

SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents\*

Section/item	Ite mN o	Description	Page number of which item is addressed
Administrative info	ormation		
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry	4, 24
	2b	All items from the World Health Organization Trial Registration Data Set	N/A
Protocol version	3	Date and version identifier	4
Funding	4	Sources and types of financial, material, and other support	25
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	1-2
	5b	Name and contact information for the trial sponsor	25
	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	25
	5d	Composition, roles, and responsibilities of the coordinating centre, 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)	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of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	5-7. benefits and harms p. 14
	6b	Explanation for choice of comparators	5-7
Objectives	7	Specific objectives or hypotheses	8
Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg,	9, 12

		superiority, equivalence, noninferiority, exploratory)	
Methods: Particinal	nts inte	erventions, 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	9
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)	10-11
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	13-14 + reference to paper in progress that will address this in more details
	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)	14
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)	15
	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 (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	16-18 and table 1.
Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	Figure 1 and Figure 2 address this
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	19-20
Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size	The study will run until sample size needed is obtained

Methods: Assignme	nt of ir	terventions (for controlled trials)	
Allocation:			
Sequence	16a	Method of generating the allocation sequence	12
generation		(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	
Allocation	16b	Mechanism of implementing the allocation	12
concealment		sequence (eg, central telephone; sequentially	
mechanism		numbered, opaque, sealed envelopes),	
		describing any steps to conceal the sequence	
		until interventions are assigned	
Implementation	16c	Who will generate the allocation sequence,	12
		who will enrol participants, and who will assign	
		participants to interventions	
Blinding (masking)	17a	Who will be blinded after assignment to	12
		interventions (eg, trial participants, care	
		providers, outcome assessors, data analysts),	
		and how	
	17b	If blinded, circumstances under which	n/a
		unblinding is permissible, and procedure for	
		revealing a participant's allocated intervention	
		during the trial	
Methods: Data colle	ction, ı	management, and analysis	
Data collection	18a	Plans for assessment and collection of	10, 16,17
methods		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	
	18b	Plans to promote participant retention and	18
		complete follow-up, including list of any	
		outcome data to be collected for participants	
		who discontinue or deviate from intervention	
		protocols	
Data management	19	Plans for data entry, coding, security, and	18-19
		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	
Statistical methods	20a	Statistical methods for analysing primary and	20
		secondary outcomes. Reference to where	

		other details of the statistical analysis plan can	
	001-	be found, if not in the protocol	00
	20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	20
	20c	Definition of analysis population relating to	18, 20
	200	protocol non-adherence (eg, as randomised	10, 20
		analysis), and any statistical methods to	
		handle missing data (eg, multiple imputation)	
Methods: Monitorin	q	The same is a second of the same is a second of the second	
Data monitoring	21a	Composition of data monitoring committee	n/a
		(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	
	21b	Description of any interim analyses and	n/a and some 14
		stopping guidelines, including who will have	
		access to these interim results and make the	
		final decision to terminate the trial	
Harms	22	Plans for collecting, assessing, reporting, and	14 and 23-24
		managing solicited and spontaneously	
		reported adverse events and other unintended	
		effects of trial interventions or trial conduct	
Auditing	23	Frequency and procedures for auditing trial	n/a
		conduct, if any, and whether the process will	
		be independent from investigators and the	
		sponsor	
Ethics and disseming	nation		
Research ethics	24	Plans for seeking research ethics	23-24
approval		committee/institutional review board	
		(REC/IRB) approval	
Protocol	25	Plans for communicating important protocol	15
amendments		modifications (eg, changes to eligibility criteria,	
		outcomes, analyses) to relevant parties (eg,	
		investigators, REC/IRBs, trial participants, trial	
		registries, journals, regulators)	
Consent or assent	26a	Who will obtain informed consent or assent	19, 23-24
		from potential trial participants or authorised	
		surrogates, and how (see Item 32)	
	26b	Additional consent provisions for collection and	n/a
		use of participant data and biological	
		specimens in ancillary studies, if applicable	
Confidentiality	27	How personal information about potential and	18-19
		enrolled participants will be collected, shared,	
		and maintained in order to protect	
		confidentiality before, during, and after the trial	

Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site	25
Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	25
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	n/a
Dissemination policy	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	15
	31b	Authorship eligibility guidelines and any intended use of professional writers	n/a
	31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	25
Appendices			
Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates	In Norwegian so not attached but consent is addressed several places in the manuscript
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

<sup>\*</sup>It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons "Attribution-NonCommercial-NoDerivs 3.0 Unported" license.