Protocol for a meta-research study of protocols for diet or nutrition-related trials published in indexed journals: general aspects of study design, rationale and reporting limitations


ABSTRACT

Introduction The Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) reporting guideline establishes a minimum set of items to be reported in any randomised controlled trial (RCT) protocol. The Template for Intervention Description and Replication (TIDieR) reporting guideline was developed to improve the reporting of interventions in RCT protocols and results papers. Reporting completeness in protocols of diet or nutrition-related RCTs has not been systematically investigated. We aim to identify published protocols of diet or nutrition-related RCTs, assess their reporting completeness and identify the main reporting limitations remaining in this field.

Methods and analysis We will conduct a meta-research study of RCT protocols published in journals indexed in at least one of six selected databases between 2012 and 2022. We have run a search in PubMed, Embase, CINAHL, Web of Science, PsycINFO and Global Health using a search strategy designed to identify protocols of diet or nutrition-related RCTs. Two reviewers will independently screen the titles and abstracts of records yielded by the search in Rayyan. The full texts will then be read to confirm protocol eligibility. We will collect general study features (publication information, types of participants, interventions, comparators, outcomes and study design) of all eligible published protocols in this contemporary sample. We will assess reporting completeness in a randomly selected sample of them and identify their main reporting limitations. We will compare this subsample with the items in the SPIRIT and TIDieR statements. For all data collection, we will use data extraction forms in REDCap. This protocol is registered on the Open Science Framework (DOI: 10.17605/OSFIO/YWEVS).

Ethics and dissemination This study will undertake a secondary analysis of published data and does not require ethical approval. The results will be disseminated through journals and conferences targeting stakeholders involved in nutrition research.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ We propose mapping the landscape of nutrition or diet-related randomised controlled trials (RCTs) and identifying the main reporting limitations of their protocols by systematically searching for all indexed publications describing such documents between 2012 and 2022.
⇒ The search strategy covers six online databases to increase the likelihood of identifying all protocols of nutrition or diet-related RCTs published in the last 10 years.
⇒ The search strategy was built based on a validated search strategy to identify nutrition or diet-related RCTs and adapted to identify protocol papers by an experienced librarian and information specialist.
⇒ Participants, intervention, comparator, outcomes and study design data of nutrition or diet-related RCTs will be used to describe this research area.
⇒ Nutrition or diet-related RCTs that did not publish their protocols as articles will not be identified by our study.

INTRODUCTION

Well-written, detailed protocols allow prospective assessment of randomised controlled trial (RCT) methods and support scientific integrity, ethical standards, safety and retrospective validation of study methods and findings. Protocols aim to describe all planned research steps comprehensively and are the key document bounding the ethical principles for medical research with human subjects. Incomplete or undisclosed reporting in RCT protocols can result in research misrepresentation, and bias that reduces the credibility and validity of research and scientific knowledge, such as bias of selective reporting.
outcomes. Thus, publishing well-reported study protocols as peer-reviewed scientific articles can be thought of as a strategy to increase research robustness and impact.

Nutrition interventions have unique challenges that require careful consideration during study design and execution and careful communication of research questions and findings that are different from the other health fields. For example, complex correlations between dietary components mean that substituting one food for another often results in simultaneous changes to many nutrients. Critical appraisal of diet or nutrition-related RCTs depends on researchers clearly describing the field-specific methodological approaches used in their studies, ideally in prospectively registered protocols and predefined statistical analysis plans. Examples of such approaches include determining baseline dietary patterns, assessing prospective food intake assessment and using appropriate data analysis techniques (eg, adjusting for total energy intake, confirmatory factor analysis and principal component analysis applied to dietary patterns). Unlike highly regulated drug trials, diet and nutrition-related RCTs are not subject to oversight by regulatory agencies, which might explain the lack of reporting of essential details in papers describing non-regulated RCTs. Indeed, the available reporting guidelines were not specifically designed for nutrition or diet-related RCTs.

The Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) reporting guideline suggests a minimum set of items to be reported in any RCT protocol. As of 1 December 2021, the primary SPIRIT publication presenting a checklist of items to include in RCT protocols had been cited more than 2000 times, according to Clarivate’s Web of Science. Reporting completeness of all RCT protocols and non-regulated RCTs has improved since SPIRIT’s publication. Item 5 of the Consolidated Standards of Reporting Trials 2010 statement and item 11 of the SPIRIT 2013 statement provide guidance for reporting an RCT’s intervention. The item was extended into a checklist called the Template for Intervention Description and Replication (TIDieR), which aimed to improve the completeness of reporting and replicability of interventions.

Published protocols are growing in importance as a source of details about interventions. The use of TIDieR alongside SPIRIT 2013 can help scientists performing nutrition-related RCTs to fully describe their protocols in peer-reviewed articles. However, little is known about the general aspects of study design of published diet or nutrition-related RCT protocols and their reporting completeness.

OBJECTIVES
This protocol describes a meta-research study that aims to use systematically identified protocols of diet or nutrition-related RCTs published as scientific articles in journals indexed in at least one of six selected databases between 2012 and 2022 to:

1. Characterise the interventions, population, primary outcomes and design features of the protocols.
2. Assess the completeness of reporting of a subsample of these protocols, measuring their adherence to the SPIRIT 2013 and TIDieR statements.

METHODS
Design
A meta-research study, whose protocol is registered in the Open Science Framework (https://doi.org/10.17605/OSF.IO/YWEVS). Box 1 shows the research questions this review aims to answer.

Eligibility criteria
We will include a sample of protocols of diet and nutrition-related RCTs published as papers in journals indexed on at least one of six selected databases in the last 10 years (01 January 2012–24 March 2022).

We will not restrict the protocols to a specific population or outcome. We will consider the self-identification of a study as an RCT as an inclusion criterion. We will consider as nutritional interventions of interest the following: (a) diets and dietary patterns; (b) formulated, fortified and enriched foods; (c) dietary products, including dietary supplements; (d) nutrients and bioactive non-nutrients naturally in foods (eg, cinnamon); and (e) nutritional education, promotion, counselling and programmes. Studies evaluating nutritional interventions combined with others (such as exercise or drugs) or as part of a lifestyle intervention will also be included. We will exclude protocols of RCTs that only assess pharmaceutical or herbal medicines. Protocols of non-RCTs and protocols not published in journals indexed on at least one of six selected databases will be excluded. We will also exclude protocols if the terms related to the nutrition interventions of interest are not described in the title or abstract.

Information source and search strategy
To identify protocols of diet or nutrition-related RCTs published as scientific articles in indexed journals, we used the search strategy developed by Durão et al, removing the term “nutrition policy” as this is not commonly investigated in RCTs and therefore not one of our nutrition interventions of interest. The Durão et al strategy was developed to identify diet and nutrition trials in PubMed and presented a high relative recall (88.6%). We combined this strategy with a modified version of the search strategy developed by Madden et
We conducted the search for PubMed (via the National Library of Medicine). We then adapted it to Embase (via Elsevier), CINAHL (via EBSCO), Web of Science (via Clarivate), PsycINFO (via Ovid) and Global Health Database (via Ovid). We have enlisted the assistance of a professional health sciences information specialist to help develop these search strategies. The complete search strategies for all databases, which were run on 24 March 2022, are presented in online supplemental appendix 1. In all databases, we limited the date of publication to between 2012 and 2022 (up to 24 March).

Selection of eligible reports

We will use EndNote as the reference management software to assist in data management. After the literature search, we will remove duplicates by first using EndNote’s automated deduplication and then manually removing the remaining duplicates. Two reviewers will independently determine the eligibility of each report in a two-stage process in Rayyan. They will screen titles and abstracts and select publications self-identified as protocols of diet or nutrition-related RCTs. They will then read the full texts to confirm eligibility based on the predefined inclusion criteria described above. Disagreements between reviewers will be resolved by a consensus and, if necessary, a third reviewer will be consulted. A flow chart will illustrate each search step and present the number of included and excluded articles.

Data collection

For all eligible protocols, we will extract information about specific protocol characteristics that may describe this field, such as PMID (a unique identifier used in the PubMed database), first author’s name, publication year, journal in which it was published, journal field according to Web of Science, funding source, whether the protocol was registered, and, if it was, the registry, date, and number. We will also extract information about the types of participants, interventions, comparators, outcomes and study designs that the protocols address. Table 1 describes these data, which are adapted from Naude et al. We will collect the clinical condition of the participants and explore if the study population involved patients with cancer or cardiovascular disease, as these are now leading causes of premature death in several countries. We also explored if the population was composed of patients with chronic or acute illness. The draft extraction form is shown in online supplemental appendix 2.

Table 1  PICOS categories in diet and nutrition-related RCT protocols

<table>
<thead>
<tr>
<th>Data domain</th>
<th>Categories used for data extraction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Participants</td>
<td>Pregnant women, Mother and infant pairs, Infants, Children and preschool-aged children, Adults, The elderly, Adults and the elderly, Postmenopausal women, Participants with a clinical condition (collect condition)</td>
</tr>
<tr>
<td>Interventions</td>
<td>Food (whole food, food products, specially formulated foods), Breast feeding, complementary feeding, weaning Complete diet or dietary pattern, Complete nutrition formulas (enteral or parenteral), Supplementation, or supplements, or fortification (single or multiple nutrients, bioactive non-nutrients, plant components), Nutrition education, counselling and coordination of care, Other</td>
</tr>
<tr>
<td>Comparator</td>
<td>Placebo, No intervention, Usual care, Different intervention, Other</td>
</tr>
<tr>
<td>Outcomes</td>
<td>Mortality, Clinical status (clinical or biochemical measures), Nutritional status (anthropometry, body composition, nutrition diagnosis), Frequency or severity of disease, Diet quality and/or variety, Food/nutrient/dietary intake, Diet-related behaviours, Other non-dietary behaviours, Withdrawal from the study, drop-out or adherence related, Adverse events, side-effects and/or safety, Cost-effectiveness or economic Quality of life, Other</td>
</tr>
<tr>
<td>Study design</td>
<td>Parallel RCT, Crossover RCT, Cluster RCT, Multicentre RCT, Single-centre RCT</td>
</tr>
</tbody>
</table>

“*Our adaptations of the Naude et al. PICOS categories: to the participant categories, we added the category ‘adults and the elderly’ and expanded the category ‘participants with a clinical condition’ to also capture the clinical condition. To the intervention categories, we added ‘complete diet or dietary pattern’ and ‘enteral or parenteral complete nutritional formulas’ and removed ‘nutrition-related policies’. From the study design categories, we removed ‘observational and experimental randomised-studies’ and included ‘cluster RCT’, ‘RCT’, randomised controlled trial.”

From the list of eligible protocols, we will select a random sample with size corresponding to the lesser of 20% or 200 to assess reporting completeness and identify the main reporting limitations in these publications. We will split the list of selected protocols according to their publication date, and select half of our random sample in a methodological systematic review of published surgical randomised trial protocols. We removed the term “Methods paper”. We included the Medical Subject Headings publication type “Clinical Trial Protocols” introduced in 2019 and free terms used to index up-to-date protocols, such as “design and methods” and “design and rationale”. As the search strategy developed by Durão et al incorporates terms to identify RCTs, we did not use any additional filter related to them.
sample from those published in 2019, and the other half from those published in 2021, considering the start of COVID-19 pandemic in 2020. These protocols will be selected based on the proportion of each category of nutrition or diet interventions described by Naube et al identified in all eligible protocols published between 2012 and 2022. Selecting a random sample of the most recently published protocols is justified by our aim to identify the current major reporting completeness limitations, rather than to explore trends over time.

We will exclude protocols for pilot or feasibility trials in this subsample: as these aim to assess the feasibility of conducting a definitive efficacy or effectiveness intervention trial, they do not assess efficacy or effectiveness per se.23

We have developed a draft data extraction form based on the items in SPIRIT14 and TIDieR,17 separating each item into discrete subitems for ease of extraction. We have excluded TIDieR items 10 and 12, as they are not applicable to reporting protocols of intervention RCTs. The draft form is presented in online supplemental appendix 3. We will evaluate whether each subitem is reported in the protocol, classifying the reporting as fully reported, partially reported, not reported or not applicable.

We will pilot test both data extraction forms in five randomly selected full texts before full data extraction to refine the form and ensure all reviewers extract data consistently, avoiding ambiguity and errors. Two reviewers will independently extract data from each report. If there is any disagreement, they will discuss to reach a consensus and, if necessary, consult a third reviewer. All relevant information will be entered directly into the study database using REDCap.24

**Summary and reporting results**

We will calculate descriptive statistics of the data extracted from the included diet and nutrition-related RCT protocols published in the last decade and present the results in diagrams and tables. Considering that we will include protocols of RCTs published before SPIRIT and TIDieR publications, a stratified analysis will be performed by base.

For the randomly selected subsample of included protocols, each item’s reporting completeness will be classified as adherent (all subitems fully reported or not applicable) or non-adherent (any subitem not reported or incompletely reported). The proportion of items adherent to will be calculated for each protocol, considering the sum of all items in the SPIRIT14 and TIDieR17 checklists, to give a final reporting completeness score. We will present the proportion of protocols that adhere to each item of SPIRIT14 and TIDieR17 and the distribution of the protocols’ reporting completeness scores. We will compare general features between protocols with above-average and below-average reporting scores, stratified by the mean or median value (depending on the distribution). Appropriate statistical tests will be performed in R software. The Student’s t-test and X² test will be used to compare quantitative and categorical variables between groups, respectively. Logistic regression models will also be constructed to define determinants of completeness reporting.

The results obtained from these analyses will provide an overview of the contemporary research landscape of nutritional and diet-related RCTs. The data gathered in this meta-research will allow the identification of major reporting limitations in protocols of nutrition or diet-related RCTs. The data will also be used to explore study features potentially associated with incomplete reporting.

**Author affiliations**

1Nutrition Department, UFCSPA, Porto Alegre, Brazil
2Centre for Healthcare Research, Coventry University, Coventry, UK
3Centre for Agroecology, Water and Resilience, Coventry University, Coventry, UK
4Nutrition Institute, UERJ, Rio de Janeiro, Rio de Janeiro, Brazil
5Pan American Health Organization, Washington, District of Columbia, USA
6UK EQUATOR Centre, Centre for Statistics in Medicine, Nuffield Department of Orthopaedics Reuamathology and Musculoskeletal Sciences, University of Oxford, Oxford, UK
7Josué de Castro Nutrition Institute, UFRJ, Rio de Janeiro, Rio de Janeiro, Brazil
8Oxford Clinical Trials Research Unit, Nuffield Department of Orthopaedics Rheumatology and Musculoskeletal Sciences, Oxford University, Oxford, UK
9Department of Clinical Nutrition and Dietetics, College of Health Sciences, University of Sharjah, Sharjah, UAE
10Nuffield Department of Women’s & Reproductive Health, University of Oxford, Oxford, UK
11School of Public Health and Preventive Medicine, Monash University, Clayton, Victoria, Australia
12Centre for Epidemiological Research in Nutrition and Health, Department of Nutrition, School of Public Health, USP, Sao Paulo, Brazil
13College of Medicine and Health, University of Exeter, Exeter, UK
14Cochrane South Africa, South African Medical Research Council, Cape Town, South Africa
15Department of Applied Health Science, Indiana University School of Public Health - Bloomington, Bloomington, Indiana, USA

**Funding**

The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

**Competing interests**

FMS received a postdoctoral fellowship from COPPETEC Foundation. MS, SK, SH, GK, JAC, SL, ARAA, CVJ and FS6 jointly conceived the idea of this project. FMS, MS, SK, SD, CC, ARAA, MJP, LCI, CVJ and GK contributed to the study design and development of research questions. FMS and SK constructed the search strategy for all databases and ran them. FMS, MS and GSC constructed the data extraction form. FMS and MS led the writing of the manuscript. All authors provided detailed comments on earlier drafts and approved this final version.

**Patient consent for publication**

Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

**Patient consent for publication**

Not required.

**Provenance and peer review**

Not commissioned; externally peer reviewed.

**Supplemental material**

This content has been supplied by the author(s). It has not been vetted by BMJ Publishing Group Limited (BMJ) and may not have been peer-reviewed. Any opinions or recommendations discussed are solely those of the author(s) and are not endorsed by BMJ. BMJ disclaims all liability and
REFERENCES
Online Supplementary Appendix 1

The search strategies for each database were run on 24th March 2022.

PubMed


#1

#2
#3

#4
#1 AND #2 AND #3

#4 Filters applied: From 2012/1/1 to 2022/3/24.

**Embase**

Database and platform: Embase 1947 to present (via Elsevier)
Search filter: SIGN RCT filter
https://www.sign.ac.uk/what-we-do/methodology/search-filters/

#7

#6
#1 AND #4 AND #5

#5
"Methodology"/de OR "Clinical Protocol"/exp OR protocol:ti OR 'study design':ti OR "design and methods":ti OR "design and rationale":ti OR "rationale and design":ti

#4
#2 NOT #3

#3
'case study'/de OR 'case report':ab,ti OR 'abstract report'/de OR 'conference paper':it OR 'conference abstract':it OR editorial:it OR letter:it OR note:it

#2
'clinical trial'/de OR 'randomized controlled trial'/de OR 'controlled clinical trial'/de OR 'multicenter study'/de OR phase 3 clinical trial'/de OR 'phase 4 clinical trial'/de OR randomization/exp OR 'single blind procedure'/de OR 'double blind procedure'/de OR 'crossover procedure'/de OR placebo/de OR 'randomized controlled trial*:ab,ti OR rct:ab,ti OR 'random* NEAR/2 allocat*':ab,ti OR 'single blind*':ab,ti OR 'double blind*':ab,ti OR ((treble:ab,ti OR triple:ab,ti) NEAR blind*:ab,ti) OR placebo*:ab,ti OR 'prospective study'/de

#1
'Nutritional Science'/exp OR 'nutritional science':kw OR 'nutritional physiological phenomena':ab,ti OR 'Nutrition'/exp OR 'nutritional assessment':kw OR 'nutritional support':kw OR 'diet therapy':kw OR 'Diet Therapy'/exp OR (nutritional:kw AND 'metabolic disorder':kw) OR 'Nutritional Disorder'/exp OR 'Metabolic Disorder'/exp OR nutrition:ab,ti OR diet:ab,ti OR feeding:ab,ti OR 'Food'/exp OR 'dietary intake':ab,ti OR 'Diet Restriction'/exp OR breastfeeding:ab,ti OR lactation:ab,ti OR 'bottle feeding':ab,ti OR 'complementary feeding':ab,ti OR weaning:ab,ti OR 'enteric feeding':ab,ti OR parenteral:ab,ti OR 'food intake':ab,ti OR 'nutritional status':ab,ti OR 'Failure to Thrive':de OR
Web of Science

Database and platform: Web of Science (All databases) 1945 to present (via Clarivate)

Search filter: Cochrane ENT group RCT filter

"overnourished") OR TS =("wasted") OR TS =("wasting") OR TS =("underweight") OR TS =("undernutrition") OR TS =("body weight") OR TS =("anthropometry") OR AK =("body weights and measures") OR TS =("growth monitoring") OR TS =("food") OR AK =("food labeling") OR AK =("food assistance") OR TS =("supplementary feeding") OR AK =("diet therapy") OR AK =("food and beverages") OR TS =("vegetable") OR TS =("fruit") OR TS =("meat") OR TS =("dairy") OR TS =("dietary fat") OR AB =("starch") OR TS =("cereal") OR AK =("food drug interactions") OR AK =("food supply") OR TS =("feeding behavio") OR TS =("eating behavio") OR TS =("food pattern") OR TS =("food hypersensitivity") OR TS =("food deprivation") OR TS =("food, organic") OR TS =("micronutrient") OR TS =("vitamin") OR TS =("thiamin") OR TS =("riboflavin") OR TS =("niacin") OR TS =("pantothenic acid") OR TS =("pyridoxine") OR TS =("pyridoxal") OR TS =("pyridoxamine") OR TS =("biotin") OR TS =("folic acid") OR TS =("folate") OR TS =("cyanocobalamin") OR TS =("choline") OR TS =("retinol") OR TS =("ascorbic acid") OR TS =("tocopherol") OR TS =("carotenoids") OR TS =("carotene") OR TS =("cryptoxanthin") OR TS =("lutein") OR TS =("lycopene") OR TS =("zeaxanthin") OR TS =("magnesium") OR TS =("calcium") OR TS =("chelation") OR TS =("phosphorus") OR TS =("potassium") OR TS =("sodium") OR TS =("sulphur") OR TS =("trace element") OR TS =("boron") OR TS =("cobalt") OR TS =("chromium") OR TS =("copper") OR TS =("fluoride") OR TS =("iodine") OR TS =("iron") OR TS =("manganese") OR TS =("molybdenum") OR TS =("selenium") OR TS =("zinc") OR TS =("trace metal") OR TS =("magnesium") OR TS =("saturated fat") OR TS =("unsaturated fat") OR TS =("polyunsaturated fat") OR TS =("mono unsaturated fat") OR TS =("saturated fat") OR TS =("unsaturated fat") OR TS =("polyunsaturated fat") OR TS =("trans fat") OR TS =("dietary fibre") OR TS =("dietary fiber") OR TS =("dietary salt") OR TS =("soft drink") OR TS =("fruit juice") OR TS =("vegetable juice") OR TS =("milk") OR TS =("tea") OR TS =("coffee") OR TS =("energy drink") OR TS =("carbonated drink") OR TS =("probiotics") OR TS =("gum") OR TS =("soda") OR TS =("calories") OR TS =("kilocalories") OR TS =("kilojoules") OR TS =("energy intake")

#4
#1 AND #2 AND #3

#5
#4 Timespan: 2012-01-01 to 2022-03-24 (Publication Date)

CINAHL

Database and platform: CINAHL with full text 1981 to present (via EBSCOHost)
Search filter: SIGN CINAHL for EBSCO RCT Filter (created by Mark Clowes)
https://www.sign.ac.uk/assets/search-filters-randomised-controlled-trials.docx

S1
(MH "Research Protocols") OR (MH "Research Methodology") OR (MH "Study Design") OR PT Protocol OR TI (protocol) OR "study design" OR "trial design" OR "research design" OR "design and methods" OR "design and rationale" OR "rationale and design")

S2
(MH "Nutrition") OR (MH "Nutritional Physiology") OR (MH "Nutritional Assessment") OR (MH "Diet Therapy") OR (MH "Nutritional and Metabolic Diseases") OR (MH "Feeding Methods") OR (MH "Diet") OR TI (nutrition* OR diet OR feeding OR dietary OR breastfeed* OR "breast feed*")
OR lactation OR "bottle feed*** OR "complementary feeding OR weaning OR enteral OR parenteral"
OR AB (nutrition* OR diet OR feeding OR dietary OR breastfeed* OR "breast feed*** OR lactation
OR "bottle feed*** OR "complementary feeding OR weaning OR enteral OR parenteral) ) OR ( TI
("nutritional status" OR overweight OR obese OR obesity OR overnutrition OR "over nutrition"
OR undernourished OR overnourished OR wasted OR wasting OR stunting OR stunted OR underweight
OR undernutrition OR "under nutrition" OR "body weight" OR anthropometry) ) OR AB ("nutritional
status" OR overweight OR obese OR obesity OR overnutrition OR "over nutrition"
OR undernourished OR overnourished OR wasted OR wasting OR stunting OR stunted OR underweight
OR undernutrition OR "under nutrition" OR "body weight" OR anthropometry ) OR ( MH "Body Weights
and Measures") OR (MH "Anthropometry") OR (MH "Body Weight") OR (MH "Food Labeling") OR (MH
"Food Assistance") OR (MH "Food and Beverages") ) OR ( TI ("growth monitoring" OR food OR
"supplementary feeding" OR vegetable* OR fruit* OR meat OR dairy OR "dietary fat*** OR starch*
OR cereal) OR AB ("growth monitoring" OR food OR "supplementary feeding" OR vegetable* OR fruit*
OR meat OR dairy OR "dietary fat*** OR starch* OR cereal) ) OR ( MH "Drug-Food
Interactions") OR (MH "Food Supply") OR (MH "Organic Food") OR (MH "Food Hypersensitivity") )
OR ( TI ("feeding behavio*" OR "eating behavio*" OR "food pattern*** OR micronutrient** OR vitamin* OR thiamin OR riboflavin OR niacin OR "pantothenic acid" OR pyridoxine OR pyridoxal
OR pyridoxamine OR biotin OR "folic acid" OR folate OR cyanocobalamin OR choline OR retinol OR
"ascorbic acid" OR tocopherol OR carotenoids OR carotene OR cryptoxanthin) OR AB ("feeding
behavio*" OR "eating behavio*" OR "food pattern*** OR micronutrient** OR vitamin* OR thiamin OR
riboflavin OR niacin OR "pantothenic acid" OR pyridoxine OR pyridoxal OR pyridoxamine OR biotin
OR "folic acid" OR folate OR cyanocobalamin OR choline OR retinol OR "ascorbic acid" OR tocopherol OR carotenoids OR carotene OR cryptoxanthin) ) OR ( TI (lutein OR lycopene OR zeaxanthin OR minerals OR calcium OR chloride OR magnesium OR phosphorus OR potassium OR sodium OR sulphur OR "trace element*** OR boron OR cobalt OR chromium OR copper OR fluoride
OR iodine OR iron OR manganese OR molybdenum OR selenium OR zinc OR "trace metal*** OR
macronutrient*** OR carbohydrate* OR "dietary protein**") ) OR AB (lutein OR lycopene OR zeaxanthin
OR minerals OR calcium OR chloride OR magnesium OR phosphorus OR potassium OR sodium OR
sulphur OR "trace element*** OR boron OR cobalt OR chromium OR copper OR fluoride OR iodine
OR iron OR manganese OR molybdenum OR selenium OR zinc OR "trace metal*** OR macronutrient*** OR carbohydrate* OR "dietary protein**") OR ( TI ("saturated fat*** OR "unsaturated fat*** OR "mono
unsaturated fat*** OR "monounsaturated fat*** OR "poly unsaturated fat*** OR "polyunsaturated fat***
OR "trans fat*** OR "dietary fibre*** OR "dietary salt*** OR "table salt*** OR "soft drink*** OR "fruit juice*** OR "vegetable juice") OR AB ("saturated fat*** OR "unsaturated fat*** OR "mono
unsaturated fat*** OR "monounsaturated fat*** OR "poly unsaturated fat*** OR "polyunsaturated fat***
OR "trans fat*** OR "dietary fibre*** OR "dietary salt*** OR "table salt*** OR "soft drink*** OR "fruit juice*** OR "vegetable juice") ) OR ( TI (milk OR tea OR coffee OR "energy drink*** OR "carbonated beverage*** OR "carbonated drink*** OR prebiotics OR probiotics OR "glycemic load*** OR "glycemic index*** OR calories OR kilocalories OR kilojoules OR "caloric intake*** OR "energy intake") OR AB (milk OR tea OR coffee OR "energy drink*** OR "carbonated beverage*** OR "carbonated drink*** OR prebiotics OR probiotics OR "glycemic load*** OR "glycemic index*** OR calories OR kilocalories OR kilojoules OR "caloric intake*** OR "energy intake") )

S3
TX allocat* random* OR (MH "Quantitative Studies") OR (MH "Placebos") OR TX placebo* OR TX
random* allocat* OR (MH "Random Assignment") OR TX randomi* control* trial* OR (TX ((singl*
n1 blind*) OR (singl* n1 mask*)) OR TX ((double* n1 blind*) OR (double* n1 mask*)) OR TX ((tripl*
n1 blind*) OR (tripl* n1 mask*)) OR TX ((trebl* n1 blind*) OR (trebl* n1 mask*)) ) OR TX clinic* n1
trial* OR PT Clinical trial OR (MH "Clinical Trials**")

S4
S1 AND S2 AND S3
Global Health

Database and platform: Global Health 1973 to 2022 Week 12 (via OVID)


1. (protocol$ OR "study design$" OR "trial design$" OR "research design$" OR "design and methods" OR "design and rationale" OR "rationale and design").ti.

2. Methodology/ OR Experimental Design/

3. 1 OR 2

4. exp Nutrition/ OR exp Nutrition Research/ OR exp Human Feeding/ OR Diets/ OR Diet/

5. Nutrition Physiology/ OR Nutritional Assessment/ OR Nutritional Disorders/ OR Nutritional Intervention/

6. (nutrition$ OR diet OR feeding OR dietary OR breastfeed$ OR "breast feed$" OR lactation OR "bottle feed$" OR "complementary feeding" OR weaning OR enteral OR parenteral).ti,ab.

7. ("nutritional status" OR overweight OR obese OR obesity OR overnutrition OR "over nutrition" OR undernourished OR overnourished OR wasted OR wasting OR stunting OR stunted OR underweight OR undernutrition OR "under nutrition" OR "body weight" OR anthropometry).ti,ab.

8. Body Weight/ OR Nutrition Labelling/ OR Diet Treatment/ OR Food Supply/ OR Nutrient Drug Interactions/ OR Food Deprivation/

9. exp Body Measurements/ OR exp Foods/ OR exp Therapeutic Diets/ OR exp Food Allergies/

10. ("growth monitoring" OR food OR "food assistance" OR "supplementary feeding" OR vegetable$ OR fruit$ OR meat$ OR dairy$ OR "dietary fat$" OR starch$ OR cereal OR "feeding behavio$" OR "eating behavio$" OR "food pattern$" OR "food group$" OR "food category$"").ti,ab.

11. ("food hypersensitivit$" OR "organic food" OR micronutrient$ OR vitamin$ OR thiam$ OR riboflavin OR niacin OR "pantothenic acid" OR pyridoxine OR pyridoxal OR pyridoxamine OR biotin OR "folic acid" OR folate OR cyanocobalamin OR choline OR retinol OR "ascorbic acid" OR tocopherol OR carotenoids OR carotene OR cryptoxanthin OR lutein OR lycopene OR zeaxanthin OR minerals OR calcium OR chloride OR magnesium OR phosphorus OR potassium OR sodium OR sulphur OR "trace element$" OR boron OR cobalt OR chromium OR copper OR fluoride OR iodine OR iron OR manganese OR molybdenum OR selenium OR zinc OR "trace metal$"").ti,ab.

12. (macronutrient$ OR carbohydrate$ OR "dietary protein$" OR "saturated fat$" OR "unsaturated fat$" OR "mono unsaturated fat$" OR "monounsaturated fat$" OR "poly unsaturated fat$" OR "polyunsaturated fat$" OR "saturated fatty acid$" OR "unsaturated fatty acid$"").ti,ab.
"polyunsaturated fat" OR "trans fat" OR "dietary fibre" OR "dietary fiber" OR "dietary salt" OR "table salt" OR "soft drink" OR "fruit juice" OR "vegetable juice" OR milk OR tea OR coffee OR "energy drink" OR "carbonated beverages" OR "carbonated drink" OR prebiotics OR probiotics OR "glycemic load" OR "glycemic index" OR calories OR kilocalories OR kilojoules OR "caloric intake" OR "energy intake".ti,ab.

13. 4 OR 5 OR 6 OR 7 OR 8 OR 9 OR 10 OR 11 OR 12

14. Randomized controlled trials/ OR Clinical Trials/ OR Placebos/

15. (randomized OR randomised OR randomly OR placebo OR trial$).ti,ab.

16. 14 OR 15

17. 3 AND 13 AND 16

18. Limit 17 to yr="2012-2022"

PsycINFO

Database and platform: PsycINFO 1806 to present (via OVID)

Search filter: Cochrane ENT Group RCT search filter for PsycINFO (OVID)


1. (protocol$ OR "study design" OR "trial design" OR "research design" OR "design and methods" OR "design and rationale" OR "rationale and design").ti.

2. ("Research Design" OR "clinical protocols").mh.

3. Methodology/

4. Experimental Design/

5. 1 OR 2 OR 3 OR 4

6. ("Nutritional Sciences" OR "Nutritional Physiological Phenomena" OR "Nutrition Assessment" OR "Nutrition Therapy" OR "Nutritional and Metabolic Diseases" OR "Feeding Methods" OR "Body Weights and Measures" OR "Food Labelling" OR "Food Assistance" OR "Diet Therapy" OR "Food and Beverages" OR "Food-drug Interactions" OR "Food Supply" OR "Food Hypersensitivity" OR "Food Deprivation" OR "Food, Organic").mh.

7. exp Nutrition/ OR exp "Nutritional Deficiencies"/ OR exp "Metabolism Disorders"/ OR exp Diets/ OR exp Food/

8. "Eating Behavior"/ OR "Failure to Thrive"/ OR "Body Weight"/ OR "Beverages (Nonalcoholic)"/ OR "Food Insecurity"/ OR "Food Allergies"/ OR "Food Deprivation"/ OR "Food Intake"/ OR "Dietary Supplements"/ OR "Dietary Restraint"/ OR "Food Preferences"/

9. (nutrition$ OR diet OR feeding OR dietary OR breastfeed$ OR "breast feed" OR lactation OR "bottle feed" OR "complementary feeding" OR weaning OR enteral OR parenteral OR "nutritional status" OR overweight OR obese OR obesity OR overnutrition OR "over nutrition" OR undernourished
OR overnourished OR wasted OR wasting OR stunting OR stunted OR underweight OR undernutrition 
OR "under nutrition" OR "body weight" OR anthropometry).ti,ab.

10. ("growth monitoring" OR food OR "supplementary feeding" OR vegetable$ OR fruit$ OR meat 
OR dairy OR "dietary fat" OR starch OR cereal OR "feeding behavio" OR "eating behavio" OR 
"food pattern") OR micronutrient$.ti,ab.

11. (vitamin$ OR thiamin OR riboflavin OR niacin OR pantothenic acid OR pyridoxine OR pyridoxal 
OR pyridoxamine OR biotin OR folic acid OR folate OR cyanocobalamin OR choline OR retinol OR 
ascorbic acid OR tocopherol OR carotenoids OR carotene OR cryptoxanthin OR lutein OR lycopene 
OR zeaxanthin OR minerals OR calcium OR chloride OR magnesium OR phosphorus OR potassium 
OR sodium OR sulphur OR "trace element" OR boron OR cobalt OR chromium OR copper OR 
fluoride OR iodine OR iron OR manganese OR molybdenum OR selenium OR zinc OR "trace 
metal").ti,ab.

12. (macronutrient$ OR carbohydrate$ OR "dietary protein" OR "saturated fat" OR "unsaturated 
fat" OR "mono unsaturated fat" OR "monounsaturated fat" OR "poly unsaturated fat" OR 
"polyunsaturated fat" OR "trans fat" OR "dietary fibre" OR "dietary fiber" OR "dietary salt" OR 
"table salt").ti,ab.

13. ("soft drink" OR "fruit juice" OR "vegetable juice" OR milk OR tea OR coffee OR "energy drink" 
OR "carbonated beverage" OR "carbonated drink" OR prebiotics OR probiotics OR "glycemic load" 
OR "glycemic index" OR calories OR kilocalories OR kilojoules OR "caloric intake" OR "energy 
intake").ti,ab.

14. 6 OR 7 OR 8 OR 9 OR 10 OR 11 OR 12 OR 13

15. Placebo/

16. ((blind* or mask*) and (single or double or triple or treble)).tw.

17. (randomised or randomized or randomisation or (random* and (allocat* or 
assign*)) or factorial* or placebo* or crossover* or (cross adj over*)).tw.

18. 15 or 16 or 17

19. 5 AND 14 AND 18

20. limit 19 to yr="2012-2022"
Online Supplementary Appendix 2:
Standardised data extraction form for protocols of diet or nutrition-related RCTs published as scientific articles in peer-reviewed journals in the last decade (2012-2022)

1. Study ID: ______
2. First author: ______________________
3. Publication Year: ______________________
4. Journal: __________________
5. PMID/ DOI: ________________________________
6. PICOS:
7.1. Participants:
7.1.1. Group of participants:
( ) Pregnant women ( ) Mother and infant pairs
( ) Infants ( ) Children and preschool-aged children
( ) Adults ( ) Elderly
( ) Adults and elderly ( ) Postmenopausal women
7.1.2. Participants with a clinical condition (s):
( ) Yes - specify: ________ ( ) No
7.1.3. Participants with cancer?
( ) Yes ( ) No
7.1.4 Participants with CVD?
( ) Yes ( ) No
7.2. Intervention:
7.2.1. Complexity:
( ) Only nutrition or diet-related intervention
( ) Nutrition or diet-related intervention combined to exercise
( ) Nutrition or diet-related intervention combined to drugs
( ) Nutrition or diet-related intervention as part of a lifestyle intervention
7.2.2. Category of nutrition or diet-intervention:
( ) Food (whole food, food products, specially formulated foods)
( ) Breastfeeding, complementary feeding, weaning
( ) Complete diet or dietary patterns
( ) Complete nutrition formulas (enteral or parenteral)
( ) Supplementation or supplements (single or multiple nutrients, bioactive non-nutrients, plant components)
( ) Nutrition education, counselling and coordination of care
( ) Other, if no component of intervention could be categorised as any of the above (specify

BMJ Publishing Group Limited (BMJ) disclaims all liability and responsibility arising from any reliance placed on this supplemental material which has been supplied by the author(s)
7.3. Comparator:
( ) Placebo
( ) Usual care
( ) Other intervention
( ) No intervention

7.4. Outcomes:
7.4.1 Primary outcome:
( ) Not specified
( ) Specified
7.4.2. Primary evaluated outcomes:
( ) Mortality
( ) Clinical status (clinical or biochemical measures)
( ) Nutritional status (anthropometry, body composition, nutrition diagnosis)
( ) Frequency or severity of disease
( ) Diet quality and/or variety
( ) Food/nutrient/dietary intake
( ) Diet-related behaviours
( ) Other non-dietary behaviours
( ) Withdrawal from the study, drop-out or adherence-related
( ) Adverse events, side-effects and/or safety
( ) Cost-effectiveness or economic
( ) Quality of life
( ) Other (specify it)______

7.5. Study design:
7.5.1. Study design_1:
( ) parallel RCT  ( ) crossover RCT
7.5.2. Study design_2:
( ) factorial RCT  ( ) non-factorial RCT
7.5.3. Study design_2
( ) cluster RCT  ( ) non-cluster RCT
7.5.4. Study design_2:
( ) unicentric  ( ) multicentric

8. Registered protocol:
( ) Yes  ( ) No

9. Reference to SPIRIT:
( ) Yes  ( ) No
Online Supplementary Appendix 3:
Standardised data extraction form to assess the reporting completeness of a subsample of protocols of diet or nutrition-related RCTs published in peer-reviewed journals in the last decade (2012-2022).

<table>
<thead>
<tr>
<th>Item</th>
<th>Description</th>
<th>Reported</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><strong>Administrative Information</strong></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>Spirit_1</td>
<td>Title - Is the study design described in the title?</td>
</tr>
<tr>
<td>2</td>
<td>Spirit_2</td>
<td>Title - Is the study population described in the title?</td>
</tr>
<tr>
<td>3</td>
<td>Spirit_3</td>
<td>Title - Is (are) the study intervention(s) described in the title?</td>
</tr>
<tr>
<td>4</td>
<td>Spirit_4</td>
<td>Title - Is the trial acronym (if applicable, check for a study acronym also in the text) described in the title?</td>
</tr>
<tr>
<td>5</td>
<td>Spirit_5</td>
<td>Trial registration – Is the trial identifier provided?</td>
</tr>
<tr>
<td>6</td>
<td>Spirit_6</td>
<td>Trial registration – Is the trial registry name or, if not yet registered, name of intended registry provided?</td>
</tr>
<tr>
<td>7</td>
<td>Spirit_7</td>
<td>Protocol version – Are the date and version of the protocol provided?</td>
</tr>
<tr>
<td>8</td>
<td>Spirit_8</td>
<td>Funding – Are the sources of support provided?</td>
</tr>
<tr>
<td>No.</td>
<td>Spirit_4</td>
<td>Funding - Are the types of support (e.g., financial, material, or other) provided? (N/A if explicitly stated that the study isn’t funded)</td>
</tr>
<tr>
<td>-----</td>
<td>----------</td>
<td>----------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>10</td>
<td>Spirit_5a</td>
<td>Roles and responsibilities - Affiliations of protocol contributors (for all paper authors)</td>
</tr>
<tr>
<td>11</td>
<td>Spirit_5a</td>
<td>Roles and responsibilities - Roles of protocol contributors (for all paper authors)</td>
</tr>
<tr>
<td>12</td>
<td>Spirit_5b</td>
<td>Roles and responsibilities - Name of the trial sponsor. Contact information for the trial sponsor.</td>
</tr>
<tr>
<td>13</td>
<td>Spirit_5c</td>
<td>Roles and responsibilities - Role of study sponsor, if any, in study design, collection, management, analysis, and interpretation of data, writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities? ('Yes' if any mention of sponsor roles or a clear statement of no participation)</td>
</tr>
<tr>
<td>15</td>
<td>Spirit_5c</td>
<td>Roles and responsibilities - Role of study funders, if any, in study design, collection, management, analysis, and interpretation of data, writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities? ('Yes' if any mention of funder roles or a clear statement of no participation)</td>
</tr>
<tr>
<td>16</td>
<td>Spirit_5d*</td>
<td>Composition of the coordinating center, steering committee, endpoint adjudication committee, data management team, and any other relevant groups overseeing the trial, if applicable (do not consider data monitoring committee for this question)</td>
</tr>
<tr>
<td>17</td>
<td>Spirit_5d*</td>
<td>Roles and responsibilities of the coordinating center, steering committee, endpoint adjudication committee, data management team, and any other individuals or groups overseeing the trial, if applicable (do not consider data monitoring committee for this question)</td>
</tr>
</tbody>
</table>

Introduction

BMJ Publishing Group Limited (BMJ) disclaims all liability and responsibility arising from any reliance placed on this supplemental material which has been supplied by the author(s).
<table>
<thead>
<tr>
<th>Page</th>
<th>Spirit</th>
<th>Section</th>
<th>Description of the content</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>18</td>
<td>Spirit_6a</td>
<td>Background and rationale</td>
<td>Description of research question</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>19</td>
<td>Spirit_6a</td>
<td>Background and rationale</td>
<td>Justification for undertaking the trial</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>20</td>
<td>Spirit_6a</td>
<td>Background and rationale</td>
<td>Summary of relevant studies (published and unpublished) examining benefits and harms for each intervention</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>21</td>
<td>Spirit_6b</td>
<td>Background and rationale</td>
<td>Explanation for choice of comparators</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>22</td>
<td>Spirit_7</td>
<td>Objectives</td>
<td>Specific objectives</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>23</td>
<td>Spirit_7</td>
<td>Objectives</td>
<td>Specific hypotheses</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>24</td>
<td>Spirit_8</td>
<td>Trial design</td>
<td>Description of trial design, including type of trial (e.g., parallel group, crossover, factorial, single group)</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>25</td>
<td>Spirit_8</td>
<td>Trial design</td>
<td>Description of trial design, including allocation ratio (e.g., 1:1 or 2:1, in two-amus parallel trials)</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>26</td>
<td>Spirit_8</td>
<td>Trial design</td>
<td>Description of trial design, including framework (e.g., superiority, equivalence, non-inferiority, exploratory)</td>
<td>No</td>
<td>Yes</td>
</tr>
</tbody>
</table>

Methods: Participants, interventions, and outcomes
<p>| | | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>27</td>
<td>Spirit_9</td>
<td>Study setting – Environment: Detailed description of study settings (e.g., community clinic, academic hospital)</td>
<td>[ ] No [ ] Yes</td>
</tr>
<tr>
<td>28</td>
<td>Spirit_9</td>
<td>Study setting - Location: List of study centres and countries where data will be collected.</td>
<td>[ ] No [ ] Yes</td>
</tr>
<tr>
<td>29</td>
<td>Spirit_10</td>
<td>Eligibility criteria - Inclusion and exclusion criteria for participants. If cluster trial, eligibility criteria for study centres should be provided</td>
<td>[ ] No [ ] Yes</td>
</tr>
<tr>
<td>Spirit_11a</td>
<td>Covered by the items of TIDieR 1-9, as outlined below.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>30</td>
<td>TIDieR_1</td>
<td>Interventions description: Provide the name or a phrase that describes the intervention</td>
<td>[ ] No [ ] Yes</td>
</tr>
<tr>
<td>31</td>
<td>TIDieR_2</td>
<td>Interventions rationale: Describe any rationale, theory, or goal of the elements essential to the intervention</td>
<td>[ ] No [ ] Yes</td>
</tr>
<tr>
<td>32</td>
<td>TIDieR_3</td>
<td>Intervention materials: Describe any physical or informational materials used in the intervention, including those provided to participants or used in intervention delivery or in training of intervention providers. Provide information on where the materials can be accessed (e.g. online appendix, URL). (‘Yes’ if all criteria fulfilled; ‘Partially’ if where the materials can be accessed is not described; ‘No’ if no information on materials is provided.)</td>
<td>[ ] No [ ] Partially [ ] Yes</td>
</tr>
<tr>
<td>33</td>
<td>TIDieR_4</td>
<td>Interventions procedures: Describe each of the procedures, activities, and/or processes will be used in the intervention, including any enabling or support activities. (‘Yes’ if all criteria fulfilled; ‘Partially’ if any enabling or support activities are not described; ‘No’ if no information on procedures is provided.)</td>
<td>[ ] No [ ] Partially [ ] Yes</td>
</tr>
<tr>
<td>34</td>
<td>TIDieR_5</td>
<td>Interventions providers description: For each category of intervention there should be a description of who will be the intervention(s) provider(s) (e.g. psychologist, nursing assistant) (‘Yes’ if all criteria fulfilled; ‘Partially’ if described for some interventions categories, but not for all; ‘No’ if no information on intervention providers is given)</td>
<td>[ ] No [ ] Partially [ ] Yes</td>
</tr>
<tr>
<td>TIDieR_5</td>
<td>Interventions providers background: For each category of intervention provider, describe their expertise, background and any specific training given. ('Yes' if all criteria fulfilled; 'Partially' if described for some interventions categories, but not for all; 'No' if no information on intervention providers background is given)</td>
<td>No</td>
<td>Partially</td>
</tr>
<tr>
<td>TIDieR_6</td>
<td>Interventions delivery modes: Describe the modes of delivery (e.g. face-to-face or by some other mechanism, such as internet or telephone) of the intervention(s). (For complex interventions, mark ‘Yes’ only if delivery modes are described for all intervention components)</td>
<td>No</td>
<td>Partially</td>
</tr>
<tr>
<td>TIDieR_6</td>
<td>Interventions delivery structure: Describe whether the intervention(s) will be provided individually or in a group. (For complex interventions, mark ‘Yes’ only if the delivery structure is described for all intervention components)</td>
<td>No</td>
<td>Partially</td>
</tr>
<tr>
<td>TIDieR_7</td>
<td>Interventions delivery environment: Describe the type(s) of location(s) where the intervention will occur, including any necessary infrastructure or relevant features. ('Yes' if all criteria fulfilled; 'Partially' if any location aspect is not described; ‘No’ if no information on procedures is provided.)</td>
<td>No</td>
<td>Partially</td>
</tr>
<tr>
<td>TIDieR_8, SPIRIT_13</td>
<td>Interventions quantity: Describe the number of times (e.g. one time or 5 sessions) the intervention(s) will be delivered. (For complex interventions, mark ‘Yes’ only if the intervention schedule is completely described for all intervention components)</td>
<td>No</td>
<td>Partially</td>
</tr>
<tr>
<td>TIDieR_8, SPIRIT_13</td>
<td>Interventions frequency: Describe the frequency (e.g. every two weeks or daily) with which the intervention(s) will be delivered. (For complex interventions, mark ‘Yes’ only if the intervention schedule is completely described for all intervention components)</td>
<td>No</td>
<td>Partially</td>
</tr>
<tr>
<td>No</td>
<td>Partially</td>
<td>Yes</td>
<td>N/A</td>
</tr>
<tr>
<td>----</td>
<td>-----------</td>
<td>-----</td>
<td>-----</td>
</tr>
</tbody>
</table>

### Interventions period
Describe the period (e.g., 6 months) over which the intervention(s) will be delivered. In cross-over trials, this must include information about any run-in and washout periods, or a statement on why these are not needed. (For complex interventions, mark ‘Yes’ only if the intervention schedule is completely described for all intervention components)

### Interventions amount
Describe the amount (length of session, or dose) of the intervention that will be delivered at each time. (For complex interventions, mark ‘Yes’ only if the intervention amount is described for all intervention components)

### Interventions - Tailoring
If the intervention was planned to be personalised, titrated or adapted, then describe what, why, when, and how. (only ‘Yes’ if all criteria fulfilled, "Partially" if any criteria of tailoring described, N/A if the intervention is not tailored)

### Interventions discontinuation
Criteria for discontinuing or modifying allocated interventions for a given trial participant (e.g., drug dose change in response to harms, participant request, or improving/worsening disease)

### Interventions adherence
Strategies to improve adherence to intervention protocols (e.g., frequent phone contact)

### Interventions adherence monitoring
Any procedures for monitoring adherence (e.g., drug tablet return, laboratory tests)

### Interventions potential interactions
Relevant concomitant care and interventions that are permitted or prohibited during the trial

### Outcomes definition
Is there a clear description of the primary outcome separately than secondary outcomes? (Yes, if discriminate primary and secondary outcome or if described that there is no secondary outcome)

### Outcomes measures of assessment
- for primary, secondary, and other outcomes, including their specific measurement variables (e.g., systolic blood pressure)

### Outcomes analysis metrics
- for primary, secondary, and other outcomes, including their analysis metric (e.g., change from baseline, final value, time to event);
| 51 | Spirit_12 | Outcomes aggregation method - for primary, secondary, and other outcomes, including their method of aggregation (e.g., median, proportion) | [ ] No | [ ] Yes |
| 52 | Spirit_12 | Outcomes endpoints - for primary, secondary, and other outcomes, including time of endpoint for each of them | [ ] No | [ ] Yes |
| 53 | Spirit_12 | Outcomes efficacy measure rationale - for primary, secondary, and other outcomes, including the explanation of the clinical relevance of chosen efficacy. | [ ] No | [ ] Yes |
| 54 | | Outcomes harm measure rationale - for primary, secondary, and other outcomes, including the explanation of the clinical relevance of chosen harm. | [ ] No | [ ] Yes |
| 55 | Spirit_13 | Participants enrollment - Detailed description of the trial's enrolment period | [ ] No | [ ] Yes |
| 56 | Spirit_13 | Participants assessments - Detailed description of the trial's schedule of assessments | [ ] No | [ ] Yes |
| 57 | Spirit_13 | Participant timeline - Time schedule as a schematic diagram, including enrolment period, interventions, assessments and visits | [ ] No | [ ] Partially |
| 58 | Spirit_14* | Sample size - Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations | [ ] No | [ ] Yes |
Methods: Assignment of interventions

|   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |  

60  | Spirit_16a* | Random sequence generation - Method of generating the allocation sequence (e.g., computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (e.g., blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions. | [ ] No | [ ] Partially | [ ] Yes
61  | Spirit_16b* | Allocation concealment mechanism - Mechanism of implementing the allocation sequence (e.g., central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned. | [ ] No | [ ] Partially | [ ] Yes
62  | Spirit_16c* | Implementation: Who will generate the allocation sequence. | [ ] No | [ ] Yes
63  | Spirit_16c* | Implementation: Who will enrol participants. | [ ] No | [ ] Yes
64  | Spirit_16c* | Implementation: Who will assign participants to interventions. | [ ] No | [ ] Yes
65  | Spirit_17a | Blinding - Details on whether trial participants were blinded and how ('Yes', if both criteria are fulfilled or if a justification is provided when blinding is not possible due to the intervention nature; 'Partially' if not described how blinded if participants were blinded). | [ ] No | [ ] Partially | [ ] Yes
66  | Spirit_17a | Blinding - Details on whether trial care providers were blinded and how ('Yes', if both criteria are fulfilled or if a justification is provided when blinding is not possible due to the intervention nature; 'Partially' if not described how blinded if care providers were blinded). | [ ] No | [ ] Partially | [ ] Yes
|   | Spirit_17a | Blinding - Details on whether trial outcomes assessors were blinded and how |
|   |           | ('Yes', if both criteria are fulfilled; 'Partially' if not described how blinded if outcomes assessors were blinded). |
|   | [   ] No | [   ] Partially | [   ] Yes |
|   | Spirit_17a | Blinding - Details on whether trial statisticians/data analysts were blinded and how |
|   |           | ('Yes', if both criteria are fulfilled; 'Partially' if not described how blinded if data analysts were blinded). |
|   | [   ] No | [   ] Partially | [   ] Yes |
|   | Spirit_17b | If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant’s allocated intervention during the trial (not required, but only ‘Yes’ if all criteria fulfilled; otherwise ‘N/A’ for open label trials, or ‘No’)

<p>|   | Methods: Data collection and management |
|   | Outcomes assessment methods - Plans for assessment and collection of outcomes, including any related processes to promote data quality (e.g., duplicate measurements, training of assessors) |
|   | [   ] No | [   ] Yes |
|   | Baseline assessment methods - Plans for assessment and collection of baseline data, including any related processes to promote data quality (e.g., duplicate measurements, training of assessors) |
|   | [   ] No | [   ] Yes |
|   | Further variables assessment methods - Plans for assessment and collection of other trials data, including any related processes to promote data quality (e.g., duplicate measurements, training of assessors) (N/A if none other trial data different from outcomes and baseline data) |
|   | [   ] No | [   ] Yes |
|   | Outcomes assessment instruments - Description of study instruments (e.g., questionnaires, laboratory tests) for assessment of outcomes |
|   | [   ] No | [   ] Yes |
|   | Baseline assessment instruments - Description of study instruments (e.g., questionnaires, laboratory tests) for assessment of baseline data |
|   | [   ] No | [   ] Yes |
|   | Further variables assessment instruments - Description of study instruments (e.g., questionnaires, laboratory tests) for assessment of other trial data (N/A if none other trial data different from outcomes and baseline data) |
|   | [   ] N/A | [   ] No | [   ] Yes |
|   | Outcomes measures reliability - Statement or reference to account for the reliability and validity for outcomes measures |
|   | [   ] No | [   ] Yes |
|   | Baseline measures reliability - Statement or reference to account for the reliability and validity for baseline data |
|   | [   ] No | [   ] Yes |</p>
<table>
<thead>
<tr>
<th></th>
<th>Spirit_18a</th>
<th>Further variables measures reliability - Statement or reference to account for the reliability and validity for other trial data (N/A if none other trial data different from outcomes and baseline data)</th>
<th></th>
<th>[   ] N/A</th>
<th>[   ] No</th>
<th>[   ] Yes</th>
</tr>
</thead>
<tbody>
<tr>
<td>79</td>
<td>Spirit_18a</td>
<td>Data collection methods - Reference to where data collection forms (DCFs) can be found, if not in the protocol (‘N/A’ for DCFs included in the publication, ‘Yes’ if DCFs not present in the publication, but info on how to obtain these is available)</td>
<td></td>
<td>[   ] N/A</td>
<td>[   ] No</td>
<td>[   ] Yes</td>
</tr>
<tr>
<td>80</td>
<td>Spirit_18b</td>
<td>Outcome data completeness - Plans to promote participant retention and complete follow-up, including a list of any outcome data to be collected for participants who discontinue (not always required, but at least a statement on why discontinuation is not relevant to the trial should be included in the text, if that’s the case)</td>
<td></td>
<td>[   ] No</td>
<td>[   ] Yes</td>
<td></td>
</tr>
<tr>
<td>81</td>
<td>Spirit_18b</td>
<td>Protocol adherence data completeness - Plans to promote participant retention and complete follow-up, including the deviance from intervention protocols (not always required, but at least a statement on why compliance with the intervention is not relevant to the trial should be included in the text, if that’s the case)</td>
<td></td>
<td>[   ] No</td>
<td>[   ] Yes</td>
<td></td>
</tr>
<tr>
<td>82</td>
<td>Spirit_19</td>
<td>Data management plans - Plans for data management (entry, coding, security, and storage, including any related processes to promote data quality - e.g., double data entry; range checks for data values).</td>
<td></td>
<td>[   ] No</td>
<td>[   ] Partially</td>
<td>[   ] Yes</td>
</tr>
<tr>
<td>83</td>
<td>Spirit_19</td>
<td>Data management documentation - Reference to where details of data management procedures can be found, if not in the protocol (‘N/A’ for DMPs included in the publication, ‘Yes’ if DMPs not present in the publication and info on how to obtain these is available)</td>
<td></td>
<td>[   ] N/A</td>
<td>[   ] No</td>
<td>[   ] Yes</td>
</tr>
</tbody>
</table>

Methods: Data analysis

|   | Spirit_20a* | Statistical methods for analyzing primary and secondary outcome(s). | | [   ] No | [   ] Yes |
| 85 | Spirit_20a* | Reference to where other details of the statistical analysis plan (SAP) can be found. | | [   ] No | [   ] Yes |
| 86 | Spirit_20b* | Statistical methods for any additional analyses (e.g., subgroup and adjusted analyses). (If a statement acknowledging that no additional analyses will be conducted, then ‘Yes’) | | [   ] No | [   ] Yes |
| 87 | Spirit_20b* | Definition of analysis population relating to protocol non-adherence (e.g., as randomised analysis) | | [   ] No |

BMJ Publishing Group Limited (BMJ) disclaims all liability and responsibility arising from any reliance on the content of this publication, and no content available here should be considered to constitute legal, medical, or any other form of advice. You should consult a professional to obtain specific advice.
<table>
<thead>
<tr>
<th>Spirit</th>
<th>Section</th>
<th>Description</th>
<th>88</th>
<th>89</th>
<th>90</th>
<th>91</th>
<th>92</th>
<th>93</th>
<th>94</th>
<th>95</th>
</tr>
</thead>
<tbody>
<tr>
<td>20c*</td>
<td>Methods</td>
<td>Statistical methods to handle missing data (e.g., multiple imputation).</td>
<td>[ ] Yes</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
| 21a*   | Monitoring | Composition of data monitoring committee (DMC).  
(If an explanation of why a DMC is not needed, then N/A.) | [ ] N/A | [ ] No | [ ] Yes | | | | | |
|        |         | Summary of DMC role and reporting structure.  
(If previous question is N/A, then N/A.) | [ ] N/A | [ ] No | [ ] Yes | | | | | |
|        |         | Data monitoring - reference to where further details about DMC charter can be found, if not in the protocol.  
(If previous question is N/A, then N/A.) | [ ] N/A | [ ] No | | | | | | |
<p>| 21b*   |         | Data monitoring - Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial. | [ ] N/A | | | | | | | |
| 22     |         | Harms data collection - Plans for collecting data on solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct | [ ] No | | | | | | | |
| 22     |         | Harms cause - Plans for assessing whether solicited and spontaneously reported adverse events and other unintended effects are related to trial interventions or trial conduct | [ ] No | | | | | | | |
| 22     |         | Harms reporting - Plans for reporting solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct | [ ] No | | | | | | | |</p>
<table>
<thead>
<tr>
<th>Spirit_22</th>
<th>Harms management - Plans for managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct (e.g. suspending intervention, removing participants from the study)</th>
<th>[ ] No [ ] Yes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spirit_23</td>
<td>Auditing Frequency – Description of frequency with which trial conduct will be audited, if any.</td>
<td>[ ] No [ ] Yes</td>
</tr>
<tr>
<td>Spirit_23</td>
<td>Auditing procedures - Description of procedures for auditing trial conduct, if any.</td>
<td>[ ] No [ ] Yes</td>
</tr>
<tr>
<td>Spirit_23</td>
<td>Auditing responsibility - Description of whether the audit process will be independent from investigators and the sponsor.</td>
<td>[ ] No [ ] Yes</td>
</tr>
</tbody>
</table>

**Ethics and dissemination**

<p>| Spirit_24 | Research ethics approval - Plans for seeking research ethics committee/institutional review board (REC/IRB) approval (If approval has already been obtained, then ‘Yes’. If instead, the authors state why they believe the trial does not need ethical approval, then ‘N/A’)) | [ ] N/A [ ] No [ ] Yes |
| Spirit_25 | Protocol amendments - Plans for communicating important protocol modifications (e.g., changes to eligibility criteria, outcomes, analyses) to relevant parties (e.g., investigators, REC/IRBs, trial participants, trial registries, journals, regulators) | [ ] No [ ] Yes |
| Spirit_26a | Consent or assent collection responsible - Who will obtain informed consent or assent from potential trial participants or authorised surrogates | [ ] No [ ] Yes |
| Spirit_26a | Consent or assent collection mode - How it will be obtained the informed consent or assent from potential trial participants or authorised surrogates | [ ] No [ ] Yes |
| Spirit_26b | Additional consent or assent - Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable (not required, but only ‘Yes’ if any ancillary study is described in the publication and info on additional consent is available; otherwise ‘N/A’ for trials without any ancillary study, or ‘No’) | [ ] N/A [ ] No [ ] Yes |
| Spirit_27 | Confidentiality - How personal information about potential and enrolled participants will be collected, shared, and maintained in | [ ] No |</p>
<table>
<thead>
<tr>
<th>SPIRIT Item</th>
<th>Description</th>
<th>Yes</th>
<th>Partially</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>106</td>
<td>Principal investigator declaration of interests - Financial and other competing interests for principal investigators for the overall trial.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>107</td>
<td>Collaborator sites declaration of interests - Financial and other competing interests for principal investigators for each study site (N/A if there is a unique study site).</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>108</td>
<td>Access to trial data - Statement of who will have access to the final trial dataset</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>109</td>
<td>Contractual agreements - disclosure of contractual agreements that limit investigators access to data.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>110</td>
<td>Ancillary and post-trial care - Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation (not required, but only ‘Yes’ if any ancillary study is described in the publication and info on if all criteria fulfilled; otherwise ‘N/A’ for trials without any ancillary study, or ‘No’).</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>111</td>
<td>Dissemination policy plans - Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (e.g., via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions (no N/A; if no mention then ‘No’). (“Partially” if it is not discriminated for different groups)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>112</td>
<td>Authorship policy - Authorship eligibility guidelines</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>113</td>
<td>Dissemination policy support - Any intended use of professional writers</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>114</td>
<td>Trial protocol sharing policy - Plans, if any, for granting public access to the full protocol</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Item #</td>
<td>Description</td>
<td>Details</td>
<td></td>
<td></td>
</tr>
<tr>
<td>-------</td>
<td>-------------</td>
<td>---------</td>
<td></td>
<td></td>
</tr>
<tr>
<td>115</td>
<td>Trial data sharing policy - Plans, if any, for granting public access to participant-level dataset</td>
<td>[ ] No  [ ] Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>116</td>
<td>Trial analysis code sharing policy - Plans, if any, for granting public access to statistical code</td>
<td>[ ] No  [ ] Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Appendices</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>117</td>
<td>Informed consent materials - Model consent form and any other related documentation given to participants and authorised surrogates (If no mention, even to state how/where these documents can be obtained, then ‘No’)</td>
<td>[ ] No  [ ] Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>118</td>
<td>Biological specimens - Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial (not required, but only ‘Yes’ if info on all criteria is provided; ‘N/A’ for trials without biological specimens data collection)</td>
<td>[ ] N/A  [ ] No  [ ] Partially  [ ] Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>119</td>
<td>Biological specimens for ancillary studies - Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis for future use in ancillary studies, if applicable (not required, but only ‘Yes’ if info on all criteria is provided; ‘N/A’ for trials without biological specimens data collection)</td>
<td>[ ] N/A  [ ] No  [ ] Partially  [ ] Yes</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Items that will be checked by a researcher with statistics expertise.