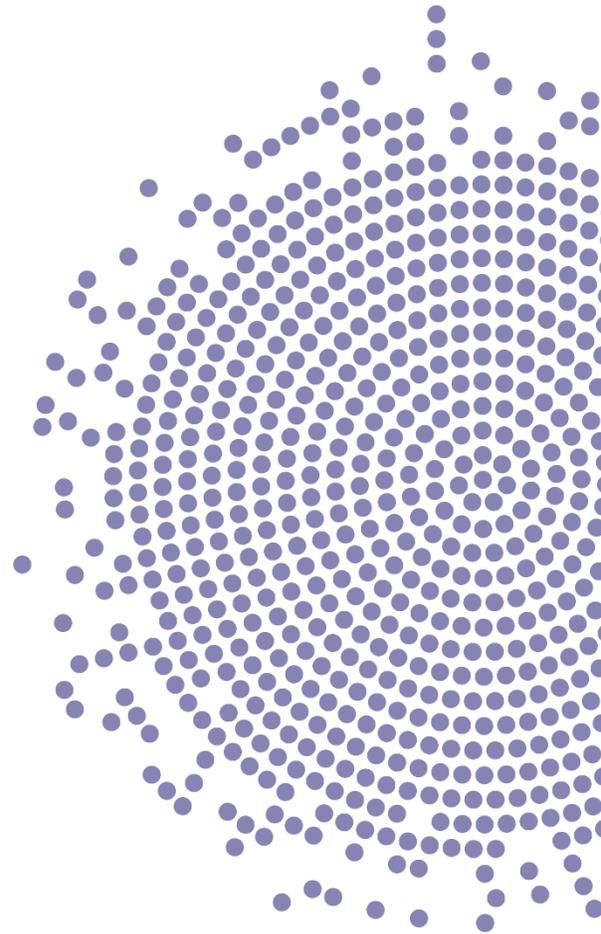




UNITED STATES DEPARTMENT OF AGRICULTURE

# USDA Nutrition Evidence Systematic Review: Methodology Manual



**Suggested citation:** USDA Nutrition Evidence Systematic Review Branch. *USDA Nutrition Evidence Systematic Review: Methodology Manual*. February 2023. U.S. Department of Agriculture, Food and Nutrition Service, Center for Nutrition Policy and Promotion, Nutrition Evidence Systematic Review. Available at: <https://nesr.usda.gov/methodology-overview>.

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# Chapter 1: Introduction to USDA's Nutrition Evidence Systematic Review

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The Nutrition Evidence Systematic Review (NESR) team was launched in 2008 by USDA's Center for Nutrition Policy and Promotion (CNPP) to conduct food- and nutrition-related systematic reviews and other evidence synthesis products. NESR supports CNPP's mission to improve the health of Americans by developing and promoting dietary guidance that links scientific research to the nutrition needs of consumers. NESR is a key resource for the Federal government when making evidence-informed decisions related to public health nutrition, such as the development of the *Dietary Guidelines for Americans*.

This chapter provides an overview of the NESR team and a brief description of how NESR works with various collaborators to conduct systematic reviews. A detailed description of these collaborations has been published elsewhere. Throughout the remaining chapters of this methodology manual, NESR's systematic review methodology is described in detail. Each chapter also describes the roles and responsibilities that the NESR team and its collaborators play in implementing this methodology.

## The Nutrition Evidence Systematic Review team

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NESR is a team of career Federal scientists, made up of analysts and librarians. NESR's work upholds the Data Quality Act,<sup>1</sup> which mandates that Federal agencies ensure the quality, objectivity, utility, and integrity of the information used to form Federal guidance. NESR also upholds the principles of USDA's Scientific Integrity Policy, which specifies that USDA employees who use scientific information to support policy- and decision-making are responsible for ensuring the quality, accuracy, and transparency of that information, and should do so without political or inappropriate influence.<sup>2</sup>

NESR analysts have doctoral (PhD, DrPH) or master's (MS, MPH) degrees in nutritional science or a related field such as public health, biochemistry, biology, or biostatistics. Some are registered dietitians (RD) or registered dietitian nutritionists (RDN). NESR analysts are scientists who have conducted research and have expertise on a range of diet and health-related topics.<sup>3</sup> Analysts also have expertise in systematic review and evidence synthesis methodology (e.g., risk of bias assessment, grading the strength of evidence, meta-analysis), technology (e.g., software for literature screening, data extraction, reference management, and statistical analyses), and have experience with project management and meeting facilitation.

NESR librarians are information specialists with master's degrees in library and information science, and experience with biomedical topics. NESR librarians have expertise in methodology and technology related to literature searching (e.g., software for literature screening, reference management used for developing, implementing, and documenting literature searches). They also have in-depth knowledge of bibliographic databases (e.g., PubMed/MEDLINE, Cochrane, Embase, CINAHL), including search terms appropriate for each database, and search refinements, such as search filters.

The NESR team also has experience with science communication, including developing and publishing peer-reviewed articles and scientific reports, writing in plain language, presenting to a wide range of audiences, and curating website content.

## Collaborators of NESR systematic reviews

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NESR systematic reviews are conducted in collaboration with expert groups, and with input from Federal and public stakeholders. Conducting reviews with the input and support of diverse collaborators helps provide informed and unique perspectives, and helps maintain the rigor, integrity, and trustworthiness of NESR systematic reviews. NESR's systematic review methodology clearly delineates the roles and responsibilities of those involved in the review process. NESR systematic reviews utilize collaborators' expertise, while managing potential biases and conflicts of interest. The sections below briefly describe the collaborators involved in the NESR systematic review process.

### Federal stakeholders

Federal stakeholders are career staff from a broad range of Federal agencies with nutrition-related mission areas, such as the USDA, U.S. Department of Health and Human Services (HHS), U.S. Department of Veterans Affairs, U.S. Environmental Protection Agency, U.S. Department of Defense, and the U.S. Agency for International Development. Federal stakeholders play numerous roles within their agencies, including as scientists, nutritionists, program- and policy analysts, or guideline and policy developers. Federal stakeholders have an interest in NESR systematic reviews and/or the evidence supporting them and may be responsible for commissioning a NESR review and/or provide input at various points during the review process. Federal stakeholders may have advanced degrees in nutritional science or a related field, subject matter expertise in topics related to diet and health, knowledge of the operations and needs of Federal guidance or nutrition-related programs, experience with systematic reviews or evidence synthesis methods, or oversight of research funding. Federal stakeholders are employees of the U.S. government and must adhere to agency scientific integrity policies, and other statutes, regulations, and agency policies governing ethical conduct.<sup>4-14</sup>

### Expert groups

Expert groups include nationally recognized scientific experts with demonstrated subject matter expertise on the topic(s) addressed in the NESR systematic review project. These scientific experts have advanced degrees in nutritional science, medicine, and/or a closely related field. Experts may be health professionals (e.g., physicians, registered dietitians, public health practitioners), researchers (e.g., trialists, epidemiologists, food scientists), and/or have specific methodology expertise (e.g., data analysis, systematic review, meta-analysis, or food pattern modeling). They may be Federal employees or external to the Federal government. Expert group members are selected to participate in NESR reviews based on their scientific expertise, but groups are also formed to ensure that membership is balanced and diverse in terms of points of view, expertise, experience, education, and institutional affiliation, as well as race and ethnicity, gender, and geographic location. Potential conflicts of interest (COI) are also assessed and taken into consideration when forming expert groups to determine whether anything could potentially bias the technical contributions of an individual or give the appearance of bias. If such potential COI are found, an expert may not be invited to participate, or, may participate, but NESR team will manage the potential conflicts. Management of COI involves ensuring that when the evidence is evaluated and synthesized, the diverse viewpoints and subject matter expertise of *all* expert group members is used to make decisions.

NESR collaborates with two types of expert groups: a Technical Expert Collaborative (TEC), or a Federal Advisory Committee (FAC) known as the Dietary Guidelines Advisory Committee.

## Technical Expert Collaborative

A TEC is a group of approximately six to eight subject matter experts who may be internal or external to the Federal government. TEC members are convened by NESR and other Federal stakeholders and work with NESR to conduct systematic reviews<sup>15-17</sup> that describe the state of the science on a particular question. However, because a TEC is not a FAC, it does not provide recommendations to the government on the basis of their review. TEC members serve without pay for a period of 1-2 years, depending on the size and scope of the project. TEC members disclose potential COI prior to their appointment and periodically during the project. Disclosures are reviewed by the USDA Office of Ethics to ensure members have no financial COI that would prohibit serving on the TEC or that would require management by the NESR team.

## Dietary Guidelines Advisory Committee

The Dietary Guidelines Advisory Committee (the Committee) is a FAC convened by USDA and HHS prior to developing an updated edition of the *Dietary Guidelines for Americans* every five years. The Committee collaborates with Federal staff, including NESR, to conduct systematic reviews, data analyses, and food pattern modeling, and integrates their findings into their Scientific Report.<sup>18</sup> This report provides HHS and USDA with the Committee's independent, science-based advice and recommendations that the Departments consider, along with input from Federal agencies and the public, when developing the next edition of the *Dietary Guidelines for Americans*.<sup>19</sup> A FAC is governed under the Federal Advisory Committee Act (FACA); thus, members undergo training for the FACA and the processes used for reviewing the evidence. The Committee consists of approximately 20 members, all of whom are external to the Federal government, and have demonstrated expertise on the topics and questions to be addressed. Members are nominated by the public and serve for up to 2 years without pay. Committee members must complete the U.S. Office of Government Ethics Form 450 Confidential Financial Disclosure Report<sup>20</sup> prior to appointment and annually throughout their term. All candidates' financial disclosures are reviewed by the USDA or HHS Office of Ethics to ensure candidates have no financial, ethical, legal, and/or criminal COI that would prohibit serving on the Committee. Members are appointed as Special Government Employees and must comply with applicable COI statutes, regulations issued by the U.S. Office of Government Ethics, supplemental agency requirements, and other applicable Federal ethics rules. Members receive ethics training on these rules and regulations prior to beginning service on the Committee.

## Public stakeholders

Public stakeholders include non-Federal individuals and organizations who have an interest in NESR systematic reviews, the evidence supporting them, and/or the decisions that will be made based on the findings and provide input at various points during the review process. Public stakeholders include individuals and organizations acting on their own behalf, or on behalf of their organization, such as consumers, health professionals, researchers, industry professionals, members of the media, students, academics, community partners, scientific societies, and others with interests in diet and health. Public stakeholders have varying expertise, which may include having advanced degrees in nutritional science or a related field, subject matter expertise in topics related to diet and health, knowledge of the operations and needs of nutrition- or public-health related policies and programs, involvement with nutrition-related communications or education, lived experience with individuals and communities, or oversight of research funding. All public stakeholders who provide written or verbal comments are requested to disclose their affiliation.

## NESR projects

NESR’s work answers nutrition questions of public health importance by conducting high-quality systematic reviews, rapid reviews, evidence scans, and continuous evidence monitoring using transparent, rigorous, and protocol-driven methods (Table A). NESR’s methodology aligns with methods used by other organizations that conduct systematic reviews,<sup>21-32</sup> and NESR’s Continuous Quality Advancement initiative ensures that its process and tools remain state of the art. NESR keeps abreast of the latest science and technology by leveraging the expertise of and collaborating with methodologists from other leading systematic review organizations.

**Table A. USDA’s Nutrition Evidence Systematic Review evidence synthesis products**

Evidence synthesis product	Definition
<b>Systematic Review</b>	A gold-standard evidence synthesis project that answers a nutrition question of public health importance using systematic, transparent, rigorous, and protocol-driven methods to search for, evaluate, synthesize, and grade the strength of the eligible body of evidence.
<b>Rapid Review</b>	An evidence synthesis project that answers a nutrition question of public health importance using streamlined systematic review methods. Methods used to search for, evaluate, synthesize, or assess the evidence may be tailored to conserve resources and produce a timelier product when full systematic review methods are not needed or feasible.
<b>Evidence Scan</b>	An exploratory evidence description project in which systematic methods are used to search for and describe the volume and characteristics of evidence available on a nutrition question or topic of public health importance. Evidence scans can be either stand-alone projects or the beginning steps of conducting a rapid or systematic review.
<b>Continuous Evidence Monitoring</b>	An evidence gathering process in which established systematic review protocols are used to periodically search for, screen, and prepare evidence for future systematic reviews.

## Funding

NESR systematic review projects are funded solely by Federal government agencies and programs, based on the needs identified by Federal stakeholders and/or in support of the development of the *Dietary Guidelines for Americans*. Federal stakeholders are responsible for identifying and describing high-priority topics that represent gaps in Federal program knowledge or dietary guidance, and for commissioning NESR to initiate systematic review projects to address these topics. Funding for NESR projects come from Federal agencies’ appropriated funds.

## Peer review

NESR systematic reviews are peer-reviewed to ensure that the graded conclusion statements are supported by the evidence synthesized. Different approaches to peer review are used depending on the project and may

involve peer review coordinated by the journal to which a manuscript has been submitted, or it may involve peer review by Federal or non-Federal subject matter experts. Regardless of the approach taken, peer reviewers are individuals who are external to, or not involved in, the project and who have either subject matter or methodological expertise. NESR analysts are responsible for submitting the draft systematic review for peer review. When peer reviewer comments are returned, the NESR team evaluates the comments and addresses any that are editorial in nature. Substantive comments are reviewed and discussed by the expert group. The NESR team documents revisions and responses and provides them back to the peer reviewing entity.

## Delineating roles and responsibilities

Systematic reviews are time and resource intensive projects conducted in accordance with NESR methodology which describes the complex, multi-step process, and involves numerous collaborators. The NESR team is responsible for designing, managing, and documenting systematic review projects within established timelines and budgets.

Each NESR systematic review project answers one or more questions of public health importance. NESR's methodology is carefully designed to reflect the delineation of roles between the NESR team and its collaborators, and to ensure a collaborative approach that promotes objectivity and minimizes bias and COI throughout the review process.

Federal stakeholders identify the need for a systematic review project, providing input on the rationale for the project and describing the context of decisions to be informed by the results of the systematic reviews. NESR coordinates, facilitates, and documents the work necessary to conduct systematic reviews in accordance with NESR systematic review protocol. The expert group develops the systematic review protocol and synthesizes the evidence to develop conclusion statements and grade the strength of the evidence. Having an external, expert group with content and methodological expertise complete these parts of the process enhances the trustworthiness of the review and reduces the perception of bias or COI. NESR analysts and librarians support the expert group by objectively executing their protocol and completing the most time and resource intensive steps - searching for and screening studies, extracting data, and conducting risk of bias assessments. This allows the expert group adequate time to review and evaluate the evidence, and ensure they are fully responsible for the results of their systematic reviews. NESR ensures that the work is accomplished in a timely manner according to the established methodology to minimize and/or manage potential bias or COI, and the expert group's time and expertise is preserved for synthesizing evidence.

The remaining chapters of this methodology manual describe how NESR conducts ([Chapter 2](#), [Chapter 3](#), [Chapter 4](#), [Chapter 5](#), [Chapter 6](#), [Chapter 7](#)) and updates ([Chapter 8](#)) systematic reviews, as well as processes for conducting evidence scans ([Chapter 9](#)), continuous evidence monitoring ([Chapter 10](#)), and rapid reviews ([Chapter 11](#)).

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## Chapter 2: Identify Systematic Review Questions

### Summary

**Purpose:** To identify high-priority public health nutrition questions that represent gaps in Federal program knowledge or dietary guidance and would benefit from a NESR systematic review or other evidence synthesis project to make evidence-informed decisions.

**Who:** NESR systematic review projects are initiated and funded by Federal stakeholders and managed by the NESR team. Federal stakeholders are responsible for defining the project scope by identifying and describing high-priority questions that represent gaps in Federal program knowledge or dietary guidance, and for commissioning NESR to initiate systematic review projects to address these questions. The NESR team supports prioritization of questions that will be examined by checking whether there are any existing NESR reviews that can be used or updated to address the question, determining whether there are any existing non-NESR reviews that can be used in place of conducting a new review, and evaluating whether there is sufficient research available to warrant conducting a review.

**What:** High-priority public health nutrition questions are identified, refined, and prioritized for NESR systematic review projects.

### Identifying systematic review questions

Systematic reviews are time and resource intensive projects conducted using complex scientific methods that are multi-step and involve numerous collaborators. NESR systematic review projects address one or more high-priority public health nutrition questions that reflect what decision makers need to make evidence-based policy and program decisions. In addition, these projects require effective project management to coordinate, facilitate, and document the work necessary to produce rigorous, transparent, and protocol-driven systematic reviews in accordance with NESR methodology. NESR systematic review projects are funded solely by Federal government agencies and programs, based on the needs identified by Federal stakeholders and/or in support of the development of the *Dietary Guidelines for Americans*. Funding for NESR projects come from Federal agencies' appropriated funds. Federal stakeholders are responsible for identifying high-priority questions that represent gaps in Federal program knowledge or dietary guidance, and for commissioning NESR to initiate systematic review projects to address the questions by considering the following factors:

- Relevance to and potential impact on Federal nutrition programs, policies, and consumer education priorities, including the *Dietary Guidelines for Americans*,
- Importance to public health, and
- Desire to avoid duplication of Federal efforts.

In general, a question is considered relevant if it addresses a food and/or nutrition issue that can inform action to promote population health or well-being, and/or reduce the risk of chronic disease in the general U.S. population or in specific population subgroups. A question is considered important when the results of a systematic review are likely to inform decisions about Federal public health food and nutrition policies and programs, and/or represents an area of major public health concern, uncertainty, and/or a knowledge gap that is critical to public health policy or programs. Finally, questions that are addressed in other Federal evidence-based guidance are lower priority, so as to avoid duplication of effort.

Systematic review questions need to be specific enough to be answered using NESR methodology, but broad enough to not unduly limit the scope of the literature search. For example, “What is the relationship between diet and cancer?” is too broad; while “What is the relationship between consuming a Mediterranean dietary pattern during adolescence and risk of postmenopausal breast cancer?” is too specific to inform Federal policy or programs. However, the question “What is the relationship between dietary patterns and risk of certain types of cancer (breast, colorectal, prostate, and lung)?” provides specificity about the type of dietary exposure and relevant outcomes without limiting the scope of literature available to answer the question.

For some projects, NESR leads the process to identify high-priority systematic review questions,<sup>1-3</sup> whereas in others, specifically Dietary Guidelines Advisory Committee projects, NESR supports both the designated team of Federal stakeholders who lead question identification as well as the Committee in their refinement and further prioritization of those questions.<sup>4, 5</sup> NESR participation ensures that questions are within scope and can be answered using NESR systematic review methodology, and that the rationale for each review question is clear and is accurately reflected in the protocol. NESR ensures that information is collected regarding the population, intervention and/or exposure, and outcome(s) of interest. Public stakeholders also participate by providing input, particularly for questions that will be examined to inform the *Dietary Guidelines for Americans*.

In some cases, the questions identified may have been previously addressed in an existing NESR systematic review, while in other cases the questions may be completely new to NESR. Once a draft list of systematic review questions has been generated, NESR and Federal stakeholders review the list to ensure that questions meet the established criteria for scope and importance. Questions that do not meet the criteria are not developed further. In some cases, based on Federal stakeholder needs and the types of questions identified, the NESR team may recommend that the question(s) identified may be better addressed by a rapid review or be further explored using an evidence scan instead of a systematic review.

## Prioritizing systematic review questions

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Federal stakeholders often identify more systematic review questions than can feasibly be addressed in available project timelines. Therefore, the NESR team, typically in collaboration with Federal stakeholders and expert groups, takes steps to prioritize the questions so that project resources are directed towards the questions with the greatest potential to impact policy or programs. These steps include: determining whether there are any existing NESR reviews that can be used or updated to address the question, whether there are any existing non-NESR reviews that can be used in place of conducting a new NESR review, and evaluating whether there is sufficient research available to conduct the review using evidence scans and continuous evidence monitoring (CEM).

## Identifying existing NESR systematic reviews

For each question, NESR analysts determine whether there is a relevant existing NESR systematic review answering the same or similar research question. NESR analysts evaluate the existing review’s protocol to determine whether it captures the most appropriate and relevant body of evidence to answer the posed question. If a relevant existing NESR systematic review is identified, the NESR analysts assess whether the existing review reflects the current state of science on the topic, or whether reviewing newly published evidence could result in changes to the conclusion statement and/or grade, thus warranting the investment of time and resources for a systematic review update. NESR’s methodology for updating NESR systematic reviews is described in [Chapter 8](#).

## Identifying existing non-NESR systematic reviews

Using an existing non-NESR systematic review to answer a question may prevent duplication of effort, save resources, and extend the breadth and depth of knowledge for making evidence-informed decisions. However, existing non-NESR systematic reviews may vary in their purpose, approach, and level of methodological rigor and transparency compared to a NESR systematic review. NESR’s methodology for identifying and determining whether existing non-NESR reviews can be used in place of conducting a new NESR review was developed based on guidance from reputable organizations on identifying and using existing systematic reviews from external groups.<sup>6-9</sup> Any existing non-NESR systematic review eligible to be considered for use by NESR must be relevant and timely, be commissioned by a national food or health authority or international scientific body, be transparently documented, include a step to grade or evaluate the strength of the body of evidence, and be high quality.

NESR identifies all potentially relevant existing non-NESR systematic reviews by conducting both a manual search and an electronic database search. To conduct the manual search, two NESR analysts independently hand search websites of nutrition and health organizations (**Table B**) to identify a preliminary list of potentially relevant sources of evidence published since a pre-determined cut-off date. To conduct the electronic database search, a NESR librarian constructs a search strategy in PubMed. Limiters are used to restrict the search based on study design (i.e., systematic reviews and meta-analyses) and publication date (e.g., published since 2020).

**Table B. Nutrition and health-related organizations that may conduct systematic reviews on topics**

U.S. Federal Government Organizations	Non-Federal Organizations
<ul style="list-style-type: none"> <li>• U.S. Department of Health and Human Services                             <ul style="list-style-type: none"> <li>○ <a href="#"><u>Agency for Healthcare Research and Quality</u></a></li> <li>○ <a href="#"><u>Centers for Disease Control and Prevention (including Office of Minority Health and Health Equity)</u></a></li> <li>○ <a href="#"><u>Food and Drug Administration</u></a></li> <li>○ <a href="#"><u>Health Resources &amp; Services Administration</u></a></li> <li>○ <a href="#"><u>National Heart, Lung, and Blood Institute</u></a></li> <li>○ <a href="#"><u>National Toxicology Program, Office of Heath Assessment and Translation</u></a></li> <li>○ <a href="#"><u>Office of Dietary Supplements</u></a></li> <li>○ <a href="#"><u>Office of Minority Health</u></a></li> </ul> </li> <li>• U.S. Department of Agriculture                             <ul style="list-style-type: none"> <li>○ <a href="#"><u>Agricultural Research Service</u></a></li> <li>○ <a href="#"><u>Economic Research Service</u></a></li> <li>○ <a href="#"><u>National Institute of Food and Agriculture</u></a></li> </ul> </li> <li>• <a href="#"><u>U.S. Environmental Protection Agency</u></a></li> </ul>	<ul style="list-style-type: none"> <li>• <a href="#"><u>Academy of Nutrition and Dietetics Evidence Analysis Library</u></a></li> <li>• <a href="#"><u>American Academy of Pediatrics</u></a></li> <li>• <a href="#"><u>American College of Cardiology/American Heart Association</u></a></li> <li>• <a href="#"><u>Campbell Collaboration</u></a></li> <li>• <a href="#"><u>Cochrane Database of Systematic Reviews</u></a></li> <li>• <a href="#"><u>European Food Safety Agency</u></a></li> <li>• <a href="#"><u>German Nutrition Society</u></a></li> <li>• <a href="#"><u>Health Canada</u></a></li> <li>• <a href="#"><u>Ministry of Health (New Zealand)</u></a></li> <li>• <a href="#"><u>National Health and Medical Research Council (Australia)</u></a></li> <li>• <a href="#"><u>Nordic Nutrition Recommendations SR Centre</u></a></li> <li>• <a href="#"><u>Scientific Advisory Committee on Nutrition (UK)</u></a></li> <li>• <a href="#"><u>The National Academies of Sciences, Engineering, and Medicine</u></a></li> <li>• <a href="#"><u>World Cancer Research Fund/American Institute for Cancer Research</u></a></li> <li>• <a href="#"><u>World Health Organization/International Agency for Research on Cancer</u></a></li> </ul>

Two NESR analysts independently screen all potentially relevant non-NESR reviews identified in the manual and electronic database searches. Existing non-NESR systematic reviews that meet all pre-specified inclusion and exclusion criteria (**Table C**) are eligible to be considered for use in place of conducting a new NESR systematic review.

Eligible existing non-NESR systematic reviews, when available, may be used to replace a *de novo* NESR systematic review (i.e., used “as is” with no updates). To determine if eligible existing non-NESR systematic review(s) can replace a *de novo* NESR systematic review, NESR will consider several factors on a case-by-case basis:

- the likelihood that the systematic review question will be addressed continuously in future editions of the *Dietary Guidelines for Americans*;
- the timeliness of the existing systematic review(s) literature search(es); and
- the extent of the analytic framework(s) addressed by the existing review(s).

If a review is likely to be addressed continuously in future editions of the *Dietary Guidelines for Americans*, then it may be preferable to conduct a *de novo* NESR systematic review that is tailored specifically to the needs of U.S. dietary guidance and can more easily be updated over time. Also, some reviews may have a publication date that meets criteria (e.g., 2020 to present), but the literature search conducted for that published review was completed several years prior to publication. If an existing non-NESR review’s search is outdated, a *de novo* NESR systematic review may be warranted. Finally, NESR may identify eligible existing non-NESR systematic reviews that are partially relevant (i.e., only answer part of the question, examining evidence only on a sub-population, intermediate outcomes, or one component of the intervention or exposures of interest). In such cases, a *de novo* NESR systematic review may be warranted in order to fully address the question of interest. If an eligible existing non-NESR systematic review is not used to replace a *de novo* NESR systematic review, it can still be used to evaluate research availability for the systematic review question and determine whether an evidence scan for primary literature needs to be conducted.

**Table C. Inclusion and exclusion criteria for eligible existing non-NESR systematic reviews**

Inclusion Criteria	Exclusion Criteria
<ul style="list-style-type: none"> <li>• Systematic review on a topic or question that sufficiently aligns with the population, intervention and/or exposure, comparator, and outcome defined in an <i>a priori</i> NESR protocol</li> </ul>	<ul style="list-style-type: none"> <li>• Systematic review does not sufficiently align with the population, intervention and/or exposure, comparator, and outcome defined in an <i>a priori</i> NESR protocol for a topic or question</li> </ul>
<ul style="list-style-type: none"> <li>• Systematic review published since a predetermined date</li> </ul>	<ul style="list-style-type: none"> <li>• Systematic review published prior to a predetermined date</li> </ul>
<ul style="list-style-type: none"> <li>• Commissioned by a national food or health authority, or an international scientific body</li> </ul>	<ul style="list-style-type: none"> <li>• Commissioned, sponsored, or funded by industry or an entity with a business or ideological interest</li> </ul>
<ul style="list-style-type: none"> <li>• Includes a clear description of the systematic review methodology and adequate reporting of the results</li> </ul>	<ul style="list-style-type: none"> <li>• Does not include a clear description of the systematic review methodology and adequate reporting of the results</li> </ul>
<ul style="list-style-type: none"> <li>• Provides an evidence grade for the strength of the evidence underlying the finding</li> </ul>	<ul style="list-style-type: none"> <li>• Does not provide an evidence grade for the strength of the evidence underlying the finding</li> </ul>
<ul style="list-style-type: none"> <li>• Systematic review rated as high quality based on AMSTAR 2<sup>10</sup> assessment</li> </ul>	<ul style="list-style-type: none"> <li>• Systematic review rated as critically low, low, or moderate quality based on AMSTAR 2 assessment</li> </ul>

## Evaluating research availability to determine if there is sufficient evidence to conduct a review

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NESR evaluates research availability to determine whether there is sufficient evidence available to conduct a new, or update an existing, systematic review, and to estimate the resource requirements for conducting or updating a review. For each proposed systematic review question, a draft protocol ([Chapter 3](#)) is developed. For questions addressed by an existing NESR review, NESR will use the protocol that was established by the expert group who conducted the existing review. For new systematic review questions, NESR will, to the greatest extent possible, use existing NESR protocols that address similar intervention/exposures and/or outcomes to develop a draft protocol that is likely to approximate one that would be developed by an expert groups, with input from Federal subject matter experts as needed. The rationale and background for why a systematic review question was identified provides NESR with important context necessary for developing a draft protocol that appropriately addresses the question of interest. These draft protocols are intended to be used in evaluating research availability only. If sufficient research is available to conduct or update the review, an expert group will be responsible for developing the protocol used in conducting that review using the processes described in [Chapter 3](#).

For proposed systematic review questions that have not previously been addressed by an existing NESR systematic review, NESR evaluates research availability by conducting an evidence scan for primary research ([Table D](#), and [Chapter 9](#)). For the *Dietary Guidelines for Americans, 2025-2030*, the first step of the evidence scan process for new questions involves determining whether there are any existing non-NESR reviews that can be used in place of conducting a new review. For proposed systematic review questions that have been previously addressed by an existing NESR systematic review, NESR evaluates new research available since the completion of the existing NESR systematic review using CEM ([Table D](#), and [Chapter 10](#)).

### Table D. NESR Evidence Scan and Continuous Evidence Monitoring

**A NESR evidence scan ([Chapter 9](#))** is an exploratory evidence description project in which systematic methods are used to search for and describe the volume and characteristics of evidence available on a nutrition question or topic of public health importance. Evidence scans can be either stand-alone projects or the beginning steps of conducting a rapid or systematic review. In general, evidence scans are conducted for proposed systematic review questions that have not previously been addressed by an existing NESR systematic review.

**NESR continuous evidence monitoring (CEM) ([Chapter 10](#))** is an evidence gathering process in which established systematic review protocols are used to periodically search for, screen, and prepare evidence for future systematic reviews. These actions can help inform protocol development and refinements, determine whether there is sufficient evidence available to conduct a new, or update an existing, NESR systematic review, or estimate the resource requirements for conducting or updating a review. In general, CEM is conducted for proposed systematic review questions that were previously addressed in an existing NESR systematic review.

Based on information gathered from CEM or an evidence scan, NESR and Federal stakeholders will determine whether there is sufficient evidence available to conduct a new NESR systematic review or update an existing NESR systematic review. Within the field of systematic review methodology, there is no established guidance on the number of studies needed to conduct a new systematic review, or to prompt an update to an existing review. Therefore, this determination must be made on a question-by-question basis, taking into consideration the volume and characteristics of studies that meet criteria for inclusion. In addition, the final decision should reflect multiple perspectives, including NESR, Federal support staff and project leadership, and Federal subject matter experts.

The following questions are used to determine whether there is sufficient evidence available to conduct a new, or update an existing, NESR systematic review:

1. Are there any studies that meet criteria for inclusion?
2. If so, how many studies meet criteria for inclusion? How comprehensively do the studies address the question of interest? Are all components of the draft analytic framework and synthesis plan addressed? What are their study designs?
3. For existing systematic review questions, do the newly published studies address previously identified gaps or limitations in the body of evidence?

In some cases, sufficient research may be available for some, but not all, components of the draft analytic framework. In those cases, a determination will be made as to whether the systematic review question will be revised to reflect a narrower scope. If sufficient research is not available, the question may not be prioritized for review by the Committee and will instead be identified as an area needing more research.

Finally, NESR and Federal stakeholders may use the information from CEM or evidence scans to evaluate time and resource requirements for conducting all of the systematic reviews determined to be high-priority and to have sufficient evidence. If the time and resources required exceed what is feasible for an expert group and NESR to complete, additional prioritization within and across questions may occur prior to finalizing the systematic review questions to be addressed in a project.

One of the end products of question refinement and prioritization is a list of systematic review questions that will be addressed as part of the project. In addition, documentation of the evidence scans and CEM that were completed to inform question selection will be prepared, including succinct, transparent descriptions of the volume and characteristics of available research, as well as the protocols, methods, and search strategies used.

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## Chapter 3: Develop a Systematic Review Protocol

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### Summary

**Purpose:** To develop a prespecified plan for how NESR’s methodology will be used to conduct a systematic review.

**Who:** An expert group develops a systematic review protocol in a process that is facilitated and documented by NESR analysts and considers input from Federal and public stakeholders.

**What:** A systematic review protocol describes the methods that will be used to conduct a systematic review, including an analytic framework, inclusion and exclusion criteria, and a synthesis plan which are tailored to the systematic review question. The systematic review protocol is posted online to provide transparency, guard against selective reporting, avoid duplication of efforts, and facilitate peer review and/or public comment.

### Developing a systematic review protocol

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After identifying systematic review questions ([Chapter 2](#)), the expert group, with support from NESR analysts, develops the systematic review protocol to transparently describe the rationale for the review and the methodology used to conduct the review (e.g., systematic review with or without meta-analysis). A NESR systematic review protocol includes the following sections:

- Introduction
- Methods
  - Develop an analytic framework and synthesis plan
  - Develop inclusion and exclusion criteria
  - Search for and screen studies
  - Extract data and assess the risk of bias
  - Synthesize the evidence
  - Develop conclusion statement and grade the evidence
  - Recommend future research
  - Peer review
  - Protocol amendments

The introduction section provides contextual information about the planned review, including the purpose/objective of the review, rationale for the question, collaborators and their role, protocol and review history, and funding source. The analytic framework, synthesis plan, and inclusion/exclusion criteria illustrate which characteristics of the available evidence will be critical to answering the systematic review question. These critical elements of NESR systematic review protocols are further described in this chapter, along with the process for making protocols and amendments publicly available. The remaining sections of the protocol describe the methods that will be used to search for and screen studies ([Chapter 4](#)), extract data and assess the risk of bias ([Chapter 5](#)), synthesize the evidence, develop conclusion statements and grade the evidence, and recommend future research ([Chapter 6](#)).

## Analytic framework and synthesis plan

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An analytic framework defines the core elements of the systematic review question, includes definitions for key terms, identifies key confounders and other factors that could affect the relationships examined, and illustrates the synthesis plan (i.e., the main comparisons of interest in the review). This helps communicate the most important contributing elements that will be examined, evaluated, synthesized, and organized in the systematic review based on each question of interest. The analytic framework serves as the foundation for the rest of the systematic review process, and informs the inclusion and exclusion criteria, literature search strategy, data extraction and risk of bias assessments, and the strategy for synthesizing the evidence to develop and grade conclusion statements.

An expert group ([Chapter 1](#)) develops an analytic framework for each systematic review question. The NESR analytic framework presents the core elements of each systematic review question based on a standard “PICO framework”, which includes the:

- **Population** (i.e., those who experience the intervention/exposure and/or outcome),
- **Intervention and/or exposure** (i.e., the independent variable of interest),
- **Comparator** (i.e., the alternative being compared to the intervention or exposure), and
- **Outcome(s)**.

Definitions for key terms are included in the NESR analytic framework because they provide the basis for how concepts are operationalized throughout the review. The definitions for key terms are based, when possible, on definitions already established by the U.S. Federal government or other leading national and international entities, as appropriate.

The expert group identifies key confounders and other factors to be considered (e.g., mediators, moderators, covariates) based on their knowledge of the literature and experience as subject matter experts. Key confounders are considered during review and evaluation of the evidence, particularly during the risk of bias assessment ([Chapter 5](#)) and evidence synthesis ([Chapter 6](#)).

The expert group, with support from NESR analysts, then develops a synthesis plan that guides how the included evidence in the systematic review will be explored, organized, and synthesized to aid development of conclusion statements. The synthesis plan is informed by input from Federal stakeholders and/or other subject matter experts during the question development phase to ensure that the end products of the review meet the needs of the end-users. The synthesis plan specifies the type of approach to be used (i.e., synthesis with or without meta-analysis), and may describe visualizations that will inform the synthesis (e.g., evidence tables, forest plots, gap maps). The synthesis plan includes details on the comparisons of interest that will be addressed, as well as the proposed methods for evaluating those comparisons. The evidence synthesis is ultimately guided by the available evidence and may be organized by a variety of different factors, including:

- Study design
- Population
- Intervention/exposures
- Outcomes
- Assessment methods
- Other factors (e.g., health status, other factors to be considered)

If a meta-analysis is planned, several additional elements are included in the synthesis plan: the plan for acquiring usable data, the methods for statistically combining data across studies, planned assessments of heterogeneity and non-reporting bias, and planned sensitivity analyses and meta-regressions.

## Inclusion and exclusion criteria

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Inclusion and exclusion criteria provide an objective, consistent, and transparent structure for determining which articles to include in each NESR systematic review. The criteria ensure that the most relevant and appropriate body of evidence is identified for each systematic review question. Additionally, these criteria are framed to increase the utility of the systematic review to inform U.S. Federal policy and programs. They are determined before any studies are reviewed to minimize bias. Revisions to the criteria after studies have been reviewed are avoided, but they are documented as protocol amendments with dates and rationales if they occur. Revisions to criteria used in updates to NESR systematic reviews are documented along with the rationale for the modification ([Chapter 8](#)).

The expert group is responsible for establishing inclusion and exclusion criteria that are tailored to the systematic review question. NESR analysts facilitate this process, and provide input to ensure that the body of evidence reviewed is:

- Applicable to the U.S. population of interest,
- Relevant to Federal public health nutrition policies and programs, and
- Rigorous and strong from a scientific perspective.

Every NESR systematic review has criteria for the following study characteristics:

- Study design
- Publication date
- Population:
  - Study participants
  - Life stage
  - Health status
- Intervention/exposure
- Comparator
- Outcome(s)
- Publication status
- Language
- Country

Additional criteria may be established, as appropriate. Some examples of criteria that have been established include:

- Population:
  - Analytic approach
- Study duration
- Size of study groups
- Confounders
- Temporality
- Sources of foods, beverages, or nutrients

Some inclusion and exclusion criteria are standard and remain the same across reviews, while some are tailored to the unique characteristics of each systematic review question. NESR standard criteria were designed to align with common practice within the field of systematic reviews and to reflect that NESR systematic reviews are used to inform U.S. Federal policy and programs. If there is a strong rationale for why a question-specific deviation from standard criteria is appropriate, the change is discussed between the expert

group, NESR, and project leadership, and the justification is documented in the protocol. Below are descriptions of considerations made when establishing various criteria.

## Study design

NESR systematic reviews are used to inform Federal policies and programs, and thus include study designs that offer the strongest evidence to establish a relationship between the intervention/exposure and the outcome(s). NESR systematic reviews typically include randomized controlled trials (RCTs, such as individual, cluster, and crossover trials), non-RCTs, observational cohort studies (e.g., prospective or retrospective), and nested case-control studies. They generally exclude uncontrolled trials, cross-sectional studies, ecological studies, case-control studies, reviews, and modeling and simulation studies. The decision to include additional study designs is determined by the expert group based on what is most appropriate for each systematic review question.

Following are some considerations used when establishing and implementing study design criteria:

- RCTs are not always ethical or practical in certain populations. Therefore, rigorously conducted observational studies can provide evidence that complements that of RCTs. For example, observational studies may allow for examination of diet as it occurs in daily life, as well as for the study of certain population groups and long-term or rare outcomes.
- When determining a study's design, NESR analysts only consider the data relevant to the systematic review question. In some cases, the study design for a particular analysis or publication differs from the design of the original study. For example, data from a prospective cohort study may have been analyzed cross-sectionally, and therefore, would be excluded if cross-sectional study designs are not part of the inclusion criteria.

## Publication date

All NESR systematic reviews include criteria for publication date. When establishing the appropriate publication date range criteria, multiple factors are considered, including whether:

- The question is building on evidence reviewed by a previous expert group or evaluated as part of an existing NESR systematic review;
- Research on the topic is emerging, and therefore, little research existed before a certain date; and
- New analytical techniques or methods have been recently established in the field, making previous research findings less valid or reliable.

## Population health status

To reflect the U.S. population, the studies included in NESR systematic reviews must be conducted with participants who are representative of the general public. In addition, because NESR systematic reviews are intended to examine questions to inform public health nutrition decision-making, and not clinical practice guidelines, studies must examine diet through a health promotion and disease prevention lens.

Thus, NESR systematic reviews include studies that exclusively enroll participants not diagnosed with a disease, including those at risk for chronic disease, or that enroll some participants diagnosed with a disease and/or with the outcome(s) of interest. Studies that exclusively enroll participants diagnosed with a disease or the outcome(s) of interest; hospitalized for an illness, injury, or surgery; and/or pre- or post-bariatric surgery are typically excluded from NESR systematic reviews. Nutrient absorption and metabolism are altered in these cases, and nutrition becomes part of specialized medical treatment of a disease and/or the outcome of interest.

The exception is obesity. Despite obesity being considered a disease, NESR systematic reviews include studies that exclusively enroll participants with obesity.

## Publication status

NESR systematic reviews include peer-reviewed studies published in research journals and typically exclude non-peer reviewed articles, unpublished data or manuscripts, pre-prints, reports, editorials, retracted articles, and conference abstracts or proceedings. This supports the reproducibility of NESR systematic reviews and the quality and objectivity of information used to inform U.S. Federal programs and policies.<sup>1</sup>

## Language

Studies published in English are included in NESR systematic reviews, while studies that are not published in English are excluded. NESR does not have the resources to translate manuscripts and our literature searches are designed to find evidence that is most relevant to U.S. Federal policies and programs.

## Country

The Human Development Index (HDI) is used to determine eligibility for inclusion in NESR systematic reviews.<sup>2</sup> Introduced by the United Nations in 1990, the HDI classifies countries based on a summary measure of average achievement in three key dimensions of human development: health, education and economics. NESR's standard criteria include studies conducted in countries classified as high or very high on the HDI, which are most generalizable to the U.S., and exclude studies conducted in countries classified as medium or low on the HDI. NESR applies the HDI classification based on the year the intervention was conducted or the exposure data were collected. If the study does not report the year(s) in which the intervention/exposure data were collected, the HDI classification for the year of publication is applied. Since the HDI was introduced in 1990, studies conducted before 1990 are classified based on the 1990 HDI classifications. If the year is more recent than the available HDI values, then the most recent HDI classifications are used. If a country is not listed in the HDI, then the current country classification from the World Bank is used, and studies conducted in countries grouped as upper-middle or high income are included.<sup>3</sup>

## Study duration

There are no standard criteria for study duration that are uniformly applied to all NESR systematic reviews because the appropriate study duration is dependent on the interventions or exposures, outcome(s), and population(s) of interest. Therefore, the expert group first determines whether study duration criteria are necessary, and then the criteria are tailored to a particular question. When establishing criteria for study duration, both the appropriate duration for the interventions or exposures of interest, as well as the appropriate follow-up duration for the outcomes of interest to occur in that population are considered. When study duration criteria are established, the rationale is documented in the protocol.

## Size of study groups

There are no standard criteria for size of study groups that are uniformly applied to all NESR systematic reviews. However, in some reviews, a minimum study group size may be important to ensure a study is adequately powered to detect an effect or association between the intervention/exposure and the outcome(s) of interest. In addition, size of study group criteria can be used to strengthen the body of evidence for a

particular question. Study group size criteria are established according to the study's design and type of analyses. When criteria for size of study groups are established, the rationale is documented in the protocol.

## Making protocols publicly available

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NESR protocols meet generally accepted standards of reporting for systematic reviews and meta-analyses (e.g., PRISMA-P<sup>4</sup>). Protocols developed in February 2023 or later are posted online for the public to view on NESR's website (<https://nesr.usda.gov/protocols>). Protocols for NESR reviews conducted prior to January 2023 can be found in their respective reports. This provides transparency to the public, guards against selective reporting, avoids duplication of efforts, and facilitates peer review and/or public comment. A protocol describes NESR's full methodology to conduct a review. Any modifications made to the protocol during the review process are documented as amendments with dates and rationales, posted online with an updated protocol (if applicable), and described in the final published systematic review report.

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## Chapter 4: Search for and Screen Literature

### Summary

**Purpose:** To identify the most complete and relevant body of evidence to answer a systematic review question.

**Who:** NESR librarians develop comprehensive literature search strategies and NESR analysts screen articles.

**What:** NESR systematically searches for and screens the scientific literature using a pre-defined analytic framework and inclusion and exclusion criteria. The entire process is documented, including a complete list of articles that meet criteria for inclusion in the systematic review and a list of excluded articles with the rationale for exclusion.

### Literature search

NESR librarians develop, implement, and document literature search strategies with input from NESR analysts using the systematic review protocol developed by the expert group. Once the inclusion and exclusion criteria are defined, the NESR librarian uses the analytic framework and inclusion and exclusion criteria to develop a comprehensive literature search strategy. The literature search strategy includes selecting and using the appropriate bibliographic databases, identifying search terms appropriate for the databases being searched, and employing search refinements, such as search filters. Each component of the literature search strategy is discussed in more detail below.

- **Bibliographic databases:** The NESR librarian identifies the most relevant electronic bibliographic databases based on the systematic review topic. PubMed/MEDLINE,<sup>1</sup> Cochrane,<sup>2</sup> and Embase<sup>3</sup> are the primary databases used to identify studies relevant to NESR systematic reviews on food, nutrition, and health. If the topic of the systematic review relates to pregnancy, lactation, or the birth to age 24 months population, CINAHL<sup>4</sup> is searched. Databases of grey and/or unpublished literature and clinical trial registries are not used to search for primary literature, as only peer-reviewed primary literature is included in NESR systematic reviews. Regional databases (e.g., African Index Medicus, Chinese Biomedical Literature Database) are typically not included in NESR reviews, since NESR's work pertains to nutrition topics that could affect U.S. Federal policies and programs.
- **Search terms:** NESR analysts help identify initial key terms and/or relevant articles to ensure that the NESR librarian has an understanding of the scope and intent of the systematic review question. The expert group may also provide help on subject or topic terminology and technical terms to aid the librarian in choosing the most appropriate and comprehensive set of search terms possible. Search terms also can be refined by reviewing key terms and the indexing of related publications such as existing systematic reviews.
- **Search filters:** For NESR searches, filters that are commonly used include: English language, human studies, date, or publication type (e.g., to filter out news, editorial, and comments). Sometimes, study design also is used as a filter (e.g., systematic reviews and meta-analyses). In some cases, searches are filtered or limited to identify studies done in subpopulations of interest, such as in a specific country or in individuals who are pregnant. In addition, filters or limits for sex (e.g., male or female) or specific age groups (e.g., children and adolescents [ages 2 to 18 years] or adults [ages 18 to 65 years]) may be applied in some cases.

NESR librarians work in collaboration with the NESR analysts and expert group members to construct a preliminary search strategy using PubMed operators and search terms. This is used to conduct a test search, preview the results, and correct any syntax, spelling, or grammatical errors. The search strategy undergoes multiple revisions to refine and adjust the search, as well as peer-review, before it is finalized for use. The search is peer-reviewed by a second designated librarian to provide additional rigor to the process. The second librarian may be a NESR librarian, or another Federal librarian who has training and expertise in conducting literature searches for systematic reviews. The peer-review librarian reviews the search strategy, and provides feedback regarding:

- The accuracy of translating the research questions into search concepts and terminology,
- Proper use of search operators, fields, limiters or filters, and spelling and syntax of search terms/strings,
- The accuracy of adapting the search strategy for each database interface,
- Inclusion of relevant subject headings, such as Medical Subject Headings (MeSH)<sup>5</sup> and Emtree thesaurus<sup>6</sup> with free-text search terms, and
- Provision of additional relevant search terms and/or original databases.

The NESR librarian uses the feedback from the designated peer-review librarian to finalize the search strategies, and shares the revised search strategy with the expert group and NESR analyst(s) for final approval. After finalizing the search strategies for each of the databases, the NESR librarian begins the process of conducting all of the electronic searches. When searching multiple databases, overlap in the literature identified is common; the librarian electronically eliminates duplicate records at the search level using a citation management program (EndNote X9; Clarivate Analytics, Philadelphia, PA). Once the electronic searches are done, the librarian documents the total number of unique articles identified, indicating how many were identified from each database searched. This documentation includes the total, raw search results, as well as search results after removal of duplicates.

## Literature screening

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Two NESR analysts independently screen all search results, which is facilitated by use of a web-based tool (i.e., DistillerSR) and screening forms developed based on the inclusion and exclusion criteria identified for each systematic review. At present, machine learning technology is selectively used by NESR to prioritize references for screening to support evidence scans and rapid reviews, but dual human screening is still used for all NESR systematic reviews. In some cases, where multiple literature searches are run to identify articles for a question or family of questions, the search results are uploaded into the web-based tool, combined, and screened together.

The goal of screening is to review the search results and exclude those that do not meet the inclusion criteria. Screening is done at 3 levels. The first level of screening is done using only the title of each article. If an article is not excluded by both analysts at this level, it is moved forward to the second level, where the abstract is screened. Finally, if an article passed the first 2 levels, it moves to the third level, where the full text of the article is screened. After the NESR analysts complete independent screening, they reconcile any discrepancies. If necessary, a third analyst is consulted to resolve differences.

If multiple articles are identified that present data from the same study or cohort, the article that most directly addresses the systematic review question is included to avoid duplicative data. If the articles address unique data related to the question, or are needed to comprehensively present information from a study or cohort, then all articles are included. Included articles from the same study or cohort are noted in the review, and this is taken into consideration when weighing the amount of evidence to answer a question.

## Manual searches

NESR analysts also complete manual searches, a mandatory part of a comprehensive search strategy, for every systematic review. Manual searching is done to find peer-reviewed published articles not identified through the electronic database search. This is typically due to inadequate indexing or filtering limitations of a database. The primary approach used for the manual search is hand searching, in which a NESR analyst systematically searches the reference sections of included articles. Additional references, such as related systematic reviews and meta-analyses and other primary articles, may also be hand searched. Potential articles also may be suggested by others engaged in the process, such as expert group members, analysts working on the project, or the general public through public comments.

Two NESR analysts independently screen all relevant citations at the abstract and full-text levels to determine whether the articles address the systematic review question and meet all inclusion and exclusion criteria, as outlined above.

If articles are identified through a manual search, the librarian reviews the search strategy to determine why they were not found through the electronic searches. If a potential gap in the literature search strategy is identified, the electronic search is updated and rerun to include additional search terms or filters, and any new references identified are screened against the inclusion and exclusion criteria, as described above.

## Making the literature search strategy and results publicly available

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After the electronic and manual searches are complete, NESR analysts and librarians prepare materials to document the literature search and screening results. They compile lists of the included and excluded citations, along with the rationale for exclusion. These lists are provided to the expert group for review and approval. The analysts and librarian also document the search strategy and results, including:

- Inclusion and exclusion criteria
- Search strings (e.g., search terms, filters, and limits) and updates used for each electronic database searched
- Date of each search
- Description of how the search was developed and implemented
- Flow chart of the number of included and excluded citations retrieved through electronic and manual searching
- List of all included articles
- List of all excluded articles with rationales for exclusion

The list of articles excluded after full text review is publicly available on the NESR website in the respective systematic review reports. The list of articles excluded after title or abstract review is documented and archived by NESR. It is uncommon for a literature search to be updated after other steps in the NESR systematic review process are under way. This is particularly true for reviews conducted in support of the Dietary Guidelines Advisory Committee. The timeframe for each review, however, is documented transparently.

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## Chapter 5: Extract Data and Assess Risk of Bias

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### Summary

**Purpose:** To objectively describe the body of evidence available that answers a systematic review question, and to determine if studies used designs and analytic methods that may have introduced bias into the results.

**Who:** NESR analysts extract data and assess risk of bias considering decisions made by the expert group during protocol development. This information is then used by the expert group to synthesize the body of evidence.

**What:** Key data relevant to the systematic review question (e.g., study design, sample size, study setting, participant characteristics, interventions/exposures, outcomes, results, funding source) is extracted using a standardized data extraction form and summarized in evidence tables and figures. Risk of bias across key domains is assessed using study design-specific tools using a dual, independent procedure and the results are displayed in tables.

### Data extraction

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NESR analysts extract and summarize data from each included article to describe the body of evidence available to answer a systematic review question. With expert group guidance, NESR analysts determine the specific types of data to extract from each included study. The focus is on information that is critical for answering the systematic review question. Types of data typically extracted include study design, country, sample size, participant characteristics (such as age, sex, race/ethnicity, socioeconomic status, and health status), the independent and dependent variables and their measurement methods, statistical adjustments, results, limitations, and funding source(s). NESR analysts develop a data extraction form to facilitate accurate and consistent extraction of the determined types of data. This form ensures that the same information from each article is extracted and formatted consistently, which makes the content easier to compare and contrast during synthesis. NESR analysts typically use tools such as DistillerSR and Excel to develop data extraction forms and collect data.

One NESR analyst extracts data from each included article. Next, a second analyst reviews the extracted data for completeness, accuracy, and consistent presentation and formatting. Any discrepancies noted by the second analyst are discussed and resolved. If a discrepancy cannot be resolved or needs additional clarification, the analysts will consult with a third NESR analyst and/or the expert group to reach resolution. In some cases, the required data is not reported in the article. In this situation, the data is recorded as “not reported.” If the required data is reported in an article’s protocol or related publication, then analysts will extract the data and note the publication from which it was extracted. If a meta-analysis is conducted it may be necessary to contact authors to request additional data when the data reported in an article cannot be statistically combined.

NESR analysts use the extracted data to create evidence tables and figures that consistently and objectively present the key data from all studies included in the systematic review. NESR analysts and the expert group determine the content and organization of evidence tables based on the analytic framework and synthesis plan. Evidence tables are used to facilitate the expert group’s review, synthesis, and grading of the body of

evidence available to answer the systematic review question. For example, some tables provide descriptive information about the study design, methods, study participants, and funding sources. Other tables present study results. The number and content of evidence tables varies depending on the size and scope of the systematic review.

## Risk of bias assessment

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Risk of bias is the likelihood of a systematic error or deviation from the truth, in results or inferences, which can lead to underestimation or overestimation of either the true effect of an intervention on an outcome or the true association between an exposure and outcome.<sup>1</sup> The design and conduct of a study affect the extent to which its results are at risk of bias. Studies with lower risk of bias (i.e., studies with rigorous designs and sound analytic methods) are more likely to report results that are closer to the truth. Systematic review methodology, including that related to risk of bias, is continuously evolving. NESR has followed these evolutions, routinely evaluating and refining its methods to ensure they remain state-of-the-art.

Each article included in a NESR systematic review undergoes a formal risk of bias assessment, which is a critical part of the systematic review process. The risk of bias assessment provides important information regarding each included article and the body of evidence under review, which the expert group considers when synthesizing the evidence, drawing conclusions, and grading the strength of evidence underlying those conclusions.<sup>2</sup> The assessment is specific to identifying the *risk* of bias because the results of a study may in fact be unbiased despite a methodological flaw.<sup>1, 3, 4</sup>

NESR conducts risk of bias assessments at the results level using a dual, independent process. For each article included in a NESR systematic review, 2 NESR analysts independently complete the risk of bias tool appropriate for the study's design. If a study includes multiple results that address the systematic review question (i.e., continuous and categorical analyses of the exposure, or multiple different outcomes of interest), the NESR analysts consider each result when responding to the items, and in some cases, complete multiple iterations of the tool to address each result independently. If necessary, analysts refer to previous and/or related publications to obtain information to complete items in the tool. The analysts compare responses and discuss and reconcile any disagreements. If a disagreement cannot be resolved by the 2 analysts, an additional NESR analyst provides a third-party consultation. The expert group also is consulted, as needed, to ensure consistency and accuracy of risk of bias assessments.

NESR uses several standardized risk of bias tools, which are study design-specific and were developed to identify specific risks of bias that different designs are subject to.<sup>5-7</sup> Each of these tools includes signaling questions that address several types, or domains, of bias. The tools also offer guidance for answering the individual signaling questions and making overall judgements for each type of bias. Analysts answer the signaling questions based only on the data that were extracted for the systematic review. The systematic review protocol developed by the expert group informs how the guidance is applied (e.g., which key confounders are evaluated). Using risk of bias tools ensures that risk of bias is assessed consistently across studies, and that the results of the assessment are transparent. Below is a summary of the study design-specific risk of bias tools that NESR uses.

## Risk of bias in randomized trials

NESR assesses the risk of bias of RCTs (including parallel group trials, cluster-randomized trials, and cross-over trials) using revised Cochrane tools for randomized trials. NESR uses the revised “Cochrane risk-of-bias tool for randomized trials” (RoB 2.0; August 2019 version)<sup>7</sup> for individually-randomized parallel group trials, and

the test versions (March 2021) for cluster-randomized parallel group trials and cross-over trials. These tools have domain-level judgements of low, some concerns, and high risk of the following types of bias:

- Bias arising from the randomization process
- Bias arising from the timing of identification and recruitment of individual participants in relation to timing of randomization (cluster randomized trials only)
- Bias due to deviations from intended interventions
- Bias due to missing outcome data
- Bias in measurement of the outcome
- Bias in selection of the reported result

## Risk of bias in non-randomized studies of interventions

NESR assesses the risk of bias of non-RCTs using the “Risk of Bias in Non-randomized Studies-of-Interventions” (ROBINS-I) tool.<sup>6</sup> This tool has domain-level judgements of low, moderate, serious, and critical risk of the following types of bias:

- Bias due to confounding
- Bias in selection of participants into the study
- Bias in classification of interventions
- Bias due to deviations from intended interventions
- Bias due to missing data
- Bias in measurement of the outcome
- Bias in selection of the reported result

## Risk of bias in observational studies

NESR assesses the risk of bias of observational studies using the “Risk of Bias in Non-randomized Studies-of-Exposures” (ROBINS-E) tool.<sup>5</sup> This tool has domain-level judgements of low, some concerns, high, and very high risk of the following types of bias:

- Bias due to confounding
- Bias arising from measurement of the exposure
- Bias in selection of participants into the study (or into the analysis)
- Bias due to post-exposure interventions
- Bias due to missing data
- Bias arising from measurement of the outcome
- Bias in selection of the reported result

NESR analysts document the results of the risk of bias assessments in a table. This table, which is found in the systematic review report, uses a color-coded system to provide transparency to the domain-level risk of bias judgements and overall risk of bias rating for each study included in the review. If a study includes multiple results to be considered in the systematic review, and the risk of bias judgements differ, then the risk of bias for each result is reported separately. The limitations identified through risk of bias assessments are frequently documented and described in evidence tables, giving transparency to the specific underlying limitations that contribute to domain-level ratings. NESR has predefined grading criteria to grade the strength of the evidence supporting each conclusion statement ([Chapter 6](#)). One of the grading criteria relies on a review of risk of bias

judgements, which considers the likelihood that systematic errors in the design and conduct of the studies could have affected reported results across the body of evidence.

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## Making extracted data and risk of bias assessments publicly available

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The extracted data and risk of bias assessments are used by the expert group to synthesize the body of evidence, develop conclusion statements, and grade the strength of the evidence. The limitations identified through risk of bias assessments frequently inform research recommendations ([Chapter 6](#)).

Evidence tables, figures, and risk of bias tables are all part of the documentation found in systematic review reports ([Chapter 7](#)), providing transparency to the evidence reviewed by the Committee.

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## Chapter 6: Synthesize Evidence, Develop Conclusion Statements, Grade the Evidence, and Identify Research Recommendations

### Summary

**Purpose:** To synthesize the evidence to develop graded conclusion statements that answer the systematic review question and communicate the level of certainty in the evidence.

**Who:** The expert group synthesizes the evidence, develops conclusion statements, grades the strength of the evidence, and identifies research recommendations. This process is facilitated and documented by NESR analysts.

**What:** Evidence synthesis is a process of combining data from included studies to examine whether the intervention or exposure is related to the outcome(s) in the population of interest. Evidence synthesis culminates in development of a conclusion statement, which is one or more summary statements carefully constructed to answer the systematic review question. Grades (Strong, Moderate, Limited, and Grade Not Assignable) are assigned based on a systematic evaluation of the underlying evidence considering consistency, precision, risk of bias, directness, and generalizability.

### Synthesize Evidence

Evidence synthesis involves describing, comparing and contrasting, and combining all included studies, to examine whether the intervention or exposure is related to the outcome(s) in the population(s) of interest. The aim of evidence synthesis is to identify overarching themes from the findings, identify and explain similarities and differences between the studies, and determine whether certain factors may have affected the relationships being examined. Meta-analysis may also be used to statistically combine eligible quantitative results from individual studies to obtain an estimated average effect size. Meta-analysis is conducted for some, but not all, NESR systematic review questions; and, for the reviews in which a meta-analysis is planned, it will be identified *a priori* and specified in the protocol ([Chapter 3](#)). NESR analysts, under the direction of the expert group, carry out meta-analyses. When conducted, the expert group considers the results of the meta-analyses in combination with the results of the systematic review in the overall synthesis.

The expert group synthesizes the evidence according to the synthesis plan, which is a strategy included in the protocol to help ensure that the systematic review will draw meaningful conclusions for the end-users. NESR analysts facilitate the expert group's synthesis by providing the full texts of included articles, evidence tables, risk of bias assessments, meta-analyses (when conducted), and other relevant data visualizations. The expert group reviews and examines these materials to collectively understand and interpret the entire body of evidence. The expert group considers study design, PICO elements, key associations or effects between the intervention/exposure and outcome(s) of interest as they assess the body of evidence. The expert group examines patterns of agreement and disagreement among the findings, and methodological differences between the studies that may explain disagreements or variations in the size or direction of the effect or association. This comprehensive approach to evidence synthesis aids the expert group in drawing conclusions, grading the strength of the evidence (see sections below), and identifying gaps in the body of evidence.

The expert group reviews, discusses, and revises the evidence synthesis until they reach agreement. Under the guidance of the expert group, NESR analysts document the evidence synthesis, finalize the data visualizations, such as evidence tables, that provide additional transparency to the synthesis process.

## Develop Conclusion Statements

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Following evidence synthesis, the expert group drafts conclusion statement(s). A conclusion statement is one or more summary statements carefully constructed to answer the systematic review question. It reflects the evidence reviewed, as outlined in the analytic framework and synthesis plan, including results from meta-analysis (if conducted), and does not take evidence from other sources into consideration. Conclusion statements do not draw implications and should not be interpreted as dietary guidance. The expert group reviews, discusses, and revises the conclusion statement(s) until they reach agreement on one or more conclusion statements that accurately reflect the body of evidence.

Conclusion statements:

- Indicate the strength of the evidence grade,
- Focus on general agreement among the studies and/or acknowledge areas of disagreement where they exist,
- Identify the relevant parameters, when appropriate (e.g., if cited papers studied only one sex, life stage, ethnicity, or level of health risk), and
- Are concise and written using elements of “plain language” so they can be understood by a broad audience.

## Grade the Evidence

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After drafting conclusion statements, the expert group begins the process of assigning a grade to each conclusion statement. The grade communicates the strength of the evidence supporting a specific conclusion statement to decision makers and stakeholders.<sup>1</sup>

NESR has predefined criteria, based on five grading elements, that the expert group uses to evaluate and grade the strength of the evidence supporting each conclusion statement. The five grading elements, described below, represent separate but related concepts:

- **Consistency** considers the degree of similarity in the direction and magnitude of effect across the body of evidence. Consistency also considers whether differences across the results can be explained by variations in study designs and methods. For example, the differences in the magnitude of effects across studies may be attributed to differences in population (e.g., baseline nutritional status), the intervention/exposure (e.g., dosage), or other study methods. If a meta-analysis is conducted, its findings may be particularly relevant to inform consistency.
- **Precision** considers the degree of certainty around an effect estimate for a given outcome. This element accounts for measures of variability within and across studies, such as the width and range of confidence intervals, the number of studies, and sample sizes. If a meta-analysis is conducted, its findings may be particularly relevant to inform precision.

- **Risk of Bias** considers the likelihood that systematic errors resulting from the design and conduct of the studies could have impacted the accuracy of the reported results across the body of evidence. Each included study in this process undergoes a formal risk-of-bias assessment specific to the study design ([Chapter 5](#)). These assessments of each individual study are documented, compiled, and used to inform consideration of risk of bias across the body of evidence.
- **Directness** considers the extent to which studies are designed to directly examine the relationship between the interventions/exposures, comparators, and outcome(s) of primary interest in the systematic review question.
- **Generalizability** considers whether the study participants, intervention and/or exposure, comparator, and outcome(s) examined in the body of evidence are applicable to the U.S. population of interest. NESR's grading process has always included generalizability as a formal grading element. Because NESR systematic reviews are conducted to inform Federal nutrition policies and programs in the U.S., it is imperative to consider how generalizable the evidence is to Americans at the population level.

The process of grading the strength of evidence underlying a conclusion statement begins by examining the body of evidence by study design. This assessment by study design ensures that the strengths and weaknesses of each design, as well as each grading element, are thoroughly considered. Study design is further taken into account with the risk of bias grading element because NESR's process utilizes risk-of-bias tools ([Chapter 5](#)) that capture design-specific concerns.

The expert group discusses their assessment of each grading element, using the NESR grading rubric (**Table E**) and select an overall grade for the entire body of evidence underlying the conclusion statement. The assessment of grading elements, as well the overall grade, get transparently documented in the report.

Definitions of NESR grades are found in **Table F**. A conclusion statement can receive a grade of Strong, Moderate, or Limited. If insufficient or no evidence is available to answer a systematic review question, then no grade is assigned (i.e., Grade Not Assignable). The overall grade is not based on a predefined formula for scoring or tallying ratings of each element. Rather, each overall grade reflects the expert group's thorough consideration of all of the grading elements, as they each relate to the specific nuances of the body of evidence under review.

NESR's grading process aligns with those used by other organizations, such as the GRADE approach and that of AHRQ.<sup>2, 3</sup> These grading processes all rely on consideration of specific elements,<sup>2-4</sup> sharing four of five grading elements in common: consistency, precision, risk of bias, and directness.<sup>3, 5-9</sup> All of these approaches take study design into consideration, and all assign an overall grade that communicates the strength of the evidence to decision makers and stakeholders.<sup>10</sup> NESR's grading process differs in its consideration of publication bias and generalizability, given its role in informing public health nutrition decisions within the U.S. government.

Even though it's not a formal element in the grading process NESR's systematic review methodology does include steps to assess the potential for publication bias. NESR recognizes the importance of publication bias in nutrition research and carefully evaluates and documents the potential for its presence during evidence synthesis. However, publication bias may not effectively differentiate the strength of bodies of evidence, and there are not widely accepted, reliable methods for assessing publication bias and its impact on systematic review conclusions.<sup>3, 7, 11</sup>

**Table E. NESR grading rubric**

Grading Elements	Strong	Moderate	Limited	Grade Not Assignable
Consistency	The body of evidence demonstrates findings with <b>strong</b> consistency in direction and magnitude of effect; or any inconsistencies in findings can be explained by methodological differences	The body of evidence demonstrates findings with <b>moderate</b> consistency in direction and magnitude of effect; some of the inconsistencies in findings can be explained by methodological differences	The body of evidence demonstrates findings with <b>limited</b> consistency in direction and magnitude of effect; few of the inconsistencies in findings can be explained by methodological differences	A <b>grade is not assignable</b> for this element because it cannot be adequately assessed
Precision	The body of evidence demonstrates <b>strong</b> precision based on a substantial number of sufficiently-powered studies with a narrow assessment of variance	The body of evidence demonstrates <b>moderate</b> precision based on an adequate number of sufficiently-powered studies with a narrow assessment of variance	The body of evidence demonstrates <b>limited</b> precision based on an inadequate number of sufficiently-powered studies with a narrow assessment of variance	A <b>grade is not assignable</b> for this element because it cannot be adequately assessed
Risk of bias	Across the body of evidence, there is a <b>strong</b> likelihood that the design and conduct of the studies has prevented or minimized bias such that the reported results are the true effects of the intervention/exposure, and plausible bias and/or potential limitations are unlikely to alter the results	Across the body of evidence, there is a <b>moderate</b> likelihood that the design and conduct of the studies has prevented or minimized bias such that the reported results are the true effects of the intervention/ exposure, and plausible bias and/or potential limitations are unlikely to alter the results	Across the body of evidence, there is a <b>limited</b> likelihood that the design and conduct of the studies has prevented or minimized bias such that the reported results may not be the true effects of the intervention/ exposure, and plausible bias and/or potential limitations may have altered the results	A <b>grade is not assignable</b> for this element because it cannot be adequately assessed
Directness	The body of evidence demonstrates <b>strong</b> directness, such that studies are designed to directly examine the relationships among intervention/exposure, comparator, and outcomes of primary interest in the systematic review question	The body of evidence demonstrates <b>moderate</b> directness, such that some studies are designed to directly examine the relationships among intervention/exposure, comparator, and/or outcomes of primary interest in the systematic review question	The body of evidence demonstrates <b>limited</b> directness, such that few studies are designed to directly examine the relationships among intervention/exposure, comparator, and/or outcomes of primary interest in the systematic review question	A <b>grade is not assignable</b> for this element because it cannot be adequately assessed
Generalizability	The body of evidence demonstrates <b>strong</b> generalizability to the U.S. population of interest with regard to: a) the participant characteristics b) the intervention/exposure and outcomes studied	The body of evidence demonstrates <b>moderate</b> generalizability to the U.S. population of interest with regard to: a) the participant characteristics b) the intervention/exposure and outcomes studied	The body of evidence demonstrates <b>limited</b> generalizability to the U.S. population of interest with regard to the: a) participant characteristics b) intervention/ exposure and outcomes studied	A <b>grade is not assignable</b> for this element because it cannot be adequately assessed

**Table F. Definitions of NESR grades**

**Strong**

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The conclusion statement is based on a strong body of evidence as assessed by consistency, precision, risk of bias, directness, and generalizability. The level of certainty in the conclusion is strong, such that if new evidence emerges, modifications to the conclusion are unlikely to be required.

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**Moderate**

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The conclusion statement is based on a moderate body of evidence as assessed by consistency, precision, risk of bias, directness, and generalizability. The level of certainty in the conclusion is moderate, such that if new evidence emerges, modifications to the conclusion may be required.

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**Limited**

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The conclusion statement is based on a limited body of evidence as assessed by consistency, precision, risk of bias, directness, and generalizability. The level of certainty in the conclusion is limited, such that if new evidence emerges, modifications to the conclusion are likely to be required.

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**Grade Not Assignable**

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A conclusion statement cannot be drawn due to either a lack of evidence, or evidence that has severe limitations related to consistency, precision, risk of bias, directness, and generalizability.

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## Identify Research Recommendations

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The expert group identifies research gaps and methodological limitations throughout the systematic review process. NESR analysts facilitate the development of research recommendations by documenting discussions and decisions of the expert group. These gaps and limitations are used to develop research recommendations that describe the research, data, and methodological advances that are needed to strengthen the body of evidence on a particular topic.<sup>12</sup> Rationales for the necessity of additional or stronger research may also be provided with the research recommendations.

## Making the evidence synthesis, graded conclusion statements, and research recommendations publicly available

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The evidence synthesis is fully documented to provide transparency to the evidence underlying each conclusion statement and rationale for assigned grades. Text, tables, and figures describe the evidence reviewed by the expert group, the assessment of that evidence during the grading process, and the gaps and limitations identified during the systematic review and are fully documented in systematic review reports ([Chapter 7](#)).

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## Chapter 7: Systematic Review Reports

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### Summary

**Purpose:** To make all completed NESR systematic reviews publicly available.

**Who:** NESR team of analysts and librarians are responsible for documenting each step of the review process and the report is reviewed and approved by the expert group.

**What:** Each systematic review report transparently documents the systematic review process, which includes a plain language summary, an abstract and the full systematic review. All systematic review reports are posted on <https://nesr.usda.gov>.

### Systematic Review Reports

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For transparency and reproducibility, all completed NESR systematic reviews are made accessible to the public. Each systematic review report contains complete documentation from each step of the review process, and includes a plain language summary, an abstract, and a full systematic review. Other NESR evidence synthesis products (i.e., rapid reviews, evidence scan and continuous evidence monitoring) follow similar transparent documenting and reporting, while taking into account some unique considerations that are applicable for each of the products ([Chapter 9](#), [Chapter 10](#), [Chapter 11](#)).

### Plain Language Summary

NESR plain language summaries provide an overview of NESR systematic reviews using concise, non-technical language. Plain language summaries include the systematic review question and the answer to that question, as well as a brief description of why the question was asked, how it was answered, what was the population of interest, what evidence was found, and how up to date the systematic review is. NESR analysts draft plain language summaries, which are then reviewed by the expert group. The intended audience of a NESR plain language summary are intended for a range of audiences, regardless of their technical or scientific expertise.

### Abstract

NESR abstracts provide a short, technical synopsis of NESR systematic reviews. The abstract is structured to help readers quickly determine the overall scope, methodology, and findings of the systematic review, without having to read the entire report. NESR abstracts are typically longer and more detailed than abstracts prepared for peer-reviewed publications and/or scientific meetings. NESR analysts draft abstracts, which are then reviewed by the expert group. The intended audiences of a NESR abstract include those with a scientific background, including scientific experts, Federal stakeholders, and researchers, as well as the general public. A NESR abstract contains the following sections:

### Background

Describes the rationale and objective of the systematic review and specifies the primary source of funding for the project.

## Methods

Describes the literature search strategy and processes used to extract data, assess risk of bias, synthesize evidence, develop conclusion statements, and grade the strength of evidence.

## Results

Includes the following:

- **Conclusion Statement(s) and Grade(s):** Answers the review question, with a grade that represents the strength of, or level of certainty in, the evidence supporting that conclusion statement.
- **Summary of Evidence:** Summarizes the body of evidence included in the review, including a description of included studies, study results, and research gaps and limitations.

## Full Systematic Review

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The purpose of the full systematic review is to present comprehensive details of the entire systematic review, including details about the methodology and protocol, as well as in-depth information about the body of evidence reviewed. The expert group's work is documented and compiled by NESR analysts throughout the course of the systematic review process. The intended audience of the full systematic review includes those with a scientific background, including scientific experts, Federal stakeholders, and researchers, as well as the general public. The full systematic review contains the following sections:

### Introduction

Describes the rationale for the systematic review and provides details about why the project happened, who funded it, the history of the project, collaborators, and the stated objective.

### Methods

Outlines the NESR methodology that was applied to the systematic review question (or the project, at large) and documents NESR's process including: 1) Develop a protocol, 2) Search for and screen studies, 3) Extract data and assess the risk of bias, 4) Synthesize the evidence, 5) Develop conclusion statement and grade the evidence, and 6) Recommend future research. The methods used to answer the systematic review question is described in detail and includes the following:

### Develop a protocol

Describes the components of the systematic review protocol, with a transparent documentation of when the protocol was posted and whether any amendments were made to the protocol.

- **Develop an analytic framework:** Represents the overall scope of the systematic review question and depicts the contributing elements that were examined and evaluated.
- **Synthesis plan:** Describes the plan for how the included evidence in the systematic review will be explored, organized, and synthesized to aid development of conclusion statements.
- **Develop inclusion and exclusion criteria:** Describes the standard NESR inclusion and exclusion criteria, rationale for question-specific deviations from standard criteria (if any), as well as rationale for establishing optional criteria (if any).

## Search for and screen studies

Describes the process for identifying the most complete and relevant body of evidence to answer a systematic review question, including the literature search strategy.

## Extract data and assess the risk of bias

Outlines NESR's data extraction process and describes how risk of bias was assessed, including the tools used.

## Synthesize the evidence

Summarizes the process for describing, comparing and combining the included studies to answer the systematic review question.

## Develop conclusion statement and grade the evidence

Answer(s) the review question, with a grade that represents the strength of evidence supporting that conclusion statement.

## Recommend future research

Describes how gaps and limitations identified in the evidence were used to develop research recommendations to strengthen the body of evidence.

## Peer review

Describes the peer review processes used for the review.

## Results

### Literature search and screening results

Transparently documents the search results after removal of duplicates and provides the number of included articles within each level of synthesis organization. Also includes a list of full-text articles that were excluded, along with the rationale for exclusion.

### Evidence synthesis

Evidence is organized according to the synthesis plan, which was drafted *a priori* as part of the protocol ([Chapter 3](#)), and leverages extracted data and risk of bias assessments ([Chapter 5](#)). This section includes:

- **Description of the evidence:** Describes the included articles, focusing on participant characteristics, interventions/exposures and outcomes examined, methodology used, and a summary of study results.
- **Synthesis of the evidence:** Discusses overall themes in the body of evidence and provides an assessment of the strength of the evidence.
- **Assessment of the evidence:** Discusses the experts' assessment of the individual grading elements including consistency, precision, risk of bias, directness, and generalizability.

## Conclusions

Answers the review question, with a grade that represents the strength of, or level of certainty in, the evidence supporting that conclusion statement. Conclusion statements and grades are drafted according to the synthesis plan.

## Research recommendations

Suggests future research based on the gaps and limitations identified in the evidence.

## Included articles

Provides reference list of articles included in the review.

## Making systematic review reports publicly available

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All completed NESR systematic reviews are made accessible to the public. Prior to conducting the systematic reviews, the protocol is posted on the NESR website (<https://nesr.usda.gov/protocols>) for the public to view. Any subsequent modifications made to the protocol during the review process are documented as amendments and posted online with an updated protocol ([Chapter 3](#)). All completed reports for each systematic review are published in entirety on the NESR website (<https://nesr.usda.gov/projects>) and made available through National Library of Medicine's National Center for Biotechnology Information website (<https://www.ncbi.nlm.nih.gov/books/>). In addition, some NESR systematic reviews are published in peer-reviewed journals, and reviews conducted with a Dietary Guidelines Advisory Committee are summarized in their respective scientific report.

## Chapter 8: Updating NESR Systematic Reviews

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### Summary

**Purpose:** To determine whether there is an existing, relevant NESR systematic review that can be used as is without updating, or whether it needs to be updated.

**Who:** An expert group updates an existing NESR systematic review. The process is facilitated and documented by NESR analysts, and Federal stakeholders may provide input.

**What:** Updating a NESR systematic review is a formal process in which the standard NESR methodology is used to search for, evaluate, analyze, and synthesize newly published evidence with the evidence included in an existing NESR systematic review.

### Identifying existing, relevant NESR systematic reviews

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Using an existing NESR systematic review to answer a research question can prevent duplication of effort, promote resource management, and provide transparency to the evolution in science supporting dietary guidance. However, depending on the status of an existing NESR systematic review, it may need to be updated. Updating a NESR systematic review is a formal process in which the standard NESR methodology is used to search for, evaluate, analyze, and synthesize newly published evidence with the evidence included in an existing NESR systematic review. NESR methods were informed by other organizations that conduct and update systematic reviews.<sup>1-4</sup> This chapter describes the NESR methodology for determining whether and how to update an existing NESR systematic review.

The process begins once the key questions for an upcoming project have been identified. For each question, NESR analysts determine if there is a relevant, existing NESR systematic review answering the same research question.

NESR analysts will evaluate the existing systematic review's protocol, which was developed in collaboration with a previous expert group, to determine whether it still captures the most appropriate and relevant body of evidence to answer the question. NESR may identify potential edits to the protocol at this point but, in most cases, the existing review remains relevant for answering the research question. The history of the protocol and edits made in the most recent protocol are reported as protocol amendments ([Chapter 3](#)). In rare instances, proposed protocol changes are so extensive that conducting a *de novo* NESR review is the more appropriate decision.

Relevance is confirmed if there is sufficient alignment between the existing protocol and the new protocol that results from any proposed changes. The protocols do not need to be identical; rather, the existing review must reasonably contribute to answering the same question.

### Determining whether or not to update an existing relevant NESR systematic review

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If an existing, relevant NESR systematic review is identified, the NESR analysts assess whether the existing review reflects the current state of science on the topic, or whether reviewing newly published evidence could result in changes to the conclusion statement(s) and/or grade(s), thus warranting the investment of time and

resources for a systematic review update. Expert feedback may be needed to make this determination. If this process occurs before the establishment of the project's expert group, Federal stakeholders may be consulted, as needed, to help develop the draft protocol and enable the NESR team to proceed with preparatory work. Upon establishment of the project's expert group, the NESR team presents any initial work that has been done, including proposed changes to the protocol, and the expert group makes final decisions.

These determinations can be facilitated using the decision tree for using as is or updating NESR systematic reviews (**Figure 1**). The considerations that contribute to this decision are **not** ranked by importance and should be considered in light of each other:

- **Timeliness: How recently the literature search was conducted for the existing review.** For example, if the review did not include articles published in the last several years, an update may be needed to capture recently published evidence. This is particularly true if the topic is actively being researched.
- **Methodology: Advancements in the field of research.** Expert knowledge of whether there have been methodological advancements in the field that justify an update to ensure the current state of the science is reflected.
- **Strength of the Evidence: The grade assigned to the conclusion statement in the existing review.** Each grade indicates the certainty in the evidence and the likelihood that new evidence would result in changes to the conclusion statement. For example, if the existing review's conclusion statement had a grade of Moderate, Limited or Grade Not Assignable, review of new evidence could be more likely to result in changes to the grade or conclusion than a grade of Strong.
- NESR analysts or the NESR librarian should also confirm if any articles included in the existing review have since been retracted. If any are found, NESR determines whether the existing conclusion statements or grades are affected, which may require expert input. If the retracted article(s) affected the conclusion statement or grade, the primary studies from the existing review should be fully re-synthesized with the new evidence (see update option 1 below).
- **Research availability: Whether there is sufficient new evidence available to warrant an update.**
  - NESR will evaluate research availability using one of two methods: evidence scans or Continuous Evidence Monitoring (CEM) ([Chapter 9](#), [Chapter 10](#)):
  - The results of evidence scans and/or CEM will inform whether there is sufficient evidence available to update an existing NESR systematic review. Within the field of systematic review methodology, there is no established rule that specifies the number of studies needed to prompt an update to an existing review. Therefore, this determination must be made on a question-by-question basis, taking into consideration the volume and characteristics of studies that meet criteria for inclusion, how newly published literature addresses gaps and limitations identified in the existing review, and multiple perspectives, such as the expert group, NESR, Federal support staff, project leadership, or Federal subject matter experts.

## Using an existing NESR systematic review, as is (without updating)

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If a relevant existing NESR review is determined to reflect the current state of science, the rationale is documented and the conclusion statements and grades from the existing review are used as they are, without being updated, to answer the systematic review question.

## Updating an existing NESR systematic review

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If updating an existing, relevant NESR review is the most appropriate choice, one of two update options can be used (discussed below). Regardless of which option is used, the new evidence is discussed as it relates to the conclusions or findings of the existing review, and the resulting conclusions and grades reflect a rigorous assessment of the entire body of evidence.

It may be appropriate to revise the existing protocol to answer the research question. Often these revisions will be minor in nature, a result of feedback from previous expert groups or insights gleaned from NESR's continuous quality advancement work that occurred since the existing review was completed. More substantial protocol changes may benefit from feedback from subject matter experts before proceeding. All protocol changes and their rationale are clearly documented, and the project's expert group is ultimately responsible for making final protocol decisions ([Chapter 3](#)). NESR systematic review methodology is then used to search for and screen studies, extract data, assess risk of bias, and describe and synthesize the evidence, based on the updated protocol.

There are two options for updating an existing NESR review. The NESR team proposes one of the two options, and the expert group selects the appropriate update option during protocol finalization:

- **Option 1: Synthesize evidence from existing review and new search as one body of evidence.** Primary studies from the existing review and new, included studies published since that review are synthesized as one body of evidence. The resulting conclusion statements and grades reflect the full body of evidence. This option will be an appropriate approach for most systematic review questions. Unique considerations in the standard NESR systematic review methodology for option 1 are described below:
  - Data extraction & Risk of bias: Extracted data from articles included in the existing review and those identified from the new evidence are presented in the same format to the expert group. Risk of bias assessments from the existing review are updated if necessary to allow comparability across the old and new sets of studies.
  - Evidence synthesis: All articles - those included in the existing review and those identified during the update process - are synthesized by the expert group as one body of evidence ([Chapter 6](#)), in accordance with a synthesis plan ([Chapter 3](#)).
  - Conclusion statement development & Grading: Conclusion statements and grades should reflect the entire body of evidence (i.e., studies included in the existing review and the update).
- **Option 2: Assess new evidence as it relates to existing evidence.** This second option allows the full body of evidence to be reflected in the updated conclusion statements and grades without a complete re-synthesis of the individual studies from the previous review. This option can be appropriate in certain situation, such as when:
  - The strength of evidence in the existing review indicates conclusions are unlikely to change (e.g., all/most conclusion statements have a grade of strong).
  - Resource limitations prohibit use of option 1 methods.
- Unique considerations in the standard NESR systematic review methodology for option 2 are described below:
  - Data extraction & Risk of bias: Data extraction and risk of bias assessment are completed for the new evidence only. Data and risk of bias assessments from the existing review remain as they are in the existing review.

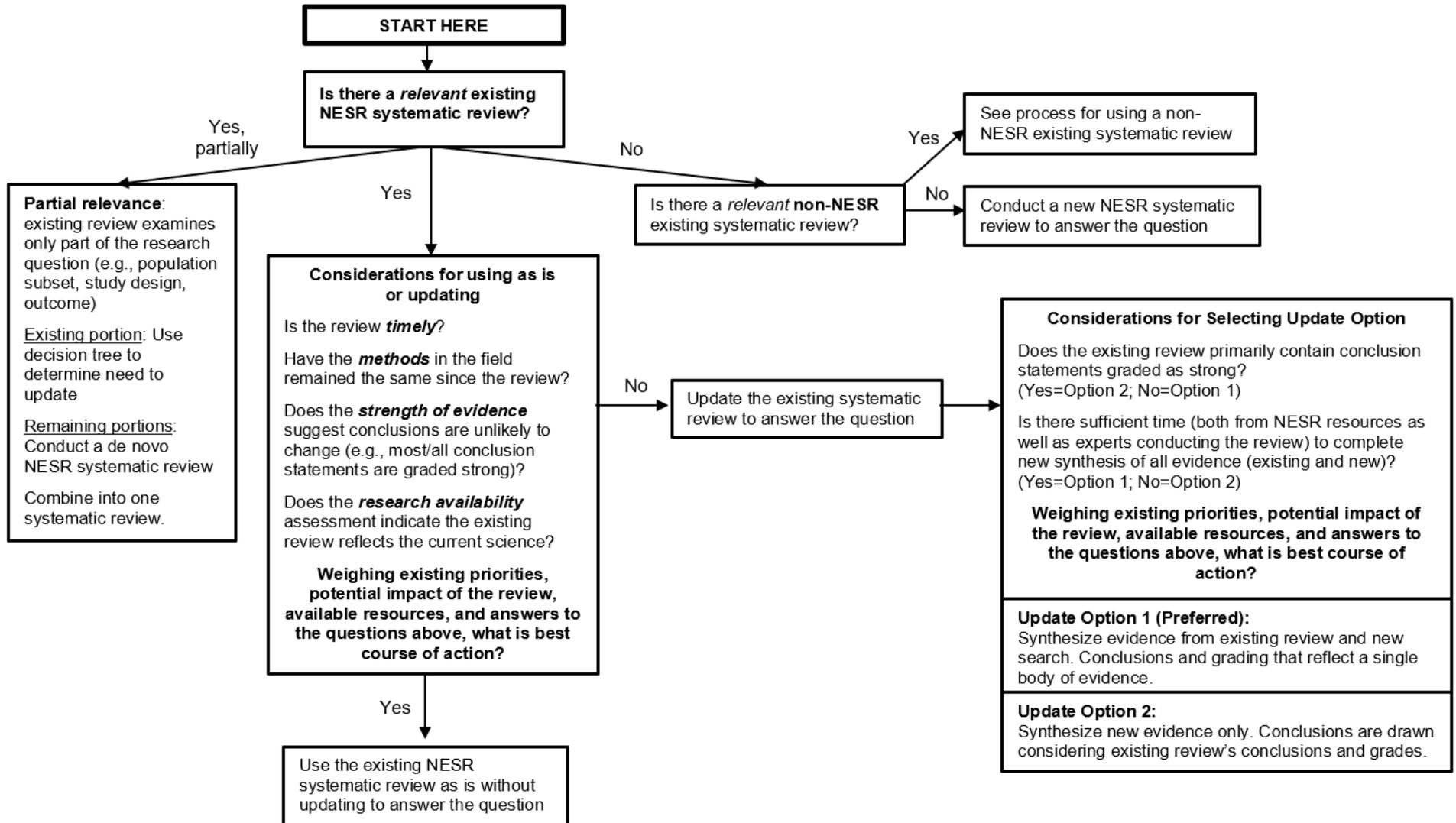
- Evidence synthesis: The more recent evidence is fully described in the description of evidence and synthesis sections as in a *de novo* NESR systematic review. A paragraph summarizing the body of evidence from the existing review should also be included. The expert group synthesizes the new evidence in accordance with the synthesis plan and then considers the new evidence in light of evidence in the existing review.
- Conclusion statement development & Grading: The expert group determines if the existing conclusion statements should be retained without any modifications or should be updated to appropriately reflect both the existing review and the newer evidence. Then, for each conclusion statement, an assessment of evidence is conducted by study design, focusing specifically on the evidence that underlies each conclusion statement – an approach consistent with NESR’s systematic review methodology. The assessment of evidence for each grading element includes the assessment of that element for the newly synthesized studies alongside the assessment of that element in the existing review (if available). Based on these considerations, the expert group will determine a grade for each conclusion statement considering both the existing review and the newer evidence. Clear rationale for each grade should be provided. The grade may be the same or different than the grade in the existing review.

## Making updated NESR systematic reviews publicly available

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Each updated NESR systematic review is thoroughly documented to provide transparency to the approach used to update the review ([Chapter 3](#), [Chapter 7](#)). The protocol for the review update is posted online for the public to view and includes a table documenting the history of the NESR systematic review question. If an existing NESR systematic review is updated using option 1, the new review will reflect the complete body of evidence and will replace the existing review. If an existing NESR systematic review is updated using option 2, the review will document the new evidence, and will refer to the existing review for the original evidence.

Figure 1. A decision tree for determining when to update a NESR systematic review



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## Chapter 9: Evidence Scans

### Summary

**Purpose:** To systematically evaluate the volume and characteristics of evidence available to inform systematic review or rapid review project planning, such as research availability, resource requirements, or protocol development.

**Who:** NESR analysts and librarians conduct evidence scans, based on input from Federal stakeholders.

**What:** A NESR evidence scan is an exploratory evidence description project in which systematic methods are used to search for and describe the volume and characteristics of evidence available on a nutrition question or topic of public health importance. Evidence scans can be either stand-alone projects or an initial step that can inform a future systematic or rapid review.

### Rationale for conducting evidence scans

A NESR evidence scan is an exploratory evidence description project in which systematic methods are used to search for and describe the volume and characteristics of evidence available on a nutrition question or topic of public health importance. Evidence scans can be either stand-alone projects or an initial step that can inform a future systematic or rapid review ([Chapter 11](#)).

NESR evidence scans use systematic methods to search, screen and describe the type and amount of evidence on a topic, but does not answer a systematic or rapid review research question. NESR evidence scans may be completed as quickly as within 2 to 4 weeks, depending on the scope of the evidence scan question and methods used.

NESR evidence scans are used to inform:

- systematic or rapid review protocol development, including
  - clarifying and refining the question,
  - evaluating and refining the analytic framework and inclusion/exclusion criteria,
  - developing and testing a search strategy,
  - identifying questions requiring clarification and input from subject matter experts,
  - informing synthesis planning;
- whether sufficient research is available to conduct a new or update an existing systematic or rapid review;
- prioritization of systematic or rapid review questions;
- the type of review project that may best meet the requesters' needs (e.g., rapid review, full systematic review, update to an existing review);
- resource requirements (e.g., approximate number of articles, characteristics of the literature, synthesis approach, etc.) for conducting a systematic or rapid review.

NESR developed a product that was descriptive in nature and did not seek to answer a systematic or rapid review research question by synthesizing evidence. In the field of evidence synthesis, there is no single, standardized methodology for conducting an evidence scan, nor is there commonly accepted terminology for this type of product. For example, some refer to this type of product as a scoping review, defined as “a type of literature that identifies and characterizes, or maps, the available research on a broad topic.”<sup>1</sup> However, others

have defined a scoping review, by including synthesis as part of the definition: “a form of knowledge *synthesis* that addresses an exploratory research question aimed at mapping key concepts, types of evidence, and gaps in research related to a defined area or field by systematically searching, selecting, and synthesizing existing knowledge.”<sup>2</sup> The terminology of “scoping review” was avoided to prevent confusion; thus this product is called an “evidence scan.”

## NESR’s evidence scan methodology

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NESR’s evidence scan methods are derived from the initial steps of NESR’s systematic review methodology ([Chapter 3](#), [Chapter 4](#), [Chapter 5](#)) but are intended to be tailored depending on the purpose of the scan and the resources and timeline available. Evidence scan methods are flexible, yet also retain scientific integrity.

A NESR evidence scan generally includes the following steps:

- Develop an evidence scan protocol
- Search for and screen studies
- Extract minimal data
- Describe the volume and characteristics of evidence

However, because a NESR evidence scan does not seek to answer a systematic or rapid review question, NESR evidence scans do not generally include:

- Extraction of study results
- Assessment of risk of bias
- Synthesis of the evidence
- Development of conclusion or summary statements
- Grading of the strength of the evidence

Methods used to conduct a NESR evidence scan are tailored to the question being addressed and designed to meet the specific needs of the requester (e.g., rationale, timeline, and circumstances). The evidence scan question and inclusion/external criteria may be broad (i.e., PICO elements less well defined) to inform a new review protocol where there is a high level of uncertainty. Methods may be streamlined in order to obtain an accurate estimate of the volume and characteristics of evidence available in an efficient way (e.g., fewer bibliographic databases searched, narrower date range, use of technology to assist screening and no evidence synthesis). It is possible that the literature search and screening done as part of these evidence scans will not be used or may need to be expanded or revised for a future systematic or rapid review. In other cases, an evidence scan may lead directly into a systematic or rapid review, and therefore, the evidence scan search and screening methods would more closely reflect the initial steps of a NESR systematic or rapid review.

## Developing an evidence scan protocol

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An evidence scan protocol is developed by NESR analysts and librarians in collaboration with Federal stakeholders, who provide input on the draft protocol. The protocol consists of the following components:

- Evidence scan question
- Rationale
- Analytic framework

- Inclusion and exclusion criteria
- Literature search strategy
- Screening methods
- Data extraction methods

The evidence scan question may be provided to the NESR team by Federal stakeholders, or the NESR team may develop the question in collaboration with the Federal stakeholders. An evidence scan question can be framed as a systematic or rapid review (i.e., What is the relationship between [intervention/exposure] and [outcome]?) or can be framed to be more exploratory (e.g., "What evidence has been published to examine the relationship between consuming high levels of protein and acute, toxicological effects in humans?"). Exploratory questions may be answered by the evidence scan; however, questions that are framed as systematic or rapid reviews are not answered by an evidence scan; instead, the scan provides a description or characterization of evidence available on that topic.

Having the rationale and background for why an evidence scan question needs to be addressed provides NESR with important context necessary for developing a draft protocol that appropriately addresses the question of interest. To the extent possible, the NESR team uses existing NESR protocols that address similar intervention and exposures and/or outcomes to develop a protocol.

The remaining components of an evidence scan protocol use NESR's systematic review methodology as a starting place and are then tailored depending on the purpose of the scan and the resources and timelines available.

## Making evidence scans publicly available

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Each evidence scan is thoroughly documented. When evidence scan results are used by Federal stakeholders or expert groups to guide important decisions, evidence scan reports or evidence scan findings may be posted on the NESR website ([nesr.usda.gov](https://nesr.usda.gov)) or shared using other means, such as public presentations. Alternatively, evidence scans may be published as part of a protocol or a rapid or systematic review report.

The description of the evidence includes a detailed summary of the volume and characteristics of the evidence which may be presented in text, figures, and/or tables. The following type of information is reported, with minimal additional information provided:

- Number of studies
- Study design
- A description of population(s), intervention(s) and exposure(s), comparator(s), and outcome(s) addressed by the evidence.

In some cases, NESR analysts may also document considerations for a future systematic or rapid review, identify gaps in the literature or research recommendations using the objective information gathered in the scan.

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# Chapter 10: Continuous Evidence Monitoring

## Summary

**Purpose:** To systematically monitor the volume and characteristics of newly published evidence over time so that resource requirements and determinations for when and whether updates to an existing NESR systematic review should be made.

**Who:** NESR analysts and librarians conduct continuous evidence monitoring, based on input from Federal stakeholders and using established systematic review protocols that were developed by a previous expert group.

**What:** An evidence gathering process in which established systematic review protocols are used to periodically search for, screen, and prepare evidence for future systematic reviews.

## Rationale for continuous evidence monitoring

Continuous Evidence Monitoring (CEM) is a process of gathering evidence in which established systematic review protocols are used to periodically search for, screen, and prepare evidence for future systematic reviews. It involves ongoing, periodic literature searching and screening, and in some cases, data extraction and risk of bias assessment, using an existing systematic review protocol that was developed by an expert group.

NESR developed CEM primarily in the context of working with a Dietary Guidelines Advisory Committee, which is reestablished every 5 years and is limited to a 2 year tenure to complete their review of the evidence ([Chapter 1](#)). Systematic reviews, particularly the literature search and screening, data extraction and risk of bias processes, are comprehensive, but time- and resource-intensive. As other systematic review organizations began to explore or adopt continuous or living review approaches, NESR staff recognized and received feedback from stakeholders that implementing evidence monitoring would improve continuity in between Dietary Guidelines Advisory Committees.<sup>1, 2</sup> NESR developed CEM as a way to monitor the evidence on high priority topics in the interim period between Committees. While CEM does not reduce the overall workloads associated with conducting systematic reviews, it does promote continuity and efficiency by redistributing the work across a longer period of time. CEM ensures that evidence will be ready for review by the next Dietary Guidelines Advisory Committee earlier in their tenure, in order to maximize the Committee's time. It is important to note that each Committee has the opportunity to review and modify a protocol as needed prior to beginning their review of evidence. However, even if a Committee does make protocol modifications, the NESR team designed CEM with flexibility in mind, to allow for adjustments if needed and still have bodies of evidence ready for synthesis in a timely fashion. In addition, CEM can be applied for systematic and rapid reviews that are conducted for projects other than the *Dietary Guidelines for Americans*.

NESR's CEM approach aligns with the methods of other organizations that conduct 'living' or 'continuous' systematic reviews. In particular, numerous organizations have applied a similar process of periodic searching, screening, extraction, and risk of bias assessment.<sup>3-9</sup> A key difference between NESR's CEM process and others is the point at which evidence is synthesized and the review is updated. Other organizations that conduct living reviews typically update the reviews based on the volume or likely impact of new evidence. The NESR CEM process is designed to occur between Dietary Guidelines Advisory Committees, which are

reestablished every 5 years. When convened, the Committee will then update the review, if the systematic review question is selected to be addressed.

## Selecting systematic review questions for CEM

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Questions eligible for CEM are (1) high priority questions that are likely to be addressed by the next Dietary Guidelines Advisory Committee and (2) those which have approved protocols with relatively high scientific confidence, indicating that substantial changes by the next Committee are not expected.

Determining if a question is likely to be addressed by the next Dietary Guidelines Advisory Committee is the responsibility of the USDA and HHS team of staff who lead and support the development of the *Dietary Guidelines for Americans* and considers the following:

- Relevance to creating the *Dietary Guidelines for Americans*,
- Importance to public health,
- Potential impact on Federal food and nutrition programs, and
- Desire to avoid duplication of Federal scientific review efforts

The second requirement for CEM eligibility is scientific confidence in the protocol, such that substantial changes are not expected to be made by the next Committee. To indicate the level of confidence in each protocol, NESR analysts review, discuss, and compile information from various sources including staff, former Committee members or other expert groups members, and public comments. Confidence in a protocol is determined to be high when little to no changes are expected. In some cases, there may be less confidence in some aspects of the protocol, and the CEM process can be tailored to account for this uncertainty, such that if protocol modifications are made by the next Committee, the NESR team could make adjustments that would account for these modifications with as little rework as possible, ensuring that evidence is still available for review early in the Committee's tenure. Finally, in cases where confidence in a protocol is determined to be low, NESR recommends against pursuing CEM until the protocol can be reviewed and updated by the next Committee or another expert group.

## Implementing the CEM process

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Once a question is selected for CEM, the remaining steps follow NESR's standard systematic review methodology ([Chapter 2](#), [Chapter 3](#), [Chapter 4](#), [Chapter 5](#), [Chapter 6](#), [Chapter 7](#)). In short, the NESR librarian will review the existing literature search strategy, making any necessary updates, conduct a search to capture studies published since the original review was completed, and then establish automated literature searches that will be run on a predetermined timeline (e.g., daily, weekly, monthly). Any literature searches that cannot be automated will be conducted manually on a predetermined timeline (e.g., quarterly). NESR analysts will then periodically screen the search results using a process that involves at least two screeners independently screening at title, abstract, and full text levels. Depending on resource availability, NESR analysts may also extract data and conduct risk of bias assessments for articles that meet criteria for inclusion on an on-going basis. However, in many cases, data extraction and risk of bias assessment will not be on-going, but rather, done at a timepoint closer to when the review may be updated by the next Committee.

CEM may also be used to evaluate research availability ([Chapter 2](#)). This evaluation helps determine whether there is sufficient evidence available to update an existing NESR systematic review, and to estimate the resource requirements for conducting or updating a review.

Documentation of the process and literature search results is maintained during CEM and published as part of the final systematic review after it is updated ([Chapter 7](#)).

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## Chapter 11: Rapid Reviews

### Summary

**Purpose:** To answer a nutrition question of public health importance in a more timely manner.

**Who:** NESR analysts and librarians conduct rapid reviews, based on input from Federal stakeholders.

**What:** An evidence synthesis project that answers a nutrition question of public health importance using streamlined systematic review methods. Methods used to search for, evaluate, synthesize, or assess the evidence may be tailored to conserve resources and produce a timelier product when full systematic review methods are not needed or feasible.

### Rationale for rapid reviews

A NESR rapid review is an evidence synthesis project that answers a nutrition question of public health importance using streamlined systematic review methods. Methods used to search for, evaluate, synthesize, or assess the evidence may be tailored to conserve resources and produce a timelier product when full systematic review methods are not needed or feasible. Although systematic review methods are modified to expedite the process, a rapid review is still characterized by rigorous, transparent, and reproducible methods.<sup>1</sup> A rapid review can be completed in a shorter timeframe than an equivalent systematic review through modifications to the scope, review methods, and desired end products. Rapid reviews are particularly useful when the extensive time requirements, resource demands, or level of detail characteristic of a full systematic review do not meet the requester's goals of timely access to evidence to inform decisions.

There is no single, standardized rapid review method; however, several reputable organizations have proposed guidance.<sup>1-5</sup> The methodology utilized for each NESR rapid review is informed by and tailored to the scientific question being answered and the specific needs of the requester (e.g., timeline, purpose, scope, circumstances, and stakeholders) while retaining scientific integrity. Process modifications vary on two important dimensions that impact resource allocation: question scope and level of process rigor. These modifications may impact question development; composition of the review team; staffing requirements; methods for the literature search, article screening, data extraction, risk of bias assessment, evidence synthesis, or assessment of evidence strength; summary or conclusion statement development; and final product preparation and dissemination, all of which affect the project timeline and cost. Best practices and recommendations from other research and health organizations, including the World Health Organization, Cochrane, the Agency for Healthcare Research and Quality, JBI, and the Center for Evidence-Based Medicine at the University of Oxford, inform the process by which NESR develops and conducts rapid reviews.<sup>1-5</sup>

Rapid reviews are characterized by the potential trade-off between reduced time and resource requirements, and level of certainty in the conclusions. They are frequently used to update existing reviews or answer focused research questions that address a targeted, concise set of interventions/exposures and outcomes.<sup>2</sup> Rapid reviews are not ideal for answering complex questions or for informing Federal policy decisions that require a greater level of certainty in the conclusions. A rapid review may be a more appropriate, cost effective, and timely approach when evidence is needed to:

- Answer urgent and emergent public health questions;
- Evaluate the effectiveness of different interventions, policies, or models of operations;

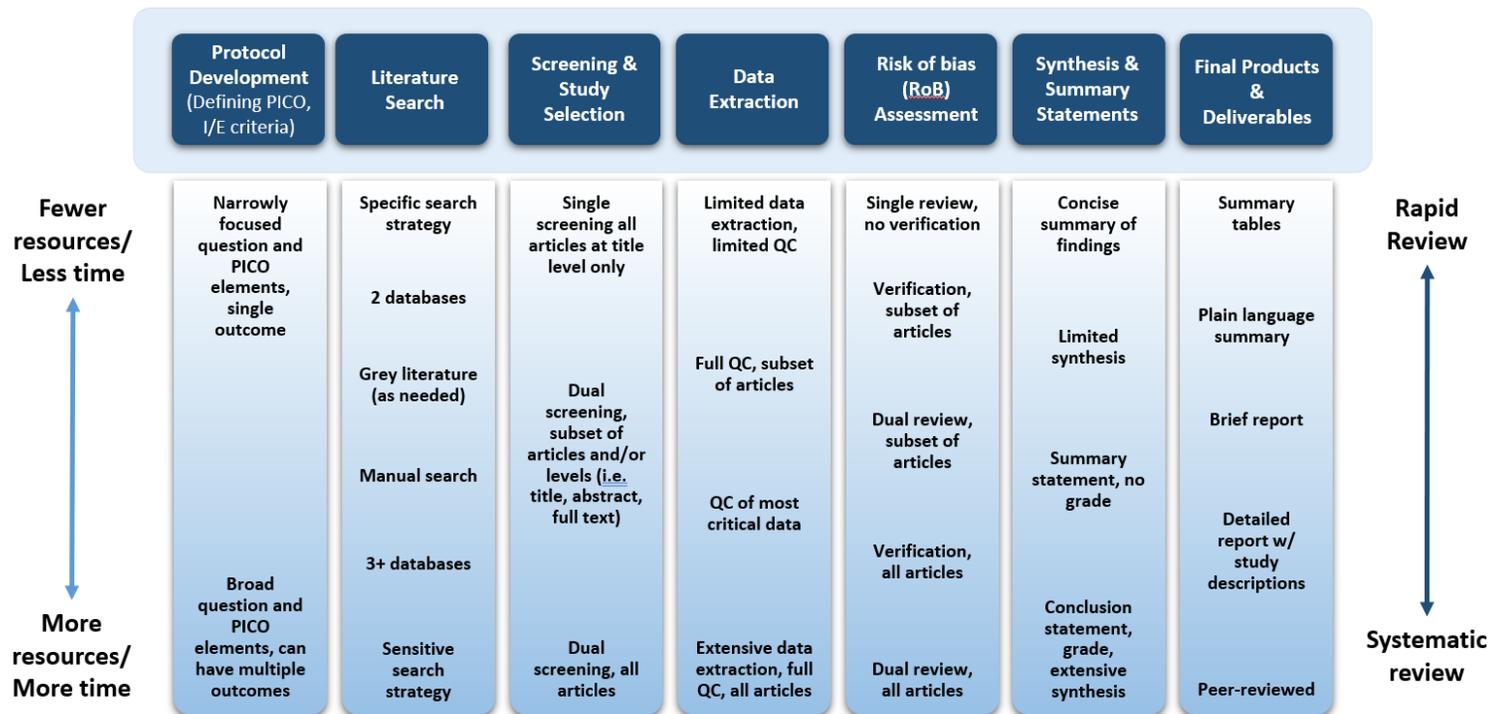
- Characterize the state-of-the-evidence on a topic;
- Identify research needs; or
- Inform communication initiatives.

The process by which NESR develops a rigorous *a priori* protocol and methods for a rapid review, the type and extent of modifications that can be made to streamline and expedite the review process, and the potential trade-offs of each type of modification are described below. However, the impact of each modification to the review process on the level of bias introduced into the results and the validity or precision of the conclusions is unclear.<sup>1, 2, 6, 7</sup> Thus, for each rapid review it is important to clearly and transparently document the modifications to NESR systematic review methods that were applied, acknowledge the limitations of the methods used, and interpret results in light of these limitations.<sup>1</sup>

## Developing a rapid review protocol and selecting streamlined methods

A rapid review protocol provides a detailed description of the approach being used to conduct the review, including the research question(s), analytic framework, inclusion and exclusion criteria, and literature search strategy. The protocol also describes the methods for literature screening, data extraction, risk of bias assessment, data analysis, and evidence synthesis. A rapid review protocol is developed using similar methods as those used for a systematic review protocol ([Chapter 3](#)), but one or all parts of a protocol may be streamlined to produce the product in a timelier fashion. The spectrum of methodology decisions that may be considered when developing a rapid review protocol are illustrated in **Figure 2** and described in the subsequent sections.

**Figure 2: Spectrum of NESR rapid review methodology streamlining options**



An analytic framework is developed to outline the population, intervention or exposure, comparator, and outcome(s) of interest. For rapid reviews, these components are defined in the most specific way possible to facilitate a targeted review of the literature.

NESR inclusion/exclusion criteria are then developed. All criteria should be as focused as possible to facilitate timely completion of the rapid review.

To improve efficiency, relevance, and applicability of the rapid review, the protocol should explain the methods selected for screening, data extraction, and risk of bias assessment. In addition, the protocol should provide the strengths and limitations discussed with the Federal stakeholders who requested the review to confirm that the approach meets their needs.

Below are streamlining options that can be considered when developing a rapid review protocol. For each, a brief description of the method used for a NESR systematic review is provided followed by options that may be considered in the rapid review.

## Literature search and screening

### Literature search strategy

NESR systematic review standard: Search strategy is developed by one librarian and peer-reviewed by a second librarian. Search strategy is developed and implemented in multiple electronic bibliographic databases, typically PubMed/MEDLINE, CENTRAL (Cochrane), and Embase, in addition to other databases appropriate to the topic (e.g., CINAHL Plus, ERIC); a manual search is conducted to find articles not identified in the electronic database search ([Chapter 4](#)).

Rapid review options:

- Search for and use existing non-NESR review(s) ([Chapter 2](#))
- Search only two electronic databases
- No peer review of the literature search strategy
- Refine search terms to prioritize specificity over sensitivity
- No manual search of existing reviews or included articles

### Screening studies

NESR systematic review standard: Results of all electronic database searches, after removal of duplicates, are screened independently by two NESR analysts using a stepwise process by reviewing titles, abstracts, and full-texts to determine which articles meet the inclusion criteria ([Chapter 4](#)).

Rapid review options:

- Use of technology, such as machine learning, to assist in screening
- Two NESR analysts independently dual screen a percentage of articles, and one NESR analyst screens the rest
- One NESR analyst screens all results at the title level

## Data extraction

NESR systematic review standard: Extraction of predefined data by one NESR analyst, full quality control by a second NESR analyst ([Chapter 5](#)).

Rapid review options:

- Minimize the amount of predefined data that are extracted
- Extract basic descriptive information during screening
- Limited quality control of only the most critical data
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## Risk of bias assessment

NESR systematic review standard: Two NESR analysts independently assess risk of bias ([Chapter 5](#)).

Rapid review options:

- One NESR analyst assesses risk of bias, and a second NESR analyst verifies the assessment
- One NESR analyst assesses risk of bias, and a second NESR analyst verifies the assessment for a percentage of articles
- One NESR analyst assesses risk of bias with no verification by a second NESR analyst

## Synthesis

NESR systematic review standard: Synthesis involves a detailed description of the body of evidence, and includes a formal, written synthesis detailing patterns of agreement and disagreement, methodological differences, limitations, and research gaps across the body of evidence ([Chapter 6](#)).

Rapid review options:

- Synthesizing data from primary analyses only, with no secondary or sub-group analyses
- Varying depth of synthesis or prioritizing by source of evidence (e.g., stronger vs. weaker study design)
- Synthesizing data from an existing review and any primary literature published since the end date of publication for included articles of that existing review

## Development of summary statement(s) and grading the evidence

NESR systematic review standard: Conclusion statements carefully summarize the answer to the systematic review and reflect areas of general agreement across studies. An overall grade for the strength of evidence is formally assigned to each conclusion statement ([Chapter 6](#)).

Rapid review options:

- Develop concise statements summarizing the main conclusion(s) from the synthesis that may or may not be formally graded.

## Making rapid reviews publicly available

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As is standard for NESR's systematic review methodology, the protocol, search strategy, and results are fully and transparently documented in the rapid review final report ([Chapter 3](#), [Chapter 7](#)). However, the description of evidence and synthesis sections are presented in the format agreed upon at the start of the project and may be much more streamlined than those developed for a systematic review. Rapid review final products and deliverables may include:

- A summary document only (plain language style), which may be presented alone or in combination with visual communications
- A short, written report with brief synthesis by topic area and evidence tables or other visuals
- A full written report with detailed synthesis and summary tables
- A peer-reviewed publication

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