

# WHAT IS THE RELATIONSHIP BETWEEN ADDED SUGARS CONSUMPTION AND RISK OF CARDIOVASCULAR DISEASE?: SYSTEMATIC REVIEW PROTOCOL

This document describes the protocol for a systematic review to answer the following question: What is the relationship between added sugars consumption and risk of cardiovascular disease?

This systematic review is being conducted by the 2020 Dietary Guidelines Advisory Committee, Beverages and Added Sugars Subcommittee and staff from USDA's Nutrition Evidence Systematic Review (NESR).

NESR methodology for answering a systematic review question involves:

- searching for and selecting articles,
- extracting data and assessing the risk of bias of results from each included article,
- synthesizing the evidence,
- developing a conclusion statement,
- grading the evidence underlying the conclusion statement, and
- recommending future research.

More information about NESR's systematic review methodology is available on the NESR website:

<https://nesr.usda.gov/2020-dietary-guidelines-advisory-committee-systematic-reviews>.

This document describes the protocol, or plan, for how the systematic review will be conducted. The protocol provides:

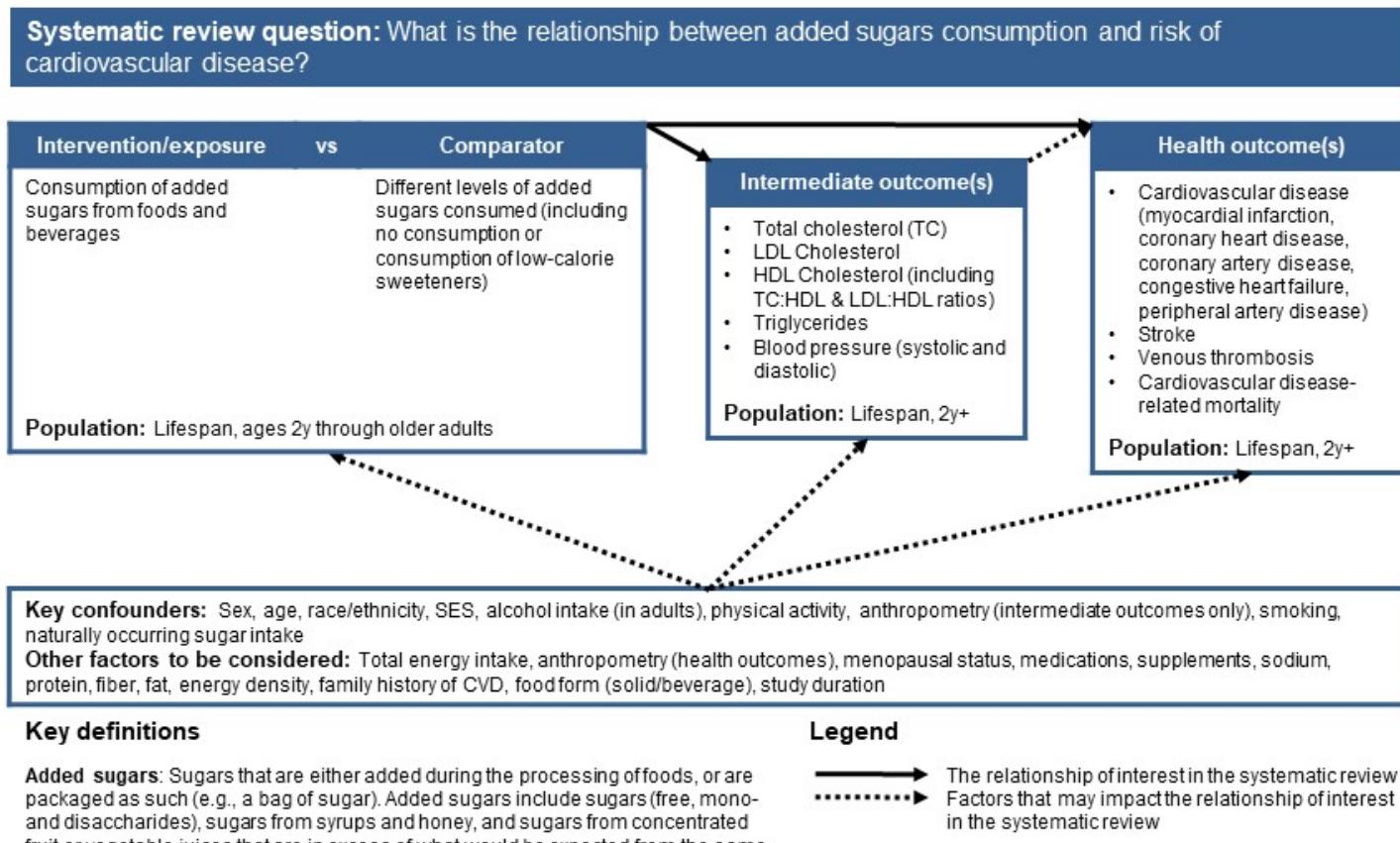
- The [analytic framework](#) (p. 2) illustrates the overall scope of the question, including the population, the interventions and/or exposures, comparators, and outcomes of interest.
- The [literature search and screening plan](#) (p. 2) details the electronic databases and [inclusion and exclusion criteria](#) (p. 3) that will be used to search for, screen, and select articles to be included in the systematic review.
- The [literature search and screening results](#) (p. 7) includes a list of included articles, and a list of excluded articles with the rationale for exclusion.

This protocol is up-to-date as of: 10/22/2019.

## ANALYTIC FRAMEWORK

The analytic framework (**Figure 1**) illustrates the overall scope of the systematic review, including the population, the interventions and/or exposures, comparators, and outcomes of interest. It also includes definitions of key terms and identifies key confounders considered in the systematic review. The inclusion and exclusion criteria that follow provide additional information about how parts of the analytic framework will be defined and operationalized for the review.

**Figure 1: Analytic framework**



DRAFT Content – for discussion only

## LITERATURE SEARCH AND SCREENING PLAN

### Electronic databases

Listed below are the databases that will be searched to identify all potentially relevant articles that have been published to address the systematic review question. Additional details regarding the search strategy will be published upon completion of the review, and are available upon request prior to publication.

- **Pubmed**
- **Cochrane**
- **Embase**

Question: What is the relationship between added sugars consumption and risk of cardiovascular disease?

## Inclusion and exclusion criteria

This table provides the inclusion and exclusion criteria for the systematic review. The inclusion and exclusion criteria are a set of characteristics used to determine which articles identified in the literature search will be included or excluded in the systematic review.

**Table 1. Inclusion and exclusion criteria**

Category	Inclusion Criteria	Exclusion Criteria
<b>Study design</b>	<ul style="list-style-type: none"> <li>• Randomized controlled trials</li> <li>• Non-randomized controlled trials including quasi-experimental and controlled before-and-after studies</li> <li>• Prospective cohort studies</li> <li>• Retrospective cohort studies</li> <li>• Nested case-control studies</li> </ul>	<ul style="list-style-type: none"> <li>• Uncontrolled trials</li> <li>• Case-control studies</li> <li>• Cross-sectional studies</li> <li>• Uncontrolled before-and-after studies</li> <li>• Narrative reviews</li> <li>• Systematic reviews</li> <li>• Meta-analyses</li> </ul>
<b>Intervention/exposure</b>	<p>Consumption of added sugars, such as:</p> <ul style="list-style-type: none"> <li>• Anhydrous dextrose</li> <li>• Brown sugar</li> <li>• Confectioner's powdered sugar</li> <li>• Corn syrup</li> <li>• Corn syrup solids</li> <li>• Dextrose</li> <li>• Fructose</li> <li>• High-fructose corn syrup (HFCS)</li> <li>• Honey</li> <li>• Invert sugar</li> <li>• Lactose</li> <li>• Malt syrup</li> <li>• Maltose</li> <li>• Maple syrup</li> <li>• Molasses</li> <li>• Nectars (e.g., peach nectar, pear nectar)</li> <li>• Pancake syrup</li> <li>• Raw sugar</li> <li>• Sucrose</li> <li>• Sugar</li> <li>• White granulated sugar</li> </ul>	<p>Consumption of:</p> <ul style="list-style-type: none"> <li>• Low-calorie sweeteners</li> <li>• Sugar alcohols</li> </ul>
<b>Comparator</b>	<ul style="list-style-type: none"> <li>• Different level of added sugars consumed, including no consumption or consumption of low-calorie sweeteners</li> </ul>	<ul style="list-style-type: none"> <li>• No comparator</li> </ul>

Category	Inclusion Criteria	Exclusion Criteria
<b>Outcomes</b>	<p><u>Intermediate outcomes:</u></p> <ul style="list-style-type: none"> <li>• Total cholesterol (TC)</li> <li>• LDL Cholesterol</li> <li>• HDL Cholesterol (including TC:HDL and LDL:HDL ratios)</li> <li>• Triglycerides</li> <li>• Blood pressure (systolic and diastolic)</li> </ul> <p><u>Health outcomes:</u></p> <ul style="list-style-type: none"> <li>• Cardiovascular disease (myocardial infarction, coronary heart disease, coronary artery disease, congestive heart failure, peripheral artery disease)</li> <li>• Stroke</li> <li>• Venous thrombosis</li> <li>• Cardiovascular disease-related mortality</li> </ul>	
<b>Date of publication</b>	<ul style="list-style-type: none"> <li>• January 2000 to August 2014 (existing NESR systematic review)</li> <li>• September 2014 – September 2019 (update)</li> </ul>	<ul style="list-style-type: none"> <li>• Articles published prior to January 2000</li> </ul>
<b>Publication status</b>	<ul style="list-style-type: none"> <li>• Articles published in peer-reviewed journals</li> </ul>	<ul style="list-style-type: none"> <li>• Articles not published in peer-reviewed journals, including unpublished data, manuscripts, reports, pre-prints, abstracts, and conference proceedings</li> </ul>
<b>Language of publication</b>	<ul style="list-style-type: none"> <li>• Articles published in English</li> </ul>	<ul style="list-style-type: none"> <li>• Articles published in languages other than English</li> </ul>
<b>Country<sup>i</sup></b>	<ul style="list-style-type: none"> <li>• Studies conducted in Very High or High Human Development Countries</li> </ul>	<ul style="list-style-type: none"> <li>• Studies conducted in Medium or lower Human Development Countries</li> </ul>
<b>Study participants</b>	<ul style="list-style-type: none"> <li>• Human subjects</li> <li>• Males</li> <li>• Females (including pregnant and lactating women)</li> </ul>	<ul style="list-style-type: none"> <li>• Animal subjects</li> <li>• Hospitalized samples</li> </ul>

Category	Inclusion Criteria	Exclusion Criteria
<b>Age of study participants</b>	<ul style="list-style-type: none"> <li>• Age at intervention or exposure*: <ul style="list-style-type: none"> <li>○ Child (2-5 years)</li> <li>○ Child (6-12 years)</li> <li>○ Adolescents (13-18 years)</li> <li>○ Adults (19 and older)Older adults (65+ years)</li> </ul> </li> <li>• Age at outcome*: <ul style="list-style-type: none"> <li>○ Child (2-5 years)</li> <li>○ Child (6-12 years)</li> <li>○ Adolescents (13-18 years)</li> <li>○ Adults (19 and older)</li> <li>○ Older adults (65+ years)</li> </ul> </li> </ul>	

\*Note: Coverage of infants and toddlers <2 years of age is still in discussion between the Beverages and Added Sugars Subcommittee and Birth to 24 Months Subcommittee.

Category	Inclusion Criteria	Exclusion Criteria
<b>Health status of study participants</b>	<ul style="list-style-type: none"> <li>• Studies that enroll participants who are healthy and/or at risk for chronic disease, including those with obesity</li> <li>• Studies that enroll <i>some</i> participants diagnosed with a disease</li> <li>• Studies that <i>exclusively</i> enroll participants with high blood pressure or high cholesterol and are evaluating cardiovascular disease endpoint outcomes (i.e., studies that aim to prevent cardiovascular disease in participants who are at high risk)</li> <li>• Studies that enroll <i>some</i> participants with endpoint outcomes of cardiovascular disease</li> </ul>	<ul style="list-style-type: none"> <li>• Studies that <i>exclusively</i> enroll participants with endpoint outcomes</li> <li>• Studies that <i>exclusively</i> enroll participants diagnosed with a disease, or hospitalized with an illness or injury. (For this criterion, studies that exclusively enroll participants with obesity will not be excluded).</li> <li>• Studies that <i>exclusively</i> enroll participants with high blood pressure or high cholesterol and are evaluating blood pressure or cholesterol outcomes (i.e., studies that aim to treat participants who already have high blood pressure or high cholesterol)</li> <li>• Studies that <i>exclusively</i> enroll participants with endpoint outcomes of cardiovascular disease (i.e., studies that aim to treat participants who have already been diagnosed with the endpoint outcomes of interest)</li> </ul>

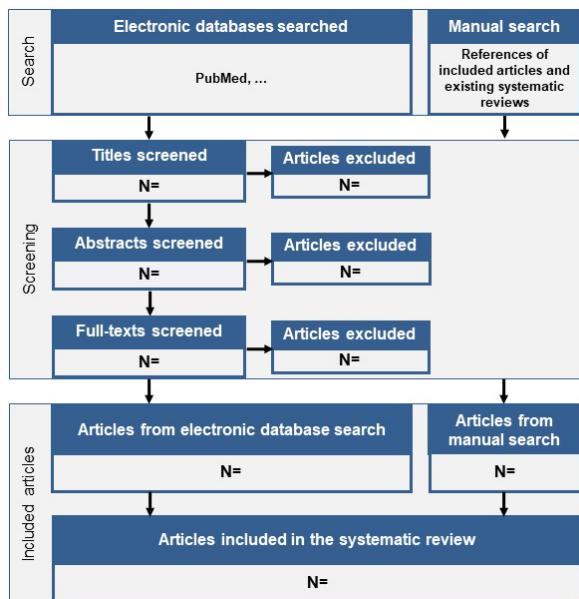
<sup>i</sup> The Human Development classification was based on the Human Development Index (HDI) ranking from the year the study intervention occurred or data was collected. If the study did not report the year in which the intervention occurred or data were collected, the HDI classification for the 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. When a country was not included in the HDI ranking, the current country classification from the World Bank is used instead.

## LITERATURE SEARCH AND SCREENING RESULTS

This protocol will be updated with the literature search and screening results after the search and screening plan has been finalized and implemented.

The flow chart (**Figure 2**) below illustrates the literature search and screening results for articles examining the systematic review question. The results of the electronic database searches, after removal of duplicates, were screened independently by two NESR analysts using a step-wise process by reviewing titles, abstracts, and full-texts to determine which articles met the inclusion criteria. A manual search was done to find articles that were not identified when searching the electronic databases; all manually identified articles are also screened to determine whether they meet criteria for inclusion.

**Figure 2: Flow chart of literature search and screening results (To be added)**



### Included Articles (To be added)

#### 1. Ref

### Excluded Articles (To be added)

The table below lists the articles excluded after full-text screening. At least one reason for exclusion is provided for each article, which may not reflect all possible reasons. Information about articles excluded after title and abstract screening is available upon request.

**Table 2. Excluded articles**

Citation	Rationale
1	