SPIRIT Checklist

		Reporting Item	Page and Line Number	Reason if not applicable
Administrative information				
Title	#1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	Page 1, lines 1–3; Page 2, lines 48–50	
Trial registration	#2a	Trial identifier and registry name. If not yet registered, name of intended registry	Page 2, lines 44–45	
Trial registration: data set	#2b	All items from the World Health Organization Trial Registration Data Set	Pages 2–5 (Structured summary {1b}; WHO trial registration data items)	
Protocol version	#3	Date and version identifier	Page 6, lines 52–53	
Funding	#4	Sources and types of financial, material, and other support	Page 36, lines 648–653	
Roles and responsibilities: contributorship	#5a	Names, affiliations, and roles of protocol contributors	Page 1, lines 4–22; Page 37, lines 654–662	
Roles and responsibilities: sponsor contact information	#5b	Name and contact information for the trial sponsor	Pages 3–4 (Structured summary {1b}, Primary Sponsor and contact information {3b})	
Roles and responsibilities: sponsor and funder	#5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	Pages 3–4 (Structured summary {1b}, Role of sponsor and funder {3c})	
Roles and responsibilities: committees	#5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and	Pages 30–31, lines 534–559	

		other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)		
Introduction				
Background and rationale	#6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	Pages 6–8, lines 55–103	
Background and rationale: choice of comparators	#6b	Explanation for choice of comparators	Page 8, lines 104–113	
Objectives	#7	Specific objectives or hypotheses	Pages 8–9, lines 114–117	
Trial design	#8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, non-inferiority, exploratory)	Page 9, lines 121–126	
Methods: Participants, interventions, and outcomes				
Study setting	#9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	Pages 9–10, lines 128–130	
Eligibility criteria	#10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	Pages 10–11, lines 133–160	

Interventions: description	#11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	Page 12, lines 171–179	
Interventions: modifications	#11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving / worsening disease)	Pages 12–13, lines 180–191	
Interventions: adherence	#11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return; laboratory tests)	Page 13, lines 192–200	
Interventions: concomitant care	#11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	Pages 13–14, lines 201–218	
Outcomes	#12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	Pages 14–15, lines 226–243	
Participant timeline	#13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is	Pages 16–18, lines 275–290	

		highly recommended (see Figure)		
Sample size	#14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	Pages 18–19, lines 291–302	
Recruitment	#15	Strategies for achieving adequate participant enrolment to reach target sample size	Pages 19–20, lines 304–330	
Methods: Assignment of interventions (for controlled trials)				
Allocation: sequence generation	#16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	Pages 20–21, lines 333–345	
Allocation concealment mechanism	#16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	Page 21, lines 346–352	
Allocation: implementation	#16c	Who will generate the allocation sequence, who will enrol participants, and	Page 21, lines 353–357	

		who will assign participants to interventions		
Blinding (masking)	#17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	Pages 21–22, lines 359–373	
Blinding (masking): emergency unblinding	#17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	Page 22, lines 374–378	
Methods: Data collection, management, and analysis				
Data collection plan	#18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	Pages 22–26, lines 380–441	
Data collection plan: retention	#18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	Page 26, lines 442–453	

Data management	#19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	Page 26, lines 454–464	
Statistics: outcomes	#20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	Pages 27–29, lines 478–531	
Statistics: additional analyses	#20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	Page 29, lines 522–523	
Statistics: analysis population and missing data	#20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	Page 29, lines 510–520	
Methods: Monitoring				
Data monitoring: formal committee	#21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	Page 31, lines 549–559	

Data monitoring: interim analysis	#21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	Page 29, lines 524–525	
Harms	#22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	Pages 15–16, lines 244–274	
Auditing	#23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	Page 31, lines 560–573	
Ethics and dissemination				
Research ethics approval	#24	Plans for seeking research ethics committee / institutional review board (REC / IRB) approval	Page 36, lines 629–635	
Protocol amendments	#25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC / IRBs, trial participants, trial registries, journals, regulators)	Page 31, lines 574–579	
Consent or assent	#26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	Page 11, lines 161–164	
Consent or assent: ancillary studies	#26b	Additional consent provisions for collection	Page 11, lines 165–168	

		and use of participant data and biological specimens in ancillary studies, if applicable		
Confidentiality	#27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	Pages 26–27, lines 465–475	
Declaration of interests	#28	Financial and other competing interests for principal investigators for the overall trial and each study site	Page 36, lines 644–647	
Data access	#29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	Pages 26–27, lines 454–464; Page 36, lines 639–643	
Ancillary and post trial care	#30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	Page 14, lines 219–225	
Dissemination policy: trial results	#31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	Page 32, lines 580–585	
Dissemination policy: authorship	#31b	Authorship eligibility guidelines and any intended use of professional writers	Page 32, lines 583–585	

Dissemination policy: reproducible research	#31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	Page 29, lines 526–531; Page 36, lines 639–643	
Appendices				
Informed consent materials	#32	Model consent form and other related documentation given to participants and authorised surrogates	Page 36, lines 636–638	
Biological specimens	#33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	N/A	No biological specimens will be collected, stored, or used in this trial (Page 11, lines 165–168).