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Perspectives on the application of CONSORT guidelines to randomised controlled trials in nutrition

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Abstract

Purpose:

Reporting guidelines facilitate quality and completeness in research reporting. The CONsolidated Standards Of Reporting Trials (CONSORT) statement is widely applied to dietary and nutrition trials but has no extension specific to nutrition. Evidence suggests poor reporting in nutrition research. The Federation of European Nutrition Societies led an initiative to make recommendations for a nutrition extension to the CONSORT statement towards a more robust reporting of the evidence base.

Methods:

An international working group was formed of nutrition researchers from 14 institutions in 12 different countries and on five continents. Using meetings over a period of one year, we interrogated the CONSORT statement specifically for its application to report nutrition trials.

Results:

We provide new nutrition-specific recommendations or emphasized recommendations for the reporting of the introduction (three), methods (twelve), results (five) and discussion (eight). We also added two additional recommendations that were not allocated under the standard CONSORT headings.

Conclusion:

We identify a need to provide guidance in addition to CONSORT to improve the quality and consistency of the reporting and propose key considerations for further development of formal guidelines for the reporting of nutrition trials. Readers are encouraged to engage in this process, provide comments and conduct specific studies to inform further work on the development of reporting guidelines for nutrition trials.

Keywords: Guidelines, CONSORT, nutrition trials, dietary interventions, reporting, expert opinion

Statements and declarations

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Author contributions

All authors contributed to the drafting of the manuscript. JRF and CW were responsible for review and editing. All authors read and approved the final manuscript.

Introduction

Randomized controlled trials (RCTs) are needed to generate causal evidence. Too often, however, causal relationships and underpinning mechanisms are poorly defined and reported. Well-conducted trials with a robust design can overcome some of these limitations and improve the quality of evidence regarding nutrition, diet and human health relationships [1].

There are specific challenges to conducting high quality dietary and / or nutrition intervention trials. Lichtenstein et al. [2] have previously summarised key concerns related to implementation of such trials. In addition, even if well-conducted, trials need to be reported accurately, with sufficient detail for correct interpretation and application of research findings. If data generated by nutrition trials are to be appropriately transcribed into health-related actions, it is critical that the results are written up completely and transparently. This is also an important requirement for comparability of trials and accumulation of findings for systematic reviews, which are crucial for health decision-making and used in drafting of programme guidance and policy. There is evidence that points towards poor reporting of nutrition research [3–6].

Reporting guidelines are widely used to improve quality and completeness of reporting research. Previous efforts, organised as an extension of the STrengthening the Reporting of OBservational studies in Epidemiology (STROBE) statement of nutritional epidemiology, have focused on the reporting of dietary assessment and observational studies [3]. However, the CONsolidated Standards Of Reporting Trials (CONSORT) statement [7, 8] for RCTs does not have an extension specific to nutrition. CONSORT details the minimum requirements for reporting RCTs, with additional guidance provided by the Template for Intervention Description and Reporting (TIDieR) checklist [9]. It remains unclear, however, if additional guidance is necessary to improve

CONSORT adherence and the utility of CONSORT guidelines in nutrition trials, and consequently, reporting quality of nutrition RCTs.

To this end and as part of the Improving Standards in the Science of Nutrition Initiative, the Federation of European Nutrition Societies (FENS) led an effort to evaluate and identify key elements of nutrition intervention trials which should be reported in a standardised way in order to provide a more robust evidence base. The present opinion piece summarises the findings from this consultation. It serves to initiate and inform further discussion on efforts to improve reporting of nutrition trials and ultimately to contribute to a better evidence base in diet, nutritional status, and health.

Methods

Responding to a call from FENS [10], a working group of nutrition experts was assembled and enlarged by recruitment of international and geographically diverse experts to ensure that the committee included a range of nutrition trial specialties and expertise and the local/national context. The working group convened nutrition researchers from 14 institutions from 12 different countries and five continents, including a representative from the American Society for Nutrition. Members of the working group were invited through contacts of existing members, or via identification as being a known expert in a trial methodology and in particular, nutrition intervention (e.g., whole diet, supplement, eating behaviour, etc.) trials. Within the expertise of the working group and calling on previous research around reproducibility, quality, and transparency of nutrition trial reporting [11–15], we applied an iterative process to interrogate the 2010 CONSORT guidelines as they relate to nutrition trials. This was achieved through a series of regular online consultations over 12 months.

We reviewed the CONSORT items specifically as applied to all types of nutrition intervention trials and where additional guidance for nutrition trials would be advantageous. Since the 25-item CONSORT checklist provides basic elements to describe, this opinion piece sets out the findings of the working group under the CONSORT framework, and proposes either enhancements to existing CONSORT items, or clear items in addition. We define “nutrition trial” as an intervention that include feeding studies that provide all foods and beverages to be consumed, or one that provide single foods or supplements, dietary advice, and/or behavioural modifications, with or without placebo or control in a nutrition or nutrition-related setting. The present considerations hence apply to both primary trials and secondary analyses of such trials. Agreement was reached on the main points. Additional considerations for diet-related trials beyond the standard CONSORT checklist identified are elaborated upon with a summary for each section provided in Boxes 1 to 5.

Results

1. Title

For nutrition trials, the title should include details of the food bioactives, food/food group, dietary pattern or eating behaviour intervention. For interventions where it is implemented by food choice guidance rather than the provision of foods or supplements or via a multi-domain eating behaviour modification approach (see below) this should be obvious from the title. For example, if the trial is investigating the impact of adopting the Mediterranean Dietary Pattern (MDP) on a health outcome, and the intervention is food choice guidance or a more holistic eating behaviour approaches (to provide individuals with the capability, opportunity, or motivation to adopt a MDP) then this should be indicated in the title with phrases such as *MDP guidance, MDP dietary intervention* or a *MDP eating behaviour intervention.*

Where nutritional status, dietary intake or eating behaviour is the primary outcome this should also be clearly stated in the title, with information on the intervention targeting these also given.

Where possible, the type of dietary comparator should be described in the title, specifically “RCT” for trials with a control group, “trial” where two intervention groups are used and “placebo-controlled trial” where a placebo is used as comparator. Furthermore, the design of the trial should be specified, e.g., cluster, cross-over, parallel, non-inferiority. Likewise, if the manuscript is reporting a secondary RCT analysis, this should always be stated in the title.

2. Abstracts

Abstracts should be clear, transparent, and sufficiently detailed to be stand-alone, given that not all health care, policy or commercial professional readers have access to the full papers with decisions often made on the abstract, e.g., the decision to include RCTs in systematic reviews is typically based initially on a title and abstract review. Though it is recognised that due to journal abstract word limit, the addition of all the information relating to RCTs is not possible, the abstract should include as much information as possible under the following standard headings: (i) background: should specify the nutrition research question; (ii) Methods: should clearly present the trial design, details of the intervention (detailed composition of the food / supplement / dietary pattern / behaviour change; whether the intervention is a (isocaloric) replacement or add on intervention), duration of the intervention, and how the intervention is delivered (supplements, food, guidance, etc.), and any details on the (dietary) comparator or control group. Methods used to assess dietary adherence should be given. The PICO (Population, Intervention, Comparator and Outcome) criteria should be clearly identifiable; (iii) Results: Main findings (including dietary adherence) based on intention-to-treat analysis with effect estimates and 95% CI or other assessment of variance; (iv) Conclusion: General scientific interpretation of the results; (v) Implementation, impact or relevance: In addition to the conclusion, an explicit statement on

implementation, impact or relevance, including to public health policy, is recommended. Although a large amount of high-quality nutrition research is conducted, this is often not effectively translated into policy and practice, such as improved population eating behaviour and nutrition status, the availability of affordable, widely consumed food products with improved composition, or effective therapeutic use of nutrition approaches in clinical medicine. Therefore, to enhance translation of findings, it is recommended the authors conclude the abstract (and highlights section of the paper if offered by the journal) with this summary on the impact, relevance, and possible implementation approach to apply the findings.

3. Keywords

To enhance visibility of information in literature reviews keywords should include the bioactive compound, food, (non) nutrient or dietary behaviour being tested, using the Medical Subject Headings (MeSH) term with preference.

4. Introduction

Although CONSORT recommends that the introduction include scientific background and explanation of rationale, reporting of the justification for undertaking nutrition trials is incomplete if all of the points described below are not clear. The introduction should clearly describe the nutrition research question and justification for undertaking the trial. This should include a summary of relevant research with reflections on effect estimates, consistency of the evidence, and its certainty [16]. This could be derived from previous well-conducted RCTs, high quality systematic reviews of RCTs, interrupted time series analyses and/or observational studies (with a focus, where available on prospective cohort data), and pre-clinical evidence (high-quality animal, *in vitro, ex vivo*, and *in silico* studies). For preclinical evidence, the physiological relevance to humans should be considered with a reflection on the human equivalent dose of the intervention and its chemical form [17].

If relevant RCT findings are available, a statement should be provided as to their scope and limitations to justify the need for further RCTs. If it is not obvious, a statement on the biological plausibility [18] of the intervention and the likely behavioural, physiological, or molecular mechanism underpinning the impact of intervention on the primary outcome measures should be provided. The introduction should provide a justification for the length of the intervention, based on the time-lag required to explore differences in change between intervention and control for primary and key secondary outcomes, which will also inform study design. An intervention period that is too short runs the risk of an underestimated treatment effect. Too long an intervention is unethical as it misuses participants, research, and financial resources. For example, when looking at the impact of supplementation with EPA+DHA on plasma triglyceride levels, an intervention period of 4-6 weeks is sufficient to achieve maximal effect (20) high-quality, whereas the maximal LDL-cholesterol lowering effect of a diet enriched with plant sterols is already visible within 1-2 weeks [19], with a cross-over study design optimal for such short intervention periods. However, if focused on a more functional endpoint, e.g., the impact of DHA on cognitive function, when the proposed mechanisms are dependent on enrichment of neuronal or glial cells with DHA, then an intervention period of one year or more, with a parallel design, should be considered, given the half-life of DHA in the brain is more than 2 years [20, 21].

Where relevant, the dietary intervention and comparator should be directly compared to current dietary recommendations or food intake in the population of interest. Where appropriate a discussion of any possible harm should also be included, particularly in vulnerable groups or in combination with other lifestyle or phenotype characteristics, such as medication use or disease status. Moreover, the studied population needs to be justified, i.e., including sex, age, morbidities (e.g., type 2 diabetes), socioeconomic status, etc. In addition to the scientific background and

rationale, the introduction should refer to any health/food/nutrition policy priorities the proposed research is addressing.

With the pleiotropic nature of food bioactives affecting multiple physiological processes, numerous secondary outcomes are typically captured. For validity and transparency, the main objectives and/or hypotheses of the research should be clearly stated at the end of the introduction.

Given the complexity of well conducted RCTs, their cost and the research-staff and participant 'burden' of completing the intervention, which may take several years to design, deliver, analyse, and publish, the publication of manuscripts based on well-conducted secondary analyses is highly encouraged. However, as with the primary analysis, such secondary analyses should be well rationalised, with a clear indication given in the introduction (and throughout the paper) that the RCT design is suitable to address the secondary research question.

Box 1: Proposed additions to CONSORT checklist for "Introduction" in manuscripts describing diet-related and nutritional trials

- State the biological plausibility of the nutrition intervention and behavioural, physiological, or molecular mechanism underpinning the intervention impact on the primary outcome measures.
- Justify the length of nutrition intervention with respect to the primary outcome
- Provide contextualisation to current dietary recommendations or food intake in the population of interest. Justify the population chosen giving details. Ensure PICO criteria are clearly identifiable.

5. Methods

Trial design

Overall design. A figure to visually explain the intervention(s) and methods is often informative, particularly if interventions are complex. CONSORT guidelines recommend a description of the trial design (such as parallel, crossover, cluster, factorial) including the allocation ratio [22]. Extensions have expanded on how to report on specific RCT designs including non-pharmacological treatments, multi-arm parallel groups, cluster, crossover, adaptive design, routinely collected data, within-person, pilot and feasibility, non-inferiority and equivalence trials, and using web-based and mobile health interventions [23–33]. Extensions for reporting effectiveness trials in communities rather than efficacy trials in controlled settings have been developed [34]. Diet-related trials can use any of these designs and should follow the relevant reporting guidelines for describing them. Properly designed RCTs reduce trial contamination and allow causal inference to be assessed. As pointed out by Lichtenstein et al. [2], the choice of the design should align with the question being asked and be part of the trial protocol. If the paper is a secondary analysis of an intervention, that should be made clear in the methods.

Length of intervention. An important aspect of the design for addressing efficacy (effect under controlled conditions) or effectiveness (pragmatic effect under real world conditions) is the duration of the intervention. The biological response of interest to an intervention may reach a stable level following exposure to the intervention that could take hours, days, weeks, or even years, which may also depend on the exposure dose, or the response may be progressive. For example, serum 25(OH)D may peak within one day following a large, acute dose [35] or it may reach a plateau after 4 or more weeks of chronic lower dose supplementation [36]. Different types of dietary interventions may require different durations to see the entire effect for the same outcome measure. For example, in a re-analysis of a four-week randomised controlled feeding study to compare the effects of a Dietary Approaches to Stop Hypertension (DASH)-style diet

high in fruits, vegetables, and low-fat dairy with a typical Western diet higher in fat, especially saturated fat, Juraschek et al. [37] found the DASH diet intervention lowered blood pressure after the first week with no subsequent further decreases, whereas, low sodium diets did not yet reach a plateau after 4 weeks, suggesting the full effects had not been achieved by 4 weeks.

Health outcomes. Health outcome measures for diet-related interventions are typically a specific validated and reliable physiological, structural, functional, or biochemical measure used to establish a causal link between the dietary intervention and the health outcome (e.g., macular pigment optical density as an indicator of eye structure associated with normal visual function, endothelium-dependent vasodilation related to healthy blood flow, bone mineral density as an indicator of fracture risk, etc.). Intermediate biomarkers should be selected that are on the causal pathway to disease. Changes in disease outcomes are difficult to achieve in diet-related interventions because of the usual long latency to see an effect, but surrogate outcomes along the causal pathway must be validated as described by Yates et al. [38]. Further, diet-related interventions typically affect many systems which may have different responses for efficacy and risk and at different doses.

Protocol modifications. Any important changes to the methods made after trial commencement should be disclosed with justification and ethical approvals. For example, in a crossover RCT evaluating the efficacy of dietary supplements for reducing bone loss in postmenopausal women compared to a positive control, the option for choosing the positive control was altered mid-study [39]. The originally approved positive control was oestradiol plus progesterone, but during the trial the results of the Women's Health Initiative hormone trial were released which led to large-scale withdrawal of hormone replacement therapy in clinical practice. The investigators received approval to offer a bisphosphonate positive control instead of oestrogen and reported the change as "Subjects were initially offered oestradiol plus medroxyprogesterone as the positive control,

but after publicity surrounding the premature termination of the Women's Health Initiative hormone trial, a bisphosphonate was offered instead."

Participants

The CONSORT checklist includes describing eligibility criteria for participants [8], but provides little more guidance. The population selected for study should align with the aims of the study. If the population may benefit from the intervention or if maximal efficacy of the intervention is of interest, the population to be studied may reflect a relatively homogenous and specific group. The broader the inclusion of the population, the more generalizable the results which may be desirable for public health recommendations compared to guidelines for treating patients. There is recent attention on including pregnant women in trials as well as underrepresented minorities. Studies with more generalizable results using a heterogeneous population come with the disadvantages of higher cost and effort as power to see an effect is reduced [2].

Eligibility criteria for diet-related interventions should include baseline nutritional consumption or status of components relating to the intervention that would influence the outcomes of interest, which should be reported This may include an objective biological assessment related to the intervention (e.g., serum ferritin for iron, serum 25(OH)D for vitamin D; red blood cell docosahexaenoic acid (DHA) for DHA intake, serum or urine metabolite specific to intake of a certain food or class of foods), or if no good biomarker of exposure exists which is the case for many nutrients, related characteristics, food and nutrient intakes or functional biomarkers may be useful, e.g., anthropometrics, clinical measures, dietary/nutrient/bioactive intake assessment. Statements to show whether exposure measurements are valid should be included. For example, in relation to iron, clinical measures such haemoglobin levels or dietary intakes of haem and non-haem iron related to iron status should be in the population under study. Consideration should be given to potential confounders of exposure; in the case of iron this could be other dietary factors

which enhance or inhibit absorption. Also, the presence of metabolic conditions, such as for the iron example, haemochromatosis, which could affect status need to be assessed. Clear statements of methods used to assess the nutritional exposure are required with a justification of method selection.

Assessing background nutritional exposure or status is an important factor in nutrition trials, that often is not considered to be a factor in other types of trials, including those outside of the nutrition field. This is important because baseline status for a given nutrient(s), can affect the response or nutritional status related to the intervention being investigated. People must consume essential nutrients; therefore, there is rarely a zero-background starting status as there is for an intervention of a xenobiotic that is absent prior to the trial. In fact, it is unethical to chronically deplete humans of an essential nutrient to determine a functional deficiency [40], making the use of placebo difficult. Moreover, standard of care has differing definitions. If the intervention has a dose threshold for an effect and the background status of the population being studied exceeds that threshold, benefits are unlikely and erroneous conclusions about the relationship of diet and physiological response may occur. This should be considered in the inclusion/exclusion criteria. This occurred in the Women's Health Initiative calcium and vitamin D trial where average status of calcium intake and serum 25(OH)D were approximately the recommended levels of these nutrients. When data were re-analysed to exclude participants who were taking their own calcium and vitamin D supplements and were compliant with the intervention, calcium and vitamin D supplementation resulted in a clinically meaningful reduction in hip fracture [41]. Too often, studies are conducted without assessing baseline status or the threshold status is unknown. Nutrient recommendations based on dose-response studies with a physiological outcome such as maximal retention have been conducted for calcium [42, 43], but for very few other nutrients. If a food allergy or avoidance is an exclusion criterion, this should be disclosed. When relevant,

disclosure of the training or characteristics (vegan, clinical, etc.) of those delivering the intervention should be disclosed.

Settings and locations

The CONSORT checklist includes settings and locations where the data were collected [8]. The study settings that might influence the intervention for diet-related studies that should be given further consideration include supervised, or free-living settings and their implementation (clinical or population-based settings). Setting and location are essential information to assess potential bias arising from the randomisation process in nutrition assessment. The STROBE-nut guidance document contains specific recommendations to report characteristics of the participants or contextual variables (season, festivities) that may influence the validity of the dietary recall [3].

Intervention

CONSORT recommends that interventions for each group be described in sufficient detail to allow replication, including how and when they were actually administered [8]. Nutrition related interventions and RCTs in which interventions are influenced by nutritional status or co-ingested nutrients or food patterns require comprehensive documentation and reporting to interpret causal relations and to support food guidance. Nutrition interventions can include feeding studies, providing all foods and beverages to be consumed or those that provide single foods or supplements, dietary guidance, or behavioural modifications. The intervention for diet-related studies should be rigorously monitored and reported. The TiDieR checklist can be used to guide elements to include about an intervention for better replication on why, what, who provided, how, where, when and how much, tailoring, and modifications [9], but it is not specific to nutrition. Not only should sufficient details of the intervention be described to be able to reproduce the study, but validation of the presence of the active constituents and validation of its stability throughout the course of the intervention should be determined and reported, and where possible, verification

of consumption. Whether foods were manufactured commercially or were developed for research purposes should be noted. Details of food preparation, cooking, and storage conditions as well guidance as to when throughout the day, with or without food, the intervention should be consumed, as these variables may affect the composition/biological activity of the intervention should be reported as relevant.

If the intervention is given via dietary advice, diet assessment is needed to provide relevant context for interpreting the effect of the intervention on outcome variables, the methods used, and their validation need to be described. For example, if dietary counselling is used, fidelity measures to ensure the consistency of delivery of the intervention should be included. Determination of diet composition should be described when assessments are used to determine intake. Further information on documentation and reporting of diet-related interventions can be found in Weaver et al. [12] and Health Canada [44].

Assessing and reporting on dietary adherence to the intervention has some unique opportunities and challenges in diet-related trials. Assessment of dietary adherence in nutrition trials using food supplement(s) may not differ substantially from drug trials. Objective biochemical assessment of exposure of an intervention with a known bioactive component or related biomarker may be feasible. In contrast, human diets are complex with well characterised difficulties with self-reporting if not provided in a controlled setting. Best practices for diet assessment and reporting were given by Kirkpatrick et al. [45].

A particular challenge in diet-related interventions is the comparator which often requires as much thought and detailed explanation as the intended intervention. This is especially true of manipulation of macronutrients or whole diet interventions. If the level of a macronutrient such as fat is being altered, the replacement (control) may have unexpected effects on the health

outcomes being measured. Such contamination has led to confusion. One recent example is the debate over whether saturated fatty acids *per se* are associated with increased risk of markers of cardiovascular disease, or whether it is their replacement with polyunsaturated fats in the comparator groups of trials that is responsible for the observed cardiovascular benefits [46–49]. Replacement foods that are thought to be neutral in their effect on the outcome measure being studied have also come under scrutiny. For example, an apple was given as the control to a plum intervention for arresting bone loss in postmenopausal women [50], but subsequently, the apple comparator was found to contain polyphenolic compounds that also benefited bone composition.

An example of documenting a whole blueberry freeze-dried powder intervention is described by Weaver and Hodges [51]. This paper discusses many elements for reporting nutrition trials using food bioactives, including description of the intervention, monitoring stability of the polyphenol bioactives, monitoring compliance through serum polyphenol metabolite biomarkers, and safety considerations.

Full reporting on the intervention may also include ethical and cultural acceptability of the product(s) being tested or used as controls. Authors should disclose any ingredients that might be prohibited for consumption for religious or cultural reasons, which therefore might introduce bias.

Outcomes

Nutrition trials need to report primary and secondary outcomes transparently. The selection of outcome needs to be clearly justified with a research hypothesis that provides a clear added value to science and/or society. Nutrition trials, however, are typically complex interventions, which present some specific challenges with regard to the multiplicity of tests and inflation of false negative findings [52], and risk of bias should be considered [53]. Specific attention is hence

required to indicate which outcomes are defined a priori, well-powered, and based on a robust hypothesis, and any other outcomes that are secondary and for which the assessment is rather exploratory. Outcomes should be adequately defined, described as “objective” (e.g., mortality) or “subjective” (e.g., quality of life), and reported at pre-specified timepoints. When reporting secondary analyses, a *post-hoc* power calculation should be included.

Randomisation

The CONSORT checklist requires details on the method used to generate the random allocation sequence and the type of randomization including restrictions. For nutrition trials, baseline nutrient status should be considered as a basis for randomization when relevant (e.g., when sample size is small), and risk of bias arising from randomisation, and in particular, allocation concealment, should be considered [53].

Blinding

The CONSORT checklist requires details on who was blinded and how, and whether the trial was single, double, or triple blinded should be clearly described [8]. Measures undertaken to reduce risk of bias such as concealed allocation strategies should be provided, including any measure taken in the case of deviations from intended interventions (e.g., blinding of participants, carers and people delivering the interventions, using appropriate analysis to estimate the effect of assignment to intervention) [53].

Blinding can be particularly challenging in diet-related trials, however. With interventions involving dietary supplements, the placebo may be well matched to the intervention, but not if commercially available dietary supplements with different packaging are being compared, as was the case with different sources of plant isoflavones [39]. Blinding of manipulations of diet or foods may be especially difficult because of their appearance, taste, smell, and texture. The participant may not

be able to see a difference in salt level if that is the only variable, but they can taste the difference between high and low salt levels. Weaver and Hodges [51] describe the problems with blinding of intensely coloured products. Even when the intervention or comparator cannot be blinded from the participants or those who deliver the intervention, the staff who perform testing and the analyses can be blinded, and this should be described. This may be particularly true for measurements that are vulnerable to observer bias such as cognitive testing or even to decide which pixels to include on an image.

Statistical Methods

Guidelines for developing an *a priori* statistical analysis plan specific to diet-related trials were recently reported [54]. The statistical analysis plan should be finalised before unblinded outcome data become available for analysis. The design and adjustments should match the appropriate analyses, and also consider measurement error. Measurement error is always a consideration in nutrition-related trials in relation to exposure or outcome measures; statistical techniques can be used to reduce the impact of this error [55]. The primary analysis should be based on the intention-to-treat principle. Compliance cut offs for per protocol analyses should be reported and defined a-priori. Methods for additional analyses such as the statistical method used to combine dietary or nutritional data, intake modelling, use of weighting factors should be identified and justified. Stratifications and adjustments as relevant should be described. Considerations of per protocol compared to intention to treat analysis and baseline nutritional status are especially important in diet related trials.

A particular challenge in nutrition research is to consider the independent effect of specific nutrients on disease outcomes. As nutrient intake can be associated with increased energy intake, adjustment for energy intake can be essential. There are various methods to make statistical adjustments and the statistical section needs to justify and report the method used [56].

In addition, description of the analysis should contain specific detail on participants that were excluded based on possible misreporting. Discuss potential effects on study power and report any data imputation or sensitivity analysis to assess potential bias of such exclusion on the findings.

Finally, methods for secondary analyses should not just refer to the primary paper when describing methods, rather include a brief summary of the key points of the methods in addition.

Box 2: Proposed additions to CONSORT checklist for “Methods” in manuscripts describing diet-related and nutritional trials

- The trial design should align with the scientific question being addressed
- Duration of the trial should be appropriate for the primary and key secondary nutritional sensitive outcomes
- Potential contaminations should be measured, including baseline nutritional status (especially for the nutrient, bioactive, diet being tested to determine if participants are already adequate) and factors that could influence nutrition trial outcomes (habitual diet, season, physical activity, knowledge of participants and interventionists, especially for education interventions), carry-over effects in crossover trials
- Target populations-efficacy vs effectiveness, clinical vs healthy population, specify particular dietary, physiological or nutritional characteristics targeted. List eligibility criteria related to baseline nutritional status (anthropometric, biochemical, clinical, diet, food allergies)

- Dietary comparators should be well described, including details if isocaloric or not, as applicable.
- Dietary adherence assessment should be clear
- Details of the diet-related intervention should be given. If given, how was it prepared, stored, checked for bioactive constituent(s), evaluated for storage stability, and biological exposure monitored? For behavioural interventions, describe the protocol that includes how it was developed and administered and by whom and when. Description of assessment of background diets is needed as relevant.
- Randomization based on nutrient intake or status (especially important in small trials) and allocation concealment should be described
- Describe any limits to blinding and who was blinded (participants, staff who delivered the intervention, analytical staff), as well as details of concealed allocation
- An a priori statistical analysis plan that aligns with the study design should be described, and primary analysis should be based on intention-to-treat, with per-protocol analysis described in addition where relevant.
- Comparisons between intention-to-treat and per protocol analysis should be considered. Additionally, per protocol compliance cut-offs should be reported, including possible exclusion criteria for misreporting
- Identify and justify data analysis choice (e.g., statistical method used to combine dietary or nutritional data, energy adjustments, intake modelling, use of weighting factors). Define stratifications and adjustments.

6. Results

Transparent, accurate and complete reporting of results is critical if data are to be considered for further use, be it in research, inclusion in systematic reviews, or to influence health policy. CONSORT guidelines provide a rigorous framework, including a strong recommendation for inclusion of a flow diagram to document the number of participants included and who finished the trial with completeness. Such flow diagrams are now considered as standard practice also in nutrition trials, though they are rarely included in those reported earlier than 2010. For example, the reputed DASH trial [57], published in 2001 may have benefited from inclusion of a flow diagram. Though the authors describe the number and percent of participants completing the study in each arm and specify that withdrawals were similar between groups, they do not elaborate on reasons for withdrawal, which is particularly relevant in nutrition trials evaluating different dietary interventions, to inform on acceptability of these interventions. Flow diagrams may be integrated with information on study design and flow, as presented by Jongstra et al. [58], who provide clear detail on ineligibility or withdrawal between screening and baseline, and then reasons for non-completion between enrolment and endpoint.

Additional detail on the flow diagram relative to nutrition trials should specify the actual interventions (i.e., treatment(s) and comparator(s)) as they were implemented, especially if differing from the described methods. Numbers of and reasons for losses and exclusions (e.g., missing, incomplete or implausible dietary/nutritional data) should be additionally present. Authors should include dates defining recruitment periods and any follow-up periods as applicable and specify if the trial ended as planned or was stopped early, providing reasons, particularly if loss of participants was due to intervention-related reasons such as adverse reactions to the intervention such as intolerability, or lack of adherence e.g., too strong restriction (unrealistic) of carbohydrate intake with very low carbohydrate diets. Details of results of adherence monitoring,

such as collection of supplement containers at points during the intervention period, should be clearly described.

The CONSORT guidelines stipulate inclusion of a table showing baseline demographic and clinical characteristics for each group. In particular, nutrition trials should provide details of where baseline differences between intervention and/or control groups may be relevant to defining the nutritional status or response to dietary intervention. This may be particularly relevant in small or underpowered trials e.g., pilot trials.

The baseline characteristics table should, as a minimum, include an assessment of variability (e.g., standard deviation, 95% CI, interquartile range), measures of status and/or recent or long-term intake of the food or bioactive of interest. Measures of status may also include proxy measures for nutrient intake, particularly if being used as a primary or secondary outcome measure. Examples might include stunting prevalence alongside serum zinc assessment [59] or household uptake of iodized salt alongside urinary iodine concentration [60]. Furthermore, though most trials seek to eliminate contamination bias, the uptake of any permitted dietary habits, in particular the use of nutritional supplements beyond that in the intervention, should be clearly recorded. Where applicable, medication use should also be considered. For example, if subjects are using statins and the trial seeks to examine the effect of diet on vascular function.

As with any trial, outcomes reported in the results should match the methods, and be strictly based on intention-to-treat analysis. It is common in systematic reviews to detect bias in selection of the reported result, which may lead to the over- or underestimation of treatment effects or harms [61]. For outcomes and estimation, reports of nutritional trials should provide details about whether measurement or ascertainment of the outcome differed between intervention groups. Further, if Bayesian analyses were performed, ‘credibility intervals’ should be reported. This is in addition to

existing CONSORT recommendations for outcomes and estimation, which state that for each primary and secondary outcome, results for each group, and the estimated effect size and its precision (e.g., 95% CI), are given, as well as presentation of both absolute and relative effect sizes for binary outcomes.

An important consideration for nutrition trials in addition to response to the intervention, is reporting of adherence. Although some level of detail may be included in the flow diagram, a specific discussion on dietary adherence is desirable, to understand how participants could adhere to the intervention, which in turn, can indicate acceptability, feasibility, and possible entry points for error. In a systematic review, Kehoe and colleagues [62] assessed the adequacy of reporting of participant adherence in RCTs investigating the effect of maternal nutritional supplements on infant outcomes. Out of 58 included RCTs, almost a third did not describe how participant adherence was assessed. Nearly half of the papers failed to report participant adherence numerically and differences in adherence data between treatment arms were not reported in 52% of publications. Soofi et al. [63] in their assessment of micronutrient powders with and without zinc on several primary outcomes including growth, diarrhoeal episodes and respiratory morbidity, report mean consumption of micronutrient powder sachets per group, but do not elaborate if data were collected on reasons why compliance was approximately half the intended dose (mean of about 16 sachets per month per group, for a daily dose intervention).

Where additional ancillary analyses, such as per-protocol, as-treated, sensitivity, subgroup and adjusted analyses are included, these should be distinguished as being pre-specified (and should thus match the methods) or exploratory. In addition to these CONSORT recommendations, nutrition trial reports should, in particular, document any interaction terms, sensitivity analysis (e.g., exclusion of under/over reporters or outliers) and data imputation, if applicable.

Finally, all unintended effects, and/or adverse outcomes beyond the incidental events that are unlikely to be associated with the intervention and possible with normal food and beverage intake, e.g., choking, minor gastrointestinal disturbances, gagging, vomiting, etc., in each group should be described.

Box 3: Proposed additions to CONSORT checklist for “Results” in manuscripts describing diet-related and nutritional trials

- Consistent use of CONSORT flow chart, including, where relevant, detail on interventions as administered, especially if different to the protocol/methods, and detail on loss to follow up due to intervention-related reasons e.g., adverse reactions to the intervention, lack of adherence, etc.
- Tabulate baseline demographic and clinical characteristics per group, highlighting nutritionally relevant differences between intervention and/or control groups and stating the participant N included in per protocol/intention to treat analyses.
- Present primary outcomes first, then secondary outcomes per trial registration, and details on whether outcomes differed between groups. If Bayesian analyses were performed, present credibility intervals in addition to usual CONSORT reporting. Results should be based on intention-to-treat analyses.
- Declare ancillary analyses as pre-specified or exploratory, reporting interaction terms, sensitivity analyses and data imputation where relevant.
- For each group, report all unintended or adverse events/outcomes beyond incidental events unlikely to be associated with normal food and beverage intake.

7. Discussion

As per general recommendations for the reporting of trials, limitations of the study, generalizability of the findings and interpretation are key sections of the discussion section of nutrition trials.

The discussion should clearly state the main findings of the paper, using intention-to-treat principles [53], with per protocol interpretations given in addition, depending on the objective of the study, e.g., if the trial outcome was to assess the effect of adhering to the intervention. The discussion should also put findings clearly into context with the research objectives and differentiate these clearly from findings from ancillary analysis. A discussion of fidelity of the intervention should follow, i.e., if the intervention as intended was feasible and/or adhered to with a discussion of the solutions where this was not possible. Dietary adherence is also essential to understand in nutrition studies, and authors should describe if an adherence assessment was conducted and include an evaluation of its adequacy. Also included here should be a discussion on how many participants were lost due to poor adherence, and how this affects statistical analyses.

Common limitations such as potential sources of bias e.g., selection bias based on uneven distribution of prognostic factors such as nutritional status, data sources or assessment methods, imprecision, and multiple testing, can also affect nutrition trials. Of particular concern for nutrition trials, however, is the potential bias due to lack of (or partial) blinding and quality control of the intervention, including the assessment of adherence, the active constituent(s) of the intervention and its stability/feasibility over time, interaction with food matrix and diet, duration of intervention. Potentially false discoveries due to the type of adjustments used in statistical analysis need to be acknowledged, as well as a consideration of the likely impact of habitual intake or nutrition status of the participants on the response to the intervention.

Authors should discuss the generalizability of the findings, considering the background diet of the participants, the likely variations in nutrition in other populations and the comparator used in the control group. Authors need to describe to the reader if the findings apply to the general population or to specific groups. A clear separation needs to be made between research findings from efficacy or effectiveness studies when inferring implications of the study findings on nutrition or health benefits of other populations.

Finally, the interpretation of the findings is a key concern. A clear separation needs to be made between statistical and findings of clinical significance as they refer to clinical/biological or health effects, e.g., a reduction in systolic blood pressure of 10 mmHg, and including both relative (risk ratio) and also absolute effects (x cases per /1000) for binary outcomes. Interpretation of effects in general needs to consider the precision of the assessment of the outcomes and whether the effects are clinically meaningful from an individual or population perspective. For example, a small risk ratio (RR, 0.95) can have a considerable absolute effect for a common disease (e.g., type 2 diabetes) at population level. Furthermore, a distinction should be made between whether the effect is from the intervention itself or food or supplement use during the intervention period. The manuscript should discuss how the findings affect clinical practice, dietary guidance, or public health recommendations. Further discussion of the findings should consider how nutritional interventions can be achieved in practice considering dietary habits, culture, socio-economic barriers, and concerns regarding environmental footprints. The feasibility of implementing the intervention in different settings should be discussed, deliberating on how each of the afore-mentioned factors can affect adherence.

Box 4: Proposed additions to CONSORT checklist for “Discussion” in manuscripts describing diet-related and nutritional trials

- Cover generalizability of the findings, interpretation, and limitations of the study clearly in key sections of the discussion.
- State the main findings of the paper, using intention-to-treat principles, with per protocol interpretations given in addition, depending on the objective of the study. Provide a clear differentiation for these findings from ancillary analyses.
- Discuss the choice of comparator, including whether isocaloric exchange was used or not, and any bias introduced.
- Discuss any assessment of dietary adherence.
- Discuss any relevant aspects on the active constituent of the intervention as revealed by the trial.
- Describe any potentially false discoveries due to any adjustments used in statistical analyses.
- Clearly discuss generalizability with consideration to background diet and any variation in other populations, ensuring a differentiation between efficacy and effectiveness.
- Distinguish clearly between statistical and clinically relevant findings, with detailed interpretation on how the findings affect clinical practice, dietary guidance, or public health recommendations, as relevant.

8. Other information

CONSORT guidelines refer to trial and protocol registration and declaration of sources of funding. The conflict of interest statement may require additional detail for nutrition trials. Rowe et al. [64] previously summarised the challenges and good practices to carry out research funded by the

private sector and food industry, in particular. The International Committee of Medical Journal Editors (ICJME), as well as many nutrition journals to date, provide instructions on how to identify and report conflicts of interest. Despite this, however, there are concerns and emerging evidence that findings of nutrition trials are affected by the funding source [65, 66]. It is essential that authors ensure transparency in sources of funding (including provision of resources such as food or food products for the trial) and potential sources of conflict. This will facilitate correct interpretation of findings, synthesis of evidence and overall transparency in reporting research.

There might be additional personal factors relating to the researchers (e.g., food preferences, restrictions,) that could induce confirmation bias and affect research findings. Authors should consider disclosing these and any other conflicts of interest that are considered essential for external readers to assess the study findings and determine potential bias.

Availability of study material is an essential aspect of reporting completeness for nutrition trials. In addition to CONSORT recommendation to share study protocol however, there is increasing attention to make other research products available i.e., questionnaires, standard operating procedures (SOP), statistical analysis plans, syntax for data manipulation and analysis, and (meta)data. Most journals have clear instructions and policies on availability of data, including provisions to handle data on a sensitive patient level. Repositories such as Github FAIRSHARING, the Open Science Framework (OSF) are at hand to enhance Findability, Accessibility, Interoperability and Re-use of resources from nutrition trials.

Box 5: Proposed additions to CONSORT checklist for “Other Information” in manuscripts describing diet-related and nutritional trials

- Include additional details in the conflict of interest statement where relevant.

- Where possible, make research products such as questionnaires, standard operating procedures, data syntax and metadata available.

Discussion

We propose important considerations that need to be addressed when assessing the CONSORT checklist to improve the rigour of reporting nutrition RCTs. The exercise illustrates the relevance and potential value of a nutrition extension to CONSORT and illustrates the extent of gaps in reporting for reproducibility and interpretation of results. In a second step, we will obtain peer feedback on our findings from the nutrition community and relevant stakeholders via (i) a workshop for attendees at the International Union of Nutritional Sciences (IUNS) conference 2022, (ii) an online forum to capture comments on this manuscript, and (iii) feedback from editors of targeted nutrition-related journals.

Further work remains to draft, test and propose authoritative reporting guidance. To date, the Enhancing the QUAlity and Transparency Of health Research (EQUATOR) network hosts hundreds of guidelines to facilitate reporting of research findings. A programme, Securing Transparency And Reproducibility in studies of NUTritional interventions (STAR-NUT), is implemented to consolidate reporting standards for randomised controlled trials and systematic reviews of nutritional interventions [67]. STAR-nut involves a comprehensive review of literature and consultation of stakeholders including journal editors to determine what guidance for nutrition trials is most appropriate, which will provide further input for drafting potential future guidelines.

It is important that care is taken to ensure consistency among reporting guidelines. The FENS working group maintains close contact with EQUATOR, the STAR-NUT study team, and the STROBE-nut development group to ensure a consistent message is presented. Care should

equally be taken to incorporate revised versions of CONSORT and SPIRIT, for which guidance is presently updated and consolidated [68]. To further improve and increase adoption of the final guidelines, we encourage readers to engage in this process, provide comments and conduct specific studies to inform further work on the development of reporting guidelines for nutrition trials.

Conclusion

We identify the need to develop guidance for the reporting of nutrition trials to increase consistency and transparency in reporting, the overall quality of the conduct of trials, and ultimately the evidence base in diet nutritional status and health. Using CONSORT as a framework, we report here the first output of this iterative process to develop such guidelines for the nutrition community. The FENS working group acknowledges the challenges to reporting of other nutrition research findings including policy interventions for nutrition-sensitive interventions that are, in essence, not specifically focused on nutrition but have a large potential to improve nutrition and diets of populations [69]. Nevertheless, as a discipline and in terms of research integrity, it is very important that the nutrition field embraces robust and consistent reporting of dietary studies and nutrition trials.

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