Preparation of Methodological Systematic Reviews in Nutrition Science

A Didactic Guide

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Systematically gathering scientific evidence is necessary to build and support safe concepts, treatments, and effective actions for health practice, policies, and recommendations in the field of nutrition. This didactic guide aimed to compile the steps necessary for a methodological systematic review in nutrition through real examples including the mandatory stages of conduct such as preparation of the central question, search strategy, inclusion and exclusion criteria, data collection, extraction of information, and methodological quality analysis of the studies. The article demonstrates that methodological systematic reviews are valuable to track the progress of concepts and practices. In this way, knowledge of the review process is important for the advancement of the field, and reviews are important resources for scientific information due to their synthesis of current evidence. Nutr Today. 2021;56(6):279–286

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This study was supported by Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES) of Brazil through the postdoctoral fellowship of researcher N.S.G. for 2 years (May 2019 to May 2021) (grant number: 88887.357990/2019-00).

The authors have no conflicts of interest to disclose.

Author Contributions: Substantial contributions for the conception or design of the manuscript: N.S.G., M.A.F., and S.M.d.F. Substantial contributions for data acquisition, analysis, or interpretation: N.S.G. Manuscript formulation: N.S.G. Critically revised the manuscript in relation to the important intellectual content: all authors. Final version's approval: all authors. Agreed to be responsible for all aspects of the work, ensuring that issues related to precision of integrity in any of the work's parts will be properly investigated and solved: N.S.G., M.A.F., and S.M.d.F.

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DOI: 10.1097/NT.0000000000000516

Evidence-based nutrition practice can be defined as the cautious, explicit, and wise use of the best scientific evidence for the development of public policies and other decisions that have the objective of promoting public health.[1–3] It is necessary for researchers to use methodological rigor as a guiding principle.[4] Systematically grouping evidence enables professionals and stakeholders to understand the scenario synthetically and critically in the face of contradictions and uncertainties in nutrition.[5–7]

The exponential increase in scientific evidence of primary and secondary studies of the science of nutrition has reinforced the commitment of researchers worldwide to improve evidence-based reviews. However, processing existing information in the face of a growing body of literature has become challenging. Considering the available methodologies and scientific designs, systematic reviews of the literature provide a way to summarize the best scientific evidence.[8,9]

Considering the absence of didactic guides so that researchers can more easily conduct methodological systematic reviews in the nutrition area, this work aims to describe crucial steps for the elaboration of methodological systematic reviews.

CONCEPTS

Literature reviews are secondary studies characterized by the collection, analysis, and presentation of information

about a specific theme, hypothesis, or guiding question to synthesize existing knowledge and summarize the subject of interest.[10] There are several types of methodological literature review studies that are classified according to the objectives and process of conducting the review.[10–14]

Narrative or traditional reviews are descriptive syntheses of studies on a broad topic without a previous protocol. The process can involve only 1 or 2 authors who choose studies without a previous definition of the methods used to select the articles. In this review, the quality of evidence must not be explicit.[15] The aim of narrative reviews is to cover a broad theme that focuses on 1 point of knowledge. An example of a narrative review is the study by Martinelli and Cavalli[16] (2019).

Integrative reviews synthesize a broad theme or subject by 2 or more authors. In this type of review, authors must outline and insert methodological steps, such as defining the inclusion and exclusion criteria, databases included in the investigation, search strategy, and number of studies found. The presentation must be described in a separate section; however, it must not present and interpret evidence quality.[17,18] The study of Gomes and collaborators[19] (2019) is an example of an integrative review.

Systematic reviews are based on a scientific research design directed by a central question in which the process includes at least 3 authors. The authors must follow rigorous, transparent, and reproducible processes of scientific data identification, selection, analysis, and interpretation as well as methodological quality. An example of a systematic review is the study by Ojha et al[20] (2020). This objective is a structured central question, and the methodology followed to answer this goal is classified as a systematic review. This design must be developed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis Protocols.[21] Other existing guidelines include handbooks by the Cochrane Collaboration[22,23] or Campbell Systematic Reviews.[24,25]

A crucial planning point differentiates this review from the others presented; the methodology used in a systematic review must be submitted to a database. For this reason, this type of methodology provides a more detailed description of the planning steps (eg, PROSPERO University of York, Campbell Collaboration, and Joanna Briggs Institute).[24,26,27]

STAGES OF SYSTEMATIC REVIEW

Planning

To begin a systematic review, we must establish a well-founded hypothesis on the subject.[28] Thus, reflection on the topic of interest and the formation of a hypothesis or question about the subject under review is a necessary and crucial step for determining the review's feasibility.[29]

Next, the authors should research and reflect on the gaps in scientific knowledge (questions that have not yet been answered clearly and explicitly in the literature). As with any other scientific investigation, systematic reviews must be performed around a well-formulated and clear question (central question or guiding question). The central question to be answered by the organized synthesis of evidence reflects the knowledge gap of a given theme.

The central question must be developed based on previous reasoning and is usually guided by an established structure.[30] Several models guide the construction of central questions (eg, PICO, PECO, POT, or SPICE) and vary according to the study objective (Figure 1).[31]

For systematic methodological reviews in the field of nutrition, PICO and PECO, differentiated by the intervention or exposure group, are used more frequently. The acronym "PICO" stands for P = population, patients, target audience; I = intervention of interest; C = comparator group; and O = outcome or result.[31] The acronym "PECO" stands for P = population, patients, target audience; E = exhibition; C = comparator group; and O = outcome. To facilitate understanding, we present the following situations in the nutrition area:

Situation 1

After extensive study of nutritional therapy in the treatment of hypercholesterolemia (dyslipidemia characterized by increased serum cholesterol levels in the body), researchers wanted to investigate whether the use of golden flaxseed is an effective therapy for reducing hypercholesterolemia compared with statin drug treatment. The critical question was "Is golden flaxseed effective in reducing hypercholesterolemia compared to drug therapy?" with the following details:

P = individuals with hypercholesterolemia
I = use of golden flaxseed
C = statin-derived drugs (eg, simvastatin or rosuvastatin)
O = improvement in serum cholesterol levels

Situation 2

After a preliminary review of the literature on alcohol consumption among university students, researchers wanted to investigate whether excessive alcohol consumption is associated with overweight or obesity among university students. Thus, the following central question was outlined: "Is there an association between excessive alcohol consumption and excess weight in university students?" with the following details:

P = university students
E = excessive consumption of alcoholic beverages
C = no, light, or moderate consumption of alcoholic beverages
O = overweight (overweight or obesity)

When the review objective requires a particular timespan for the search or design of the included studies, structural derivations are possible. The acronym "T" stands for the timespan included in the search (in situation 1, the starting

Acronyms	Definitions
PICO	P=population or patients; I=intervention; C=control group; O=outcomes
PECO	P=population or patients; E=exposure; C=control group; O=outcomes
POT	P=population or patients; O=outcomes; T=type of study
SPICE	S = Setting – where?; P = Perspective – for whom?; I= Intervention – what?; C= Comparison – compared with what?; E= Evaluation – with what result?

FIGURE 1. Models to guide the construction of central questions.

year could be stipulated as the year of statin manufacture), and the acronym "S" stands for the type (design) of studies that must be investigated to answer the central question (eg, controlled clinical trials, case reports).

After developing the objective, it is necessary to consult bibliographic records such as the Cochrane Library (https://www.cochranelibrary.com/), Turning Research Into Practice (https://www.tripdatabase.com/), and Prospective International Registry of Systematic Reviews.[32] After updating or confirming that the central question is unique, it is necessary to reflect on the potential application of the central question. The suggested questions are as follows:

- Does the guiding question instigate decision making?
- Is the central question relevant to clinical practice and/or health services?
- Will the elaborated central question add guidance to nutritionists, other health professionals, and health managers?
- Is the question relevant to the progress of nutrition science; that is, does it guide future research?
- Is there biological plausibility for the action and outcome of the nutrient under study?

For these reflections to be productive, it is suggested that the group of researchers performing the review relies on the opinion of 1 or more external collaborator(s) who are specialists in the subject of interest.

Data Collection

Information sources, also known as platforms or databases, may or may not be electronic. For the field of nutrition, among the various existing electronic data platforms, PubMed,[33] Excerpta Medica Database (EMBASE),[34] Cochrane Library (Central),[35] and Latin American and Caribbean Literature in Health Sciences (LILACS) stand out.[36]

PubMed is the most widely used scientific literature data platform in the health sciences worldwide. This platform is operated by the National Center for Biotechnology Information at the National Library of Medicine, one of the National Institutes of Health. It currently includes approximately 30 million references and encompasses the Medical Literature Analysis and Retrieval System database online (MEDLINE or PubMed). EMBASE is a scientific literature data platform with the widest range of scientific research in health sciences that is operated by Elsevier.[37] The Cochrane Library (Central) is a scientific literature data platform run and administered by the Cochrane Collaboration, a nonprofit organization with the purpose of preparing, maintaining, and promoting access to high-quality information. This platform has the largest framework for randomized clinical trials worldwide.[38,39] LILACS is operated by the Latin American and Caribbean Center on Health Sciences Information and includes the Scientific Electronic Library Online database (https://scielo.org/) as well as official institutional databases (such as documents published by the Brazilian Ministry of Health). The main databases used in systematic methodological reviews in the area of nutrition are described in Figure 2, which includes the electronic address and the comparison of the potential and access form of each of the databases presented.

Other sources should be considered depending on the guiding question of the review. These sources can be identified through a manual search by checking the list of publications in printed sources. Among the types of documents in a manual search are the proceedings of congresses, monographs, dissertations, theses, scientific initiation reports, clinical trial records, government reports, and reference lists. Such literature, often called the gray literature, is not an easily accessible document or source. These sources will be included in the gray literature section of the systematic review.[40,41] The gray literature encompasses materials with negative results; thus, it helps researchers minimize the publication/selection bias of the included studies.

Electronic base	Site	Potentialities/ Access form
PubMed	https://pubmed.ncbi.nlm.nih.gov/	Extensive scientific literature / Free
Embase	https://www.embase.com/login	Extensive scientific literature / Pay
Cochrane Library	http://www.cochrane.org	Extensive scientific literature of systematic reviews or clinical trials / Free
Lilacs	https://lilacs.bvsalud.org/	Literature limited to Latin America / Free

Note: Embase -Excerpta Medica Database; LILACS - Literatura Latino-Americana e do Caribe em Ciências da Saúde

FIGURE 2. Description of the electronic addresses of databases used in systematic methodological reviews in the nutrition science. EMBASE, Excerpta Medica Database; LILACS, Literatura Latino-Americana e do Caribe em Ciências da Saúde.

Situation 3

Suppose a team of researchers wants to conduct a systematic review that aims to survey the evidence on the number of new cases of obese patients given a diagnosis of COVID-19 using mechanical ventilation. This group, after structuring the guiding question of the review and searching for the information in the chosen databases, should search hospital records and epidemiological bulletins because these materials are essential to increasing the investigated response. These materials, which have not been officially published in electronic databases, are part of the so-called gray literature.

After selecting the databases and/or gray literature, researchers must understand the databases chosen, especially the controlled vocabulary used by each one. This indexed and specific vocabulary is referred to as "terminology," "uniterms," "descriptors," and "keywords," whereas the use of these in various combinations is called the "search strategy."

Each database uses a specific vocabulary and, consequently, has specific descriptor bases. The most standardized descriptor bases are medical subject headings (MeSH; PubMed), DeCS (LILACS), and Emtree (EMBASE). The links to these databases are available in the Supplementary Materials (https://www.ncbi.nlm.nih.gov/mesh, http://decs.bvs.br/, and https://www.embase.com, respectively).

Situation 4

Take the following central question: "Is the transtheoretical model an effective tool for assessing the change in eating behavior of adolescents with binge eating?" with the following details:

P = adolescents with binge eating
I = transtheoretical model
O = change in eating behavior

When searching for the descriptors for "I" (intervention = transtheoretical model or Transtheoretical Model) in MeSH, the term is indexed under "Biobehavioral Sciences," whereas there is no index for the item in DeCS.

The search strategy is defined as a standardized set of rules for researching a central question in a specific database. In other words, the search strategy is the most effective resource for the recovery of potential studies to answer a question. Among the items belonging to the search strategy are Boolean operators. The Boolean operator "AND" is used to intersect acronyms, whereas the Boolean operator "OR" is used to sum them. The "NOT" and "AND NOT" operators, used by PubMed and LILACS, respectively, have exclusion functions. Methodologists or librarians are professionals responsible for the proper use of search vocabulary. The specific search strategy is of utmost importance because an inadequate search strategy may overestimate or underestimate the potential studies found.

Here is an example of the search strategy used in PubMed: sensitive search strategy: (infant, newborn[MeSH] OR newborn OR neonate OR neonatal OR premature OR low birth weight OR VLBW OR LBW or infan* or neonat*) AND (randomized controlled trial [pt] OR controlled clinical trial [pt] OR randomized [tiab] OR placebo [tiab] OR drug therapy [sh] OR randomly [tiab] OR trial [tiab] OR groups [tiab]) NOT (NOT animals [mh])) ➜ studies found 15 673 results. The search was conducted on October 1, 2020. Nonsensitive search strategy: infant, newborn, and trial ➜ studies found 36 257 results. The search was conducted on October 1, 2020.

Data Eligibility

Selection

The selection of data (scientific studies) eligible for a systematic review should, as a rule, be performed independently by at least 2 researchers. At this stage, eligibility criteria are used, encompassing criteria for inclusion or exclusion from the final data analysis, that must be applied in stages (analysis of titles, abstracts, and texts).[42] Consider this example of the inclusion and exclusion criteria.

> Relationship of different fruit and vegetable sources with incident cardiovascular outcomes: a systematic review and meta-analysis of prospective cohort studies.[43]
> Aim: To evaluate the relationship between fruit and vegetable sources and cardiovascular outcomes.
>
> Inclusion criteria: adults and the elderly; cohort studies; studies that quantified fruits and vegetables and showed an association with cardiovascular outcomes.
>
> Exclusion criteria: children and adolescents; other study designs; revisions; studies that did not quantify fruits and vegetables and/or did not show an association with cardiovascular outcomes.

After the application of search strategies in the bibliographic databases, repositories are formed that must be merged to identify duplicates. In this step, reference manager software such as EndNote, Mendeley, Rayyan, and Zotero is extremely useful.

Software can also be very useful for assisting in the organization of eligibility. Covidence, for example, is software integrated with RevMan to assist with study eligibility assessments; however, it is available only to Cochrane researchers or by subscription for a price. Other software such as RevMan or SUMARI from the Joanna Briggs Institute can be used after the initial eligibility process to organize the layout of the chosen studies.

The first stage of the eligibility process is performed by at least 2 researchers screening the titles and abstracts. If there are disagreements in the eligibility process, a third researcher resolves any disagreements, or disagreements are settled through consensus meetings.[42]

After this stage, a full-text review is necessary. This is the stage in which each study, obtained in PDF format, should be read, checked for the central question, and, finally, reviewed for the PICO or PECO elements. In the full-text review, each study must also be evaluated independently by at least 2 researchers. If there are disagreements in the eligibility of the studies, they should also be resolved by a third researcher.[42,44]

The included or excluded studies must be registered through the standard flowchart of systematic reviews as requested by Preferred Reporting Items for Systematic Reviews and Meta-Analysis.[26] Proper registration of the flowchart contributes to its reproducibility.

Extraction of Information

The information should be extracted from the selected studies and placed in a summary table to avoid standardization of the final text. In general, data are extracted about the author, date, place of publication, study design, general information about the participants of the research (number, sex, age), intervention or exposure, outcomes, and main results.

Quality of Evidence

The methodological quality of a study was associated with a lower risk of bias. The results of good-quality studies are more reliable. On the other hand, a higher degree of uncertainty is present in the results of low-quality studies. Because more uncertainty is present in low-quality studies, their use is not recommended because the risk of bias is elevated. This step to reduce the risk of bias is very important in the development of a systematic review.[45]

During the analysis of evidence quality, the reviewers determined whether the methodology was adequate for the given results.[46] For the design of reviews involving nutrition, the validated scales presented in Figure 3 are useful. In addition, at least 2 independent reviewers should evaluate the quality of the studies included in the review and any differences between them should be resolved by consensus or a third reviewer.

Evaluating the Certainty of Evidence

The GRADE system evaluates the quality of evidence based on a hierarchy of study design.[47] The advantage of GRADE is that it recognizes that the strength of observational evidence is more uncertain due to study design heterogeneity, exposure measurement errors, confounding factors, and adjustments for them. Thus, GRADE evaluates the certainty of evidence and weighs it appropriately.[48]

Summary, Synthesis, and Presentation of Information

The extracted information must be synthesized to obtain valid conclusions. Thus, the synthesis of information involves the collection, approximation, combination, and, finally, a summary of the results of the individual studies included in the systematic review.

The purpose of the data synthesis, however, is to understand whether the results stated in the primary studies are

Scale of evidence quality	Study type	Electronic address
Cochrane risk of bias (RoB) tool	Clinical trials	https://methods.cochrane.org/bias/risk-bias-tool
Oxford Quality Scoring System (JADAD)	Clinical trials	https://onlinelibrary.wiley.com/doi/pdf/10.1002/9780470988343.app1
The Newcastle-Ottawa Scale (NOS)	Cohorts, Case-Controls	http://www.ohri.ca/programs/clinical_epidemiology/nosgen.pdf
Joanna Briggs critical appraisal tools	Cross-sectionals	https://jbi.global/sites/default/files/2019-05/JBI_Critical_Appraisal-Checklist_for_Analytical_Cross_Sectional_Studies2017_0.pdf
Quality Assessment of Diagnostic Accuracy Studies (QUADAS-2)	Diagnostic accuracy studies	https://pubmed.ncbi.nlm.nih.gov/22007046/
SYRCLE's risk of bias tool for animal studies	Experimental studies (pre-clinical)	https://bmcmedresmethodol.biomedcentral.com/articles/10.1186/1471-2288-14-43
Collaborative Approach to Meta-Analysis and Review of Animal Data from Experimental Studies (CAMARADES)	Experimental studies (pre-clinical)	https://www.ed.ac.uk/clinical-brain-sciences/research/camarades
A MeaSurement Tool to Assess Systematic Reviews (AMSTAR)	Systematic Reviews	https://amstar.ca/Amstar_Checklist.php
Risk Of Bias In Systematic reviews (ROBIS)	Systematic Reviews	https://www.jclinepi.com/article/S0895-4356(15)00308-X/fulltext
Appraisal of Guidelines for Research and Evaluation (AGREE)	Clinical Guidelines	https://www.agreetrust.org/
International Network of Agencies for Health Technology Assessment (INAHTA)	Health Technology Assessment Reports	http://www.inahta.org/hta-tools-resources/briefs/

FIGURE 3. Description of the electronic addresses of the scales used to evaluate the quality of evidence of primary studies in systematic methodological reviews of the nutrition science.

consistent. If not, the summary should investigate possible reasons for this.

The synthesis can be performed quantitatively using statistical treatment (called a meta-analysis) or through the narrative approach, in which the data are not quantitatively analyzed.

The entire process of planning, executing, and writing the systematic review requires resources, whether personal or financial, to acquire the minimum necessary elements. The research team should consist of at least 3 researchers with advanced scientific knowledge; at least one should be an expert in the subject of the central question, whereas another should understand the methodology of conducting and presenting the research review.

Financial resources include the purchase of computers, office supplies, access to fee-based platforms (such as the EMBASE database), and perhaps other services such as translation or submission and publication fees for certain scientific journals.

Scoping Reviews in Nutrition

Scoping reviews are used to map the concepts underpinning a research area and the main sources and types of available evidence. Scoping reviews are a relatively new approach to synthesizing evidence, and there is currently little guidance regarding the decision to choose between a systematic review or scoping review approach when synthesizing evidence. Scoping reviews are useful for examining emerging evidence when it remains unclear what other, more specific questions can be posed and valuably addressed by a more precise systematic review.[49]

The reasons for conducting a scoping review according to Munn et al[50] (2018) are as follows:

- To identify the types of available evidence in a given field
- To clarify key concepts/definitions in the literature
- To examine how research is conducted on a certain topic or field
- To identify key characteristics or factors related to a concept
- As a precursor to a systematic review
- To identify and analyze knowledge gaps

CONCLUSIONS

The description of a systematic review involving central questions in nutrition or other sciences requires transparency and explicit researcher objectivity. For this, knowledge of the concepts and a description of the process are extremely important for progress in the construction and discovery of treatments and/or effective actions for nutrition practice, assistance, policies, and recommendations.

Acknowledgments

The researcher Dr Nathalia Sernizon Guimarães would like to thank all the researchers who helped her in her training and improvement as a methodologist of systematic reviews with or without meta-analysis, especially her MSc and PhD advisors Professor Maria Arlene Fausto and Professor Unaí Tupinambás and the respective postgraduate programs represented by them.

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Disclosure Statement: The author and planners have disclosed no potential conflicts of interest, financial or otherwise.