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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

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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/OSF.IO/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[1] and are the key document bounding the ethical principles for medical research with human subjects.[2] 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.[3] 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.[4] 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.[5–7] 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,[8] confirmatory factor analysis[9] and principal component analysis applied to dietary patterns[10]). Unlike highly regulated drug trials, diet and nutrition-related RCTs are not subject to oversight by regulatory agencies,[11] which might explain the lack of reporting of essential details in papers describing non-regulated RCTs.[12 13] 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.[14] 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[15] and non-regulated RCTs[11] has improved since SPIRIT's publication. Item 5 of the Consolidated Standards of Reporting Trials 2010 statement[16] 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.[17]

Published protocols are growing in importance as a source of details about interventions. The use of TIDieR[17] alongside SPIRIT 2013[14] 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.

Box 1 Review research questions

⇒ What are the main characteristics of published protocols of diet and nutrition-related randomised controlled trials (RCTs)?
⇒ What are the main reporting limitations of a random sample of published protocols of diet and nutrition-related RCTs?

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.[18] 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*,[19] 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*

al[20] 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*[19] incorporates terms to identify RCTs, we did not use any additional filter related to them.

We constructed 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.[21] 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*.[18] 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.[22] 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

Data domain	Categories used for data extraction
Participants	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)*
Interventions	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, if no component of intervention could be categorised as any of the above
Comparator	Placebo No intervention Usual care Different intervention Other
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
Study design*	Parallel RCT Crossover RCT Cluster RCT Multicentre RCT Single-centre RCT

*Our adaptations of the Naude *et al*.[18] 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 non-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 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 SPIRIT[14] 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 this.

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 adhered to will be calculated for each protocol, considering the sum of all items in the SPIRIT[14] and TIDieR[17] checklists, to give a final reporting completeness score. We will present the proportion of protocols that adhere to each item of SPIRIT[14] and TIDieR[17] 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 X^2 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.

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Contributors All authors have made substantial contributions to the development of this protocol through discussions on the topic. MS, SK, SH, GK, JAC, SL, ARAA, CJV and FSG jointly conceived the idea of this project. FMS, MS, SK, SD, CC, ARAA, MJP, LCI, CJV 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.

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