Appendix A
Search strategy

('protocol'/exp OR (protocol):ti) AND ('randomized controlled trial'/exp OR 'randomized controlled trial (topic)'/de OR ((random* NEAR/3 trial*)):ab,ti) AND [2008-2012]/py

('protocol'/exp OR (protocol):ti) AND ('randomized controlled trial'/exp OR 'randomized controlled trial (topic)'/de OR ((random* NEAR/3 trial*)):ab,ti) AND [2014-2019]/py

Appendix B

Inter-rater agreement of checklist items from the SPIRIT statement

Section/Item	No.	Checklist Items	Kappa Score	Agreement (%)
Administrative information				
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	0.49	92.3
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry	1	100
	2b	All items from the World Health Organization (WHO) Trial Registration Data Set	0.01	75.3
Protocol version	3	Date and version identifier	0.61	83.9
Funding	4a	Funding Sources: Sources of financial, material, and other support	0.39	91.4
	4b	Funding Types: Sources of financial, material, and other support	0.15	70.7
Roles and responsibility	5a	Names, affiliations, and roles of protocol contributors	0.58	95.7
	5b	Name and contact information for the trial sponsor	0.19	78.3
	5c	Role of study sponsor and funders	0.67	83.7
	5d	Composition, roles, and responsibilities of the coordinating center, steering committee, end point adjudication committee, data management team, and other individuals or groups overseeing the trial	0.35	72
Introduction				
Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies examining benefits and harms for each intervention	1	100
	6b	Explanation for choice of comparators	1	100
Objectives	7	Specific objectives or hypotheses	0.24	73.1
Trial design	8	Description of trial design, including type of trial, allocation ratio, and framework	0.27	67.7
Methods: Participants, interventions, and outcomes				
Study setting	9	Description of study settings and list of countries where data will be collected. Reference to where list of study sites can be obtained	0.29	67
Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centers and individuals who will perform the interventions	0.35	90.3
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered.	0.07	87.1
	11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant	0.33	69.9
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence	0.50	76.3
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	0.54	85
Outcomes	12a	Primary, secondary, and other outcomes, including the specific measurement variable	0.15	79.6

		pressure), analysis metric, method of aggregation, and time point for each outcome.		
	12b	Explanation of the clinical relevance of chosen efficacy and harm outcomes	0.12	66.7
Participant timeline	13	Time schedule of enrolment, interventions, assessments, and visits for participants	0.46	80.7
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	0.49	97.8
Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size	0.47	75.3
Assignment of interventions (for controlled trials)				
Allocation Sequence generation	16a	Method of generating the allocation sequence, and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction should be provided in a separate document that is unavailable to those who enrol participants or assign interventions.	0.50	83.9
Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence, describing any steps to conceal the sequence until interventions are assigned	0.44	72.8
Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	0.38	71
Blinding (masking)	17a	Who will be blinded after assignment to interventions, and how	0.24	71.6
	17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	0.73	93.8
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 and a description of study instruments along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol.	0.25	68.8
	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	0.46	74.2
Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality.	0.67	83.9
Statistical methods	20a	Statistical methods for analyzing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol.	-0.03	91.4
	20b	Methods for any additional analyses	0.61	80.7
	20c	Definition of analysis population relating to protocol nonadherence, and any statistical methods to handle missing data	0.25	64.5
Monitoring				
Data monitoring	21a	Composition of 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	0.60	81.7

		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 stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	0.76	90.3
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	0.67	83.9
Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	0.35	83.9
Ethics and dissemination				
Research ethics approval	24	Plans for seeking REC/IRB approval	-0.06	87.1
Protocol amendments	25	Plans for communicating important protocol modifications to relevant parties	0.70	89.3
Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorized surrogates, and how	0.68	83.9
	26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	0.25	92.2
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	0.70	85
Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site	0.13	83.9
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	0.65	83.9
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	0.31	83.9
Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, health care professionals, the public, and other relevant groups, including any publication restrictions	0.65	82.8
	31b	Authorship eligibility guidelines and any intended use of professional writers	0.29	88.2
	31c	Plans, if any, for granting public access to the full protocol, participant-level data set, and statistical code	0.55	81.7
Appendices				
Informed consent materials	32	Model consent form and other related documentation given to participants and authorized surrogates	0.66	98.9
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	0.62	80

Appendix C

Checklist items from the SPIRIT statement by mean completeness in RCT protocols

Section/Item	Item Number	Checklist Items	Before SPIRIT N=150	After SPIRIT N=150
Administrative information				
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	126 (84%)	134 (89%)
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry	147 (98%)	149 (99%)
	2b	All items from the World Health Organization (WHO) Trial Registration Data Set	133 (89%)	135 (90%)
Protocol version	3	Date and version identifier	14 (9%)	42 (28%)
Funding	4a	Funding Sources: Sources of financial, material, and other support	131 (88%)	145 (97%)
	4b	Funding Types: Sources of financial, material, and other support	111 (75%)	108 (73%)
Roles and responsibility	5a	Names, affiliations, and roles of protocol contributors	145 (97%)	134 (89%)
	5b	Name and contact information for the trial sponsor	17 (11%)	19 (13%)
	5c	Role of study sponsor and funders	23 (15%)	69 (47%)
	5d	Composition, roles, and responsibilities of the coordinating center, steering committee, end point adjudication committee, data management team, and other individuals or groups overseeing the trial	21 (14%)	39 (26%)
Introduction				
Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies examining benefits and harms for each intervention	150 (100%)	150 (100%)
	6b	Explanation for choice of comparators	150 (100%)	149 (99%)
Objectives	7	Specific objectives or hypotheses	100 (67%)	104 (69%)
Trial design	8	Description of trial design, including type of trial, allocation ratio, and framework	92 (61%)	105 (70%)
Methods: Participants, interventions, and outcomes				
Study setting	9	Description of study settings and list of countries where data will be collected. Reference to where list of study sites can be obtained	80 (55%)	84 (56%)
Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centers and individuals who will perform the interventions	143 (95%)	135 (90%)

Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered.	148 (99%)	141 (94%)
	11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant	30 (20%)	54 (36%)
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence	52 (35%)	54 (36%)
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	23 (15%)	28 (19%)
Outcomes	12a	Primary, secondary, and other outcomes, including the specific measurement variable pressure), analysis metric, method of aggregation, and time point for each outcome.	146 (97%)	143 (95%)
	12b	Explanation of the clinical relevance of chosen efficacy and harm outcomes	129 (86%)	103 (69%)
Participant timeline	13	Time schedule of enrolment, interventions, assessments, and visits for participants	50 (33%)	114 (76%)
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	138 (92%)	137 (92%)
Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size	42 (28%)	50 (33%)
Assignment of interventions (for controlled trials)				
Allocation Sequence generation	16a	Method of generating the allocation sequence, and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction should be provided in a separate document that is unavailable to those who enrol participants or assign interventions.	127 (85%)	124 (83%)
Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence, describing any steps to conceal the sequence until interventions are assigned	85 (57%)	90 (60%)
Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	37 (25%)	58 (39%)
Blinding (masking)	17a	Who will be blinded after assignment to interventions, and how	94 (71%)	102 (76%)
	17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a	10 (8%)	20 (15%)

		participant's allocated intervention during the trial		
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 and a description of study instruments along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol.	117 (78%)	88 (59%)
	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	25 (17%)	56 (37%)
Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality.	61 (41%)	108 (72%)
Statistical methods	20a	Statistical methods for analyzing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol.	150 (100%)	144 (96%)
	20b	Methods for any additional analyses	38 (25%)	55 (37%)
	20c	Definition of analysis population relating to protocol nonadherence, and any statistical methods to handle missing data	110 (73%)	95 (63%)
Monitoring				
Data monitoring	21a	Composition of 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.	25 (17%)	53 (36%)
	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	28 (19%)	41 (27%)
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	70 (47%)	99 (66%)
Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be	14 (9%)	21 (14%)

		independent from investigators and the sponsor		
Ethics and dissemination				
Research ethics approval	24	Plans for seeking REC/IRB approval	145 (97%)	145 (97%)
Protocol amendments	25	Plans for communicating important protocol modifications to relevant parties	3 (2%)	44 (29%)
Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorized surrogates, and how	46 (31%)	81 (54%)
	26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	3 (2%)	10 (7%)
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	41 (27%)	93 (62%)
Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site	147 (98%)	135 (90%)
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	7 (5%)	54 (36%)
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	14 (9%)	20 (13%)
Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, health care professionals, the public, and other relevant groups, including any publication restrictions	23 (15%)	88 (59%)
	31b	Authorship eligibility guidelines and any intended use of professional writers	2 (1%)	10 (7%)
	31c	Plans, if any, for granting public access to the full protocol, participant-level data set, and statistical code	5 (3%)	59 (39%)
Appendices				
Informed consent materials	32	Model consent form and other related documentation given to participants and authorized surrogates	0 (0%)	6 (4%)
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	6 (29%)	8 (35%)