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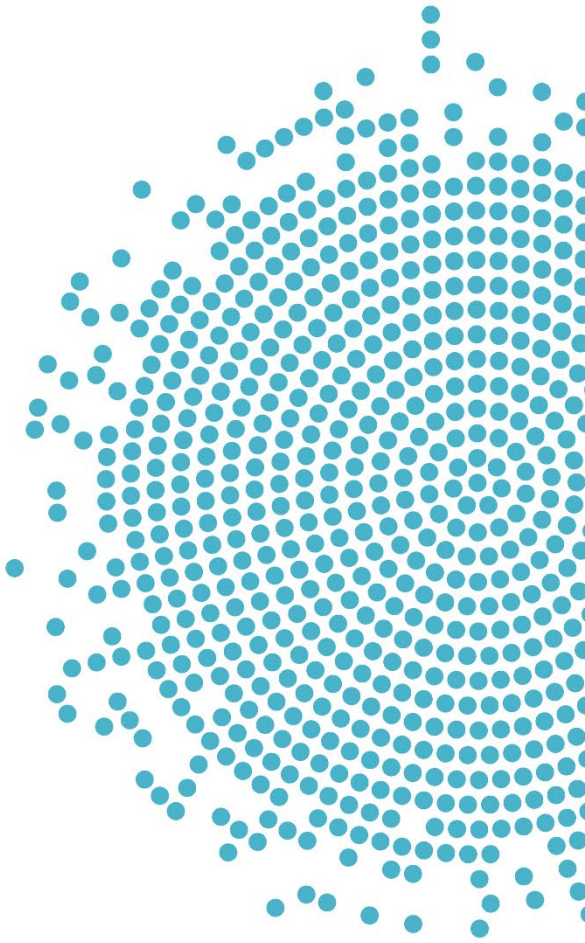
Sugar-Sweetened Beverages and Growth, Body Composition, and Risk of Obesity: A Systematic Review with Meta-Analysis Protocol



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Related citation: Mayer-Davis E, Leidy H, Mattes R, Naimi T, Novotny R, Schneeman B, Kingshipp BJ, Spill M, Cole NC, Bahnfleth CL, Butera G, Terry N, Obbagy J. Beverage Consumption and Growth, Size, Body Composition, and Risk of Overweight and Obesity: A Systematic Review. July 2020. U.S. Department of Agriculture, Food and Nutrition Service, Center for Nutrition Policy and Promotion, Nutrition Evidence Systematic Review. Available at: https://doi.org/10.52570/NESR.DGAC2020.SR0401

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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 sugar-sweetened beverage consumption and growth, body composition, and risk of obesity? The Committee will conduct a systematic review with meta-analysis to address this question, with support from USDA's Nutrition Evidence Systematic Review (NESR) team. This question will update the systematic review conducted by the 2020 Dietary Guidelines Advisory Committee (**Table 1)**.

Table 1. Review history

Date	Description	Citation
July 2020	Original systematic review conducted by the 2020 Dietary Guidelines Advisory Committee published	Mayer-Davis E, Leidy H, Mattes R, Naimi T, Novotny R, Schneeman B, Kingshipp BJ, Spill M, Cole NC, Bahnfleth CL, Butera G, Terry N, Obbagy J. Beverage Consumption and Growth, Size, Body Composition, and Risk of Overweight and Obesity: A Systematic Review. July 2020. U.S. Department of Agriculture, Food and Nutrition Service, Center for Nutrition Policy and Promotion, Nutrition Evidence Systematic Review. Available at: https://doi.org/10.52570/NESR.DGAC2020.SR0401

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 sugar-sweetened beverage consumption and growth, body composition, and risk of obesity?

This systematic review updates an existing NESR systematic review completed as part of the 2020 Dietary Guidelines Advisory Committee[‡], which included evidence published from January 2012 to June 2019. This

[*] 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

[‡] Mayer-Davis E, Leidy H, Mattes R, Naimi T, Novotny R, Schneeman B, Kingshipp BJ, Spill M, Cole NC, Bahnfleth CL, Butera G, Terry N, Obbagy J. Beverage Consumption and Growth, Size, Body Composition, and Risk of Overweight and Obesity: A Systematic Review. July 2020. U.S. Department of Agriculture, Food and Nutrition Service, Center for Nutrition Policy and Promotion, Nutrition Evidence Systematic Review. Available at: https://doi.org/10.52570/NESR.DGAC2020.SR0401

updated systematic review will synthesize the studies from the existing reviews with eligible studies published since June 2019 as one body of evidence, according to the methods described below.

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 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. When updating an existing review, the Committee uses the analytic framework and the inclusion and exclusion criteria from the existing review and makes adjustments to the protocol, if necessary. Differences in the inclusion and exclusion criteria between existing and updated reviews are documented in **Appendix 1**.

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 sugar-sweetened beverage (SSB) consumption in infants, toddlers, children, adolescents, adults, older adults, and individuals during pregnancy and postpartum. The comparators are consumption of a different amount of SSB (including no consumption and versions diluted with water), SSB vs. water, and SSB vs. low- and no-calorie sweetened beverages. 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 and 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 race and/or ethnicity, socioeconomic position, and anthropometry at baseline (all populations); sex (infants, toddlers, children, adolescents, adults, older adults); age, physical activity, and diet quality (children, adolescents, adults, older adults, pregnancy, postpartum); smoking (adults, older adults, pregnancy, postpartum); milk feeding practices (human milk, infant formula, or both), birth size, and gestational age (infants and toddlers); parity (pregnancy, postpartum), diabetes mellitus in the current pregnancy (pregnancy), hypertensive disorders in the current pregnancy (pregnancy), and human milk feeding (postpartum).

Figure 1. Analytic framework for the systematic review question: What is the relationship between sugar-sweetened beverage consumption and growth, body composition, and risk of obesity?

Population	***Intervention/ exposure***	***Comparator***	***Outcome***	***Key confounders***
Infants and toddlers (birth up to 24 months)	Sugar-sweetened beverage (SSB) consumption	Consumption of a different amount of SSB (including no consumption and versions diluted with water) SSB vs. water SSB vs. low- and no-calorie sweetened beverages	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	• Sex • Race and/or ethnicity • Socioeconomic position • Anthropometry at baseline • Milk feeding practices (human milk, infant formula, or both) • Birth size • Gestational age
Children and adolescents (2 up to 19 years)			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	• Sex • Age • Race and/or ethnicity • Socioeconomic position • Anthropometry at baseline • Physical activity • Diet quality
Adults and older adults (19 years and older)			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 • Race and/or ethnicity • Socioeconomic position • Anthropometry at baseline • Physical activity • Diet quality • Smoking
Individuals during pregnancy and postpartum			Pregnancy and postpartum-related weight change (in individuals during pregnancy or postpartum) • Gestational weight gain • Postpartum weight change	• Age • Race and/or ethnicity • Socioeconomic position • Anthropometry at baseline • Physical activity • Diet quality • Smoking • Parity • Diabetes mellitus in the current pregnancy (pregnancy) • Hypertensive disorders in the current pregnancy (pregnancy) • Human milk feeding (postpartum)

Synthesis organization:

I. ***Population:*** Infants and toddlers; Children and adolescents; Adults; Older adults; Individuals during pregnancy; Individuals during postpartum

Outcome: Growth; Body composition; Risk of obesity; Weight loss and maintenance; Pregnancy and postpartum-related weight change

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 2**). 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 2: 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 • Mendelian randomization studies	• Uncontrolled trials[†] • Case-control studies • Cross-sectional studies • Ecological studies • Narrative reviews • Systematic reviews • Meta-analyses • Modeling and simulation studies
Publication date	• January 2000 – May 2023[‡]	• Before January 2000, after May 2023
Population: Study participants	• Human	• Non-human
Population: Life stage	• At intervention or exposure and outcome: o Infants and toddlers (birth up to 24 months) o Children and adolescents (2 up to 19 years) o Adults and older adults (19 years and older) o Individuals during pregnancy o Individuals during postpartum	• At intervention or exposure and outcome: o N/A

[*] 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 January 2012 to June 2019

Category	Inclusion Criteria	Exclusion Criteria

Population: Health status	• Studies that exclusively enroll participants not diagnosed with a disease[*]
	• Studies that enroll some participants:
	  ○ diagnosed with a disease;
	  ○ diagnosed with a disorder that affects feeding/eating or growth (e.g., autism spectrum disorder, attention-deficit/hyperactivity disorder, eating disorder);
	  ○ with severe undernutrition, failure to thrive/underweight, stunting, or wasting;
	  ○ born preterm,[†] with low birth weight,[‡] and/or small for gestational age;
	  ○ who became pregnant using Assisted Reproductive Technologies;
	  ○ with multiple gestation pregnancies;
	  ○ receiving pharmacotherapy to treat obesity;
	  ○ pre- or post-bariatric surgery;
	  ○ and/or hospitalized for an illness, injury, or surgery
		• Studies that exclusively enroll participants:
		  ○ diagnosed with a disease;[§]
		  ○ diagnosed with a disorder that affects feeding/eating or growth (e.g., autism spectrum disorder, attention-deficit/hyperactivity disorder, eating disorder);
		  ○ with severe undernutrition, failure to thrive/underweight, stunting, or wasting;
		  ○ born preterm,[†] with low birth weight,[‡] and/or small for gestational age;
		  ○ who became pregnant using Assisted Reproductive Technologies;
		  ○ with multiple gestation pregnancies;
		  ○ receiving pharmacotherapy to treat obesity;
		  ○ pre- or post-bariatric surgery;
		  ○ and/or hospitalized for an illness, injury, or surgery[**]

Intervention/ exposure	• SSB consumption • Multi-component intervention in which the isolated effect of the intervention of interest on the outcome(s) of interest is provided or can be determined despite multiple components	• Infant milk, infant formula, toddler formula/milks • Other beverage types, such as nutritional beverages (e.g., protein shakes, smoothies) • Studies focusing on specific nutrients added to beverages instead of a beverage as a whole (i.e., studies where beverages are the delivery mechanism for a nutrient) • Beverages that are not commercially available (e.g., experimentally manipulated beverages) • Supplements • Alcohol • Soups • 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 due to multiple components
Comparator	• Consumption of a different amount of SSB (including no consumption and versions diluted with water) • SSB vs. water • SSB vs. low- and no-calorie sweetened beverages	• No comparator

[*] 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
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, 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 (individuals during pregnancy or postpartum) • Gestational weight gain • Postpartum weight change	• N/A
Study duration*	• Intervention length ≥12 weeks (in children, adolescents, adults, and older adults only) • Follow-up duration ≥6 months for weight loss • Follow-up duration ≥12 months for weight maintenance	• Intervention length <12 weeks (in children, adolescents, adults, and older adults only) • Follow-up duration <6 months for weight loss • Follow-up duration <12 months for weight maintenance
Publication status	• Peer-reviewed articles published in research journals	• Non-peer-reviewed articles, unpublished data or manuscripts, pre-prints, reports, editorials, retracted articles, 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

* Study duration criteria were developed to enable focus on the strongest body of evidence.

† 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. 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. 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 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. 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.

To avoid duplication of efforts, studies including infants and toddlers will be identified as part of another systematic review answering the systematic review question: What is the relationship between complementary feeding and growth, body composition, and risk obesity?[*]

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.[†‡§ **††]

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

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[*] Fisher JO, Abrams SA, Andres A, Byrd-Bredbenner C, Deierlein A, Eicher-Miller HA, Odoms-Young A, Palacios C, Obbagy J, Bahnfleth C, Kim JH, Nevins J, Higgins M, Bokay K, Butera G, Terry N. Complementary Feeding and Growth, Body Composition, and Risk of Obesity: A Systematic Review Protocol. May 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

[†] 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

[**] Observational studies included in the existing review were assessed using the "Risk of Bias for Nutrition Observational Studies" tool (RoB-NObs) (Dietary Guidelines Advisory Committee. 2020. Scientific Report of the 2020 Dietary Guidelines Advisory Committee: Advisory Report to the Secretary of Agriculture and the Secretary of Health and Human Services. U.S. Department of Agriculture, Agricultural Research Service, Washington, DC.

[††] Randomized controlled trials included in the existing review were assessed using the "Cochrane Risk-of-bias 2.0" tool (RoB 2.0) (August 2016 version)" (Higgins JPT, Sterne JAC, Savović J, Page MJ, Hróbjartsson A, Boutron I, Reeves B, Eldridge S. A revised tool for assessing risk of bias in randomized trials In: Chandler J, McKenzie J, Boutron I, Welch V (editors). Cochrane Methods. Cochrane Database of Systematic Reviews 2016, Issue 10 (Suppl 1). dx.doi.org/10.1002/14651858.CD201601.)

by similar outcome based on the available evidence. Depending on the available evidence, the next level of organization may be based on participant characteristics such as race and/or ethnicity, socioeconomic position, and health status.

Quantitative synthesis plan

The primary objective of the quantitative synthesis is to estimate the average effect of sugar-sweetened beverage consumption on growth, body composition, and risk of obesity. Further, this meta-analysis aims to identify whether the association between the consumption of sugar-sweetened beverages and growth, body composition, and risk of obesity varies across subgroups of the population (e.g., by age at intervention/exposure), and will explore whether differences in other study-specific variables (e.g., reasons for risk of bias, funding sources, dietary intake assessment method) impact the size or direction of the association. Finally, the quantitative synthesis will explore whether a dose-response relationship exists between the consumption of sugar-sweetened beverages and growth, body composition, and risk of obesity.

The outcomes for the quantitative synthesis are growth, body composition, and risk of obesity. For each of the outcomes, the Committee will separately analyze results reported for infants, toddlers, children, and adolescents (birth up to 19 years) and adults or older adults (19 years and older). Pending data availability, the Committee will also evaluate results for infants and toddlers (birth up to 24 months) and children and adolescents (2 up to 19 years) separately in sub-group analyses. Within each age group, the Committee will conduct series of meta-analyses on the following relationships:

- Absolute intake of sugar-sweetened beverages and
    - growth (weight, weight-for-age; BMI-for-age, weight-for-length/stature; body circumferences (arm, neck, thigh))
    - body composition (skinfold thickness; fat mass; fat-free, lean mass; waist circumference, waist-to-hip ratio)
    - risk of obesity (BMI; overweight and obesity; underweight; normal weight)
- Change in intake of sugar-sweetened beverages and
    - growth (weight, weight-for-age; BMI-for-age, weight-for-length/stature; body circumferences (arm, neck, thigh))
    - body composition (skinfold thickness; fat mass; fat-free, lean mass; waist circumference, waist-to-hip ratio)
    - risk of obesity (BMI; overweight and obesity; underweight; normal weight)

Measures associated with central obesity (i.e., weight, BMI, overweight and obesity), measures of whole body fat mass or fat-free mass, and measures associated with the distribution of body fat (i.e., waist circumference, waist-to-hip ratio, and skinfold thickness) are particularly important for informing Federal dietary guidance, and thus for informing conclusion statements.

Data preparation

Studies will only be combined statistically if they are sufficiently homogenous in study design, intervention/exposure, comparator, and effect size measure. To maximize the data available for inclusion in the meta-analysis, analysts will convert results to a common effect size based on the outcome. Analysts will also convert units (for both the exposure and the outcome) to analyze results on the same scale based on the available data. When possible, analysts will select the effect size, categorical comparisons, and/or units that allow the most data to be included in the analysis, using the most fully adjusted results. For example, a standardized outcome (e.g., z-score for normally distributed data) may be created to allow for the combination of results when the outcome is measured differently across studies.

For the categorical outcome of overweight/obesity, the analyst will combine the results from studies reporting overweight and/or obesity BMI categories. When possible, the analyst will combine data from studies reporting

either absolute measures or z-scores (e.g., BMI, weight-for-age) for infants, toddlers, and children, according to the sex and mean age in months of study participants. The analyst will not combine results of outcomes measured at a single time point with outcomes measuring change over time, as these results are not similarly scaled (e.g., weight-for-age and change in weight-for-age).

For cohort studies that report continuous exposure data, results will be scaled to 4-oz servings/day for infants and toddlers, to 8-oz servings/day for children and adolescents, and 12-oz servings/day for older age groups. If studies do not specify a serving, the analyst will assume the standard serving size 4-oz servings/day for infants and toddlers, to 8-oz servings/day for children and adolescents, and 12-oz servings/day for older age groups. When feasible based on the available evidence, the analyst will also explore the relationship between the outcomes and each 1-oz difference in intake. For cohort studies that report categorical exposure data, the analyst will select the most common comparison(s) across studies (e.g., ≥1 serving sugar-sweetened beverages/d vs never/rarely) to be included in the analysis. If studies do not report the selected most common comparison(s), or if reported details are insufficient to permit transformation, analysts will contact study authors to obtain useable data. If data transformations and/or contacting authors is unsuccessful, studies will be excluded from the meta-analysis.

Where possible, we will analyze data that are not adjusted for total energy intake, which mediates the relationship between sugar-sweetened beverages intake and growth, body composition, and risk of obesity.

We will use the software R (version 4.3.0)[*] for data preparation.

Meta-analyses

For each series of analyses, we will complete a main analysis which includes the results of all studies that report that relationship of interest. Studies will be examined separately by study design (RCTs, NRCTs, observational studies). We will conduct meta-analyses when there are at least two studies per planned analysis. When possible, standard mean differences will be calculated for continuous outcomes. Regression coefficients (i.e., beta values), transformed to equivalent units, will be used as the effect size for continuous outcomes if they are more commonly reported than mean differences. When dichotomous outcomes are presented, we will use relative risk as the effect size, or odds ratios if they are more commonly reported. In all cases, the average effect size and 95% confidence interval (CI) will be calculated using random-effects models using the restricted maximum-likelihood (REML) estimator.[†] Statistical significance will be set at a two-sided alpha of 0.05. If multiple acceptable measures of the intervention/exposure and/or multiple assessments of the outcome are reported within a study, all data will be analyzed using multi-level meta-analysis to account for the multiplicity.

All meta-analyses will be conducted using the metafor package[‡] (version 4.2-0) in the software R (version 4.3.0). Dose-response models will be fitted either by using general linear and nonlinear (e.g., quadratic, spline) model fitting routines in R, or by way of the R package dosresmeta[§] (version 2.0.1).

Sub-group analyses, which restrict analyses to a subset of studies, will be conducted to examine the influence of the following factors on all intervention/exposure-outcome relationships when data are available:

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[*] R Core Team (2023). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. URL https://www.R-project.org/.

[†] Langan, D, Higgins, JP, Jackson, D, Bowden, J, Veroniki, AA, Kontopantelis, E, et al. A comparison of heterogeneity variance estimators in simulated random-effects meta-analyses. *Research synthesis methods* 2019; 10(1): 83-98. doi: 10.1002/jrsm.1316

[‡] Viechtbauer W. Conducting Meta-Analyses in R with the metafor Package. *Journal of Statistical Software* 2010; 36(3): 1–48. doi: 10.18637/jss.v036.i03

[§] Crippa, A, Orsini, N. Dose-response meta-analysis of differences in means. *BMC Medical Research Methodology* 2016; 16(1): 91. doi: 10.1186/s12874-016-0189-0

- Age group at intervention/exposure

The following meta-regression analyses will be conducted for all exposure-outcome relationships when data are available:

- Dose-response meta-analysis
- Sex
- Age at intervention/exposure
- Reasons for risk of bias, including the presence/absence of key confounders
- Funding source

Prior to the conduct of these analyses, moderators will be examined and checked for multicollinearity by using intercorrelations and contingency-table analyses, as appropriate. Sensitivity and/or meta-regression analyses in addition to those identified above may be needed. Those analyses will be clearly labeled as *post-hoc* in the report and results will be interpreted with caution.

Assessment of heterogeneity

Analysts will create forest plots according to study design, type of intervention/exposure, and outcome, and will visually analyze the plots for overlap of CIs. The following measures of statistical heterogeneity will be reported: tau^2, I^2 (95% CI), and the 95% prediction interval. When data are available, analysts will complete subgroup analyses and/or meta-regressions to identify factors that may explain heterogeneity, as described above, and report appropriate tests of between-groups differences or moderator (predictor) significance. Sensitivity analyses will be conducted as needed. Any deviations from this protocol will be detailed and explained in the final report.

Assessment of non-reporting bias

When there are at least 10 unique studies or data points in an analysis and the included studies/data points vary in precision/sample size, non-reporting bias will be evaluated with a visual assessment of a contoured-enhanced funnel plot, a statistical test of funnel plot asymmetry (e.g., Egger's Test), and an exploration of alternative causes of funnel plot asymmetry (e.g., heterogeneity). If a limited number of studies are included publication bias will not be assessed using a funnel plot, but it will be addressed qualitatively.

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

After the Committee synthesizes the body of evidence, including all results from meta-analyses, 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.

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 and meta-analysis 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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Appendix

Appendix 1: Inclusion and exclusion criteria comparison between existing[*] and updated systematic reviews for the research question: What is the relationship between sugar-sweetened beverage (SSB) consumption and growth, body composition, and risk of obesity?

Category	Existing Review	Updated Review	Change and Rationale
Study design	Included: • Randomized controlled trials • Non-randomized controlled trials (including quasi-experimental and controlled before and after studies) • Prospective cohort studies • Retrospective cohort studies • Nested case-control studies • Mendelian randomization studies	Included: • Randomized controlled trials • Non-randomized controlled trials[†] • Prospective cohort studies • Retrospective cohort studies • Nested case-control studies • Mendelian randomization studies	No changes were made. Formatting was edited for clarity. Modeling and simulation studies, which were always excluded, were added explicitly to the exclude list.
	Excluded: • Uncontrolled trials • Case-control studies • Cross-sectional studies • Uncontrolled before-and-after studies • Narrative reviews • Systematic reviews • Meta-analyses	Excluded: • Uncontrolled trials[‡] • Case-control studies • Cross-sectional studies • Ecological studies • Narrative reviews • Systematic reviews • Meta-analyses • Modeling and simulation studies	

[*] Mayer-Davis E, Leidy H, Mattes R, Naimi T, Novotny R, Schneeman B, Kingshipp BJ, Spill M, Cole NC, Bahnfleth CL, Butera G, Terry N, Obbagy J. Beverage Consumption and Growth, Size, Body Composition, and Risk of Overweight and Obesity: A Systematic Review. July 2020. U.S. Department of Agriculture, Food and Nutrition Service, Center for Nutrition Policy and Promotion, Nutrition Evidence Systematic Review. Available at: https://doi.org/10.52570/NESR.DGAC2020.SR0401

[†] Including quasi-experimental and controlled before-and-after studies

[‡] Including uncontrolled before-and-after studies

Category	Existing Review	Updated Review	Change and Rationale
Publication date	Included: • January 2000 – June 2019 (Milk, 100% Juice, LNCSB) • January 2012 – June 2019 (SSB) * Excluded: • Before January 2000, after June 2019	Included: • January 2000 – May 2023† Excluded: • Before January 2000, after May 2023	Dates were modified to enable focus on the most recent evidence.
Population: Study participants	Included: • Human Excluded: • Non-human	Included: • Human Excluded: • Non-human	No change
Population: Life stage	Included: • At intervention/exposure and outcome: o Children and adolescents (2 up to 19 years) o Adults (19 years and older) o Older adults (65 years and older) Excluded: • At intervention/exposure and outcome: • Infants and toddlers (birth up to 24 months)	Included: • At intervention/exposure and outcome: o Infants and toddlers (birth up to 24 months) o Children and adolescents (2 up to 19 years) o Adults and older adults (19 years and older) o Individuals during pregnancy o Individuals during postpartum Excluded: o N/A	Infants, toddlers, and individuals during pregnancy and postpartum will be included in the updated review on SSB rather than being addressed in separate questions.

* This publication date range criteria was applied to the review of SSB evidence because the 2015 Dietary Guidelines Advisory Committee reviewed evidence on the relationship between added sugars, including SSB, and body weight/obesity, published up to January 2012.

† This review update date range encompasses the original systematic review date range, which included articles published from January 2012 to June 2019

Category	Existing Review	Updated Review	Change and Rationale
Population: Health Status	Included: • Studies that enroll participants who are healthy and/or at risk for chronic disease • Studies that enroll some participants diagnosed with a disease • Studies that enroll some participants who are classified as underweight, stunted, wasted, or obese	Included: • Studies that exclusively enroll participants not diagnosed with a disease* • Studies that enroll some participants: o diagnosed with a disease; o diagnosed with a disorder that affects feeding/eating or growth (e.g., autism spectrum disorder, attention-deficit/hyperactivity disorder, eating disorder); 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 receiving pharmacotherapy to treat obesity; o pre- or post-bariatric surgery; o and/or hospitalized for an illness, injury, or surgery	Study samples where 100% of participants have obesity will be included
	Excluded: • Studies that exclusively enroll participants diagnosed with a disease, or hospitalized with an illness or injury • Studies that exclusively enroll participants classified as obese (i.e., studies that aim to treat participants who have already been classified as obese)	Excluded: • Studies that exclusively enroll participants: o diagnosed with a disease;‡ o diagnosed with a disorder that affects feeding/eating or growth (e.g., autism spectrum disorder, attention-deficit/hyperactivity disorder, eating disorder); 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 receiving pharmacotherapy to treat obesity; o pre- or post-bariatric surgery; o and/or hospitalized for an illness, injury, or surgery§	

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

Category	Existing Review	Updated Review	Change and Rationale
Intervention/exposure	Included: Type and amount of beverage consumption of the following beverage types: • Milk (dairy milk and milk substitutes, including flavored milk) • 100% Juice • Low- and no-calorie sweetened beverages (LNCSB) • Sugar-sweetened beverages (SSB)	Included: • SSB consumption • Multi-component intervention in which the isolated effect of the intervention of interest on the outcome(s) of interest is provided or can be determined despite multiple components	The existing systematic review conducted by the 2020 Dietary Guidelines Advisory Committee (Committee) examined multiple beverages: milk, 100% juice, LNCSB, and SSB. The proposed question will update the review of SSB, which will be examined as an individual systematic review.
	Excluded: • Other beverage types, including: Coffee, tea, water, and nutritional beverages (e.g., protein shakes, smoothies) • Studies focusing on specific nutrients added to beverages instead of a beverage as a whole (i.e., studies where beverages are the delivery mechanism for a nutrient) • Beverages that are not commercially available (e.g., experimentally manipulated beverages) • Supplements • Alcohol • Soups	Excluded: • Infant milk, infant formula, toddler formula/milks • Other beverage types, such as nutritional beverages (e.g., protein shakes, smoothies) • Studies focusing on specific nutrients added to beverages instead of a beverage as a whole (i.e., studies where beverages are the delivery mechanism for a nutrient) • Beverages that are not commercially available (e.g., experimentally manipulated beverages) • Supplements • Alcohol • Soups • 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 due to multiple components	

[*] 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	Existing Review	Updated Review	Change and Rationale
Comparator	Included: • Different amount of the same beverage (including no consumption and versions diluted with water) • Beverage vs. solid • Beverage vs. water • Sugar-sweetened beverages vs. low- and no-calorie sweetened beverages • Dairy milk with different amounts of fat Excluded: • No comparator • Studies comparing different types of beverages (with the exception of studies comparing a beverage to plain water, dairy milk with different amounts of fat, and sugar-sweetened beverages to low- or no-calorie sweetened beverages)	Included: • Consumption of a different amount of SSB (including no consumption and versions diluted with water) • SSB vs. water • SSB vs. low- and no-calorie sweetened beverages Excluded: • No comparator	No change

Category	Existing Review	Updated Review	Change and Rationale

Outcome(s)	Included:
	• Weight, weight-for-age
	• Height, length/stature-for-age
	• BMI, BMI z-score, weight-for-length
	• Body circumferences: head, arm, waist, thigh, neck
	• Body composition and distribution (e.g., % fat mass, % fat free mass)
	• Incidence and prevalence of:
	  ○ Underweight, failure to thrive, stunting, wasting
	  ○ Healthy weight
	  ○ Overweight
	  ○ Obesity
	
	Excluded
	• N/A
		Included:
		Growth (in infants, toddlers, children, adolescents):
		• Height
		• Length/stature-for-age (in infants and toddlers only)
		• Weight
		• Weight-for-age (in infants and toddlers only)
		• Stunting, failure to thrive, wasting
		• BMI-for-age
		• Weight-for-length/stature (in infants and toddlers only)
		• Body circumference (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
		• Gestational weight gain (during pregnancy)
		• Postpartum weight change (during postpartum)
		Excluded
		• N/A
			The existing systematic review conducted by the 2020 Dietary Guidelines Advisory Committee (Committee) examined growth, size, body composition, and risk of overweight and obesity.
			The proposed question will update the relationships examined by the 2020 Committee and expand that work by including additional outcomes of weight loss and maintenance. This expansion was recommended by the 2020 Committee, Federal stakeholders, and the public. In addition, gestational weight gain and postpartum weight change will be included in the updated review rather than addressed in separate systematic review questions.

Category	Existing Review	Updated Review	Change and Rationale
Study duration	Included • N/A Excluded • N/A	Included • Intervention length ≥12 weeks (in children, adolescents, adults, and older adults only) • Follow-up length ≥6 months from baseline for weight loss • Follow-up length ≥12 months from baseline for weight maintenance Excluded • Intervention length <12 weeks (in children, adolescents, adults, and older adults only) • Follow-up length <6 months from baseline for weight loss • Follow-up length <12 months from baseline for weight maintenance	Study duration criteria were developed to enable focus on the strongest body of evidence.
Publication status	Included • Articles published in peer-reviewed journals Excluded • Articles not published in peer-reviewed journals, including unpublished data, manuscripts, reports, pre-prints, abstracts, and conference proceedings	Included • Peer-reviewed articles published in research journals Excluded • Non-peer-reviewed articles, unpublished data or manuscripts, pre-prints, reports, editorials, retracted articles, and conference abstracts or proceedings	No change
Language	Included • Articles published in English Excluded • Articles published in language other than English	Included • Published in English Excluded • Not published in English	No change

Category	Existing Review	Updated Review	Change and Rationale
Country*	Included • Studies conducted in very high or high Human Development countries Excluded • Studies conducted in medium or lower Human Development countries	Included • Studies conducted in countries classified as high or very high on the Human Development Index the year(s) the intervention/exposure data were collected Excluded • Studies conducted in countries classified as medium or low on the Human Development Index the year(s) the intervention/exposure data were collected	Clarification added that Human Development Index classification is based on the year(s) when intervention/exposure data were collected.

* In order to determine the inclusion exclusion criteria for country, the Human Development classification was used. This classification is based on the Human Development Index (HDI) ranking from the year the study intervention occurred or data were collected (UN Development Program. HDI 1990-2017 HDRO calculations based on data from UNDESA (2017a), UNESCO Institute for Statistics (2018), United Nations Statistics Division (2018b), World Bank (2018b), Barro and Lee (2016) and IMF (2018). Available from: http://hdr.undp.org/en/data). If the study did not report the year in which the intervention occurred or data were collected, the HDI classification for the year of publication was applied. HDI values are available from 1980, and then from 1990 to present. If a study was conducted prior to 1990, the HDI classification from 1990 was applied. If a study was conducted in 2018 or 2019, the most current HDI classification was applied. When a country was not included in the HDI ranking, the current country classification from the World Bank was used instead (The World Bank. World Bank country and lending groups. Available from: https://datahelpdesk.worldbank.org/knowledgebase/articles/906519-world-country-and-lending-groups)