Supplementary Table 1. SPIRIT (Standard Protocol Items: Recommendations for Interventional Trials) 2013 checklist: recommended items to address in a clinical trial protocol and related documents*

Section/item	Item no.	Description	Page
Administrative information			
Title	1	Descriptive title identifying the study design, population, interventions, and trial acronym (if applicable)	1
Trial registration	2a	Trial identifier and registry name. If not yet registered, the name of the intended registry	5
	2b	All items from the World Health Organization Trial Registration Data Set	5
Protocol version	3	Date and version identifier	5
Funding	4	Sources and types of financial, material, and other support	Author page
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	Author page
	5b	Name and contact information for the trial sponsor	Author page
	5c	Role of study sponsor and funders (if any) in the 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	Author page
	5d	Composition, roles, and responsibilities of the coordinating center, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable [see Item 21a for data-monitoring committee (DMC)]	N/A
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of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	3, 4
	6b	Explanation for choice of comparators	3, 4
Objectives	7	Specific objectives or hypotheses	4, 5
Trial design	8	Description of trial design including type of trial (e.g., parallel group, crossover, factorial, or single group), allocation ratio, and framework (e.g., superiority, equivalence, noninferiority, or exploratory)	4–6
Methods: participants, interventions, and outcomes			
Study setting	9	Description of study settings (e.g., community clinic or academic hospital) and list of countries where data will be collected. Provide reference to where list of study sites can be obtained	5
Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centers and individuals who will perform the interventions (e.g., surgeons or psychotherapists)	5, 6, 26
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	7–12
	11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (e.g., change in drug dose in response to harms, participant request, or improving/worsening disease)	14
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (e.g., drug tablet return, or laboratory tests)	10, 12–14
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	14
Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (e.g., systolic blood pressure), analysis metric (e.g., change relative to baseline, final value, or time to event), method of aggregation (e.g., median or proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	12–14, 30
Participant timeline	13	Time schedule of enrollment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (Fig. 1)	14 Fig. 1
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	14, 15
Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size	5
Methods: assignment of interventions (for controlled trials)			
Allocation:			
Sequence generation	16a	Method of generating the allocation sequence (e.g., computer-generated random numbers), and list of any factors for stratification. To reduce the predictability of a random sequence, details of any planned restriction (e.g., blocking) should be provided in a separate document that is not available to those who enroll participants or assign interventions	6
Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence (e.g., central telephone, or sequentially numbered, opaque, sealed envelopes), describing any steps used to conceal the sequence until interventions are assigned	6
Implementation	16c	Who will generate the allocation sequence, who will enroll participants, and who will assign participants to interventions	6
Blinding (masking)	17a	Who will be blinded after assignment to interventions (e.g., trial participants, care providers, outcome assessors, and data analysts), and how	6
	17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	N/A
Methods: data collection, management, and analysis			
Data collection methods	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to improve data quality (e.g., duplicate measurements and training of assessors) and a description of study instruments (e.g., questionnaires and laboratory tests) along with their reliability and validity, if known. Provide reference to where data collection forms can be found, if they are not in the protocol	13, 14, 31
	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 the intervention protocols	10, 14
Data management	19	Plans for data entry, coding, security, and storage, including any related processes to improve data quality (e.g., double data entry or range checks for data values). Provide reference to where details of data management procedures can be found, if they are not in the protocol	14
Statistical methods	20a	Statistical methods used to analyze primary and secondary outcomes. Provide reference to where other details of the statistical analysis plan can be found, if they are not in the protocol	15
	20b	Methods used in any additional analyses (e.g., subgroup and adjusted analyses)	N/A
	20c	Definition of analysis population relating to protocol nonadherence (e.g., as randomized analysis), and any statistical methods for handling missing data (e.g., multiple imputation)	15
Methods: monitoring			
Data monitoring	21a	Composition of the 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 they are not in the protocol. Alternatively, explain why a DMC is not needed	14
	21b	Description of any interim analyses and stopping guidelines, including who will have access to the interim results and make the final decision to terminate the trial	N/A
Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or the trial conduct	14
Auditing	23	Frequency and procedures for auditing the trial conduct (if any), and whether the process will be independent from investigators and the sponsor	N/A
Ethics and dissemination			
Research ethics approval	24	Plans for seeking research ethics committee (REC) or Institutional Review Board (IRB) approval	15, 16
Protocol amendments	25	Plans for communicating important protocol modifications (e.g., changes to eligibility criteria, outcomes, and analyses) to relevant parties (e.g., investigators, REC/IRBs, trial participants, trial registries, journals, and regulators)	16
Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorized surrogates, and how (see Item 32)	16
	26b	Additional consent provisions for the collection and use of participant data and biological specimens in ancillary studies, if applicable	16
Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect their confidentiality before, during, and after the trial	16
Declaration of interests	28	Financial and other competing interests of the principal investigators for the overall trial and each study site	Author page
Access to data	29	Statement of who will have access to the final trial data set, and disclosure of contractual agreements that limit such access for investigators	N/A
Ancillary and posttrial care	30	Provisions (if any) for ancillary and posttrial care, and for compensation to those who suffer harm from participating in the trial	N/A
Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (e.g., via publication, reporting in results databases, or other data-sharing arrangements), including any publication restrictions	16
	31b	Authorship eligibility guidelines and any intended use of professional writers	16
	31c	Plans (if any) for granting public access to the full protocol, participant-level data set, and statistical code	16
Appendices			
Informed consent materials	32	Model consent form and other related documentation given to participants and authorized surrogates	N/A
Biological specimens	33	Plans for the 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

Adapted from SPIRIT Group. *It is strongly recommended for this checklist to be read in conjunction with the SPIRIT 2013 Explanation and Elaboration for important clarifications of the items. Amendments to the protocol should be tracked and dated.