Protocol and Results Report Annotation Guide

Version 2.21
April 12, 2023

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Aims

To identify text related to SPIRIT and CONSORT items in clinical trial protocols and reports.

Annotation Levels

1. Term: Annotate the string that describes the item (e.g., the specific method used). If there is more than one item, annotate each item separately; for example, in a trial recruiting from two settings, label both of the settings). If the document does not include information about a term (e.g, the title does not include an acronym, the manuscript does not state the allocation ratio), do not annotate.
2. Trigger: Annotate the string that indicates that the sentence contains information about the checklist item, even if the document is *not* compliant with all or part of the relevant SPIRIT/CONSORT item. Trigger text might occur anywhere in the sentence (beginning, middle, or end). If multiple sentences are related to an item, annotate the trigger text in each relevant sentence (or use Section annotation as described below). Annotate each sentence separately; i.e., a single annotation should not include more than one sentence. If there is no relevant text (e.g., the manuscript says nothing about discontinuing or modifying allocated interventions for a given trial participant), do not annotate.
3. Section: If there is a relevant section heading, annotate the heading to indicate that most or all sentences / paragraphs under the heading are related to the SPIRIT/CONSORT item. Annotations of major headings will be applied to subheadings (e.g., annotating the highest level heading “Study outcomes” will automatically include subheadings “Primary outcomes” and “Secondary outcomes”). If there is no heading, annotate the relevant sentences using Trigger annotation. If a section is mostly about one item (item X) with the exception of a few sentences that belong to other categories (items Y, Z), annotate the section header (with item X) and annotate the relevant sentences with other items (Y and Z). Annotating a sentence within a section (i.e., annotating items Y and Z) will exclude the sentence from the header annotation (i.e., not item X) unless the sentence is also annotated using the header annotation (annotated as X and Y, or X and Z).

Section level exceptions

Although annotating a sentence within a section will exclude usually the sentence from the header annotation, there are several exceptions to this rule. In the following cases, section level annotations will be applied to sentences with additional annotations without the need to add the header annotation:

In a section with this annotation	**sentences with this annotation will not be excluded**
11a_Intervention_Description	17e_Masking_Similarity

11a_Intervention_Description	11b_Intervention_Modification
11c_Intervention_Monitoring	18a_Data_Collection
12a_Outcomes_Definitions	18a_Data_Collection
14b_Sample_Calculation	8b_Design_Framework
14b_Sample_Calculation	8d_Design_Ratio
14b_Sample_Calculation	14a_Sample_size
18a_Data_Collection	18b_Data_Retention
19_Data_Management	27_Confidentiality
31d_Sharing_Data	29_Data_access
38a_Outcome_results	38b_Binary_results

Instructions

Annotation for this project will identify text *needed to make a decision* about whether a protocol or results report adheres to one or more items/sub-items in SPIRIT or CONSORT. For brevity and consistency, we have combined related items and used consistent wording. Some items that appear in only SPIRIT or only CONSORT will be annotated for both protocols and results reports. Other items that appear in only SPIRIT or only CONSORT will be annotated for only protocols or results reports, respectively.

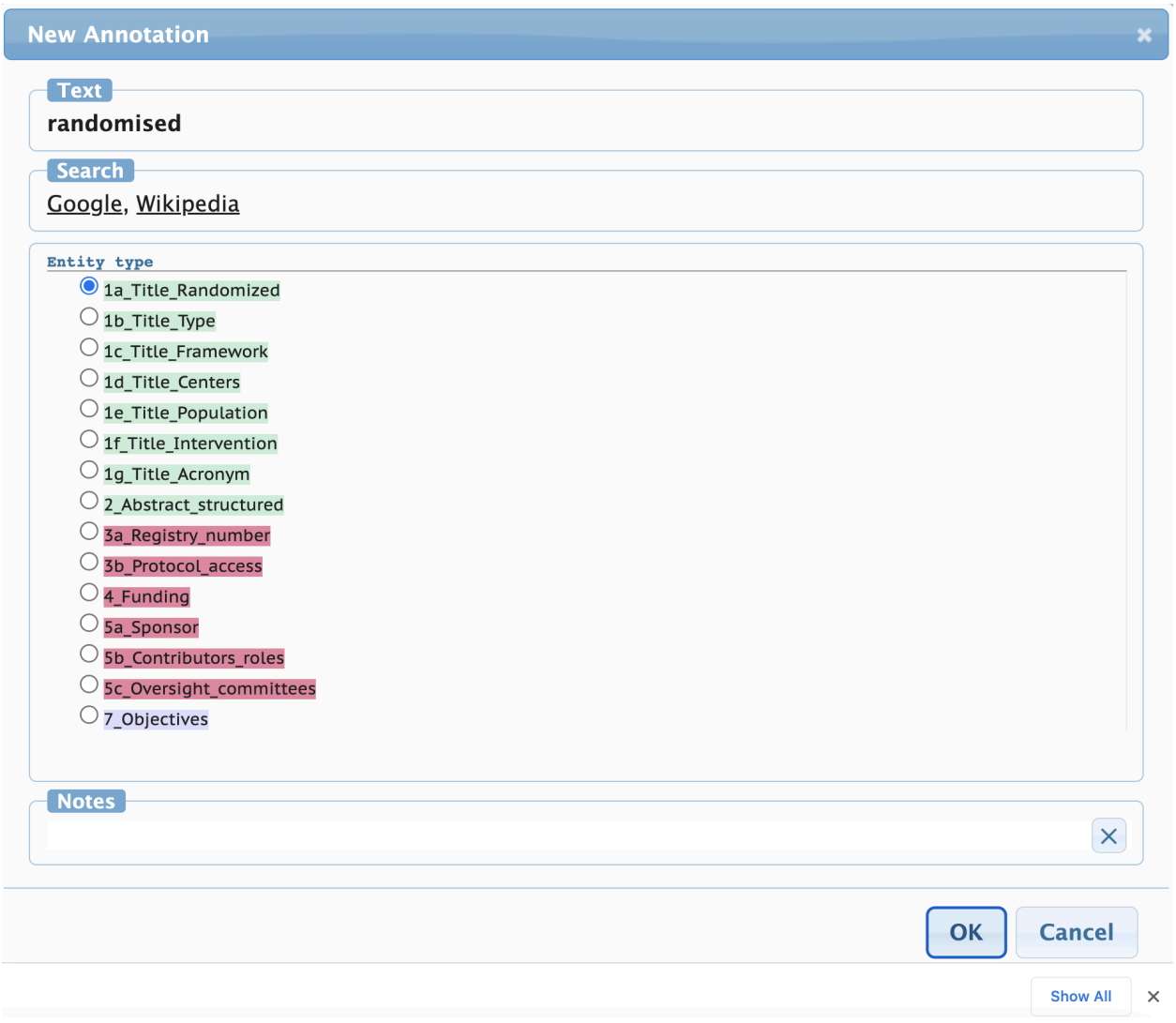
We will use the *brat* tool[1] for annotation. The annotation URL is: http://3.135.137.158/brat/#/SPIRIT_CONSORT/. To annotate, a username/password is needed (*brat/annotate*). To login, hover over the document bar at the top of the page, which will display the login button on the right, as shown below. You can view annotations without logging in.

Each annotator has their own annotation folder and should only annotate in that folder. Under the folder with your name, you will find two subfolders: *Protocols* for protocol publications and *Results* for result publications. In the screenshot above, we see the *Protocols* folder of the annotator *Halil (*note */SPIRIT_CONSORT/Halil/Protocols* at the top). The names of the documents in Protocols and Results folders have the form <id>_<PubMed Central ID>, where

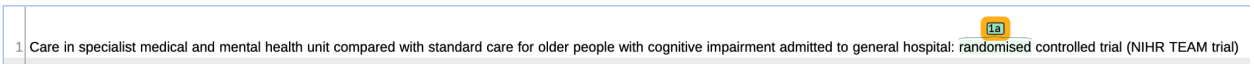
[1] For a more detailed user guide on brat, see https://brat.nlplab.org/manual.html.

<id> are used to pair the protocols and their corresponding results publications. In other words, for example, Protocols/1_PMC3117715 and Results/1_PMC3698942 are protocol and results publications related to the same RCT.

To annotate a checklist item, select the text span that is relevant for the item. If the relevant text span is a single word, you can also double-click on that word. This will pop up the New Annotation window with checklist items. Select the checklist item and click OK. In the example below, the text span 'randomised' is highlighted, and '1a_Title_Randomized' is selected as the type.



Once the selection is confirmed, the text span will be shown with the relevant annotation, as shown below.



If you want to edit an annotation (change its type, delete it, or move it (to another text span)), you can double-click on the label which will bring up the Edit Annotation window, similar to the New Annotation window above.

Brat tips/quirks:

- It is easy to miss a character or annotate an additional character, when selecting spans for annotation with brat. After you add your annotation, make sure to check that the span is captured correctly, by hovering over the label which will show the annotated text.
- When two annotations overlap, brat puts a red border around their labels, indicating this might be an error. Ignore these errors.
- Alert us if you see warning/error messages in red when you open a brat document.

For items 1a to 1f, annotate only the title.

For item 2, annotate the abstract header to indicate that the article abstract is structured.

For all other items, annotate the main text of the protocol or results report; annotate an Abstract, special section (e.g., “What’s New”?”), table,or figure (including footnotes) only if information appears in an Abstract/special section/table/footnote that does not also appear in the main text. For example, annotate the trial registration number if it appears in the abstract and does not in the main manuscript. Many annotations will appear in the Methods and Results sections; it is not necessary to annotate the Introduction and Discussion for items that have been annotated in the Methods and Results section. For example, design features such as “cluster” might be repeated in the Introduction and Discussion, but they do not need to be annotated every time they appear in these sections.

The same text may be annotated multiple times if it is relevant to more than one item.

Make each section as short as possible and do not annotate more words in a sentence than is necessary. In general, annotations should be as short as possible to improve precision and consistency. For trigger annotations, highlight the fewest words needed to infer that the sentence is related to the item.

For Figures and Tables, annotate the descriptive title but do not annotate the Figure/Table number. For example, annotate “Baseline characteristics”; do not annotate “Table 1”.

We anticipate that the instructions below might need to be revised and clarified during the project. If you have a question, or if you encounter a novel issue and need to make a decision, please complete the Questions and Coding Decisions Form. This form will allow us to maintain a time-stamped record of these events throughout the project.

Because trials selected for this project have common characteristics (e.g., they are all parallel trials), there will be little variation in annotations for some items. Additional trials might be added at a later time to provide different examples of describing trial designs and methods.

Structure of this document

For each item, this document uses the following structure:

> **Annotation name**
> [Type of annotation]: instructions for this specific annotation
>
> Example: An example given with annotated item underlined
>
> SPIRIT 2013 Item: SPIRIT guideline number, if applicable
> CONSORT 2010 Item: CONSORT guideline number, if applicable
> Reports annotated: Protocols, Results, or Protocols and Results

Protocol changes

January 18, 2023: After completing pilot testing of Annotation Guide version 1 using 3 trials (i.e., protocol/results pairs), we completed revisions and began using Annotation Guide version 2.00. The guide was locked for editing. Further comments and changes were recorded using a Google form.

February 9, 2023. After completing further pilot testing, we identified some inconsistencies in coding. Many of these inconsistencies were related to identifying trigger text (rather than terms) and to identifying the minimum amount of text needed for each annotation. Additionally, coders found it difficult to determine what information about the participant timeline should be annotated when it appeared in different places throughout the text. We completed revisions and began using Annotation Guide version 2.10.

February 15, 2023. Minor updates following further consultation. Updated to version 2.11. The first 11 pairs of reports have been annotated.

February 16, 2023. Updated the link to brat to make it “elastic”. Updated to version 2.12.

April 6, 2023. Made multiple changes to clarify instructions in response to questions arising during coding and reconciliation. Added examples. Addressed comments up to row 68 in the Questions and Coding Decisions form. Updated to version 2.20.

April 18, 2023. After annotating 32 pairs, we changed annotation 9_Setting from “Term” to “Section/Trigger” annotation. We updated the instructions and examples to match.

Annotations

1a_Title_Randomized

Term: Select the word "random" or "randomized," or an acronym indicating the trial was randomized (e.g., RCT, cRCT), if included in the title. For 1a, label only whether the trial is identified as randomized; do not label other words about the design.

Example: *GI-CBT: A multi-site randomized parallel non-inferiority trial of group- versus -individual cognitive behavioral therapy for veterans with post-traumatic stress disorder*

SPIRIT 2013 Item: 1
CONSORT 2010 Item: 1a
Reports annotated: Protocols and Results

1b_Title_Type

Term: Select the word or phrase describing the design of the trial, such as "parallel," "crossover," "factorial," or "cluster." For 1b, do not label words describing the comparative intent (e.g., "superiority," "equivalence"). Abbreviations or terms indicating both randomization and type (e.g., cRCT) may be annotated for 1a and 1b.

Example: *GI-CBT: A multi-site randomized parallel non-inferiority trial of group- versus -individual cognitive behavioral therapy for veterans with post-traumatic stress disorder*

SPIRIT 2013 Item: 1
CONSORT 2010 Item: Not applicable
Reports annotated: Protocols and Results

1c_Title_Framework

Term: Select the word or phrase describing the comparative intent of the trial, such as "superiority," "equivalence," "noninferiority," or "exploratory." For 1c, do not label words describing the level or type of randomization (e.g., "crossover," "cluster," "stratified,"). If the title does not include the comparative intent, do not annotate. Vague terms such as "effectiveness" should not be annotated, but explicitly comparative phrases such as "more effective than" may be annotated. Likewise, do not label "placebo-controlled"; although most placebo-controlled trials are superiority trials, some non-inferiority and equivalence trials include placebo.

Example: *GI-CBT: A multi-site randomized parallel non-inferiority trial of group- versus -individual cognitive behavioral therapy for veterans with post-traumatic stress disorder*

SPIRIT 2013 Item: Not applicable
CONSORT 2010 Item: Not applicable
Reports annotated: Protocols and Results

1d_Title_Centers

Term: Select the word or phrase describing the number of centers, such as “single center,” “multi-center,” or “multi-site.” Select words or phrases that indicate a trial is single-center (e.g., “in a community hospital” or multi-center (e.g., “in six states”). For 1d, do not label place names (e.g., “Baltimore,” “Malawi”) unless the number of places named indicates that the trial is multiple-center (e.g., “a randomized trial in Baltimore and Philadelphia”).

Example: *GI-CBT: A multi-site randomized parallel non-inferiority trial of group- versus -individual cognitive behavioral therapy for veterans with post-traumatic stress disorder*

Example: *Effect of administration of ramelteon, a melatonin receptor agonist, on the duration of stay in the ICU: A single-center randomized placebo-controlled trial*

SPIRIT 2013 Item: Not applicable
CONSORT 2010 Item: Not applicable
Reports annotated: Protocols and Results

1e_Title_Population

Term: Select the word or phrase describing the populations or health problems examined in the trial, such as “nursing home residents” or “depression.” Annotate words such as “adults with” and “men with” that refer to specific characteristics of the population, but do not annotate non-specific words such as “participants with” or “subjects with”.

Example: *GI-CBT: A multi-site randomized parallel non-inferiority trial of group- versus -individual cognitive behavioral therapy for veterans with post-traumatic stress disorder*

Example: *Implementing comprehensive prevention of mother-to-child transmission and HIV prevention for South African couples*

SPIRIT 2013 Item: 1
CONSORT 2010 Item: Not applicable
Reports annotated: Protocols and Results

1f_Title_Intervention

Term: Select the word or phrase describing the intervention or interventions evaluated in the trial, such as the drug name (e.g., “quetiapine”), a type of behavioral or physical intervention (e.g., “acupuncture”), or a name for a specific intervention (e.g., “Incredible Years”). Label both test and comparator interventions (e.g., “placebo,” “sham”). Label each intervention separately. If the title does not include information about the intervention(s), do not annotate.

Example: *GI-CBT: A multi-site randomized parallel non-inferiority trial of group- versus -individual cognitive behavioral therapy for veterans with post-traumatic stress disorder*

Example: *Effects of tranexamic acid on death, disability, vascular occlusive events and other morbidities in patients with acute traumatic brain injury (CRASH-3): a randomised, placebo-controlled trial*

SPIRIT 2013 Item: 1
CONSORT 2010 Item: Not applicable
Reports annotated: Protocols and Results

1g_Title_Acronym

Term: Select the trial acronym.

Example: *GI-CBT: A multi-site randomized parallel non-inferiority trial of group- versus -individual cognitive behavioral therapy for veterans with post-traumatic stress disorder*

SPIRIT 2013 Item: 1
CONSORT 2010 Item: Not applicable
Reports annotated: Protocols and Results

2_Abstract_structured

Document: Annotate the heading "Abstract" to classify the document as "structured" if the abstract is a structured summary of the trial (e.g., background, methods, results, and conclusions). If there is no heading called "Abstract", annotate the first heading of the structured abstract (e.g., Background"). Do not annotate to classify the document as "unstructured" if the abstract is not organized using structured headings.

SPIRIT 2013 Item: Not applicable
CONSORT 2010 Item: 1b
Reports annotated: Protocols and Results

3a_Registry_number

Term: Select the registration number (e.g., "NCT03766165"). If more than one registration number is reported, label each registration number separately. Do not label the name of the register. All trials in this study are registered on ClinicalTrials.gov, and some are also registered elsewhere. If the main text or abstract does not include a registration number, do not annotate.

Example: *Trial registration: ClinicalTrials.gov, NCT03766165 . Registered on 4 December 2018.*

SPIRIT 2013 Item: 2a
CONSORT 2010 Item: 23
Reports annotated: Protocols and Results

3b_Protocol_access

Trigger: Label the string of text that indicates that the sentence contains information about where the protocol and/or statistical analysis plan (SAP) can be accessed, or that the manuscript contains a reference to where the protocol/SAP can be accessed. If the protocol/SAP is included in the reference list but the text does not explain or imply that it includes a reference to the protocol/SAP, do not annotate. Do not annotate the reference list. Authors sometimes conflate trial registrations and protocols/SAP; do not annotate the trial registration as a protocol/SAP, even if the authors identify the trial registration as the protocol.

Example: *Full details of the trial protocol can be found in the Supplementary Appendix, available with the full text of this article at www.nejm.org.*

Example: *We conducted a trial as previously described.*

Example: *Following a published protocol, we compared the effect of quetiapine and placebo for adults with bipolar depression.*

Example: *The trial protocol was not published.*

SPIRIT 2013 Item: Not applicable
CONSORT 2010 Item: 24
Reports annotated: Results only

4_Funding

Section/Trigger: Label the applicable heading "Funding" if there is one. Otherwise, label the string of text that indicates that the sentence contains information about financial or other material support (e.g., supply of drugs), including the role of the funder (e.g., 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.). CONSORT 2010 includes reporting requirements related to the trial "sponsor," which may or may not be the funder; unless the same string describes the funder and the sponsor, do NOT use this code to label text about the sponsor (see 5b).

Example (Section annotation): *Funding: The study was partially supported by a grant from Bayer Italy and sponsored by the University of Insubria in Varese, Italy. No Bayer employees were members of the steering committee or had any role in the study. The funders had no role in considering the study design or in the collection, analysis, interpretation of data, writing of the report, or decision to submit the article for publication.*

Example (Trigger annotation): *LSHTM [London School of Hygiene and Tropical Medicine] is funding the run-in costs for the WOMAN trial and up to 2,000 patients' recruitment. The main phase is funded by the UK Department of Health and the Wellcome Trust. Funding for this trial covers meetings and central organisational costs only. Pfizer, the manufacturer of tranexamic acid, have provided the trial drug and placebo used for this trial.*

SPIRIT 2013 Item: 4
CONSORT 2010 Item: 25
Reports annotated: Protocols and Results

5a_Sponsor

Trigger: Label the string of text that indicates that the sentence contains information about the name, contact information, and/or role of the trial sponsor. [A trial sponsor is responsible for many aspects of study conduct and might or might not be the trial funder. For industry trials, the funder and the sponsor are often the same (e.g., Pfizer), so the same text might be annotated for item 4 and item 5b. For investigator-initiated trials, the funder and sponsor are often different. For example, NIH might be the funder of a trial initiated by an investigator at Johns Hopkins University; in this case, Johns Hopkins University would be the likely sponsor. If the manuscript indicates the name of the funder but does not name the sponsor explicitly, do not annotate.]

Example: *Trial Sponsor: University of Nottingham*

SPIRIT 2013 Item: 5b
CONSORT 2010 Item: Not applicable
Reports annotated: Protocols and Results

5b_Contributors_roles

Section: Label the heading (or if no heading, the sentences) that contains information about the roles of contributors to the protocol or results report.

Example: *Authors Contributions: RTL conceived of the study. AK, EN, SB, PR, WJ, JH, and MC initiated the study design and JK and LG helped with implementation. RTL, JK, LG, and FP are grant holders. LT and EM provided statistical expertise in clinical trial design and RN is conducting the primary statistical analysis. All authors contributed to refinement of the study protocol and approved the final manuscript.*

SPIRIT 2013 Item: 5a
CONSORT 2010 Item: Not applicable
Reports annotated: Protocols and Results

5c_Oversight_committees

Section: Label the heading (or if no heading, the sentences) that contains information about the members and responsibilities of trial oversight committees. Committees might include coordinating center, steering committee, endpoint adjudication committee, data management team, and other individuals or groups. Do *not* use 5c to annotate information about a data monitoring committee (see Item 21a for data monitoring committee).

Example: *Steering Committee (SC): See title page for members. Agreement of final protocol….Trial management committee (TMC): Study planning…*

SPIRIT 2013 Item: 5d
CONSORT 2010 Item: Not applicable
Reports annotated: Protocols and Results

7_Objectives

Trigger/Section: Label the string of text that indicates that the sentence or section describes the study objectives or hypothesis. Label the heading "Objectives" if it exists ("Section" annotation). The relevant section might be annotated for other items as well, such as "framework" (8b). The Background section will often end with a statement of the trial objectives; if the objectives are stated in both places, then label both the Objectives section and any relevant sentences in the Background section.

Example: *The purpose of this study is to evaluate the efficacy of the KRG extract in reducing the frequency, severity and duration of ILI symptoms in healthy adults.*

Example: *To determine if apixaban is noninferior to warfarin (INR [international normalized ratio] target range 2.0-3.0) in the combined endpoint of stroke (hemorrhagic, ischemic or of unspecified type) and systemic embolism, in subjects with AF and at least one additional risk factor for stroke.*

Example: *In the current study we tested the hypothesis that a policy of active management of nulliparous labour would: 1. reduce the rate of caesarean section, 2. reduce the rate of prolonged labour; 3. not influence maternal satisfaction with the birth experience.*

SPIRIT 2013 Item: 7
CONSORT 2010 Item: 2b
Reports annotated: Protocols and Results

8a_Design_Type

Term: Select the word or phrase describing the design of the trial, which might include "parallel", "cluster", or "factorial". Do not tag terms such as "pragmatic" that are not related to the basic structure of the trial. If you identify an excluded design, such as "crossover" complete the Questions and Coding Decisions form. If the design is not stated explicitly, label any word or phrases from which you could infer the design (e.g., phrases that imply clusters were assigned) but do not tag potentially ambiguous phrases such as "randomly allocated patients", which might appear in a section describing different designs (e.g., either individual- or cluster-level randomization) . For 8a, do not label words describing the comparative intent.

Example: *The PROUD trial is designed as a randomised, controlled, observer, surgeon and patient blinded multicenter superiority trial with two parallel groups and a primary endpoint of wound infection during 30 days after surgery…*

SPIRIT 2013 Item: 8
CONSORT 2010 Item: 3a
Reports annotated: Protocols and Results

8b_Design_Framework

Term: Select the word or phrase describing the comparative intent of the trial, such as "superiority," "equivalence," "noninferiority". Vague terms (such as "effectiveness" and "compared the effect") should not be annotated, but phrases that are explicit concerning the comparative intent (such as "more effective than" or added value of") may be annotated. That is, if the comparative intent is not described using a term such as "superiority" or "non-inferiority"), then select the words or phrases from which the intent can be inferred, such as "lower," "better," fewer," "greater," or "more." If you identify an excluded framework, including "pilot," "feasibility," or "exploratory," complete the Questions and Coding Decisions form. Do not label words describing the level or type of randomization.

Example: *The PROUD trial is designed as a randomised, controlled, observer, surgeon and patient blinded multicenter superiority trial with two parallel groups and a primary endpoint of wound infection during 30 days after surgery…randomization will be performed as block randomization with a 1:1 allocation.*

SPIRIT 2013 Item: 8
CONSORT 2010 Item: 3a
Reports annotated: Protocols and Results

8c_Design_Centers

Term: Select the word or phrase describing the number of centers, such as "single center," "multi-center," or "multi-site." Select words or phrases that indicate a trial is single-center (e.g., "in a community hospital" or multi-center (e.g., "in six states"). For cluster randomized trials, centers might be the unit of randomization and also considered "multi-center" when centers are enrolling or data are being collected for individual participants. For 8c, do not label place names (e.g., "Baltimore," "Malawi"). If the document does not state or imply the number of centers, do not annotate.

Example: *The PROUD trial is designed as a randomised, controlled, observer, surgeon and patient blinded multicenter superiority trial with two parallel groups and a primary endpoint of wound infection during 30 days after surgery…randomization will be performed as block randomization with a 1:1 allocation.*

Example: *Randomization sequence was created using Stata 9.0 (StataCorp, College Station, TX) statistical software and was stratified by center with a 1:1 allocation using random block sizes of 2, 4, and 6.*

Example: …*a large British National Health Service hospital.*

SPIRIT 2013 Item: 8
CONSORT 2010 Item:4b
Reports annotated: Protocols and Results

8d_Design_Ratio

Term: Select the word or phrase describing the allocation ratio (i.e., the ratio of participants or clusters assigned to each group), such as "1:1" or "2 to 3". Select words or phrases that clearly imply the allocation ratio (e.g., "equally", "92 per group").

Example: *Participants will be randomly assigned to either control or experimental group with a 1:1 allocation as per a computer generated randomisation schedule stratified by site and the baseline score of the Action Arm Research Test (ARAT; <=21 versus >21) using permuted blocks of random sizes.*

Example: *To detect a reduction in PHS (postoperative hospital stay) of 3 days (SD 5 days), which is in agreement with the study of Lobo et al17 with a two-sided 5% significance level and a power of 80%, a sample size of 50 patients per group was necessary, given an anticipated dropout rate of 10%.*

Example: *To allow for 30% drop out, 170 will be recruited per arm, ie, 340 in total.*

SPIRIT 2013 Item: 8
CONSORT 2010 Item: 3a
Reports annotated: Protocols and Results

9_Setting

Section/Trigger: Label the string of text that indicates the sentence or section describes the setting. If applicable, label a heading such as "Setting" ("Section" annotation).

Example: *100 subjects will be recruited through local advertising and doctor referrals from hospital outpatients and general practice clinics.*

Example: *The study took place at the antiretroviral therapy clinic of Queen Elizabeth Central Hospital in Blantyre, Malawi, from January 2006 to April 2007. Blantyre is the major commercial city of Malawi, with a population of 1 000 000 and an estimated HIV prevalence of 27% in adults in 2004.*

Example: *The study is currently being carried out at four primary healthcare centers (PHC) in low-income communities in peri-urban areas of Karachi (Fig 1).*

Example: *Between July 20, 2012, and Jan 31, 2019, we recruited patients with TBI from 175 hospitals in 29 countries.*

Example (Section annotation)
Study Site
The trial is being conducted in four predominantly rural districts of Brong- Ahafo region in central Ghana. The study districts, which are under demographic surveillance by the Kintampo Health Research Centre…

SPIRIT 2013 Item: 9
CONSORT 2010 Item: 4b
Reports annotated: Protocols and Results

10a_Participants_inclusion

Trigger: Label the string of text that indicates the sentence or section describes the inclusion and/or exclusion criteria for the people on whom outcomes will be assessed (e.g., patients). Unless the main outcomes are assessed for intervention providers or places, do not use this code to label text concerning inclusion criteria for them (see 10b).

Example: *Eligible participants were all adults aged 18 or over with HIV who met the eligibility criteria for antiretroviral therapy according to the Malawian national HIV treatment guidelines (WHO clinical stage III or IV or any WHO stage with a CD4 count <250/mm3) and who were starting treatment with a BMI <18.5. Exclusion criteria were pregnancy and lactation or participation in another supplementary feeding programme.*

SPIRIT 2013 Item: 10
CONSORT 2010 Item: 4a
Reports annotated: Protocols and Results

10b_Center_interventionist_inclusion

Trigger: Label the string of text that indicates the sentence or section describes the inclusion and/or exclusion criteria for intervention providers (e.g., doctors, psychologists) or centers (e.g., hospitals, schools).

Example: *To qualify, physicians responsible for PAC [pulmonary-artery catheter] placements will be required to show proof of insertion of ≥50 PACs in the previous year with a complication rate of <5%.*

Example: *Hospitals participating in IST-3 [third International Stroke Trial] should have an organized acute stroke service.*

SPIRIT 2013 Item: 10
CONSORT 2010 Item: 4b
Reports annotated: Protocols and Results

i11a_Intervention_Description

Section/Trigger: Label a heading such as "Intervention description" if one exists ("Section" annotation). Otherwise, label the string of text that indicates the sentence or section describes the intervention(s) and/or comparator(s). Complex interventions may include multiple components that are delivered or not delivered depending on participant characteristics; these components should be described as part of the intervention (11a) and criteria for delivering different components to different participants may be considered intervention modification (11b).

Example: *Eligible patients will be randomised in equal proportions between IL-1ra [interleukin-1 receptor antagonist] and placebo, receiving either a once daily, subcutaneous (s.c.) injection of IL-1ra (dose 100 mg per 24 h) for 14 days, or a daily s.c. injection of placebo for 14 days…*

SPIRIT 2013 Item: 11a
CONSORT 2010 Item: 5
Reports annotated: Protocols and Results

11b_Intervention_Modification

Trigger: Label the string of text that indicates the sentence or section describes criteria for discontinuing or modifying allocated interventions for a given trial participant (e.g., drug dose change in response to harms, participant request, improving/worsening disease). Complex interventions may include multiple components that are delivered or not delivered depending on participant characteristics; these components should be described as part of the intervention (11a) and criteria for delivering different components to different participants may be considered intervention modification (11b).

Example: *The tablets may be taken in two equally divided doses, if necessary, to improve gastro-intestinal tolerance. Should it be necessary the daily dose may be reduced by one tablet at a time to improve gastro-intestinal tolerance.*

SPIRIT 2013 Item: 11b
CONSORT 2010 Item: 5
Reports annotated: Protocols and Results

11c_Intervention_Monitoring

Trigger: For protocols and results reports, label the string of text that indicates the sentence or section describes strategies to improve adherence to intervention protocols and/or procedures for monitoring adherence (e.g., drug tablet return, laboratory tests, monitoring session attendance). In results reports, also annotate results concerning intervention monitoring (e.g., average number of sessions attended).

Example: *To enhance validity of data, multiple methods will be used to assess medication adherence including pill count; an electronic medication event monitoring system (MEMS® cap) [reference]; and ACASI [audio-computer administered interview] questionnaire items including a one month visual analogue scale,[reference] reasons for non-compliance, and use of the MEMS® cap.*

Example: *Intervention fidelity*

SPIRIT 2013 Item: 11c
CONSORT 2010 Item: 5
Reports annotated: Protocols and Results

11d_Intervention_Concomitant

Trigger: Label the string of text that indicates the sentence or section describes relevant concomitant care and interventions that are permitted or prohibited during the trial. Include text describing interventions that both groups will or might receive, such as “usual care” or “standard of care”, or interventions that might be prescribed “as needed”. Complex interventions may include multiple components that are delivered or not delivered depending on participant characteristics; in these cases, flexibility of intervention components may be considered part of the intervention definition and should be annotated 11a or 11b.

Example: *For weeks 0-3, topical mometasone furoate 0.1% cream or ointment (30 g/week) will be permitted with participants preferably using ointment. Participants will be instructed to apply the topical mometasone furoate to blisters/lesions as required (not to areas of unaffected skin). If the participant is allergic to mometasone furoate or the hospital pharmacy does not stock it, then an alternative topical steroid may be prescribed but this must be in the potent class. In addition, participants will be advised that they can apply a light moisturiser to blisters/lesions at any time during the study.*

Example: *Any other pharmacological treatment will be allowed*.

SPIRIT 2013 Item: 11d
CONSORT 2010 Item: 5
Reports annotated: Protocols and Results

12a_Outcomes_Definitions

Trigger: Label the string of text that indicates the sentence or section describes the names and/or definitions of the primary, secondary, and/or other outcomes. Where possible, do not label the outcome definitions *per se*; instead, label the text that indicates the sentence contains information about the outcomes. Baseline variables that are not expected to be affected by the intervention (e.g., predictors, moderators) are not outcomes and should not be labeled 12a.

Example: *The primary endpoint with respect to efficacy in psoriasis was the proportion of patients achieving a 75% improvement in psoriasis activity from baseline to 12 weeks as measured by the PASI…Additional analyses were done on the percentage change in PASI scores and improvement in target psoriasis lesions.*

Example: *Follow-up data will be obtained for…*

Example: *Primary outcome measures: Difference between the two treatment arms in the proportion of participants classed as treatment success at 6 weeks. Treatment success is defined as 3 or less significant blisters present on examination at 6 weeks. Significant blisters are defined as intact blisters containing fluid which are at least 5 mm in diameter. However, if the participant has popped a blister, or the blister is at a site that makes it susceptible to bursting such as the sole of the foot, it can be considered part of the blister count, providing there is a flexible (but not dry) roof present over a moist base. Mucosal blisters will be excluded from the count.*

SPIRIT 2013 Item: 12
CONSORT 2010 Item: 6a
Reports annotated: Protocols and Results

12b_Outcomes_Changes

Trigger: Label the string of text that indicates the sentence or section describes changes to outcomes after trial commencement (e.g., modifications to outcome definition, addition of new outcomes). Do not annotate other changes to the trial (see 25).

Example: *The original primary endpoint was all-cause mortality, but, during a masked analysis, the data and safety monitoring board noted that overall mortality was lower than had been predicted and that the study could not be completed with the sample size and power originally planned. The steering committee therefore decided to adopt co-primary endpoints of all-cause mortality (the original primary endpoint), together with all-cause mortality or cardiovascular hospital admissions (the first prespecified secondary endpoint).*

SPIRIT 2013 Item: Not applicable
CONSORT 2010 Item: 6b
Reports annotated: Results only

13_Participant_timeline

Trigger: Label the string of text that indicates the sentence or section describes the complete time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. If a sentence in the text refers to a figure for this information, annotate that sentence. If this information appears only in a figure, annotate the text in the label and/or caption. For vague figure titles, refer to the article on PMC to determine whether the title describes a SPIRIT figure or other participant timeline. Although a reader might attempt to construct a timeline from information that appears in multiple places, piecemeal information is not consistent with the goals of this item; do not label pieces of information about the timing or duration of activities that appear throughout the report.

Example: *A timeline for the intervention and assessments is included in Figure 2.*

Example if the information appears only in a figure: *Figure 2. Participant timeline*

SPIRIT 2013 Item: 13
CONSORT 2010 Item: Not applicable
Reports annotated: Protocols and Results

14a_Sample_size

Term: Label the text describing the estimated sample size (i.e., number of participants planned to be enrolled and allocated overall, to each group, or both overall and to each group). For cluster randomized trials, label both the number of clusters and the number of individual participants if reported. If the sample size was revised (e.g., following an interim analysis), then label both the planned and revised sample size if both are reported. This information will normally appear in the Methods section rather than the Results section. Do not label the number actually enrolled, receiving treatment, or analyzed (see 34). Do not annotate words such as “patients” or “participants” that refer to the entire sample. If the sample size is reported in parts (e.g., number assigned to each group), annotate words that indicate the number refers to part of the sample (e.g., “per group”, “at each site”). Unless it falls within a longer span of text that has to be annotated, do not annotate “n=”.

Example: *We plan to recruit 210 patients.*

Example: *We plan to recruit 100 men and 100 women.*

Example: *Number and size of clusters were increased to 43 clusters of 12 children to allow for potential loss to follow-up.*

Example: *These findings suggest that improvements in social functioning may accrue over 1 year, hence we expect to find a greater magnitude of response at the 72 week follow-up than we did in the exploratory trial. Therefore, we have powered this trial to be able to detect a difference in SFQ score of 2 points. SFQ standard deviations vary between treatment, control,*

and the wait-list samples, ranging from 3.78 to 4.53. We have based our sample size estimate on the most conservative (ie, largest) SD [standard deviation]. To detect a mean difference in SFQ score of 2 point (SD = 4.53) at 72 weeks with a two-sided significance level of 1% and power of 80% with equal allocation to two arms would require 120 patients in each arm of the trial. To allow for 30% drop out, 170 will be recruited per arm, ie, 340 in total.

Example: *To detect a reduction in PHS (postoperative hospital stay) of 3 days (SD 5 days), which is in agreement with the study of Lobo et al17 with a two-sided 5% significance level and a power of 80%, a sample size of 50 patients per group was necessary, given an anticipated dropout rate of 10%. To recruit this number of patients a 12-month inclusion period was anticipated.*

SPIRIT 2013 Item: 14
CONSORT 2010 Item: 7a
Reports annotated: Protocols and Results

14b_Sample_Calculation

Section/Trigger: Label a heading such as “Sample size” if one exists (“Section” annotation). Otherwise, label the string of text that indicates the sentence or section describes how the investigators arrived at the number to be allocated, including text that indicates statistical choices (e.g., percentage power) and assumptions (e.g., percentage dropout).

Example (Trigger annotation): *These findings suggest that improvements in social functioning may accrue over 1 year, hence we expect to find a greater magnitude of response at the 72 week follow-up than we did in the exploratory trial. Therefore, we have powered this trial to be able to detect a difference in SFQ score of 2 points. SFQ standard deviations vary between treatment, control, and the wait-list samples, ranging from 3.78 to 4.53. We have based our sample size estimate on the most conservative (ie, largest) SD [standard deviation]. To detect a mean difference in SFQ score of 2 point (SD = 4.53) at 72 weeks with a two-sided significance level of 1% and power of 80% with equal allocation to two arms would require 120 patients in each arm of the trial. To allow for 30% drop out, 170 will be recruited per arm, ie, 340 in total.*

Example (Trigger annotation): *To detect a reduction in PHS (postoperative hospital stay) of 3 days (SD 5 days), which is in agreement with the study of Lobo et al17 with a two-sided 5% significance level and a power of 80%, a sample size of 50 patients per group was necessary, given an anticipated dropout rate of 10%. To recruit this number of patients a 12-month inclusion period was anticipated.*

SPIRIT 2013 Item: 14
CONSORT 2010 Item: 7a
Reports annotated: Protocols and Results

15_Recruitment

Trigger: Label the string of text that indicates the sentence or section describes strategies for achieving adequate participant enrolment to reach target sample size.

Example: *The Asthma Clinical Research Center at the Brigham & Women's Hospital utilizes three primary resources for identifying and recruiting potential subjects as described below…*

SPIRIT 2013 Item: 15
CONSORT 2010 Item: Not applicable
Reports annotated: Protocols and Results

16a_Randomization_Generation

Term: Label the text describing the *method* used to generate the random sequence (e.g., computerized).

Example: *Participants will be randomly assigned to either control or experimental group with a 1:1 allocation as per a computer generated randomisation schedule stratified by site and the baseline score of the Action Arm Research Test (ARAT; <=21 versus >21) using permuted blocks of random sizes. The block sizes will not be disclosed, to ensure concealment.*

Example: *Determination of whether a patient would be treated by streptomycin and bed-rest (S case) or by bed-rest alone (C case) was made by reference to a statistical series based on random sampling numbers drawn up for each sex at each centre by Professor Bradford Hill; the details of the series were unknown to any of the investigators or to the co-ordinator.*

Example: *Independent pharmacists dispensed either active or placebo inhalers according to a computer generated randomisation list.*

SPIRIT 2013 Item: 16a
CONSORT 2010 Item: 8a
Reports annotated: Protocols and Results

16b_Randomization_Type

Term: Label the text describing the type of randomization, which might be "simple" or might include restrictions such as stratification or blocking. Label each term separately; if a trial reports that "stratified block" randomization was used, annotate the word "stratified" and the work "block" separately. Terms such as "cluster randomized" and "group randomized" describe the unit of assignment rather than the type of randomization and should not be labeled (see 8a). ["Stratification" refers to generating different random assignment lists for participants depending on certain characteristics to prevent imbalance. For example, a trial might stratify by site such that participants at different clinics are randomized separately. "Blocking" refers to creating small sequences within the overall sequence in which the allocation ratio is met. These

are sometimes called “permuted blocks” because the order of assignments in a block can be any permutation of the group assignments (e.g., for a 1:2 allocation ABB, BAB, BBA). Blocking is used to prevent imbalance over time and to reduce the likelihood of imbalance that might occur within a stratum (e.g., to reduce the likelihood that a site recruiting 20% of the total study sample is imbalanced at the end of recruitment). One method does not necessarily imply that the other was used; however, when stratification is used, blocking is often used also.]

Example: *Participants will be randomly assigned to either control or experimental group with a 1:1 allocation as per a computer generated randomisation schedule stratified by site and the baseline score of the Action Arm Research Test (ARAT; <=21 versus >21) using permuted blocks of random sizes.*

Example: *For each arm, balanced randomization of subjects, stratified by site, gender, and fracture type (intracapsular versus extracapsular), was carried out via permuted block randomization with a variable block size. The randomization seed and actual algorithm was kept by the study Biostatistician, and randomization was performed centrally through the study electronic data management system.*

Example: *The randomization technique is stratified block randomization with varying sized blocks of 4,6, 8, and 10 to prevent prediction of next assignment and to ensure sequence allocation concealment.*

SPIRIT 2013 Item: 16a
CONSORT 2010 Item: 8b
Reports annotated: Protocols and Results

16c_Randomization_Block_size

Term: Label the text describing the block size, which may be fixed (e.g., 4) or variable (e.g., 2 to 8). Variable blocks might be described as “random” when the size of each block in the sequence is selected randomly. Do not use this label if participants are randomized in pairs (similar to a block size of 2). [Block size should be a function of the allocation ratio (e.g., an even number for 1:1, a multiple of 3 for 1:2).]

Example: *Participants will be randomly assigned to either control or experimental group with a 1:1 allocation as per a computer generated randomisation schedule stratified by site and the baseline score of the Action Arm Research Test (ARAT; <=21 versus >21) using permuted blocks of random sizes. The block sizes will not be disclosed, to ensure concealment.*

Example: *For each arm, balanced randomization of subjects, stratified by site, gender, and fracture type (intracapsular versus extracapsular), was carried out via permuted block randomization with a variable block size.*

SPIRIT 2013 Item: 16a

CONSORT 2010 Item: 8b
Reports annotated: Protocols and Results

16d_Randomization_Strata

Term: Label the text describing each stratification variable or each variable used for minimization. Do not label text that states stratification was not used (which should be labelled "Randomization Type"). [Stratification and minimization use different methods to balance groups with respect to prognostic variables; annotate the variables on which the groups were deliberately balanced using these methods. In multi-center trials, center is typically a stratification variable and should be labeled if the text says or implies that randomization was stratified by center.]

Example: *Participants will be randomly assigned to either control or experimental group with a 1:1 allocation as per a computer generated randomisation schedule stratified by site and the baseline score of the Action Arm Research Test (ARAT; <=21 versus >21) using permuted blocks of random sizes. The block sizes will not be disclosed, to ensure concealment.*

Example: *Determination of whether a patient would be treated by streptomycin and bed-rest (S case) or by bed-rest alone (C case) was made by reference to a statistical series based on random sampling numbers drawn up for each sex at each centre by Professor Bradford Hill; the details of the series were unknown to any of the investigators or to the co-ordinator.*

Example: *Patients deemed eligible for study inclusion at this point were randomly assigned on the day of surgery to one of the two treatment regimens (described in a 1:1 ratio via an automated algorithm constructed by the study Biostatistician. For each arm, balanced randomization of subjects, stratified by site, gender, and fracture type (intracapsular versus extracapsular), was carried out via permuted block randomization with a variable block size.*

SPIRIT 2013 Item: 16a
CONSORT 2010 Item: 8b
Reports annotated: Protocols and Results

16e_Allocation_Mechanism

Term: Label the text describing the mechanism of implementing the allocation sequence (e.g., central telephone; sequentially numbered, opaque, sealed envelopes).

Example: *Participants will be randomised using TENALEA, which is an online, central randomisation service…Allocation concealment will be ensured, as the service will not release the randomisation code until the patient has been recruited into the trial, which takes place after all baseline measurements have been completed.*

Example: *The doxycycline and placebo were in capsule form and identical in appearance. They were prepacked in bottles and consecutively numbered for each woman according to the randomisation schedule. Each woman was assigned an order number and received the capsules in the corresponding prepacked bottle.*

Example: *The randomization seed and actual algorithm was kept by the study Biostatistician, and randomization was performed centrally through the study electronic data management system. Site staff obtained the randomization assignment electronically from the data management system and communicated the treatment assignment to the anesthesia team on the day of surgery verbally in person or by telephone, e-mail, text, or other appropriate modality. In the event that the data management system was not available or could not be accessed by study personnel (e.g., password lockout), randomization assignment was communicated to site staff via telephone by the study PI or designated clinical coordinating center staff.*

Example: *To ensure blinding, self-adhesive, pre-coded sticking labels with the unique identification numbers are prepared at the CTU and applied to the opaque medication bottles before providing to the study physicians. 4 digit randomization codes are used with two prefix characters for different age groups (e.g., IN0000, CH0000). Differentiation in code by age is to minimize chances of error in prescribing the wrong bottle. The codes will be kept safe with a person completely unrelated with the trial and broken only after analysis or upon the recommendation of the DSMB. This will ensure blinding of both the allocating physician as well as the one performing the outcome assessment. Moreover, medication will be dispensed by community health workers who are not involved in treatment allocation and outcome assessment.*

SPIRIT 2013 Item: 16b
CONSORT 2010 Item: 9
Reports annotated: Protocols and Results

16f_Allocation_Concealment

Term: Label the text describing steps to conceal the sequence until interventions are assigned. Adequate concealment often includes separating the generation of the sequence (e.g., generated by a statistician at a coordinating center) from the administration of the sequence (e.g., assessment, enrollment, and notification of assignment by a research nurse). Allocation concealment is a process, so sentences describing the mechanism of allocation might also contain information about concealment, and vice versa. Some steps to conceal allocation can also be used for blinding/masking; text can be annotated multiple times, and you should annotate steps that are relevant to allocation concealment even if they are also annotated for blinding/masking (item 17). Do not annotate if the document does not describe steps to conceal allocation.

Example: *Participants will be randomised using TENALEA, which is an online, central randomisation service…Allocation concealment will be ensured, as the service will not release the randomisation code until the patient has been recruited into the trial, which takes place after all baseline measurements have been completed.*

Example: *Patients deemed eligible for study inclusion at this point were randomly assigned on the day of surgery to one of the two treatment regimens (described in a 1:1 ratio via an automated algorithm constructed by the study Biostatistician. For each arm, balanced randomization of subjects, stratified by site, gender, and fracture type (intracapsular versus extracapsular), was carried out via permuted block randomization with a variable block size. The randomization seed and actual algorithm was kept by the study Biostatistician, and randomization was performed centrally through the study electronic data management system. Site staff obtained the randomization assignment electronically from the data management system and communicated the treatment assignment to the anesthesia team on the day of surgery verbally in person or by telephone, e-mail, text, or other appropriate modality. In the event that the data management system was not available or could not be accessed by study personnel (e.g., password lockout), randomization assignment was communicated to site staff via telephone by the study PI or designated clinical coordinating center staff.*

Example: *The doxycycline and placebo were in capsule form and identical in appearance. They were prepacked in bottles and consecutively numbered for each woman according to the randomisation schedule. Each woman was assigned an order number and received the capsules in the corresponding prepacked bottle.*

Example: *To ensure blinding, self-adhesive, pre-coded sticking labels with the unique identification numbers are prepared at the CTU and applied to the opaque medication bottles before providing to the study physicians. 4 digit randomization codes are used with two prefix characters for different age groups (e.g., IN0000, CH0000). Differentiation in code by age is to minimize chances of error in prescribing the wrong bottle. The codes will be kept safe with a person completely unrelated with the trial and broken only after analysis or upon the recommendation of the DSMB. This will ensure blinding of both the allocating physician as well as the one performing the outcome assessment. Moreover, medication will be dispensed by community health workers who are not involved in treatment allocation and outcome assessment.*

SPIRIT 2013 Item: 16b
CONSORT 2010 Item: 9
Reports annotated: Protocols and Results

16g_Personnel_Sequence

Trigger: Label the string of text that indicates who will generate the allocation sequence, including text indicating that the allocation sequence will be generated by a computer (i.e.,

consider “personnel” to include computers) or text indicating where the sequence will be generated (e.g., “centralized randomization”).

Example: *The trial biostatistician will prepare the sequence of treatments.*

Example: *The allocation sequence will be generated by the Institute for Medical Biometry (IMB) applying a permuted block design with random blocks stratified by study centre and medication compliance (favourable vs. unfavourable)...*

Example: Example: *Patients deemed eligible for study inclusion at this point were randomly assigned on the day of surgery to one of the two treatment regimens (described in a 1:1 ratio via an automated algorithm constructed by the study Biostatistician. For each arm, balanced randomization of subjects, stratified by site, gender, and fracture type (intracapsular versus extracapsular), was carried out via permuted block randomization with a variable block size.*

Example: *Determination of whether a patient would be treated by streptomycin and bed-rest (S case) or by bed-rest alone (C case) was made by reference to a statistical series based on random sampling numbers drawn up for each sex at each centre by Professor Bradford Hill; the details of the series were unknown to any of the investigators or to the co-ordinator.*

Example: *Randomization will be performed at a site remote from the trial location".*

SPIRIT 2013 Item: 16c
CONSORT 2010 Item: 10
Reports annotated: Protocols and Results

16h_Personnel_Enrollment

Trigger: Label the string of text that indicates who will assess the eligibility criteria and enroll participants.

Example: *After acceptance of a patient by the panel, and before admission to the streptomycin centre, the appropriate numbered envelope was opened at the central office; the card inside told if the patient was to be an S or a C case, and this information was then given to the medical officer of the centre.*

Example: *Randomisation took place at the end of the 2nd stage of labour when the midwife considered a vaginal birth was imminent. To enter a women into the study, the midwife opened the next consecutively numbered envelope.*

Example: After the research nurse had obtained the patient’s consent, she telephoned a contact who was independent of the recruitment process for allocation consignment.

SPIRIT 2013 Item: 16c

CONSORT 2010 Item: 10
Reports annotated: Protocols and Results

17a_Masking_People_masked

Term: Label the text describing whether people are masked/blinded after assignment according to the study design. Label specific groups (e.g., participants, care providers, those assessing outcomes) including vague statements (e.g., trial staff). Do not label categories such as "double blind" (see 17c).

Example: *Assessments regarding clinical recovery will be conducted by an assessor blind to treatment allocation. The assessor will go through a profound assessment training program . . . Due to the nature of the intervention neither participants nor staff can be blinded to allocation, but are strongly inculcated not to disclose the allocation status of the participant at the follow up assessments. An employee outside the research team will feed data into the computer in separate datasheets so that the researchers can analyse data without having access to information about the allocation.*

Example: *Whereas patients and physicians allocated to the intervention group were aware of the allocated arm, outcome assessors and data analysts were kept blinded to the allocation.*

SPIRIT 2013 Item: 17a
CONSORT 2010 Item: 11a
Reports annotated: Protocols and Results

17b_Masking_Not_masked

Term: Label the text describing personnel who are NOT masked/blinded after assignment according to the study design. Do not annotate if the document does not mention masking/blinding, even if it seems obvious that some persons could not have been masked (e.g., participants assigned to either psychological therapy or drug would be aware of their assignment, surgeons would know whether they are performing a real or sham surgery). Label specific groups (e.g., participants, care providers, those assessing outcomes) including vague statements (e.g., trial staff). Do not label categories such as "double blind" (see 17c).

Example: *Assessments regarding clinical recovery will be conducted by an assessor blind to treatment allocation. The assessor will go through a profound assessment training program . . . Due to the nature of the intervention neither participants nor staff can be blinded to allocation, but are strongly inculcated not to disclose the allocation status of the participant at the follow up assessments. An employee outside the research team will feed data into the computer in separate datasheets so that the researchers can analyse data without having access to information about the allocation.*

Example: *Whereas patients and physicians allocated to the intervention group were aware of the allocated arm, outcome assessors and data analysts were kept blinded to the allocation.*

SPIRIT 2013 Item: 17a
CONSORT 2010 Item: 11a
Reports annotated: Protocols and Results

17c_Masking_Type

Term: Label text describing a categorical description of masking (e.g., open-label, single blind, double blind, assessor-blinded). (CONSORT 2010 explains that these descriptions are used inconsistently, and it argues that they should be abandoned.)

SPIRIT 2013 Item: 17a
CONSORT 2010 Item: 11a
Reports annotated: Protocols and Results

17d_Masking_Unblinding

Trigger: Label the string of text that indicates the sentence or section describing conditions under which unblinding is/was permissible, and procedure for revealing a participant's allocated intervention during the trial. Do not annotate text concerning accidental unblinding (e.g., because of adverse events).

Example: *If unblinding is deemed to be necessary, the investigator should use the system for emergency unblinding through the PHRI toll-free help line as the main system or through the local emergency number as the back-up system.*

SPIRIT 2013 Item: 17b
CONSORT 2010 Item: Not applicable
Reports annotated: Protocols and Results

17e_Masking_Similarity

Trigger: Label the string of text that indicates the sentence or section describes the similarity of interventions. This includes treatment packaging and physical aspects of the intervention. Label "matching placebo" and similar phrases if reported.

Example: *Jamieson Laboratories Inc provided 500-mg immediate release niacin in a white, oblong, bisect caplet. We independently confirmed caplet content using high performance liquid chromatography … The placebo was matched to the study drug for taste, color, and size, and contained microcrystalline cellulose, silicon dioxide, dicalcium phosphate, magnesium stearate, and stearic acid.*

SPIRIT 2013 Item: 17a
CONSORT 2010 Item: 11b
Reports annotated: Protocols and Results

18a_Data_Collection

Trigger: Label the string of text that indicates the sentence or section describes plans for (protocols) or methods for (results reports) assessment and collection of outcome, baseline, and other trial data. Look for sentences that are about data collection rather than sentences that merely mention outcomes or other variables. For example, if a sentence explains that an outcome will be assessed using a particular scale (e.g., "depression will be assessed using the Montgomery Asberg Depression Rating Scale), then the label 12a would be more appropriate than 18a. Sections about data collection often describe processes to promote data quality (eg, duplicate measurements, training of assessors). Do not annotate data management procedures such as double entry (see 19) and do not annotate time points.

Example: *The study will collect demographic and baseline functional information from the patient's legally authorized representative and/or caregivers. Cognitive function status will be obtained by interviewing the patient's legally authorized representative using the Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE). IQCODE is a questionnaire that can be completed by a relative or other caregiver to determine whether that person has declined in cognitive functioning.*

Example: *Assessments regarding clinical recovery will be conducted by an assessor blind to treatment allocation. The assessor will go through a profound assessment training program . . . Due to the nature of the intervention neither participants nor staff can be blinded to allocation, but are strongly inculcated not to disclose the allocation status of the participant at the follow up assessments. An employee outside the research team will feed data into the computer in separate datasheets so that the researchers can analyse data without having access to information about the allocation.*

SPIRIT 2013 Item: 18a
CONSORT 2010 Item: Not applicable
Reports annotated: Protocols and Results

18b_Data_Retention

Trigger: Label the string of text that indicates the sentence or section describes plans (protocols) or methods (results reports) to promote participant retention and complete follow-up, including any outcome data to be collected for participants who discontinue or deviate from intervention protocols. Label also plans concerning the absence of data retention.

Example: *Once an infant is enrolled or randomized, the study site will make every reasonable effort to follow the infant for the entire study period…Study site staff are responsible for developing and implementing local standard operating procedures to achieve this level of follow-up.*

Example: *The investigator can decide to withdraw a subject from the study for urgent medical reasons or in case of demonstrable poor adherence to the study medication.*

SPIRIT 2013 Item: 18b
CONSORT 2010 Item: Not applicable
Reports annotated: Protocols and Results

19_Data_Management

Trigger: Label the string of text that indicates the sentence or section describes plans (protocols) or methods (results reports) for data entry, coding, security, and storage, including any related processes to promote data quality (e.g., double data entry; range checks for data values). Do not annotate data collection procedures such as training assessors (see 18a).

Example: *Data from the Core Lab will be securely transmitted in batches and quality controlled in the same manner as Core Coordinating Center data; ie data will be entered and verified in the database on the Cleveland Clinic Foundation SUN with a subset later selected for additional quality control. Appropriate edit checks will be in place at the key entry (database) level. The Core Lab is to have an internal quality control system established prior to analyzing any FSGS [focal segmental glomerulosclerosis] samples. This system will be outlined in the Manual of Operations for the Core Lab(s) which is prepared and submitted by the Core Lab to the DCC [data coordinating centre] prior to initiating of the study.*

SPIRIT 2013 Item: 19
CONSORT 2010 Item: Not applicable
Reports annotated: Protocols and Results

20a_Statistical_methods_Outcomes

Section/Trigger: Label a heading such as “Primary analysis” if one exists (“Section” annotation). Otherwise, label the string of text that indicates the sentence or section describes planned (protocols) or actual (results reports) statistical methods for analyzing primary and secondary outcomes. Include both benefits and systematically assessed harms (i.e., harms assessed in the same way for all trial participants). For trigger annotation, annotate phrases that indicate the sentence is about the methods (e.g., “to compare”, “calculated the difference between groups”) rather than the methods themselves (e.g., do not annotate “log-rank test”) if possible.

Example (Section annotation): *Secondary analyses*

Example (Trigger annotation): *We will use chi-squared test for binary outcomes, and T-test for continuous outcomes. For subgroup analyses, we will use regression methods with appropriate interaction terms (respective subgroup×treatment group). Multivariable analyses will be based on logistic regression . . . for binary outcomes and linear regression for continuous outcomes. We will examine the residual to assess model assumptions and goodness-of-fit. For timed endpoints such as mortality we will use the Kaplan-Meier survival analysis followed by multivariable Cox proportional hazards model for adjusting for baseline variables. We will calculate Relative Risk (RR) and RR Reductions (RRR) with corresponding 95% confidence intervals to compare*

dichotomous variables, and difference in means will be used for additional analysis of continuous variables. P-values will be reported to four decimal places with p-values less than 0.001 reported as p < 0.001. Up-to-date versions of SAS (Cary, NC) and SPSS (Chicago, IL) will be used to conduct analyses. For all tests, we will use 2-sided p-values with alpha≤0.05 level of significance. We will use the Bonferroni method to appropriately adjust the overall level of significance for multiple primary outcomes, and secondary outcomes.

SPIRIT 2013 Item: 20a
CONSORT 2010 Item: 12a
Reports annotated: Protocols and Results

20b_Statistical_methods_Other_Analyses

Trigger: Label the string of text that indicates the sentence or section describes plans (protocols) or methods (results reports) for any additional analyses (e.g., subgroup and adjusted analyses). Annotate sentences about statistical methods, but do not annotate sentences that merely describe which groups will be compared or that describe non-specific sensitivity analyses. Where possible, label the triggers that indicate sentences are about statistical methods (e.g., "we also compared") but do not label the name of the statistical model (e.g., "using logistic regression").

Example: *We will use chi-squared test for binary outcomes, and T-test for continuous outcomes. For subgroup analyses, we will use regression methods with appropriate interaction terms (respective subgroup×treatment group).*

SPIRIT 2013 Item: 20b
CONSORT 2010 Item: 12b
Reports annotated: Protocols and Results

20c_Statistical_methods_Analysis_population

Term: Label any term used to describe a population (e.g., intention-to-treat, per-protocol) and label text describing the definition of the analysis population (e.g., everyone randomized, people who received one or more doses). Include text that indicates the sentence or section describes whether the analysis was by original assigned groups.

Example: *The primary analysis was intention-to-treat and involved all patients who were randomly assigned.*

Example: *One patient in the alendronate group was lost to follow up; thus data from 31 patients were available for the intention-to-treat analysis. Five patients were considered protocol violators ... consequently 26 patients remained for the per- protocol analyses.*

Example: *Nevertheless, we propose to test non-inferiority using two analysis sets; the intention-to-treat set, considering all patients as randomized regardless of whether they received the randomized treatment, and the "per protocol" analysis set.*

Example: *In order for an enrolled child to be included in the modified per protocol analysis, s/he must have received 5 out of 6 doses, including 4 doses in the first two days.*

SPIRIT 2013 Item: 20c
CONSORT 2010 Item: 16
Reports annotated: Protocols and Results

20d_Statistical_methods_Missing_data

Term: Label the text describing any statistical methods to handle missing data (e.g., multiple imputation), including sensitivity analyses to assess the impact of missing data.

Example: *The effect that any missing data might have on results will be assessed via sensitivity analysis of augmented data sets. Dropouts (essentially, participants who withdraw consent for continued follow-up) will be included in the analysis by modern imputation methods for missing data.*

Example: *Missing data were filled in by multiple imputation assuming a missing at-random mechanism of dropout. The Monte Carlo Markov Chain technique implemented in SAS Proc MI was used to obtain 50 imputed datasets. Rubin rules implemented in SAS Proc MIANALYZE were used to combine effect estimates and to estimate 95% CIs to allow for uncertainty attributable to missing data. For the post hoc analysis, the last observation carried forward technique was used to complete missing values for patients who did not complete the study.*

SPIRIT 2013 Item: 20c
CONSORT 2010 Item: Not applicable
Reports annotated: Protocols and Results

21a_Data_monitoring_committee

Trigger: Label the string of text that indicates the sentence or section describes the data monitoring committee an explanation of why a DMC is not needed. This might include: 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.

Example: *A Data Monitoring Committee (DMC) has been established. The DMC is independent of the study organisers. During the period of recruitment to the study, interim analyses will be supplied, in strict confidence, to the DMC, together with any other analyses that the committee may request.…..*

SPIRIT 2013 Item: 21a
CONSORT 2010 Item: Not applicable
Reports annotated: Protocols and Results

21b_Interim_analyses

Trigger: Label the string of text that indicates the sentence or section describes planned (protocols) or actual (results reports) methods/results for interim analyses, including explicit statements that no interim analyses will be (protocols) or were (results reports) conducted..

Example: *An interim-analysis is performed on the primary endpoint when 50% of patients have been randomised and have completed the 6 months follow-up. The interim-analysis is performed by an independent statistician, blinded for the treatment allocation. The statistician will report to the independent DSMC [data and safety monitoring committee]. The DSMC will have unblinded access to all data and will discuss the results of the interim-analysis with the steering committee in a joint meeting. The steering committee decides on the continuation of the trial and will report to the central ethics committee. The Peto approach is used: the trial will be ended using symmetric stopping boundaries at P < 0.001 [reference]. The trial will not be stopped in case of futility, unless the DSMC during the course of safety monitoring advices [sic] otherwise. In this case DSMC will discuss potential stopping for futility with the trial steering committee.*

Example: *An independent data and safety monitoring board periodically reviewed the efficacy and safety data. Stopping rules were based on modified Haybittle-Peto boundaries of 4 SD in the first half of the study and 3 SD in the second half for efficacy data, and 3 SD in the first half of the study and 2 SD in the second half for safety data. Two formal interim analyses of efficacy were performed when 50% and 75% of the expected number of primary events had accrued; no correction of the reported P value for these interim tests was performed.*

Example: *No interim analyses will be conducted*.

SPIRIT 2013 Item: 21b
CONSORT 2010 Item: 7b
Reports annotated: Protocols and Results

21c_Stopping_guidelines

Trigger: Label the string of text that indicates the sentence or section describes any stopping guidelines. Label text that states a data monitoring committee may stop the trial at their discretion, including for reasons not prespecified.

Example: *The DSMC will have unblinded access to all data and will discuss the results of the interim-analysis with the steering committee in a joint meeting. The steering committee decides on the continuation of the trial and will report to the central ethics committee. The Peto*

approach is used: the trial will be ended using symmetric stopping boundaries at P < 0.001 [reference]. The trial will not be stopped in case of futility, unless the DSMC during the course of safety monitoring advices [sic] otherwise. In this case DSMC will discuss potential stopping for futility with the trial steering committee.

Example: *An independent data and safety monitoring board periodically reviewed the efficacy and safety data. Stopping rules were based on modified Haybittle-Peto boundaries of 4 SD in the first half of the study and 3 SD in the second half for efficacy data, and 3 SD in the first half of the study and 2 SD in the second half for safety data.*

SPIRIT 2013 Item: 21b
CONSORT 2010 Item: 7b
Reports annotated: Protocols and Results

22_Harms_non-systematic

Trigger: Label the string of text that indicates the sentence or section describes planned (protocols) or actual (results reports) methods related to non-systematically assessed harms. These might include methods for collecting, assessing, or reporting adverse events that are not measured in the same way for all participants (e.g., using standardized scales or instruments at prespecified times).

Example: *The study will monitor for the following movement-related adverse effects daily through patient examination and chart review: dystonia, akathisia, pseudoparkinsonism, akinesia, and neuroleptic malignant syndrome. Study personnel will use the Simpson-Angus [reference] and Barnes Akathisia [reference] scales to monitor movement-related effects.*

SPIRIT 2013 Item: 22
CONSORT 2010 Item: Not applicable
Reports annotated: Protocols and Results

23_Auditing

Trigger: Label the string of text that indicates the sentence or section describes frequency and procedures for auditing trial conduct. For example, audits might be conducted to ensure that sites are storing medications correctly, that allocation is being concealed, and the records are being kept in a manner that preserves patient confidentiality. Audits are generally not focused on study results per se; reviewing safety and conducting interim analyses might be functions of the Data Monitoring Committee (DMC) or Data Safety Monitoring Board (DSMB) rather than auditors (see 21a).

Example: *Both the European and US DCCs will conduct monitoring of source documents via fax at all enrolling ARUBA [A Randomised trial of Unruptured Brain Arteriovenous malformations] sites and will conduct at least one on-site monitoring visit per year over the course of the study*

at 100% of clinical sites (with repeat visits to sites where performance is a concern). Monitoring of European study sites will be assured by the European Coordinating Center (Paris). The primary objectives of the DCC during the on-site visits are to educate, support and solve problems. The monitors will discuss the protocol in detail and identify and clarify any areas of weakness.

SPIRIT 2013 Item: 23
CONSORT 2010 Item: Not applicable
Reports annotated: Protocols

34_Flow

Trigger: Label the string of text that indicates the sentence or section describes the number of participants who were enrolled and randomly assigned, received intended intervention, lost or excluded after randomization and analyzed for the primary outcome (overall, to each group, or both overall and to each group). If a sentence in the text refers to a figure for this information, annotate that sentence. If this information appears only in a figure, annotate the text in the label and/or caption. Do not label the planned sample size (see 14a and 14b).

Example: 202 participants were randomly assigned, 187 completed treatment as allocated, 185 completed follow-up as planned. All 202 randomized participants were included in the intention to treat analysis.

Example: T*he monitoring led to withdrawal of nine centres, in which existence of some patients could not be proved, or other serious violations of good clinical practice had occurred.*

Example: *The CONSORT Flow Diagram is shown in Figure 2.*

Example: *Figure 2. CONSORT Flow Diagram*

SPIRIT 2013 Item: Not applicable
CONSORT 2010 Item: 13a
Reports annotated: Results

35a_Recruitment_dates

Trigger: Label the string of text that indicates the sentence or section describes planned (protocols) or actual (results reports) dates defining the period of recruitment. Where possible, do not label the specific dates.

Example: *Age-eligible participants were recruited … from February 1993 to September 1994 … Participants attended clinic visits at the time of randomisation (baseline) and at 6-month intervals for 3 years.*

SPIRIT 2013 Item: Not applicable

CONSORT 2010 Item: 14a
Reports annotated: Protocols and Results

35b_Followup_dates

Trigger: Label the string of text that indicates the sentence or section describes dates defining the planned (protocols) or actual (results) period of follow-up. Annotate sentences that describe follow-up periods after the recruitment dates, but do not annotate sentences that merely describe the duration of the study, which might be mentioned several times (e.g., do not annotate "We conducted a 12-month trial.").

Example: *Recruitment was conducted between January and April 2022 and follow-up for each participant occurred 12-months later.*

Example: *Recruitment was conducted between January and April 2022 and follow-up occurred from January and April 2023.*

Example: *Age-eligible participants were recruited … from February 1993 to September 1994 … Participants attended clinic visits at the time of randomisation (baseline) and at 6-month intervals for 3 years.*

SPIRIT 2013 Item: Not applicable
CONSORT 2010 Item: 14a
Reports annotated: Protocols and Results

35c_Stopping

Trigger: Label the string of text that indicates the sentence or section describes why the trial ended or was stopped, or that states the trial was stopped early. Do not annotate if the document does not give a reason for stopping or does not say that the trial stopped early; for example there might be nothing to annotate for trials that are not stopped early and that do not state explicitly that they completed the scheduled recruitment and follow-up.

Example: *In January 2000, problems with vaccine supply necessitated the temporary nationwide replacement of the whole cell component of the combined DPT/Hib vaccine with acellular pertussis vaccine. As this vaccine has a different local reactogenicity profile, we decided to stop the trial early.*

SPIRIT 2013 Item: Not applicable
CONSORT 2010 Item: 14b
Reports annotated: Results

36_Baseline_data

Trigger: Label the string of text that indicates the sentence or section describes the baseline characteristics of participants or that it refers to a table showing baseline demographic and clinical characteristics for each group.

Example: *Table 1. Baseline characteristics.*

Example: *The randomization process achieved balance between oxytocin and control clusters on a range of women's characteristics (Table 1) and on indicators of recruitment, enrollment, and measurement procedures (Table 2).*

SPIRIT 2013 Item: Not applicable
CONSORT 2010 Item: 15
Reports annotated: Results

37a_Analysis_Numbers

Trigger: Label the string of text that indicates the sentence or section describes the number of participants included in each analysis (overall, in each group, or both overall and in each group). Do not annotate tables (e.g., column headings, footers) unless this is the only place that the sample size is reported.

Example: *One patient in the alendronate group was lost to follow up; thus data from 31 patients were available for the intention-to-treat analysis. Five patients were considered protocol violators … consequently 26 patients remained for the per-protocol analyses.*

SPIRIT 2013 Item: Not applicable
CONSORT 2010 Item: 16
Reports annotated: Results

38a_Outcome_results

Section/Trigger: Label a heading such as "Primary results" if one exists ("Section" annotation). Otherwise, label the string of text that indicates the sentence or section describes the results for primary and secondary outcomes. Not all reports will adhere to CONSORT guidelines, which specifically require results for each group and the estimated effect size and its precision.

Example (Section annotation): *Secondary results*

Example (Trigger annotation): *The etanercept group had statistically better outcomes for all clinical endpoints (table 2, figure 2). The primary endpoint for psoriatic arthritis, the number of patients who met the PsARC at 12 weeks, was achieved by 26 (87%) etanercept-treated patients compared with seven (23%) placebo-treated patients (p<0·0001). The response was significantly greater at all measured time points in patients who received etanercept relative to those*

receiving placebo. The ACR response rates were also significantly higher in the etanercept-treated group. At 12 weeks, the ACR20 was achieved by 22 (73%) etanercept-treated patients compared with four (13%) placebo-treated patients (p<0·0001).

SPIRIT 2013 Item: Not applicable
CONSORT 2010 Item: 17a
Reports annotated: Results

38b_Binary_results

Trigger: Label the string of text that indicates the sentence or section describes, for binary outcomes, presentation of absolute or relative effect sizes, or both. Where applicable, rates should be labeled 38a rather than 38b. Sentences annotated 38b may also meet the definition of 38a but do not also need to be labeled 38a (i.e., do not annotate them twice).

Example: *The risk of oxygen dependence or death was reduced by 16% (95% CI 25% to 7%). The absolute difference was −6.3% (95% CI −9.9% to −2.7%); early administration to an estimated 16 babies would therefore prevent 1 baby dying or being long-term dependent on oxygen.*

Example: *Treatment failures were 51(2.6%) with amoxicillin and 95(4.9%) with placebo, including one death in each arm. Relapses were 58(3.1%) in the amoxicillin arm and 40(2.2%) in placebo.*

SPIRIT 2013 Item: Not applicable
CONSORT 2010 Item: 17b
Reports annotated: Results

39_Ancillary_results

Trigger: Label the string of text that indicates the sentence or section describes results of any other analyses performed such as subgroup analyses, adjusted analyses, and analyses concerning dropout. All ancillary results should be labeled 39, including both continuous and dichotomous outcomes; do not label ancillary results 38b, even if they are binary.

Example: *We prespecified our primary subgroup analysis on the basis of the revised cardiac risk index scoring system. We also did prespecified secondary subgroup analyses based on sex, type of surgery, and use of an epidural or spinal anaesthetic. For all subgroup analyses, we used Cox proportional hazard models that incorporated tests for interactions, designated to be significant at p<0.05 … Figure 3 shows the results of our prespecified subgroup analyses and indicates consistency of effects … Our subgroup analyses were underpowered to detect the modest differences in subgroup effects that one might expect to detect if there was a true subgroup effect.*

SPIRIT 2013 Item: Not applicable

CONSORT 2010 Item: 18
Reports annotated: Results

40_Harms_results

Trigger: Label the string of text that indicates the sentence or section describes results for non-systematic harms. Include any harms that are not defined clearly as systematic or non-systematic (e.g., "adverse events"). Systematic harms are measured in the same way for all participants using the same instrument at predefined timepoints; systematic harms may be listed as primary or secondary outcomes and labeled 12a.

Example: *The proportion of patients experiencing any adverse event was similar between the rBPI21 [recombinant bactericidal/permeability-increasing protein] and placebo groups: 168 (88.4%) of 190 and 180 (88.7%) of 203, respectively, and it was lower in patients treated with rBPI21 than in those treated with placebo for 11 of 12 body systems … the proportion of patients experiencing a severe adverse event, as judged by the investigators, was numerically lower in the rBPI21 group than the placebo group: 53 (27.9%) of 190 versus 74 (36.5%) of 203 patients, respectively. There were only three serious adverse events reported as drug-related and they all occurred in the placebo group.*

SPIRIT 2013 Item: Not applicable
CONSORT 2010 Item: 19
Reports annotated: Results

41_Generalizability

Trigger: Label the string of text that indicates the sentence or section describes generalizability (external validity, applicability) of the trial findings, including limits to generalizability.

Example: *As the intervention was implemented for both sexes, all ages, all types of sports, and at different levels of sports, the results indicate that the entire range of athletes, from young elite to intermediate and recreational senior athletes, would benefit from using the presented training programme for the prevention of recurrences of ankle sprain. By including non-medically treated and medically treated athletes, we covered a broad spectrum of injury severity. This suggests that the present training programme can be implemented in the treatment of all athletes. Furthermore, as it is reasonable to assume that ankle sprains not related to sports are comparable with those in sports, the programme could benefit the general population.*

SPIRIT 2013 Item: Not applicable
CONSORT 2010 Item: 21
Reports annotated: Results

24_Ethics

Trigger: Label the string of text that indicates the sentence or section describes research ethics committee/institutional review board (REC/IRB) approval or plans for seeking approval. Although often followed by information about ethical approval, phrases such as "this study was approved by" might refer to other types of approvals (e.g., financial support). Therefore,, annotations should include information related to ethics specifically (e.g., "IRB", "ethics committee").

Example: *This protocol and the template informed consent forms contained in Appendix II will be reviewed and approved by the sponsor and the applicable IRBs/ECs [institutional review boards/ethical committees] with respect to scientific content and compliance with applicable research and human subjects regulations.*

Example: *This study has been approved by the Ethics Committee in Verona.*

SPIRIT 2013 Item: 24
CONSORT 2010 Item: Not applicable
Reports annotated: Protocols and Results

25_Amendments

Trigger: Label the string of text that indicates the sentence or section describes plans for protocol modifications or changes to methods after trial commencement (e.g., modifications to the eligibility criteria, modifications to to the allocation ratio, increased sample size). Do not annotate changes to the outcomes (see 12b).

Example: *During the trial, this committee recommended that the group receiving the lowest dose of otamixaban (0·035 mg/kg/h) be discontinued because of clinical evidence of inadequate anticoagulation. The protocol was immediately amended in accordance with that recommendation, and participants were subsequently randomly assigned in 2:2:2:2:1 ratio to the remaining otamixaban and control groups, respectively.*

Example: *Any modifications to the protocol which may impact on the conduct of the study, potential benefit of the patient or may affect patient safety, including changes of study objectives, study design, patient population, sample sizes, study procedures, or significant administrative aspects will require a formal amendment to the protocol. Such amendment will be agreed upon by BCIRG [Breast Cancer International Research Group] and Aventis, and approved by the Ethics Committee/IRB [institutional review board] prior to implementation and notified to the health authorities in accordance with local regulations.*

SPIRIT 2013 Item: 25
CONSORT 2010 Item: 3b
Reports annotated: Protocols and Results

26a_Consent_Obtaining

Trigger: Label the string of text that indicates the sentence or section describes how informed consent or assent from potential trial participants or authorized surrogates will be (protocols) or was (results reports) obtained. Do not label text referring to the consent materials (see 32).

Example: *Trained Research Nurses will introduce the trial to patients who will be shown a video regarding the main aspects of the trial. Patients will also receive information sheets. Research Nurses will discuss the trial with patients in light of the information provided in the video and information sheets. Patients will then be able to have an informed discussion with the participating consultant. Research Nurses will obtain written consent from patients willing to participate in the trial….*

SPIRIT 2013 Item: 26a
CONSORT 2010 Item: Not applicable
Reports annotated: Protocols and Results

26b_Consent_Provisions

Trigger: Label the string of text that indicates the sentence or section describes additional consent provisions for collection and use of participant data and biological specimens in ancillary studies. Do not annotate if the document does not describe consent for future research.

Example: *Additional biological samples will be obtained to be stored for use in future studies of the pathobiology of FSGS [focal segmental glomerulosclerosis]. A materials consent will be obtained to specifically address the collection of these . . . urine, serum and plasma specimen.*

SPIRIT 2013 Item: 26b
CONSORT 2010 Item: Not applicable
Reports annotated: Protocol

27_Confidentiality

Trigger: Label the string of text that indicates the sentence or section relates to confidentiality of personal information about potential and enrolled participants (e.g., how that information will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial).

Example: *All study-related information will be stored securely at the study site. All participant information will be stored in locked file cabinets in areas with limited access. All laboratory specimens, reports, data collection, process, and administrative forms will be identified by a coded ID [identification] number only to maintain participant confidentiality. All records that contain names or other personal identifiers, such as locator forms and informed consent forms, will be stored separately from study records identified by code number. All local databases will*

be secured with password-protected access systems. Forms, lists, logbooks, appointment books, and any other listings that link participant ID numbers to other identifying information will be stored in a separate, locked file in an area with limited access.

SPIRIT 2013 Item: 27
CONSORT 2010 Item: Not applicable
Reports annotated: Protocols and Results

28_Financial_interests

Section/Trigger: Label the string of text that indicates the sentence or section relates to financial and other competing interests (e.g., for principal investigators for the overall trial and for each study site).

Example: *GG received honoraria and speaker fees from: Boehringer Ingelheim, Sanofi Synthlabo Aventis, Hoffman La Roche and Novo Nordisk.*

SPIRIT 2013 Item: 28
CONSORT 2010 Item: Not applicable
Reports annotated: Protocols and Results

29_Data_access

Trigger: Label the string of text that indicates the sentence or section relates to data access (e.g., who will have access to the final trial dataset, disclosure of contractual agreements that limit such access for investigators).

Example: *The Data Management Coordinating Center will oversee the intra-study data sharing process, with input from the Data Management Subcommittee. All Principal Investigators (both US and host country) will be given access to the cleaned data sets. Project data sets will be housed on the Project Accept Web site and/or the file transfer protocol site created for the study, and all data sets will be password protected. Project Principal Investigators will have direct access to their own site's data sets, and will have access to other sites data by request. To ensure confidentiality, data dispersed to project team members will be blinded of any identifying participant information.*

SPIRIT 2013 Item: 29
CONSORT 2010 Item: Not applicable
Reports annotated: Protocol

30_Post_trial_care

Trigger: Label the string of text that indicates the sentence or section describes provisions, if any, for ancillary and post-trial care, including compensation to those who suffer harm from trial participation.

Example: *Patients that are enrolled into the study are covered by indemnity for negligent harm through the standard NHS [National Health Service] Indemnity arrangements. The University of Sheffield has insurance to cover for non-negligent harm associated with the protocol . . . This will include cover for additional health care, compensation or damages whether awarded voluntarily by the Sponsor, or by claims pursued through the courts. Incidences judged to arise from negligence (including those due to major protocol violations) will not be covered by study insurance policies. The liability of the manufacturer of IL1RA (Amgen Corporation) is strictly limited to those claims arising from faulty manufacturing of the commercial product and not to any aspects of the conduct of the study.*

SPIRIT 2013 Item: 30
CONSORT 2010 Item: Not applicable
Reports annotated: Protocol

31a_Dissemination

Trigger: Label the string of text that indicates the sentence or section describes dissemination, including how the investigators and sponsor plan to communicate (protocols and results reports) or have communicated (results reports) 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. Do not lebel a statement that the funder has no role in decision to publish (see 4_Funding)

Example: *The Publications subcommittee will review all publications following the guidelines given below and report its recommendations to the Steering Committee…Each paper or abstract, as described below, must be submitted to the appropriate Subcommittee for review of its appropriateness and scientific merit prior to submission. The Subcommittee may recommend changes to the authors and will finally submit its recommendations to the Steering Committee for approval.*

SPIRIT 2013 Item: 31a
CONSORT 2010 Item: Not applicable
Reports annotated: Protocols and Results

31b_Authorship

Trigger: Label the string of text that indicates the sentence or section describes authorship eligibility guidelines and any planned (protocols) or actual (results reports) use of professional writers.

Example: *Topics suggested for presentation or publication will be circulated to the PIs [principal investigators] of the CCCs [core coordinating centers], the DCC [data coordinating centre], Core Lab and the NIH [National Institutes of Health]. These groups are requested to suggest and*

justify names for authors to be reviewed by the PC [publications committee]. . . If a topic is suggested by a participant of the FSGS-CT [focal segmental glomerulosclerosis—clinical trial], the writing committee will be formed as just described except that the person making the suggestion may be considered as the lead author. The PI of an ancillary study should be considered for lead author of material derived from this study. Disputes regarding authorship will be settled by the Study Chair after consultation with the Chair of the PC.

SPIRIT 2013 Item: 31b
CONSORT 2010 Item: Not applicable
Reports annotated: Protocols and Results

31c_Sharing_Materials

Trigger: Label the string of text that indicates the sentence or section relates to granting (or not) public access to research materials, such as the intervention protocol. Do not label headings that appear to be relevant (e.g., "Data and Materials Sharing") unless the section actually contains information about sharing materials.

Example: Data and Materials Sharing

SPIRIT 2013 Item: 31c
CONSORT 2010 Item: Not applicable
Reports annotated: Protocols and Results

31d_Sharing_Data

Section/Trigger: Label a heading such as "Data sharing" if one exists ("Section" annotation). Otherwise, label the string of text that indicates the sentence or section relates to granting (or not) public access to participant-level data.

Example (Section annotation): *Data sharing statement No later than 3 years after the collection of the 1-year postrandomisation interviews, we will deliver a completely deidentified data set to an appropriate data archive for sharing purposes.*

SPIRIT 2013 Item: 31c
CONSORT 2010 Item: Not applicable
Reports annotated: Protocols and Results

31e_Sharing_Code

Trigger: Label the string of text that indicates the sentence or section relates to granting (or not) public access to statistical code.

SPIRIT 2013 Item: 31c
CONSORT 2010 Item: Not applicable

Reports annotated: Protocols and Results

32_Informed_consent_materials

Trigger: Label the string of text that indicates the sentence or section relates to accessing a model consent form and other related documentation given to participants and authorized surrogates.

Example: *The informed consent form is included in Appendix 1.*

SPIRIT 2013 Item: 32
CONSORT 2010 Item: Not applicable
Reports annotated: Protocols and Results

33_Biological_specimens

Section/Trigger: Label a heading such as "Sample bank procedures" if one exists ("Section" annotation). Otherwise, label the string of text that indicates the sentence or section describes planned (protocols) or actual (results reports) methods for handling biological specimens (e.g., collection, laboratory evaluation, and storage for genetic or molecular analysis in the current trial and for future use in ancillary studies).

Example: *The PCPT WBC [white blood cell] sample will be available to PCPT investigators as well as outside researchers who have important, timely hypotheses to test. Because the sample bank is a limited resource, proposals to use it will be evaluated in terms of scientific relevance, significance, and validity as well as the potential impact of the proposed study. The amount and type of material needed will also be considered and the efficient use of material will be required. Strict confidentiality will be exercised and the information provided to investigators will not contain personal identifiers… NCI-Frederick Cancer Research Development Center (FCRDC) in Frederick, Maryland will serve as the processing, aliquotting and storage facility. Upon arrival at FCRDC the blood will be pooled and centrifuged. Plasma will be separated into 5 x 1.8 ml aliquots and frozen. All samples will be logged in and aliquots will be bar coded with a unique storage ID. These data will be electronically transmitted to the Statistical Center for verification.*

SPIRIT 2013 Item: 33
CONSORT 2010 Item: Not applicable
Reports annotated: Protocols and Results