SPIRIT 2013 and SPIRIT-PRO Extension Checklist: Recommended Items to Address in a Clinical Trial Protocol

Calvert M, Kyte D, Mercieca-Bebber R, et al. Guidelines for Inclusion of Patient-Reported Outcomes in Clinical Trial Protocols: The SPIRIT-PRO Extension. JAMA : the journal of the American Medical Association 2018;319(5):483-94 doi: 10.1001/jama.2017.21903[published Online First: Epub Date])

Section/item	ItemNo	Description	SPIRIT-PRO Item No.	SPIRIT-PRO Extension or Elaboration Item Description	Addressed on Page No.
Administrative information					
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			3
	2b	All items from the World Health Organization Trial Registration Data Set			See below
Protocol version	3	Date and version identifier			3
Funding	4	Sources and types of financial, material, and other support			25

Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors			1; 25
	5b	Name and contact information for the trial sponsor	SPIRIT-5a-PRO Elaboration	Specify the individual(s) responsible for the PRO content of the trial protocol.	1; BS
	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)			8-9; 25
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of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	SPIRIT-6a-PRO Extension	Describe the PRO-specific research question and rationale for PRO assessment and summarize PRO findings in relevant studies.	5-6
	6b	Explanation for choice of comparators			5-6
Objectives	7	Specific objectives or hypotheses	SPIRIT-7-PRO Extension	State specific PRO objectives or hypotheses (including relevant PRO concepts/domains).	7
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, noninferiority, exploratory)			7
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			7

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)	SPIRIT-10-PRO Extension	Specify any PRO-specific eligibility criteria (eg, language/reading requirements or prerandomization completion of PRO). If PROs will not be collected from the entire study sample, provide a rationale and describe the method for obtaining the PRO subsample.	8
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered			9-11; Figure 1; Figure 2, Supplemental Table 1
	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)			15
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)			2, 10-11, 15-18
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial			8-9

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	SPIRIT-12-PRO Extension	Specify the PRO concepts/domains used to evaluate the intervention (eg, overall health-related quality of life, specific domain, specific symptom) and, for each one, the analysis metric (eg, change from baseline, final value, time to event) and the principal time point or period of interest.	17-20; Supplemental Table 2
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)	SPIRIT-13-PRO Extension	Include a schedule of PRO assessments, providing a rationale for the time points, and justifying if the initial assessment is not prerandomization. Specify time windows, whether PRO collection is prior to clinical assessments, and, if using multiple questionnaires, whether order of administration will be standardized.	Supplemental Table 2; Supplemental Figure 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	SPIRIT-14-PRO Extension	When a PRO is the primary end point, state the required sample size (and how it was determined) and recruitment target (accounting for expected loss to follow-up). If sample size is not established based on the PRO end point, then discuss the power of the principal PRO analyses.	8

Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size			8-9
Methods: Assignment of interventions (for controlled trials)					
Allocation:					9
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			9
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			9
Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions			8-9

Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how			9
	17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial			9
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 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	SPIRIT-18a (i)-PRO Extension	Justify the PRO instrument to be used and describe domains, number of items, recall period, and instrument scaling and scoring (eg, range and direction of scores indicating a good or poor outcome). Evidence of PRO instrument measurement properties, interpretation guidelines, and patient acceptability and burden should be provided or cited if available, ideally in the population of interest. State whether the measure will be used in accordance with any user manual and specify and justify deviations if planned.	14-15
			SPIRIT-18a (ii)-PRO Extension	Include a data collection plan outlining the permitted mode(s) of administration (eg, paper, telephone, electronic, other) and setting (eg, clinic, home, other).	14-15

			SPIRIT-18a (iii)-PRO Extension	Specify whether more than 1 language version will be used and state whether translated versions have been developed using currently recommended methods.	NA
			SPIRIT-18a (iv)-PRO Extension	When the trial context requires someone other than a trial participant to answer on his or her behalf (a proxy-reported outcome), state and justify the use of a proxy respondent. Provide or cite evidence of the validity of proxy assessment if available.	NA
	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	SPIRIT-18b (i)-PRO Extension	Specify PRO data collection and management strategies for minimizing avoidable missing data.	21
			SPIRIT-18b (ii)-PRO Elaboration	Describe the process of PRO assessment for participants who discontinue or deviate from the assigned intervention protocol.	21, Supplemental File 2
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			21

Statistical methods	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	SPIRIT- 20a-PRO Elaboration	State PRO analysis methods, including any plans for addressing multiplicity/type I (α) error.	21-23
	20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)			21-23
	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)	SPIRIT- 20c-PRO Elaboration	State how missing data will be described and outline the methods for handling missing items or entire assessments (eg, approach to imputation and sensitivity analyses).	21-23
Methods: Monitoring					
Data monitoring	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			21

	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			NA
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	SPIRIT- 22-PRO Extension	State whether or not PRO data will be monitored during the study to inform the clinical care of individual trial participants and, if so, how this will be managed in a standardized way. Describe how this process will be explained to participants; eg, in the participant information sheet and consent form.	15; Patient Information Sheet and Informed Consent Form (English, German versions)
Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor			NA
Ethics and dissemination					
Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval			24-25

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)			Study protocol (Supplemental Files 2 an 3; English and German versions)
Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)			24-25
	26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable			NA
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			21
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			15
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			25
	31b	Authorship eligibility guidelines and any intended use of professional writers			25
	31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code			26
Appendices					

Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates			Supplemental Files 2 and 3; Patient Information Sheet and Informed Consent Form (English, German versions)
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			NA

Abbreviations: SPIRIT, Standard Protocol Items: Recommendations for Interventional Trials; PRO, patient-reported outcome.
*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 and is reproduced with permission.

Spirit Item 2B WHO Trial Registration Dataset

Data Category	Information

Primary registry and trial identifying number	German Clinical Trials Register https://www.drks.de/drks_web/ Trial ID: DRKS00023395
Date of registration in primary registry	14.01.2021
Secondary identifying numbers	1304/2020
Source(s) of monetary or material support	Investigator-funded academic study; an open-access publication fee will be covered by VASCage, Research Centre on Vascular Ageing and Stroke, Innsbruck, Austria.
Primary sponsor	Medical University of Innsbruck, Austria
Secondary sponsor(s)	N/A
Contact for public queries	Miriam Wanner, BSc, Phone: +435050483500, Email: miriam.wanner@tirol-kliniken.at
Contact for scientific queries	Assoz. Prof. PD Dr. Michael Knoflach, Phone: +435050481697 Email: michael.knoflach@tirol-kliniken.at

Public Title	Feasibility of an individualised, task-oriented, video-supported home exercise programme in people after stroke (INAUVIS)
Scientific Title	Use of an individualised, task-oriented, video-supported home exercise programme in people after subacute stroke with mild to moderate arm paresis: a randomised, single blinded, controlled feasibility study (INAUVIS)
Countries of recruitment	Austria
Health condition(s) or problem(s) studied	Stroke
Intervention(s)	Intervention group 1 (Video-group): video-based individualised, task-oriented, video-supported home exercise programme Intervention group 2 (Paper-group): paper-based individualised, task-oriented, video-supported home exercise programme
Key inclusion and exclusion criteria	Inclusion criteria: first-ever stroke leading to a mild to moderate arm paresis, as assessed by the Motricity Index (MI); minimum pinch grip of 19 points and elbow flexion / shoulder abduction of 14 points; subacute phase, from seven days to five months after a stroke; age of >18 years; sufficient

	cognitive abilities (Mini Mental Status Test ≥24); Tyrolean residency; after discharge from the hospital or living at home. Exclusion criteria: severe disability (modified Rankin Scale (mRS) score ≥4); comorbidity potentially restraining participation e.g., a life expectancy <12 months or malignant disease, any physical or mental condition restricting participation in the study e.g., heart failure, being under guardianship, serious neuropsychological disorders, neglect, severe aphasia, severe cognitive deficits or dementia, psychiatric disorders, hemianopia, severe visual impairment, pregnancy; military service providers.
Study type	Single-centre, randomised, parallel-group, assessor-blinded controlled feasibility trial Allocation: stratified blocked randomisation Intervention model: parallel assignment Masking: assessor-blinded Primary purpose: to explore the feasibility of the methods and of conducting a full-scale randomised controlled trial.

Date of first enrolment	01.04.2021
Target sample size	24
Recruitment status	Not yet recruiting
Primary outcome(s)	Explore the feasibility of the methods and of conducting a full-scale randomised controlled trial.
Key secondary outcomes	Changes in self-perceived arm and hand use arm function (Motor Activity Log-30 (MAL-30)); arm motor function (Action Research Arm Test (ARAT)); finger dexterity (Nine Hole Peg Test (NHPT)); gross motor dexterity (Box and Block Test (BBT)); hand strength (Jamar grip dynamometer); independence in activities of daily living (Scores of Independence for Neurologic and Geriatric Rehabilitation (SINGER)); health-related quality of life (EuroQol-5 Dimensions 5-level (EQ-5D-5L) questionnaire and individual goal achievement (Goal Attainment Scaling (GAS)).