USDA
UNITED STATES DEPARTMENT OF AGRICULTURE

Ultra-Processed Food Dietary Patterns and Growth, Body Composition, and Risk of Obesity: A Systematic Review Protocol

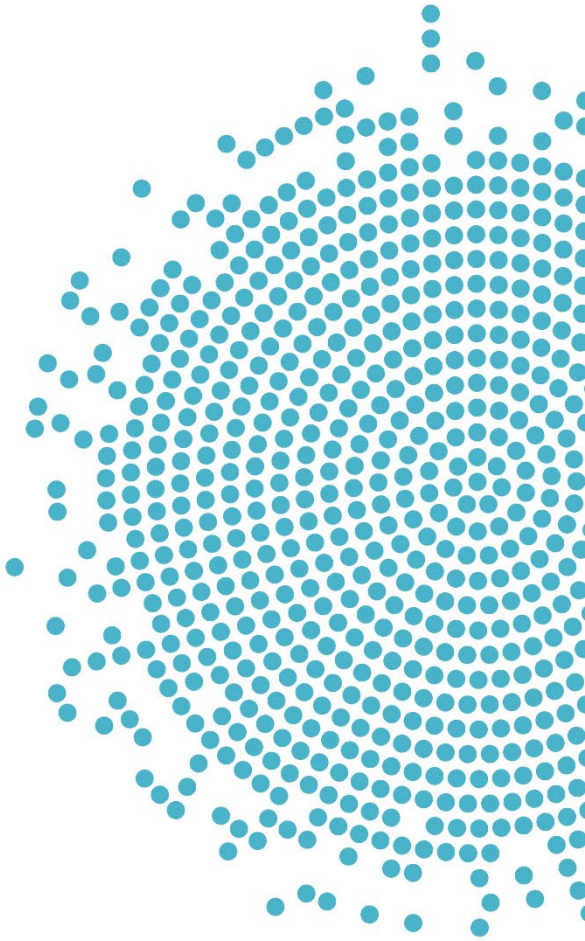

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Table of contents

Introduction

To prepare for the development of the *Dietary Guidelines for Americans, 2025-2030*, the U.S. Departments of Health and Human Services (HHS) and Agriculture (USDA) identified a proposed list of scientific questions based on relevance, importance, potential federal impact, and avoiding duplication, which were posted for public comment.[*] The Departments appointed the 2025 Dietary Guidelines Advisory Committee (Committee) in January 2023 to review evidence on the scientific questions. The proposed scientific questions were refined and prioritized by the Committee for consideration in their review of the evidence. Their review forms the basis of their independent, science-based advice and recommendations to HHS and USDA, which is considered as the Departments develop the next edition of the *Dietary Guidelines*. As part of that process, the following systematic review question has been identified: What is the relationship between dietary patterns with varying amounts of ultra-processed foods consumed and growth, body composition, and risk of obesity?

The Committee will conduct a new systematic review to address this question, with support from USDA's Nutrition Evidence Systematic Review (NESR) team (**Table 1**).

Table 1. Review history

Date	Description	Citation
October 2023	Systematic review protocol for the 2025 Dietary Guidelines Advisory Committee published online	Hoelscher DM, Anderson CAM, Booth S, Deierlein A, Fung T, Gardner C, Giovannucci E, Raynor H, Stanford FC, Talegawkar S, Taylor C, Tobias D, Obbagy J, English LK, Higgins M, Butera G, Terry N. Ultra-Processed Dietary Patterns and Growth, Body Composition, and Risk of Obesity: A Systematic Review Protocol. March 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/protocols

Methods

The NESR methodology manual [†] has a detailed description of the NESR methodology as it will be applied in the systematic reviews for the Dietary Guidelines for Americans, 2025-2030 Project. This section presents an overview of the specific methods that will be used to by the Committee to answer the systematic review question: What is the relationship between dietary patterns with varying amounts of ultra-processed foods consumed and growth, body composition, and risk of obesity?

Develop a protocol

A systematic review protocol is the plan for how NESR's methodology will be used to conduct a specific systematic review and is established by the Committee, *a priori*, before any evidence is reviewed. The protocol is designed to capture the most appropriate and relevant body of evidence to answer the systematic review question. Development of the protocol involves discussion of the strengths and limitations of various methodological approaches relevant to the question, which then inform subsequent steps of the systematic

[*] Dietary Guidelines for Americans: Learn About the Process. 2022. Available at: https://www.dietaryguidelines.gov/work-under-way/learn-about-process

[†] 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

review process. The protocol describes all of the methods that will be used throughout the systematic review process. Additionally, the protocol includes the following components, which are tailored to each systematic review question: the analytic framework, the inclusion and exclusion criteria, and the synthesis plan.

Revisions to the systematic review protocol were made during the review process. These revisions are documented in **Table 2**.

Table 2. Protocol revisions

Date	Protocol revision	Description
July 2023	Inclusion and exclusion criteria were added for confounders, specifying that studies must control for at least one key confounder listed in the analytic framework to be included.	This revision was made to enable focus on a stronger body of evidence. The revision was made before any evidence was synthesized.
July 2023	The inclusion and exclusion criteria for the outcome of gestational weight gain were revised to include only those studies that examine adequacy of total gestational weight gain (i.e., in relation to recommendations based on pre-pregnancy BMI). Studies that examine gestational weight gain during certain time periods or trimesters of pregnancy or total gestational weight gain not in relation to recommendations will be excluded.	This revision was made to focus on the most clinically meaningful measure of gestational weight gain. The revision was made before any evidence was synthesized.
July 2023	The inclusion and exclusion criteria for the intervention/exposure and comparator were revised to clarify that: • a study must provide a description of the foods and beverages in both the intervention/exposure and comparator groups to be included. • studies that examine consumption of and/or adherence to similar dietary patterns of which only a specific component or food source differs between groups are excluded.	These revisions were made before evidence synthesis to clarify the intent of the intervention/exposure and comparator criteria, but do not represent a change in how the criteria were applied.
September 2023	The inclusion criteria for study duration for weight loss and weight loss maintenance was reduced from ≥6 months and 12 months, respectively, to ≥12 weeks.	This revision was made so that study duration criteria is consistent across all growth, body composition, and risk of obesity outcomes. Longer-term studies on weight loss and weight loss maintenance will be prioritized in evidence synthesis. The revision was made before any evidence was synthesized.
September 2023	The exclusion criteria for outcome were revised to specify that studies that only report unintentional weight loss (i.e., a component of frailty) will be excluded.	This revision was made to clarify the intent of the outcome criteria but does not represent a change in how the criteria were applied.

Develop an analytic framework

An analytic framework visually represents the overall scope of the systematic review question and depicts the contributing elements that will be examined and evaluated. **Figure 1** is the analytic framework for the systematic review and shows that the intervention or exposure of interest is dietary patterns with varying amounts of ultra-processed foods consumed by infants, toddlers, children, adolescents, adults, individuals during pregnancy, individuals during postpartum, and older adults. The comparators are different dietary patterns or different levels of adherence to/consumption of the same dietary pattern. The outcomes are Growth

(in infants, toddlers, children, adolescents) including: height, length/stature-for-age, weight, weight-for-age, stunting, failure to thrive, wasting, BMI-for-age, weight-for-length/stature, body circumferences (arm, neck, thigh), head circumference; Body composition (in infants, toddlers, children, adolescents, adults, older adults) including: skinfold thickness, fat mass, ectopic fat, fat-free mass or lean mass, waist circumference, waist-to-hip-ratio; Risk of obesity (in children, adolescents, adults, older adults) including: BMI, underweight, normal weight, overweight and/or obesity, weight loss and maintenance (in adults, older adults); Pregnancy and postpartum-related weight change (in individuals during pregnancy or postpartum) including: gestational weight gain and postpartum weight change. The key confounders may impact the relationships of interest and are sex, age, physical activity, anthropometry at baseline, socioeconomic position, race and/or ethnicity in all populations, alcohol intake in adults and older adults, smoking in adults, older adults, and pregnancy, parity (pregnancy, postpartum), diabetes mellitus in the current pregnancy (pregnancy), hypertensive disorders in the current pregnancy (pregnancy), and human milk feeding (postpartum). Dietary patterns are defined as the quantities, proportions, variety, or combination of different foods, drinks, and nutrients (when available) in diets, and the frequency with which they are habitually consumed.

Figure 1. Analytic framework for the systematic review question: What is the relationship between dietary patterns with varying amounts of ultra-processed foods consumed and growth, body composition, and risk of obesity?

Population	***Intervention/ exposure***	***Comparator***	***Outcome***	***Key confounders***
Infants and toddlers (birth up to 24 months) Children and adolescents (2 up to 19 years) Adults and older adults (19 years and older)	Consumption of a dietary pattern with varying amounts of ultra-processed foods (UPF)	Different dietary pattern(s) Different adherence/ consumption levels to the same dietary pattern	Growth (in infants, toddlers, children, adolescents) • Height, length/stature-for-age • Weight, weight-for-age • Stunting, failure to thrive, wasting • BMI-for-age, weight-for-length/stature • Body circumferences (arm, neck, thigh) • Head circumference Body composition (in infants, toddlers, children, adolescents, adults, older adults) • Skinfold thickness • Fat mass, ectopic fat • Fat-free mass or lean mass • Waist circumference, waist-to-hip-ratio Risk of obesity (in children, adolescents, adults, older adults) • BMI • Underweight • Normal weight • Overweight and/or obesity • Weight gain • Weight loss and maintenance (in adults, older adults)	• Sex • Age • Physical activity • Race and/or ethnicity • Socioeconomic position • Anthropometry at baseline • Smoking (adults, older adults) • Alcohol intake (adults, older adults)
Individuals during pregnancy and postpartum			Pregnancy and postpartum-related weight change (in individuals during pregnancy or postpartum) • Gestational weight gain • Postpartum weight change	• Age • Physical activity • Race and/or ethnicity • Socioeconomic position • Anthropometry at baseline • Smoking • Parity • Diabetes mellitus in the current pregnancy (pregnancy) • Hypertensive disorders in the current pregnancy (pregnancy) • Human milk feeding status (postpartum)

Synthesis organization:

I. ***Population***: Infants and toddlers; Children and adolescents; Adults; Older adults; Individuals during pregnancy; Individuals during postpartum
   i. ***Outcome:*** Growth; Body composition; Risk of obesity; Weight loss and maintenance; Pregnancy and postpartum-related weight change

Key definitions:

Dietary patterns: the quantities, proportions, variety, or combination of different foods, drinks, and nutrients (when available) in diets, and the frequency with which they are habitually consumed.

Develop inclusion and exclusion criteria

The inclusion and exclusion criteria provide an objective, consistent, and transparent framework for determining which articles to include in the systematic review (see **Table 3**). These criteria ensure that the most relevant and appropriate body of evidence is identified for the systematic review question, and that the evidence reviewed is:

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

Table 3. Inclusion and exclusion criteria

Category	Inclusion Criteria	Exclusion Criteria
Study design	• Randomized controlled trials • Non-randomized controlled trials* • Prospective cohort studies • Retrospective cohort studies • Nested case-control studies	• Uncontrolled trials† • Case-control studies • Cross-sectional studies • Ecological studies • Narrative reviews • Systematic reviews • Meta-analyses • Modeling and simulation studies
Publication date	• January 1980 – May 2023‡	• Before January 1980
Population: Study participants	• Human	• Non-human
Population: Life stage	At intervention or exposure and outcome: • Infants and toddlers (birth up to 24 months) • Children and adolescents (2 up to 19 years) • Adults and older adults (19 years and older) • Individuals during pregnancy • Individuals during postpartum	At intervention or exposure and outcome: • Individuals before pregnancy

* Including quasi-experimental and controlled before-and-after studies

† Including uncontrolled before-and-after studies

‡ This review update date range encompasses the original systematic review date range, which included articles published from 1980 to 2013

Category	Inclusion Criteria	Exclusion Criteria
Population: Health status	• Studies that <u>exclusively</u> enroll participants not diagnosed with a disease[*] • Studies that enroll <u>some</u> participants: o diagnosed with a disease; o with severe undernutrition, failure to thrive/underweight, stunting, or wasting; o born preterm,[†] with low birth weight,[‡] and/or small for gestational age; o and/or with the outcome of interest o who became pregnant using Assisted Reproductive Technologies; o with multiple gestation pregnancies; o pre- or post-bariatric surgery; o and/or receiving pharmacotherapy to treat obesity	• Studies that <u>exclusively</u> enroll participants: o diagnosed with a disease;[§] o hospitalized for an illness, injury, or surgery;[**] o with severe undernutrition, failure to thrive/underweight, stunting, or wasting; o born preterm,[†] with low birth weight,[‡] and/or small for gestational age o who became pregnant using Assisted Reproductive Technologies; o with multiple gestation pregnancies; o pre- or post-bariatric surgery; o and/or receiving pharmacotherapy to treat obesity
Intervention/ exposure	• Studies that examine consumption of and/or adherence to a dietary pattern [i.e., the quantities, proportions, variety, or combination of different foods, drinks, and nutrients (when available) in diets, and the frequency with which they are habitually consumed] with varying amounts of ultra-processed foods, including, at a minimum, a description of the foods and beverages in the pattern of each intervention/exposure and comparator group o Dietary patterns may be measured or derived using a variety of approaches, such as adherence to a priori patterns (indices/scores), data driven patterns (factor or cluster analysis), reduced rank regression, or other methods, including clinical trials • Multi-component intervention in which the isolated effect of the dietary pattern with varying amounts of ultra-processed foods on the outcome(s) of interest is provided or can be determined	• Studies that do not provide a description of the dietary pattern, which at minimum, must include the foods and beverages in the pattern (i.e., studies that examine a labeled dietary pattern, but do not describe the foods and beverages consumed in each intervention/exposure and comparator group) • Multi-component intervention in which the isolated effect of the intervention of interest on the outcome(s) of interest is not provided or cannot be determined (e.g., due to multiple intervention components within groups)

[*] Studies that enroll participants who are at risk for chronic disease will be included

[†] Gestational age <37 weeks and 0/7 days

[‡] Birth weight <2500g

[§] Studies that exclusively enroll participants with obesity will be included

[**] Studies that exclusively enroll participants post-cesarean section will be included

Category	Inclusion Criteria	Exclusion Criteria
Comparator	• Consumption of and/or adherence to a different dietary pattern • Different levels of consumption of and/or adherence to a dietary pattern	• Consumption of and/or adherence to a similar dietary pattern of which only a specific component or food source s differs between groups

Outcome(s)	• Growth (in infants, toddlers, children, adolescents)
	  ○ Height, length/stature-for-age
	  ○ Weight, weight-for-age
	  ○ Stunting, failure to thrive, wasting
	  ○ BMI-for-age, weight-for-length/stature
	  ○ Body circumferences (arm, neck, thigh)
	  ○ Head circumference
	• Body composition (in infants, toddlers, children, adolescents, adults, older adults)
	  ○ Skinfold thickness
	  ○ Fat mass, ectopic fat
	  ○ Fat-free mass or lean mass
	  ○ Waist circumference, waist-to-hip-ratio
	• Risk of obesity (in children, adolescents, adults, older adults)
	  ○ BMI
	  ○ Underweight
	  ○ Normal weight
	  ○ Overweight and/or obesity
	  ○ Weight gain
	  ○ Weight loss and maintenance (in adults, older adults)
	• Pregnancy and postpartum-related weight change (in individuals during pregnancy or postpartum)
	  ○ Adequacy of total gestational weight gain (i.e., in relation to recommendations based on pre-pregnancy BMI)
	  ○ Postpartum weight change
		• Gestational weight gain only during certain time periods or trimesters of pregnancy
		• Absolute total gestational weight gain (i.e., not in relation to recommendations based on pre-pregnancy BMI)
		• Weight loss that is specifically classified as unintentional weight loss (e.g., a component of Frailty)

Category	Inclusion Criteria	Exclusion Criteria
Confounders	• Studies that control for at least one of the key confounders listed in the analytic framework	• Studies that do not control for any of the key confounders listed in the analytic framework
Study duration (not applied to pregnancy and postpartum studies)	• Intervention length ≥12 weeks	• Intervention length <12 weeks
Size of study groups (not applied to pregnancy and postpartum studies)	• For intervention studies: ○ ≥30 participants per study group for between-subject analyses, ○ or a power calculation indicating that the study is appropriately powered for the outcome(s) of interest • For observational studies: ○ Analytic sample size of ≥1000 participants (only for adults and older adults)	• For intervention studies: ○ <30 participants per study group for between-subject analyses, ○ and no power calculation indicating that the study is appropriately powered for the outcome(s) of interest • For observational studies: ○ Analytic sample size n<1000 (only for adults and older adults)
Publication status	• Peer-reviewed articles published in research journals	• Non-peer reviewed articles, unpublished data or manuscripts, pre-prints, reports, and conference abstracts or proceedings
Language	• Published in English	• Not published in English
Country*	• Studies conducted in countries classified as high or very high on the Human Development Index the year(s) the intervention/exposure data were collected	• Studies conducted in countries classified as medium or low on the Human Development Index the year(s) the intervention/exposure data were collected

* The classification of countries on the Human Development Index (HDI) is based on the UN Development Program Human Development Report Office (http://hdr.undp.org/en/data) for the year the study intervention occurred or data were collected. Studies conducted prior to 1990 are classified based on 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 (The World Bank. World Bank country and lending groups. Available from: https://datahelpdesk.worldbank.org/knowledgebase/articles/906519-world- country-and-lending-groups)

Search for and screen studies

NESR librarians, in collaboration with NESR analysts and the Committee, will use the analytic framework and inclusion and exclusion criteria to develop a comprehensive literature search strategy. The literature search strategy will include selecting and searching the appropriate bibliographic databases, translating search using syntax appropriate for the databases being searched, and employing search refinements, such as search filters. For existing reviews, search strategies will be updated, as appropriate, for each database. The full literature search will be available upon request, and will be fully documented in the final review.

The results of all electronic database searches, after removal of duplicates, will be screened independently by two NESR analysts using a step-wise process by reviewing titles, abstracts, and full-texts to determine which articles meet the inclusion criteria. Manual searching will be conducted to find peer-reviewed published articles not identified through the electronic database search. These articles will also be screened independently by two NESR analysts at the abstract and full-text levels.

Extract data and assess the risk of bias

NESR analysts will extract all essential data from each included article to describe key characteristics of the available evidence, such as the author, publication year, cohort/trial name, study design, population life stage at intervention/exposure and outcome, intervention/exposure and outcome assessment methods, and outcomes. One NESR analyst will extract the data and a second NESR analyst will review the extracted data for accuracy. Each article included in the systematic review will undergo a formal risk of bias assessment, with two NESR analysts independently completing the risk of bias assessment using the tool that is appropriate for the study design.[*†‡] For review updates, data extraction and risk of bias assessment will be updated, if needed.

Synthesize the evidence

The Committee will describe, compare, and combine the evidence from all included studies to answer the systematic review question. Synthesis of the body of evidence will involve identifying overarching themes or key concepts from the findings, identifying and explaining similarities and differences between studies, and determining whether certain factors impact the relationships being examined. The first level of synthesis organization will be by population. Then, within each of the population groups, the evidence will be organized by similarity in outcome. Depending on the available evidence, the synthesis may be organized by participant characteristics such as race/ethnicity, socioeconomic position, and health status.

Develop [a] conclusion statement[s] and grade the evidence

After the Committee synthesizes the body of evidence, they will draft a conclusion statement or conclusion statements. 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 (e.g., PICO elements) and synthesis plan, and does not take evidence from other sources into consideration. The Committee will review, discuss, and revise the conclusion statement until they reach agreement on wording that accurately reflect the body of evidence.

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[*] Sterne JAC, Savovic J, Page MJ, et al. RoB 2: a revised tool for assessing risk of bias in randomised trials. *BMJ*. Aug 28 2019;366:l4898.doi:10.1136/bmj.l4898

[†] Sterne JA, Hernan MA, Reeves BC, et al. ROBINS-I: a tool for assessing risk of bias in non-randomised studies of interventions. *BMJ*. Oct 12 2016;355:i4919.doi:10.1136/bmj.i4919

[‡] ROBINS-E Development Group., Higgins J, Morgan R, et al. Bias In Non-randomized Studies - of Exposure (ROBINS-E). 2022. https://www.riskofbias.info/welcome/robins-e-tool

The Committee will then assign a grade to each conclusion statement (i.e., strong, moderate, limited, or grade not assignable). The grade communicates the strength of the evidence supporting a specific conclusion statement to decision makers and stakeholders. NESR has predefined criteria, based on five grading elements that the Committee will use to evaluate and grade the strength of the evidence supporting each conclusion statement. The five grading elements are: consistency, precision, risk of bias, directness and generalizability of the evidence. Study design will also be considered during the grading process.

Recommend future research

The Committee will identify and document research gaps and methodological limitations throughout the systematic review process. These gaps and limitations will be 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. Rationales for the necessity of additional or stronger research may also be provided with the research recommendations.

Acknowledgments and funding

The Committee members are involved in: establishing all aspects of the protocol, which presents the plan for how they are planning to examine the scientific evidence, including the inclusion and exclusion criteria; reviewing all studies that meet the criteria the Committee sets; deliberating on the body of evidence for each question; and writing and grading the conclusion statements. The NESR team, with assistance from Federal staff from HHS and USDA (Jean Altman, MS; Kara Beckman, PhD; Dana DeSilva, PhD, RD; Kevin Kuczynski, MS, RD; TusaRebecca Pannucci, PhD, MPH, RD; Julia Quam, MSPH, RND; Elizabeth Rahavi, RD) and Project Leadership (HHS: Janet de Jesus, MS, RD; USDA: Eve Stoody, PhD), supports the Committee by facilitating, executing, and documenting the work necessary to ensure the reviews are completed in accordance with NESR methodology. Contractor support was also provided by Panum Telecom (Emily Madan, PhD; Verena McClain, MSc).

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