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Added Sugars Consumption and Risk of Cardiovascular Disease: A Systematic Review

2020 Dietary Guidelines Advisory Committee,
Beverages and Added Sugars Subcommittee

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Nutrition Evidence Systematic Review
Center for Nutrition Policy and Promotion
Food and Nutrition Service
U.S. Department of Agriculture
Braddock Metro Center II
1320 Braddock Place
Alexandria, Virginia 22314

This systematic review was conducted by the 2020 Dietary Guidelines Advisory Committee in collaboration with the Nutrition Evidence Systematic Review (NESR) team at the Center for Nutrition Policy and Promotion, Food and Nutrition Service, U.S. Department of Agriculture (USDA). All systematic reviews from the 2020 Advisory Committee Project are available on the NESR website: <https://nesr.usda.gov/2020-dietary-guidelines-advisory-committee-systematic-reviews>.

Conclusion statements drawn as part of this systematic review describe the state of science related to the specific question examined. Conclusion statements do not draw implications, and should not be interpreted as dietary guidance. This portfolio provides the complete documentation for this systematic review. A summary of this review is included in the 2020 Advisory Committee's Scientific Report available at www.DietaryGuidelines.gov.

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Beverages and Added Sugars Subcommittee:

- Elizabeth Mayer-Davis, PhD, RD, University of North Carolina at Chapel Hill, Subcommittee Chair
- Heather Leidy, PhD, University of Texas at Austin
- Richard Mattes, PhD, MPH, RD, Purdue University
- Timothy Naimi, MD, MPH, Boston University
- Rachel Novotny, PhD, RDN, LD, University of Hawaii
- Barbara Schneeman, PhD, University of California, Davis, Chair of the 2020 Dietary Guidelines Advisory Committee

Nutrition Evidence Systematic Review (NESR) Team:

- Brittany James Kingshipp, PhD, Analyst, Panum Groupⁱ
- Maureen Spill, PhD, Analyst, Panum Groupⁱ
- Natasha Chong Cole, PhD, MPH, RD, Analyst, Panum Groupⁱ
- Gisela Butera, MLIS, MEd, Systematic Review Librarian, Panum Groupⁱ
- Nancy Terry, MS, MLS, Biomedical Librarian, National Institutes of Health Library, U.S. Department of Health and Human Services (HHS)
- Julie Obbagy, PhD, RD, Project Lead, Office of Nutrition Guidance and Analysis (ONGA), Center for Nutrition Policy and Promotion (CNPP), Food and Nutrition Service (FNS), U.S. Department of Agriculture (USDA)

Federal Liaisons:

- Jennifer Seymour, PhD, Division of Nutrition, Physical Activity, and Obesity, Centers for Disease Control and Prevention, HHS
- Julia Quam, MSPH, RDN, Division of Prevention Science (DPS), Office of Disease Prevention and Health Promotion (ODPHP), HHS
- Clarissa (Claire) Brown, MS, MPH, RD, ONGA, CNPP, FNS, USDA
- Meghan Adler, MS, RD, FAND, ONGA, CNPP, USDA

Project Leadership:

- Eve Essery Stody, PhD, Designated Federal Officer and Director, ONGA, CNPP, FNS, USDA
- Janet de Jesus, MS, RD, Nutrition Advisor, DPS, ODPHP, Office of the Assistant Secretary for Health (OASH), HHS
- Richard (Rick) Olson, MD, MPH, Director, DPS, ODPHP, OASH, HHS

USDA and HHS implemented a process to identify topics and scientific questions to be examined by the 2020 Dietary Guidelines Advisory Committee. The Committee conducted its review of evidence in subcommittees for discussion by the full Committee during its public meetings. The role of the Committee members involved establishing all aspects of the protocol, which presented the plan for how they would

ⁱ Under contract with the Food and Nutrition Service, United States Department of Agriculture.

examine the scientific evidence, including the inclusion and exclusion criteria; reviewing all studies that met the criteria they set; deliberating on the body of evidence for each question; and writing and grading the conclusion statements to be included in the scientific report the 2020 Committee submitted to USDA and HHS. The NESR team with assistance from Federal Liaisons and Project Leadership, supported the Committee by facilitating, executing, and documenting the work necessary to ensure the reviews were completed in accordance with NESR methodology. More information about the 2020 Dietary Guidelines Advisory Committee, including the process used to identify topics and questions, can be found at www.DietaryGuidelines.gov. More information about NESR can be found at NESR.usda.gov.

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TABLE OF CONTENTS

Acknowledgements.....	3
Table of contents	5
Introduction.....	7
What is the relationship between added sugars consumption and risk of cardiovascular disease?	9
Plain language summary.....	9
Technical abstract.....	11
Full review	14
Systematic review question	14
Conclusion statements and grades	14
Summary of the evidence	14
Description of the evidence	16
Evidence synthesis.....	17
Research recommendations.....	21
Included articles.....	22
Methodology	51
Analytic framework.....	52
Literature search and screening plan	53
Inclusion and exclusion criteria.....	53
Electronic databases and search terms.....	57
Literature search and screening results	61
Excluded articles	62
Table 1: Evidence in children on added sugars consumption and risk of cardiovascular disease	24
Table 2: Risk of bias for the randomized controlled trial examining added sugars consumption and risk of cardiovascular disease in children.....	27
Table 3: Risk of bias for observational studies examining added sugars consumption and risk of cardiovascular disease in children	27
Table 4: Evidence in adults on added sugars consumption and risk of cardiovascular disease	28
Table 5: Risk of bias for randomized controlled trials examining added sugars consumption and risk of cardiovascular disease in adults.....	49
Table 6: Risk of bias for observational studies examining added sugars consumption and risk of cardiovascular disease in adults	50
Table 7. Inclusion and exclusion criteria	53
Table 8. Articles excluded after full text screening with rationale for exclusion.....	62

Figure 1: Analytic framework	52
Figure 2: Flow chart of literature search and screening results.....	61

INTRODUCTION

This document describes a systematic review conducted to answer the following question: What is the relationship between added sugars consumption and risk of cardiovascular disease? This systematic review was conducted by the 2020 Dietary Guidelines Advisory Committee, supported by USDA's Nutrition Evidence Systematic Review (NESR).

More information about the 2020 Dietary Guidelines Advisory Committee is available at the following website: www.DietaryGuidelines.gov.

NESR specializes in conducting food- and nutrition-related systematic reviews using a rigorous, protocol-driven methodology. More information about NESR is available at the following website: NESR.usda.gov.

NESR's systematic review methodology involves developing a protocol, searching for and selecting studies, extracting data from and assessing the risk of bias of each included study, synthesizing the evidence, developing conclusion statements, grading the evidence underlying the conclusion statements, and recommending future research. A detailed description of the systematic reviews conducted for the 2020 Dietary Guidelines Advisory Committee, including information about methodology, is available on the NESR website: <https://nesr.usda.gov/2020-dietary-guidelines-advisory-committee-systematic-reviews>. In addition, starting on page 51, this document describes the final protocol as it was applied in the systematic review. A description of and rationale for modifications made to the protocol are described in the 2020 Dietary Guidelines Advisory Committee Report, Part D: Chapter 12. Added Sugars.

The systematic review described in this document updates an existing systematic review that was conducted by the 2015 Dietary Guidelines Advisory Committee with support from USDA's Nutrition Evidence Systematic Review (NESR) team. Information about the 2015 Dietary Guidelines Advisory Committee's review of the evidence on added sugars and risk of cardiovascular disease can be found in their report, which is available at the following website: <https://nesr.usda.gov/cross-cutting-topics-public-health-importance-subcommittee> and <https://www.dietaryguidelines.gov/current-dietary-guidelines/process-develop-2015-2020-dg/advisory-committee>

List of abbreviations

Abbreviation	Full name
BMI	Body mass index
CNPP	Center for Nutrition Policy and Promotion
CVD	Cardiovascular disease
DBP	Diastolic blood pressure
DPS	Department of Prevention Science
FNS	Food and Nutrition Service
HDI	Human development index
HDL-C	High-density lipoprotein cholesterol
HHS	Department of Health and Human Services
LDL-C	Low-density lipoprotein cholesterol
NESR	Nutrition Evidence Systematic Review
OASH	Office of the Assistant Secretary for Health
ODPHP	Office of Disease Prevention and Health Promotion
ONGA	Office of Nutrition Guidance and Analysis
PAD	Peripheral artery disease
PCS	Prospective cohort study
RCT	Randomized controlled trial
SBP	Systolic blood pressure
SSB	Sugar-sweetened beverage
TEI	Total energy intake
UK	United Kingdom
US	United States
USDA	United States Department of Agriculture

WHAT IS THE RELATIONSHIP BETWEEN ADDED SUGARS CONSUMPTION AND RISK OF CARDIOVASCULAR DISEASE?

PLAIN LANGUAGE SUMMARY

What is the question?

- The question is: What is the relationship between added sugars consumption and risk of cardiovascular disease?

What is the answer to the question?

- Limited evidence from prospective cohort studies that were based primarily on sugar-sweetened beverages suggests that higher consumption of added sugars in adulthood is associated with increased risk of cardiovascular disease mortality.
- Insufficient evidence is available to determine the relationship between added sugars consumption and risk of cardiovascular disease in children.
- Insufficient evidence is available to determine the relationship between added sugars intake in adulthood and cardiovascular disease risk profile.
- Insufficient evidence is available to determine the relationship between added sugars intake in adulthood and risk of stroke.
- Insufficient evidence is available to determine the relationship between added sugars intake in adulthood and incident ischemic cardiovascular disease events.
- Insufficient evidence is available to determine the relationship between added sugars intake in adulthood and risk of peripheral artery disease.
- Insufficient evidence is available to determine the relationship between added sugars intake in adulthood and risk of heart failure.

Why was this question asked?

- This important public health question was identified by the U.S. Departments of Agriculture (USDA) and Health and Human Services (HHS) to be examined by the 2020 Dietary Guidelines Advisory Committee.

How was this question answered?

- The 2020 Dietary Guidelines Advisory Committee, Beverages and Added Sugars Subcommittee conducted a systematic review to answer this question with support from the Nutrition Evidence Systematic Review (NESR) team.

What is the population of interest?

- The population of interest for the intervention/exposure was all ages (birth through older adulthood).
- The population of interest for the intermediate outcomes was all ages 2 years and older for controlled trials and ages 2-18 years for observational studies.
- The population of interest for the endpoint health outcomes was all ages 2 years and older.

What evidence was found?

- This review includes 23 studies: 3 in children, 20 in adults
- The exposure or intervention of interest was added sugars. This included total

added sugars and added sugars from single, substantial sources like sugar-sweetened beverages (SSB).

- Evidence in children:
 - All 3 studies examined intermediate outcomes, primarily lipid profiles. Two found greater added sugars intake related to worse lipid profiles in children. The third found no relationship.
 - Evidence was limited by the small number of studies, wide variability in participant age, and inconsistency in outcomes measured.
- Evidence in adults:
 - Four of the 6 articles reporting intermediate outcome data found no relationship with added sugars. The remaining 2 found added sugars related to both total cholesterol and triglyceride levels.
 - Cardiovascular disease-related mortality risk was positively related to greater added sugars intake when the exposure was measured multiple times.
 - No conclusions could be drawn for peripheral artery disease, stroke, or heart failure.
 - Evidence was limited by poor adjustment for confounders, use of different exposures and outcomes, and measuring the exposure only once.

How up-to-date is this systematic review?

- This review searched for studies from September 2014 to September 2019.

TECHNICAL ABSTRACT

Background

- This important public health question was identified by the U.S. Departments of Agriculture (USDA) and Health and Human Services (HHS) to be examined by the 2020 Dietary Guidelines Advisory Committee.
- The 2020 Dietary Guidelines Advisory Committee, Beverages and Added Sugars Subcommittee conducted a systematic review to answer this question with support from the Nutrition Evidence Systematic Review (NESR) team.
- The goal of this systematic review was to examine the following question: What is the relationship between added sugars consumption and risk of cardiovascular disease?

Conclusion statements and grades

- Limited evidence from prospective cohort studies that were based primarily on sugar-sweetened beverages suggests that higher consumption of added sugars in adulthood is associated with increased risk of cardiovascular disease mortality. (Grade: Limited)
- Insufficient evidence is available to determine the relationship between added sugars consumption and risk of cardiovascular disease in children. (Grade: Grade not assignable)
- Insufficient evidence is available to determine the relationship between added sugars intake in adulthood and cardiovascular disease risk profile. (Grade: Grade not assignable)
- Insufficient evidence is available to determine the relationship between added sugars intake in adulthood and risk of stroke. (Grade: Grade not assignable)
- Insufficient evidence is available to determine the relationship between added sugars intake in adulthood and incident ischemic cardiovascular disease events. (Grade: Grade not assignable)
- Insufficient evidence is available to determine the relationship between added sugars intake in adulthood and risk of peripheral artery disease. (Grade: Grade not assignable)
- Insufficient evidence is available to determine the relationship between added sugars intake in adulthood and risk of heart failure. (Grade: Grade not assignable)

Methods

- A literature search was conducted using 3 databases (PubMed, Cochrane, and Embase) to identify articles that evaluated the intervention or exposure of added sugar consumption and the outcomes of cardiovascular disease. A manual search was conducted to identify articles that may not have been included in the electronic databases searched. Articles were screened by two NESR analysts independently for inclusion based on pre-determined criteria.
- Data extraction and risk of bias assessment were conducted for each included study, and both were checked for accuracy. The Committee qualitatively synthesized the body of evidence to inform development of a conclusion statement(s), and graded the strength of evidence using pre-established criteria for risk of bias, consistency, directness, precision, and generalizability.

Summary of the evidence

- 23 studies examined the relationship between added sugars consumption and the risk of cardiovascular disease (CVD):
 - Children: 3 studies, including 1 randomized controlled trial (RCT) and 2 prospective cohort studies (PCSs)
 - Adults: 20 studies, including 4 RCTs, 2 crossover studies, and 14 PCSs
- The added sugars intervention/exposure included:
 - Total added sugars intake from foods and beverages
 - Added sugars from a single substantial source of overall added sugars intake (e.g., sugar-sweetened beverages [SSB], total sucrose intake)
- CVD outcomes considered:
 - Intermediate outcomes: Total cholesterol, LDL-C, HDL-C, triglycerides, and blood pressure (systolic and diastolic)
 - Children: included intermediate outcome data from RCTs and observational studies
 - Adults: included intermediate outcome data from RCTs and crossover studies only
 - Endpoint outcomes: CVD (including myocardial infarction, coronary heart disease, and coronary artery disease; congestive heart failure; and peripheral artery disease), stroke (separating ischemic and hemorrhagic when possible), venous thrombosis, and CVD-related mortality
 - Children and adults: included endpoint outcome data from RCTs, crossover, and observational studies
- Evidence in children:
 - Three studies reported on intermediate CVD outcomes in children; no studies looking at endpoint CVD outcomes in children met the inclusion criteria.
 - Findings from the 1 RCT and 1 cohort study found greater added sugars intake related to worse lipid profiles in children, namely detrimental change in total cholesterol and HDL-C over time.
 - The third study did not find a significant relationship between added sugars consumption and CVD outcomes.
 - The body of evidence was limited substantially by the small number of studies, the variability in age of the participants, and inconsistency in outcomes measured.
- Evidence in adults:
 - Intermediate outcomes:
 - Three RCTs reported in 4 articles and 2 crossover studies examined intermediate CVD outcomes; 4 of these studies found no significant effect of added sugars consumption.
 - One RCT found that reducing added sugars consumption led to improved triglyceride levels, and the second article from a larger sample of participants from the same RCT found that continued high levels of SSB consumption led to detrimental changes in total cholesterol and triglyceride levels.
 - RCT evidence was limited by small sample sizes and inconsistency in exposures and outcomes measured.
 - Endpoint outcomes:

- CVD-related mortality was assessed by 8 PCSs; 6 of the 8 found no significant relationship; 1 found a relationship before adjustment for adiposity, and the other reported repeat exposure assessment in 2 independent cohorts and found a significant, positive association.
- A small number of studies examined ischemic CVD events, peripheral artery disease, stroke, and heart failure, which limited the ability to draw conclusions.
- Most studies adjusted for adiposity, though four studies presented data both with and without adjustment, and all but one found the relationship did not change.
- Observational evidence was limited by inadequate adjustment for confounders, inconsistency in exposures and outcomes measured, and measures of exposure taken at baseline only.

FULL REVIEW

Systematic review question

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

Conclusion statements and grades

Limited evidence from prospective cohort studies that were based primarily on sugar-sweetened beverages suggests that higher consumption of added sugars in adulthood is associated with increased risk of cardiovascular disease mortality. (Grade: Limited)

Insufficient evidence is available to determine the relationship between added sugars consumption and risk of cardiovascular disease in children. (Grade: Grade not assignable)

Insufficient evidence is available to determine the relationship between added sugars intake in adulthood and cardiovascular disease risk profile. (Grade: Grade not assignable)

Insufficient evidence is available to determine the relationship between added sugars intake in adulthood and risk of stroke. (Grade: Grade not assignable)

Insufficient evidence is available to determine the relationship between added sugars intake in adulthood and incident ischemic cardiovascular disease events. (Grade: Grade not assignable)

Insufficient evidence is available to determine the relationship between added sugars intake in adulthood and risk of peripheral artery disease. (Grade: Grade not assignable)

Insufficient evidence is available to determine the relationship between added sugars intake in adulthood and risk of heart failure. (Grade: Grade not assignable)

Summary of the evidence

- 23 studies examined the relationship between added sugars consumption and the risk of cardiovascular disease (CVD)¹⁻²³:
 - Children: 3 studies, including 1 randomized controlled trial (RCT) and 2 prospective cohort studies (PCSs)
 - Adults: 20 studies, including 4 RCTs, 2 crossover studies, and 14 PCSs
- The added sugars intervention/exposure included:
 - Total added sugars intake from foods and beverages
 - Added sugars from a single substantial source of overall added sugars intake (e.g., sugar-sweetened beverages [SSB], total sucrose intake)
- CVD outcomes considered:
 - Intermediate outcomes: Total cholesterol, LDL-C, HDL-C, triglycerides, and blood pressure (systolic and diastolic)
 - Children: included intermediate outcome data from RCTs and observational studies
 - Adults: included intermediate outcome data from RCTs and crossover studies only

- Endpoint outcomes: CVD (including myocardial infarction, coronary heart disease, and coronary artery disease; congestive heart failure; and peripheral artery disease), stroke (separating ischemic and hemorrhagic when possible), venous thrombosis, and CVD-related mortality
 - Children and adults: included endpoint outcome data from RCTs, crossover, and observational studies
- Evidence in children:
 - Three studies reported on intermediate CVD outcomes in children; no studies looking at endpoint outcomes in children met the inclusion criteria.
 - Findings from the 1 RCT and 1 cohort study found greater added sugars intake related to worse lipid profiles in children, namely detrimental change in total cholesterol and HDL-C over time.
 - The third study did not find a significant relationship between added sugars consumption and CVD outcomes.
 - The body of evidence was limited substantially by the small number of studies, the variability in age of the participants, and inconsistency in outcomes measured.
- Evidence in adults:
 - Intermediate outcomes:
 - Three RCTs reported in 4 articles and 2 crossover studies examined intermediate CVD outcomes; 4 of these studies found no significant effect of added sugars consumption.
 - One RCT found that reducing added sugars consumption led to improved triglyceride levels, and the second paper from a larger sample of participants from the same RCT found that continued high levels of SSB consumption led to detrimental changes in total cholesterol and triglyceride levels.
 - RCT evidence was limited by small sample sizes and inconsistency in exposures and outcomes measured.
 - Endpoint outcomes:
 - CVD-related mortality was assessed by 8 PCSs; 6 of the 8 found no significant relationship; 1 found a relationship before adjustment for adiposity, and the other reported repeat exposure assessment in 2 independent cohorts and found a significant, positive association.
 - A small number of studies examined ischemic CVD events, peripheral artery disease, stroke, and heart failure, which limited the ability to draw conclusions.
 - Most studies adjusted for adiposity, though four studies presented data both with and without adjustment, and all but one found the relationship did not change.
 - Observational evidence was limited by inadequate adjustment for confounders, inconsistency in exposures and outcomes measured, and measures of exposure taken at baseline only.

Description of the evidence

This systematic review examining the relationship between added sugars consumption and risk of CVD included 23 articles published between September 2014 and September 2019. Three studies were conducted in children and 20 in adults.

Study designs:

- Children: 3 articles
 - RCTs: 1 article⁴
 - Prospective cohort studies: 2 articles^{8,9}
- Adults: 20 articles
 - Parallel-arm RCTs: 4 articles^{2,5,6,11}
 - Crossover RCTs: 2 articles^{13,22}
 - Prospective cohort studies: 14 articles^{1,3,7,10,12,14-21,23}

In children, the RCT was conducted in Brazil,⁴ one prospective cohort study was conducted in the United States,⁸ and the other in the Netherlands.⁹

The studies in adults were conducted in the following countries: six studies in the United States^{1,3,12,17,18,20}; four in Sweden^{7,19,21,23}; two each in Denmark,^{2,5} Mexico,^{6,11} and the United Kingdom^{13,22}; one each in Hong Kong,¹⁰ Japan,¹⁵ and Singapore¹⁶; and one multi-country European cohort.¹⁴

Population

Studies were included if the participants were generally healthy or at risk for chronic disease.

The three studies in children enrolled a range of ages, with the RCT studying 478, 11-year-old children and following them for one school year⁴; one prospective cohort study studying 2,223, 9-10-year-old children with a 10-year follow up⁸; and the other studying 1,390 children approximately 13-months old and following them through age 6.⁹ Two of the samples were racially diverse with 59% 'non-white skin' participants in the RCT⁴ and 51% Black in the US cohort,⁸ while the third study, conducted in the Netherlands, did not report race/ethnicity data.⁹

The four RCTs and two crossover studies conducted in adults enrolled a broad range of ages, primarily middle-aged adults, with one focusing specifically on older men²² and another exclusively enrolling women.⁶ The sample sizes ranged from 27 to 268. Only one study reported race/ethnicity data, and the sample was 80% white.¹³ The prospective cohort studies were similar, enrolling large cohorts of predominantly white, middle-aged adults. Sample sizes ranged from 2,888 to 202,907.

Intervention/exposure/comparator

The intervention or exposure of interest for this question was added sugars, which included studies examining total added sugars intake from foods and beverages as well as studies assessing added sugars from a single substantial source of overall added sugars intake (e.g., SSBs or total sucrose intake).

Two of the three studies in children, including the RCT, focused on SSB intake,^{4,9} while one of the prospective cohort studies examined added sugars intake from all foods and beverages.⁸

For adults, two RCTs and one crossover study used total added sugars as the intervention,^{11,13,22} while the remaining studies focused specifically on SSBs.^{2,5,6}

The prospective cohort studies also assessed a variety of exposures, with eight examining SSB intake^{1,3,12,14,16-19}; three examining total added sugars intake^{10,15,20}; and three specifically examining sucrose intake.^{7,21,23}

Outcomes

The outcomes of interest in children included both intermediate and endpoint outcomes; however, the eligible data only looked at intermediate outcomes. Total cholesterol and HDL cholesterol were assessed in two studies, while SBP, DBP, LDL, and triglycerides were each measured in one study.⁹

In order to focus on the strongest available evidence, included outcomes in adults differed by study design. For experimental designs, intermediate and endpoint outcomes were included; for observational studies, only endpoint CVD outcomes were included. The eligible data were synthesized according to the following categories: CVD risk profile, which included blood pressure, cholesterol, and triglycerides (4 RCTs and 2 crossover studies); CVD-related mortality (8 prospective cohort studies); ischemic CVD event incidence (3 prospective cohort studies); peripheral artery disease incidence (PAD, 2 prospective cohort studies); stroke incidence (1 prospective cohort study); and heart failure incidence (1 prospective cohort study).

Evidence synthesis

Children

The RCT⁴ and one cohort study⁸ examined similarly-aged children and showed greater SSB and total added sugars intake related to worse lipid profiles, though they examined different outcomes, total cholesterol and HDL, respectively. The remaining cohort study examined a broader range of outcomes in younger children and did not find any significant associations (**Table 1**).⁹

Lipid profile

De Moraes et al⁴ used school-based cluster randomization to test a behavioral approach to reduce SSB intake in 4th grade Brazilian children in which the intervention group received water-promoting messaging, education, and supplies (i.e., water bottles). The control group received general health education and consumed their usual diet. The intervention ran for one full school year and resulted in significantly lower total cholesterol and lower incidence of moderately high total cholesterol (≥ 150 mg/dL) and hypercholesterolemia (≥ 170 mg/dL) compared to the control group.

Lee et al⁸ assessed added sugar intake from all foods and beverages in girls age 9-10 years-old at baseline and then annually for 10-years of follow-up. Consuming $\geq 10\%$ of total energy from added sugars was associated with an annual decrease in HDL. Over the 10-year follow up, consuming less than 10% total energy as added sugars was associated with higher HDL.

Leermakers et al⁹ examined consumption of sugar-containing beverages in 13-month-old toddlers and outcomes at 6 years of age. Intake of sugar-containing beverages at baseline was not associated with the outcomes examined five years later, including

systolic and diastolic blood pressure, total cholesterol, HDL, LDL, and triglycerides.

These findings were limited by the small number of studies, and the individual studies were impacted by inconsistency in population ages, exposures, and outcome assessed; inadequate adjustment for confounders; inconsistent findings with limited directness to the outcome of interest; and poor generalizability (see **Table 2** and **Table 3**). Due to these limitations, the evidence was insufficient to draw a conclusion to the systematic review question.

Adults

CVD-related mortality

Three large prospective cohort studies examined total added sugars intake and CVD-related mortality.^{10,15,20} Findings were mixed; two found no significant association with CVD-related mortality,^{15,20} while one found greater added sugars intake was related to lower risk but only before adjustment for adiposity.¹⁰ All other studies on this outcome adjusted for adiposity in all analyses (**Table 4**).

Five additional prospective cohort studies examined the relationship between added sugars in the form of SSBs and CVD-related mortality^{1,3,12,14,16}; four of the five found no significant effect.^{1,3,14,16} The fifth study found that greater intake of SSBs was related to higher risk of CVD-related mortality in two large, independent cohorts.¹²

Adjusting for total energy did not explain discrepant findings across the prospective cohort studies. Anthropometry, a likely mediator of this relationship, was adjusted for in all studies and likely attenuated the relationship between added sugars consumption and CVD-related mortality. The study that showed a significant deleterious effect in both men and women measured SSB intake at baseline and multiple times thereafter in two separate cohorts¹²; all other studies assessed intake at baseline only in a single cohort.

CVD risk profile

Four RCTs and two crossover studies examined the relationship between added sugars intake and intermediate CVD outcomes.^{2,5,6,11,13,22}

Two articles reported results from the same parallel arm RCT.^{2,5} This study randomized participants to a 6-month intervention of either 1 L/day of sucrose-sweetened soft drinks or aspartame-sweetened diet cola. Bruun et al² found that triglyceride levels were significantly lower in the diet cola group at the end of intervention. Engel et al⁵ found total cholesterol and triglyceride levels were significantly higher in the sugar-sweetened soft drink group at the end of the intervention, but that differences in LDL, HDL, SBP, and DBP were not significant. These analyses were limited by small sample sizes.

The remaining parallel-arm RCTs found no significant relationships.^{6,11} A 9-month intervention in women with overweight or obesity promoted decreased SSB consumption compared to an education-only control and found no significant between-group differences in triglycerides, total cholesterol, LDL, HDL, SBP, or DBP.⁶ The fourth parallel-arm RCT compared a 4-week low-fructose + low-sodium diet to a low-

sodium diet and found no significant differences in blood pressure, total cholesterol, or triglycerides.¹¹

Of the crossover studies, one found no significant differences between consuming a sugar-reduced diet versus a regular diet for eight weeks in SBP, DBP, total cholesterol, LDL, HDL, or triglycerides.¹³ The other crossover trial found no significant differences between consuming high-sugar and low-sugar diets for 12 weeks in triacylglycerol, total cholesterol, LDL, or HDL in a sample of men.²²

Ischemic CVD events

Three prospective cohort studies measured the incidence of ischemic CVD events.^{18,21,23} Sonestedt et al²¹ examined intake of sucrose from all sources at baseline and incidence of ischemic CVD event, defined as coronary events and ischemic stroke, over a 14-year average follow-up. They also considered individual sources of sucrose, assessing the relationship between SSBs, cookies and cakes, and sweets with the outcome, independently. There was no significant association between baseline intake and incident events. Similarly, Pase et al¹⁸ showed no significant relationship between sugar-sweetened soft drink intake over an average of 8 years and risk of ischemic stroke in the following 10 years.

The third prospective cohort study found total sucrose intake >15% of total energy intake at baseline was related to greater incidence of coronary events over 17 years of follow-up.²³ Incidence was not significantly different between groups at lower intake levels.²³

Peripheral artery disease (PAD) incidence

Two prospective cohort studies examined incidence of peripheral artery disease.^{7,17} The first measured sucrose intake in middle-aged adults relative to the Swedish dietary guidelines (sucrose intake \leq 10% total energy) and found there was no significant difference in risk of PAD between those consuming above and those consuming below the recommended amount.⁷ The second study examined intake of SSBs in middle-aged US adults and found that baseline intake of 2-6 servings per week was related to lower risk relative of PAD compared to those who consumed lower and higher levels, but this was no longer significant after adjustment for baseline diabetes status.¹⁷

Stroke

One study examined the relationship between SSBs and total stroke risk. Pase et al¹⁸ found that average intake of sugar-sweetened soft drinks over eight years was not related to risk of stroke over the subsequent 10-year period.

Heart failure incidence

Only one study examining the association between added sugars intake and incident heart failure was eligible for inclusion.¹⁹ The authors assessed SSB intake and found that individuals consuming two or more servings per day at baseline had a higher risk of heart failure over a 12-year average follow-up compared to non-consumers.

Across all outcomes, adiposity (or prevalence of obesity) was an important variable to consider when answering this question, particularly since this review aimed to examine the direct link between added sugar consumption and risk of CVD independent of

obesity. Over 75 percent of studies in this body of evidence adjusted for adiposity (e.g., BMI, weight), which, as adiposity is a likely mediator, may have affected the observed magnitude of relationship between added sugars and risk of CVD in these studies. One study found the relationship was significant only before adjustment for adiposity,¹⁰ while three other studies examined the effect of adjustment for adiposity using sensitivity analysis, and results remained the same both with and without adjustment.^{18,19,23}

Funding source(s) of each study were extracted and considered during synthesis.

Assessment of the evidence: Adultsⁱⁱ

The conclusion statement “evidence from prospective cohort studies that were based primarily on SSBs suggests that higher consumption of added sugars in adulthood is associated with increased risk for cardiovascular disease mortality” was assigned a grade of limited. Publication bias is another concern. Insufficient evidence was available to draw conclusion statements related to CVD risk profile, stroke, ischemic CVD events, peripheral artery disease, or heart failure.

As outlined and described below, the body of evidence examining added sugars consumption and risk of cardiovascular disease was assessed for the following elements used when grading the strength of evidence.

Consistency: The study combining two cohorts with repeat exposure assessment showed a significant relationship with CVD-related mortality, while the studies that only examined one exposure time point showed no significant relationship. This remained true regardless of whether the study looked at total added sugars intake or SSBs as the exposure.

Directness: All evidence comes from prospective cohort studies that were not likely designed to answer this specific question; however, the relationships studied are sufficient for answering this research question. More than half of the studies examined SSBs, specifically, while the others assessed total added sugars intake.

Precision: Most cohorts were large in size, with only one study enrolling fewer than 5,000 participants, and findings were consistent across sample sizes.

Generalizability: The majority of studies enrolled middle-aged adults that were primarily white, suggesting good generalizability for that population, but less generalizability for younger, older, and non-white adults.

Risk of bias: Multiple areas of potential risk of bias impacted these studies, primarily inadequate adjustment for confounders, exposure measurement at baseline only, and failure to account for missing data. (see **Table 5** and **Table 6**)

ⁱⁱ A detailed description of the methodology used for grading the strength of the evidence is available on the NESR website: <https://nesr.usda.gov/2020-dietary-guidelines-advisory-committee-systematic-reviews> and in Part C of the following reference: 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.

Research recommendations

- Distinguish between food and beverage sources of added sugars when conducting intervention or assessing exposure
- Measure added sugars consumption with more accuracy, including use of validated measures and repeat assessment of intake across time
- Consider the important role of obesity and adiposity measures when examining this relationship, including consideration both with and without statistical adjustment for these measures

Included articles

1. Barrington WE, White E. Mortality outcomes associated with intake of fast-food items and sugar-sweetened drinks among older adults in the Vitamins and Lifestyle (VITAL) study. *Public Health Nutr.* 2016;19(18):3319-3326. doi: 10.1017/s1368980016001518.
2. Bruun JM, Maersk M, Belza A, Astrup A, Richelsen B. Consumption of sucrose-sweetened soft drinks increases plasma levels of uric acid in overweight and obese subjects: a 6-month randomised controlled trial. *Eur J Clin Nutr.* 2015;69(8):949-953. doi: 10.1038/ejcn.2015.95.
3. Collin LJ, Judd S, Safford M, Vaccarino V, Welsh JA. Association of sugary beverage consumption with mortality risk in us adults: a secondary analysis of data from the REGARDS Study. *JAMA Netw Open.* 2019;2(5):e193121. doi: 10.1001/jamanetworkopen.2019.3121.
4. de Moraes MM, Mediano MFF, de Souza RAG, Moura AS, da Veiga GV, Sichieri R. Discouraging soft drink consumption reduces blood glucose and cholesterol of Brazilian elementary students: secondary analysis of a randomized controlled trial. *Prev Med.* 2017;100:223-228. doi: 10.1016/j.ypmed.2017.04.035.
5. Engel S, Tholstrup T, Bruun JM, Astrup A, Richelsen B, Raben A. Effect of high milk and sugar-sweetened and non-caloric soft drink intake on insulin sensitivity after 6 months in overweight and obese adults: a randomized controlled trial. *Eur J Clin Nutr.* 2018;72(3):358-366. doi: 10.1038/s41430-017-0006-9.
6. Hernandez-Cordero S, Barquera S, Rodriguez-Ramirez S, et al. Substituting water for sugar-sweetened beverages reduces circulating triglycerides and the prevalence of metabolic syndrome in obese but not in overweight Mexican women in a randomized controlled trial. *J Nutr.* 2014;144(11):1742-1752. doi: 10.3945/jn.114.193490.
7. Kulezic A, Bergwall S, Fatemi S, et al. Healthy diet and fiber intake are associated with decreased risk of incident symptomatic peripheral artery disease - a prospective cohort study. *Vasc Med.* 2019;24(6):511-518. doi: 10.1177/1358863x19867393.
8. Lee AK, Binongo JN, Chowdhury R, et al. Consumption of less than 10% of total energy from added sugars is associated with increasing HDL in females during adolescence: a longitudinal analysis. *J Am Heart Assoc.* 2014;3(1):e000615. doi: 10.1161/jaha.113.000615.
9. Leermakers ET, Felix JF, Jaddoe VW, Raat H, Franco OH, Kiefte-de Jong JC. Sugar-containing beverage intake at the age of 1 year and cardiometabolic health at the age of 6 years: the Generation R Study. *Int J Behav Nutr Phys Act.* 2015;12:114. doi: 10.1186/s12966-015-0278-1.
10. Liu ZM, Tse LA, Chan D, Wong C, Wong SYS. Dietary sugar intake was associated with increased body fatness but decreased cardiovascular mortality in Chinese elderly: an 11-year prospective study of Mr and Ms OS of Hong Kong. *Int J Obes.* 2018;42(4):808-816. doi: 10.1038/ijo.2017.292.
11. Madero M, Rodriguez Castellanos FE, Jalal D, et al. A pilot study on the impact of a low fructose diet and allopurinol on clinic blood pressure among overweight and prehypertensive subjects: a randomized placebo controlled trial. *J Am Soc Hypertens.* 2015;9(11):837-844. doi: 10.1016/j.jash.2015.07.008.

12. Malik VS, Li Y, Pan A, et al. Long-term consumption of sugar-sweetened and artificially sweetened beverages and risk of mortality in US adults. *Circulation*. 2019;139(18):2113-2125. doi: 10.1161/circulationaha.118.037401.
13. Markey O, Le Jeune J, Lovegrove JA. Energy compensation following consumption of sugar-reduced products: a randomized controlled trial. *Eur J Nutr*. 2016;55(6):2137-2149. doi: 10.1007/s00394-015-1028-5.
14. Mullee A, Romaguera D, Pearson-Stuttard J, et al. Association between soft drink consumption and mortality in 10 European countries. *JAMA Intern Med*. 2019. doi: 10.1001/jamainternmed.2019.2478.
15. Nagata C, Wada K, Yamakawa M, et al. Intake of starch and sugars and total and cause-specific mortality in a Japanese community: the Takayama Study. *Br J Nutr*. 2019;122(7):820-828. doi: 10.1017/s0007114519001661.
16. Odegaard AO, Koh WP, Yuan JM, Pereira MA. Beverage habits and mortality in Chinese adults. *J Nutr*. 2015;145(3):595-604. doi: 10.3945/jn.114.200253.
17. Ogilvie RP, Lutsey PL, Heiss G, Folsom AR, Steffen LM. Dietary intake and peripheral arterial disease incidence in middle-aged adults: the Atherosclerosis Risk in Communities (ARIC) Study. *Am J Clin Nutr*. 2017;105(3):651-659. doi: 10.3945/ajcn.116.137497.
18. Pase MP, Himali JJ, Beiser AS, et al. Sugar- and artificially sweetened beverages and the risks of incident stroke and dementia: a prospective cohort study. *Stroke*. 2017;48(5):1139-1146. doi: 10.1161/strokeaha.116.016027.
19. Rahman I, Wolk A, Larsson SC. The relationship between sweetened beverage consumption and risk of heart failure in men. *Heart*. 2015;101(24):1961-1965. doi: 10.1136/heartjnl-2015-307542.
20. Shah NS, Leonard D, Finley CE, et al. Dietary patterns and long-term survival: a retrospective study of healthy primary care patients. *Am J Med*. 2018;131(1):48-55. doi: 10.1016/j.amjmed.2017.08.010.
21. Sonestedt E, Hellstrand S, Schulz CA, et al. The association between carbohydrate-rich foods and risk of cardiovascular disease is not modified by genetic susceptibility to dyslipidemia as determined by 80 validated variants. *PLoS One*. 2015;10(4):e0126104. doi: 10.1371/journal.pone.0126104.
22. Umpleby AM, Shojaee-Moradie F, Fielding B, et al. Impact of liver fat on the differential partitioning of hepatic triacylglycerol into VLDL subclasses on high and low sugar diets. *Clin Sci*. 2017;131(21):2561-2573. doi: 10.1042/cs20171208.
23. Warfa K, Drake I, Wallstrom P, Engstrom G, Sonestedt E. Association between sucrose intake and acute coronary event risk and effect modification by lifestyle factors: Malmo Diet and Cancer Cohort Study. *Br J Nutr*. 2016;116(9):1611-1620. doi: 10.1017/s0007114516003561.

Table 1: Evidence in children on added sugars consumption and risk of cardiovascular diseaseⁱⁱⁱ

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	TEI, Confounders, and Study Limitations
<p>de Moraes, 2017^{1*} Cluster RCT, Brazil (secondary analyses using participants who consented to blood draw, 42% of original sample) Baseline N=1140, Analytic N=478 (Attrition: NR); Power: 80% power and a 5% significance level to detect a difference of 0.5 cup in soda consumption between the two groups, with 140 students in each arm of the trial; final sample size with available blood samples of about 480 would be able to detect weight changes and associated changes in metabolic markers</p> <p>Recruitment: 22 public schools in the metropolitan area of Rio de Janeiro, Brazil</p> <p>Participant characteristics: fourth-grade children</p> <ul style="list-style-type: none"> • Total energy intake: ~2297 kcal/d • Sex (female): ~44% • Age: ~10.8y • Race/ethnicity: 59% Non-white skin • SES: NR • Anthropometrics: BMI~18.2 kg/m²; 19% Overweight • Physical activity: NR • Smoking: NR <p>Summary of findings: An 8-month lifestyle intervention to reduce soft drink intake in children resulted in significant reductions in total cholesterol in the intervention group compared to control.</p>	<p>Intervention: Soft drink intake A healthy lifestyle education program using simple messages encouraging water consumption instead of soft drinks. Education delivered via classroom activities; banners promoting water consumption, and water bottles with the logo of the campaign given to children and school teachers; n=238</p> <p>Comparator: Control; received two 1hr sessions on general health issues and printed guidelines on healthy eating; n=240</p> <p><u>Intervention duration:</u> 7mo of one school year</p> <p><u>Intervention compliance:</u> two 24hr dietary recalls and frequency questionnaire on beverage consumption</p> <p>Study added sugars intake: Soft drinks</p> <ul style="list-style-type: none"> • Never to 4 times/mo: 29% • 2-6 times/wk: 51% • ≥1 time/d: 16% <p>Outcome assessment methods/timing:</p> <ul style="list-style-type: none"> • Baseline, ~8mo follow-up • Intermediate outcomes measured: Total cholesterol • Fasting blood samples collected in schools by trained laboratory technician; serum cholesterol obtained by enzymatic-colorimetric method • Moderately high total cholesterol defined as ≥150 mg/dL and hypercholesterolemia ≥170 mg/dL 	<p>Intermediate outcomes: Total Cholesterol, mg/dL Within group, change over 1yr: Control: +2.14 Intervention: -10.34 Between groups: P<0.001, Effect size=0.06</p> <p>Cholesterol ≥150 mg/dL, % (n) Change within group over time: Baseline, f/u Control: 53.2 (125), 56.7 (89) Intervention: 70.7 (159), 55.6 (84) Between groups: P=0.002</p> <p>Cholesterol ≥170 mg/dL, % (n) Change within group over time: Baseline, f/u Control: 26.0 (61), 28.7 (45) Intervention: 39.1 (88), 29.1 (44) Between groups: P=0.03</p>	<p>TEI adjusted: Yes TEI, kcal/d Within group, change over 1yr: Control: -193.7 Intervention: -384.0 Between groups: P=0.03, Effect size=0.15</p> <p>Confounders accounted for:</p> <ul style="list-style-type: none"> • Key confounders: sex, age, race/ethnicity, anthropometry • Other factors considered: total energy intake, protein, fat, food form (beverage) <p>Confounders NOT accounted for:</p> <ul style="list-style-type: none"> • Key confounders: SES, physical activity, smoking, naturally occurring sugar intake • Other factors considered: medications, supplements, sodium, fiber, energy density, family history of CVD <p>Additional model adjustments: Baseline cholesterol, cluster (class)</p> <p>Limitations:</p> <ul style="list-style-type: none"> • Not all key confounders accounted for • Frequency of participants who consumed soft drinks ≥1/d was higher among ppts with no blood samples compared to those included here who had at least one blood sample • No analysis plan <p>Funding source: Brazilian National Research Institute</p>

ⁱⁱⁱ Abbreviations: Avg: average; B: beta; BMI: body mass index; CI: confidence interval; CVD: cardiovascular disease; d: day(s); DBP: diastolic blood pressure; dL: deciliter(s); FFQ: food frequency questionnaire; f/u: follow-up; g: gram(s); HDL: high-density lipoprotein cholesterol; hr: hour; kg/m²: kilograms per meters squared; LDL: low-density lipoprotein cholesterol; mg: milligram(s); ml: milliliter(s); mo: month(s); NS: not significant; NR: not reported; RCT: randomized controlled trial; REF: reference group; SBP: systolic blood pressure; SD: standard deviation; SE: standard error; SES: socioeconomic status; sv: serving(s); TC:

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	TEI, Confounders, and Study Limitations
Prospective Cohort Studies			
<p>Lee, 2014² Prospective Cohort Study, National Heart Lung and Blood Institute's Growth and Health Study (NGHS), United States Analytic N=2223; Power: NR</p> <p>Recruitment: three study sites (Richmond, CA; Cincinnati, OH; Washington, DC)</p> <p>Participant characteristics: adolescent girls (9-10y)</p> <ul style="list-style-type: none"> Sex (female): 100% Age: 9-10y Race/ethnicity: 51% African-American, 49% Caucasian SES: Parent education, ≥College graduate 35% Anthropometrics: 69% Normal weight, 13% Obese Physical activity: score, 32.2 Smoking: Current (≥7 cigarettes/wk) 0.5% <p>Summary of findings: Among adolescent girls, consuming ≥10% of total energy from added sugars was associated in an annual decline in HDL. Over the 10y follow-up, consumption of added sugars <10% total energy was associated with higher HDL.</p>	<p>Exposure of interest: Added sugar intake from all sugar-containing foods and beverages (such as sucrose, fructose, and glucose from soda, desserts, and sweetened grain products)</p> <p>Comparators: categorical</p> <ul style="list-style-type: none"> Low (0 to <10% of total energy) High (≥10% of total energy) <p>Exposure assessment method and timing:</p> <ul style="list-style-type: none"> 3-d food record (validated); represents dietary intake on both weekdays and weekends At baseline, annually for 10y <p>Outcome assessment methods/timing:</p> <ul style="list-style-type: none"> At visits 1, 3, 5, 7, and 10y Intermediate outcomes measured: HDL cholesterol Fasting and non-fasting blood samples obtained; non-fasting HDL levels used for analysis 	<p>Intermediate outcomes: HDL, by consumption level, mg/dL, β (95% CI)</p> <p>Change per consumption level: Low (ref) High: -0.26 (0.48 to 0.04), P=0.02</p> <p>Predicted change over 10yr study period for nonsmoking adolescents of normal weight: Low: 2.2 (0.09, 4.32), P=0.04 High: -0.4 (-1.32, 0.52), P=0.4 P difference: 0.045</p> <p><i>Interaction of added sugars with BMI: P=0.45</i></p> <p><i>Sensitivity analyses assessing impact of assumptions used to calculate amount of added and naturally occurring sugars in foods (e.g., lactose and galactose in dairy products) found no substantial differences in the results.</i></p>	<p>TEI adjusted: Yes</p> <p>Confounders accounted for:</p> <ul style="list-style-type: none"> Key confounders: sex, age, race/ethnicity, physical activity, anthropometry, smoking, naturally occurring sugar intake Other factors considered: total energy intake, fiber, fat <p>Confounders NOT accounted for:</p> <ul style="list-style-type: none"> Key confounders: SES Other factors considered: menopausal status, medications, supplements, sodium, protein, energy density, family history of CVD, food form (solid/beverage) <p>Additional model adjustments: Puberty stage, nutrient residuals for other carbohydrates</p> <p>Limitations:</p> <ul style="list-style-type: none"> Not all key confounders accounted for No information on non-completers Results not clearly reported No preregistered data analysis plan <p>Funding sources: NR</p>

total cholesterol; TEI: total energy intake; TG: triglyceride; wk: week(s); y: year(s)

Red font indicates a statistically significant detrimental relationship, and green font indicates a statistically significant beneficial relationship.

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	TEI, Confounders, and Study Limitations
<p>Leermakers, 2015³ Prospective Cohort Study, Generation R Study, the Netherlands Analytic N= 1390-1950; Power: NR</p> <p>Participant characteristics: toddlers</p> <ul style="list-style-type: none"> Sex (female): 34% Age: ~ 13mo <p>Summary of findings: There were no significant associations between sugar-containing beverage intake at 12 month and CVD-related outcomes (TC, HDL, LDL, TG, SBP, DBP) at ~6 years old.</p>	<p>Exposure of interest: Sugar-containing beverages (Total SCBs including fruit juices, fruit concentrates, lemonades, soft drinks and sports drinks); 1 svg = 150 mL</p> <p>Comparators: categorical; sex-specific tertiles</p> <p>Exposure assessment method and timing:</p> <ul style="list-style-type: none"> Primary caregiver completed FFQ, representing past month; validated At baseline (~13mo) <p>Outcome assessment methods/timing:</p> <ul style="list-style-type: none"> At ~5.9yo Intermediate outcomes measured: total cholesterol (TC), HDL, LDL, TG, SBP, DBP Non-fasting blood samples drawn and TC, HDL, LDL, and TG measured with enzymatic methods; SBP and DBP measured four times using validated automatic sphygmomanometer (average of three measurements used) 	<p>Systolic Blood Pressure, Linear regression, β (95% CI) Total population (n=1950): NS Boys: NS Girls: NS</p> <p>Diastolic Blood Pressure, Linear regression, β (95% CI) Total population (n=1950): NS Boys: NS Girls: NS</p> <p>Total Cholesterol, Linear regression, β (95% CI); Total population: NS Boys: NS Girls: NS</p> <p>HDL Cholesterol, Linear regression, β (95% CI); Total population (n=1390): NS Boys: NS Girls: NS</p> <p>LDL Cholesterol, Linear regression, β (95% CI); Total population: NS Boys: NS Girls: NS</p> <p>Triglycerides, Linear regression, β (95% CI) Total population (n=1387): NS Boys: NS Girls: NS</p>	<p>TEI adjusted: Yes</p> <p>Confounders accounted for:</p> <ul style="list-style-type: none"> Key confounders: maternal age, sex, SES (parent), feeding practices (e.g., human milk/infant formula history) Other factors considered: smoking (maternal), maternal anthropometry <p>Confounders NOT accounted for:</p> <ul style="list-style-type: none"> Key confounders: gestational age, race/ethnicity, anthropometry at birth or baseline Other factors considered: maternal diet, parity, participation in a supplemental food program, family history of CVD, complementary feeding practices <p>Additional model adjustments: Total energy intake, folic acid supplementation during pregnancy, child diet quality score, hours of watching TV at age 2</p> <p>Limitations:</p> <ul style="list-style-type: none"> Not all key confounders accounted for No information on non-completers Exposure data only measured once No preregistered data analysis plan <p>Funding sources: Erasmus Medical Centre, Rotterdam, the Erasmus University Rotterdam and the Netherlands Organization for Health Research and Development; the Netherlands Organization for Health Research and Development; Nestlé Nutrition (Nestec Ltd.), Metagenics Inc. and AXA</p>

Table 2: Risk of bias for the randomized controlled trial examining added sugars consumption and risk of cardiovascular disease in children^{iv,v}

	Randomization	Identification of participants - randomization	Deviations from intended interventions	Missing outcome data	Outcome measurement	Selection of the reported result
de Moraes, 2017 ¹	High	Some concerns	Low	Low	Low	Some concerns

Table 3: Risk of bias for observational studies examining added sugars consumption and risk of cardiovascular disease in children^{vi}

	Confounding	Selection of participants	Classification of exposures	Deviations from intended exposures	Missing data	Outcome measurement	Selection of the reported result
Lee, 2014 ²	Serious	Low	Low	Low	Low	Low	Serious
Leermakers, 2015 ³	Serious	Low	Low	Moderate	Moderate	Low	Moderate

^{iv} A detailed description of the methodology used for assessing risk of bias is available on the NESR website: <https://nesr.usda.gov/2020-dietary-guidelines-advisory-committee-systematic-reviews> and in Part C of the following reference: 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.

^v Possible ratings of low, some concerns, or high determined using the "[Cochrane Risk-of-bias 2.0](#)" (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.)

^{vi} Possible ratings of low, moderate, serious, critical, or no information determined 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.)

Table 4: Evidence in adults on added sugars consumption and risk of cardiovascular disease^{vii}

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	TEI, Confounders, and Study Limitations
RCTs			

^{vii} Abbreviations/short-hand: Avg: average; B: beta; BMI: body mass index; CI: confidence interval; CVD: cardiovascular disease; d: day(s); DBP: diastolic blood pressure; dL: deciliter(s); FFQ: food frequency questionnaire; f/u: follow-up; g: gram(s); HDL: high-density lipoprotein cholesterol; hr: hour; kg/m²: kilograms per meters squared; L: liter(s); LDL: low-density lipoprotein cholesterol; mg: milligram(s); ml: milliliter(s); mo: month(s); N/A: not applicable; NS: not significant; NR: not reported; RCT: randomized controlled trial; REF: reference group; SBP: systolic blood pressure; SD: standard deviation; SE: standard error; SES: socioeconomic status; svg: serving(s); TC: total cholesterol; TEI: total energy intake; TG: triglyceride; wk: week(s); y: year(s)
 Red font indicates a statistically significant detrimental relationship, and green font indicates a statistically significant beneficial relationship.

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	TEI, Confounders, and Study Limitations
<p>Bruun, 2015^{4*} RCT, Denmark Baseline N=60, Analytic N=47 (Attrition: 22%); Power: NR Recruitment: two centers at Aarhus University Hospital and Department of Nutrition, Exercise and Sports, Faculty of Science, Copenhagen University</p> <p>Participant characteristics: adults with overweight and obesity</p> <ul style="list-style-type: none"> Total energy intake: NR Sex (female): 72% Age: 38.6 (1.1)y (Range 20-50y) Race/ethnicity: NR SES: NR Anthropometrics: BMI 32.1 (0.5) kg/m² Physical activity: ≤10hr/wk (inclusion criteria) Smoking: 100% nonsmokers <p>Summary of findings: In overweight adults and those with obesity, drinking sucrose-sweetened cola (1 L/d) for 6 months significantly increased triglycerides, and triglycerides were significantly higher in the SSSD group than in the groups randomized to consume diet cola (aspartame-sweetened cola, 1 L/d). * Additional information obtained from primary study: Maersk M, et al. <i>Am J Clin Nutr</i> 2012; 95: 283–289.</p>	<p>Intervention: Sucrose-sweetened soft drink (SSSD; Coca Cola; 1 L/d), n=10</p> <p>Comparator: Aspartame-sweetened diet cola (diet Coca Cola; 1 L/d), n=12</p> <p>Other interventions: milk, water</p> <p><u>Intervention duration:</u> 6mo</p> <p><u>Intervention compliance:</u> empty bottles or cartons every 3-4wk; 7-d dietary records at baseline, 3mo, 6mo; compliance NR</p> <p>Study added sugars intake:</p> <ul style="list-style-type: none"> SSSD at baseline: NR <p>Outcome assessment methods/timing:</p> <ul style="list-style-type: none"> At baseline, 6mo follow-up Intermediate outcomes measured: triglycerides Circulating triglycerides measured using routine laboratory methods at hospital 	<p>Intermediate outcomes: Triglycerides Change over time, between groups: Diet Cola < SSSD, P=0.0007</p>	<p>TEI adjusted: Yes (Between-group differences NS at baseline or during study)</p> <p>Confounders accounted for:</p> <ul style="list-style-type: none"> Key confounders: sex, age, anthropometry, smoking Other factors considered: total energy intake, medications, food form (beverage) <p>Confounders NOT accounted for:</p> <ul style="list-style-type: none"> Key confounders: race/ethnicity, SES, alcohol intake, physical activity, naturally occurring sugar intake Other factors considered: menopausal status, supplements, sodium, protein, fiber, fat, energy density, family history of CVD <p>Additional model adjustments:</p> <ul style="list-style-type: none"> NS at baseline: liver fat, triglycerides, fasting plasma insulin, uric acid <p>Limitations:</p> <ul style="list-style-type: none"> Randomization and allocation methods NR No power calculation and likely underpowered Trial registry did not include data analysis plan <p>Funding Sources: Danish Council for Strategic Research; The Food Study Group/Danish Ministry of Food, Agriculture and Fisheries; Novo Nordic Foundation; Clinical Institute at Aarhus University, Denmark; Danish Dairy Company, Arla Foods</p>

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	TEI, Confounders, and Study Limitations
<p>Engel, 2018⁵ RCT, Denmark Baseline N=73, Analytic N=60; Attrition: 18%; Power: none, as the outcome (OGTT) was secondary and explorative</p> <p>Recruitment: healthy, nondiabetic participants from two study sites at Aarhus University Hospital and University of Copenhagen</p> <p>Participant characteristics: overweight and obese adults</p> <ul style="list-style-type: none"> Sex (female): 67% Age: ~38y Race/ethnicity: NR SES: NR Anthropometrics: BMI ~32 kg/m² Physical activity: ≤10hr/wk (inclusion criteria) Smoking: 100% non-smokers (inclusion criteria) <p>Summary of findings: Among overweight and obese adults, those who consumed SSSD every day for 6mo had increased total cholesterol and triacylglycerol compared to NCSD consumers. SSSD consumers did not differ in changes of LDL, HDL, Total:HD cholesterol, or systolic and diastolic blood pressure compared to NCSD consumers.</p>	<p>Intervention: Sugar-sweetened soft drink (SSSD); specifically, 1 L/d of sucrose-sweetened regular cola (50% glucose and 50% fructose), n=14</p> <p>Comparator: Artificially sweetened non-caloric soft drink (NCSD); specifically, 1 L/d of aspartame-sweetened diet cola, n=15</p> <p>Other interventions: semi-skimmed milk (n=15) and still mineral water (n=16)</p> <p><u>Intervention duration:</u> 6mo</p> <p><u>Intervention compliance:</u> all participants were instructed to bring back empty bottles/cartons for monitoring compliance</p> <p>Study added sugars intake:</p> <ul style="list-style-type: none"> NR <p>Outcome assessment methods/timing:</p> <ul style="list-style-type: none"> At baseline, and 6mo follow-up Intermediate outcomes measured: Total cholesterol, LDL, HDL, Total:HDL, triacylglycerol, systolic and diastolic blood pressure Fasted blood samples collected; Total and HDL cholesterol, and triacylglycerol analyzed using routine laboratory methods at hospital and LDL cholesterol calculated by Friedewald equation; blood pressure recorded with digital blood pressure apparatus after 10min rest 	<p>Intermediate outcomes:</p> <p>Total cholesterol, mmol/L, Mean (SE) Within group, over time: 0mo, 6mo NCSD: 5.45 (0.84), 4.95 (0.18) SSSD: 4.84 (0.84), 5.25 (0.28) Between groups: P=0.007</p> <p>LDL cholesterol, mmol/L, Mean (SE) Within group, over time: 0mo, 6mo NCSD: 3.50 (0.98), 3.17 (0.18) SSSD: 3.07 (0.82), 3.32 (0.23) Between groups: P=NS</p> <p>HDL cholesterol, mmol/L, Mean (SE) Within group, over time: 0mo, 6mo NCSD: 1.18 (0.29), 1.17 (0.07) SSSD: 1.16 (0.23), 1.21 (0.09) Between groups: P=NS</p> <p>Total:HDL cholesterol, mmol/L, Mean (SE) Within group, over time: 0mo, 6mo NCSD: 4.83 (1.15), 4.41 (0.28) SSSD: 4.26 (0.80), 4.49 (0.24) Between groups: P=NS</p> <p>Triacylglycerol, mmol/L, Mean (SE) Within group, over time: 0mo, 6mo NCSD: 1.73 (0.63), 1.37 (0.11) SSSD: 1.35 (0.73), 1.60 (0.23) Between groups: P=0.045</p> <p>Systolic blood pressure, mmHg, Mean (SE) Within group, over time: 0mo, 6mo NCSD: 131.5 (14.1), 126.8 (2.4) SSSD: 123.4 (8.9), 125.9 (2.9) Between groups: P=NS</p> <p>Diastolic blood pressure, mmHg, Mean (SE) Within group, over time: 0mo, 6mo NCSD: 81.2 (7.9), 77.4 (2.3) SSSD: 74.4 (9.7), 77.5 (2.0) Between groups: P=NS</p>	<p>TEI adjusted: Yes</p> <p>Confounders accounted for:</p> <ul style="list-style-type: none"> Key confounders: sex, age, alcohol intake, physical activity, anthropometry, smoking Other factors considered: total energy intake, menopausal status, medications, supplements, protein, fat, food form (beverage) <p>Confounders NOT accounted for:</p> <ul style="list-style-type: none"> Key confounders: race/ethnicity, SES, naturally occurring sugar intake Other factors considered: menopausal status, supplements, sodium, fiber, energy density, family history of CVD <p>Additional model adjustments:</p> <ul style="list-style-type: none"> NS at baseline: Carbohydrate, calcium, OGTT glucose and insulin, fasting glucose and insulin, Matsuda index, HOMA-IR, PAI-1, FFA <p>Limitations:</p> <ul style="list-style-type: none"> No power calculation No information on non-completers No preregistered data analysis plan <p>Funding Sources: Arla Foods; Danish Dairy Research Foundation; Global Dairy Platform; Danish Agriculture and Food Foundation; Dairy Institute; Dairy Research Industry; Danish Agriculture and Food Council</p>

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	TEI, Confounders, and Study Limitations
<p>Hernandez-Cordero, 2014⁶ RCT, Mexico Baseline N=268, Analytic N=240; Attrition: 10%; Power: powered to observe a 31±58 mg/dL decrease in plasma [TG] and a weight loss of 1.8±3.4 kg; needed a sample size of 120 cases, which considered 2-sided tests, with 90% power, α=0.05, and allowed for >75% attrition</p> <p>Recruitment: advertising campaign</p> <p>Participant characteristics: Mexican women with overweight or obesity who habitually consumed ≥250 kcal/d of SSB</p> <ul style="list-style-type: none"> Sex (female): 100% Age: 33.3 (6.7) y (18-45y) Race/ethnicity: NR SES: 45% completed middle and high school Anthropometrics: 46% Overweight, 54% Obese; BMI 31.2 (3.7) kg/m² Physical activity: NR Smoking: 31% Yes <p>Summary of findings: A 9-month lifestyle intervention to reduce SSB intake in Mexican women with overweight and obesity did not result in changes in plasma triglycerides or cholesterol (total, LDL, HDL), or systolic and diastolic blood pressure in the intervention group compared to control.</p>	<p>Intervention: Decreasing SSB intake (nutrition counseling sessions included activities to encourage increased water intake, reduced SSB intake, and substitution of water for SSBs; received bottled water every 2wk), n=120</p> <p>Comparator: Control; education provision, n=120</p> <p><u>Intervention duration:</u> 9mo</p> <p><u>Intervention compliance:</u> Examined change in SSB intake using 3, 24-h recalls at baseline, 3, 6, and 9mo – SSB was significantly lower in both groups at 3, 6, and 9mo</p> <p>Study added sugars intake:</p> <ul style="list-style-type: none"> Habitual SSB intake ≥250 kcal/d (inclusion criteria) <p>Outcome assessment methods/timing:</p> <ul style="list-style-type: none"> At baseline, and 3, 6, 9mo follow-up Intermediate outcomes measured: Plasma triglycerides, total cholesterol, LDL, HDL, and systolic/diastolic blood pressure Fasting blood samples analyzed using standard laboratory procedures; resting blood pressure measured using digital sphygmomanometer (mean of 3 measurements used) 	<p>Intermediate outcomes: Triglycerides, mg/dL, Mean (SE) Within group, over time: Δ3, Δ6, Δ9mo Control: 1.8 (6.6), 1.2 (11.3), 10.7 (9.90) Intervention: 5.6 (8.0), -2.4 (9.1), -5.7 (10.0) Between groups: P-interaction=NS P=NS for all stages</p> <p>Total cholesterol, mg/dL, Mean (SE) Within group, over time: Δ3, Δ6, Δ9mo Control: 5.7 (5.2), 1.2 (7.6), -3.0 (8.9) Intervention: 1.5 (4.7), 5.8 (5.6), 1.9 (8.7) Between groups: P-interaction=NS P=NS for all stages</p> <p>LDL cholesterol, mg/dL, Mean (SE) Within group, over time: Δ3, Δ6, Δ9mo Control: 4.6 (3.7), -1.6 (4.6), -5.0 (4.7) Intervention: 1.1 (3.5), 4.9 (4.0), 0.2 (4.0) Between groups: P-interaction=NS P=NS for all stages</p> <p>HDL cholesterol, mg/dL, Mean (SE) Within group, over time: Δ3, Δ6, Δ9mo Control: 1.20 (1.4), 1.1 (4.6), -1.7 (1.8) Intervention: -0.3 (1.3), 1.9 (8.5), 0.3 (1.40) Between groups: P-interaction=NS P=NS for all stages</p> <p>Systolic blood pressure, mmHg, Mean (SE) Within group, over time: Δ3, Δ6, Δ9mo Control: -1.3 (1.0), -3.8 (1.4), -2.8 (1.7) Intervention: 0.05 (0.09), -2.4 (1.0), -0.9 (1.2) Between groups: P-interaction=NS P=NS for all stages</p> <p>Diastolic blood pressure, mmHg, Mean (SD) Within group, over time: Δ3, Δ6, Δ9mo Control: -1.9 (0.8), -4.7 (1.1), -3.9 (1.5) Intervention: -1.0 (0.9), -3.7 (1.0), -3.4 (1.1) Between groups: P-interaction=NS P=NS for all stages</p>	<p>TEI adjusted: Yes TEI, kcal/d, Mean (SE) Within group, over time: Δ3, Δ6, Δ9mo Control: -447 (52), -478 (60), -567 (66) SSB: -553 (56), -575 (54), -585 (55) Between groups: P-interaction=NS P=NS for all stages</p> <p>Confounders accounted for:</p> <ul style="list-style-type: none"> Key confounders: sex, age, (race/ethnicity), SES, physical activity, anthropometry, smoking Other factors considered: total energy intake, food form (beverage) <p>Confounders NOT accounted for:</p> <ul style="list-style-type: none"> Key confounders: alcohol intake, naturally occurring sugar intake Other factors considered: menopausal status, medications, supplements, sodium, protein, fiber, fat, energy density, family history of CVD <p>Additional model adjustments:</p> <ul style="list-style-type: none"> NS at baseline: parity, marital status, fasting plasma glucose, HbA1c, serum and urine osmolality, beverages with sugar, water consumption, baseline intermediate outcomes <p>Limitations:</p> <ul style="list-style-type: none"> Allocation methods NR No a priori analysis plan <p>Funding Source: Danone Research Center</p>

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	TEI, Confounders, and Study Limitations
<p>Madero, 2015⁷ RCT, Mexico</p> <p>Baseline N=78, Analytic N=72; Attrition: 3%; Power: post hoc calculations of power analyses made with the differences found in SBP and DBP among allopurinol and placebo groups yielded in a power of 94%</p> <p>Recruitment: clinic</p> <p>Participant characteristics: overweight, prehypertensive adults</p> <ul style="list-style-type: none"> Sex (female): 39% Age: 46 (8) y Race/ethnicity: NR SES: NR Anthropometrics: all overweight; mean ~88kg Physical activity: NR Smoking: NR <p>Summary of findings:</p> <p>There were no differences between groups of overweight prehypertensive adults that were on a low-fructose and sodium diet or a low sodium diet for 4 weeks for any CVD outcomes: blood pressure, total cholesterol, and triglycerides.</p>	<p>Intervention: Low fructose (<20g/d) and sodium diet (<2500mg/d); n= 34</p> <p>Comparator: Low sodium diet (<2500mg/d); n=38</p> <p><u>Intervention duration:</u> 4wks</p> <p><u>Intervention compliance:</u> Adherence was defined as attending at least 80% of the scheduled clinic visits and having blood work during this last visit; fructose intake decreased significantly in low fructose group (P<0.05 within and between groups)</p> <p>Study added sugars intake:</p> <ul style="list-style-type: none"> Inclusion criteria: history of high fructose consumption from sources of added sugar (excluding fruits) of >70 g/d. <p>Outcome assessment methods/timing:</p> <ul style="list-style-type: none"> Baseline, 4wks Intermediate outcomes measured: Total cholesterol, Triglycerides, Systolic and diastolic BP (3 BP measures: clinic, global-ABPM, Day-ABPM) ABPM: Ambulatory Blood Pressure Monitoring 	<p>Intermediate outcomes:</p> <p>Blood pressure: mm Hg, Mean (SD)</p> <ul style="list-style-type: none"> Clinic SBP Within group, over time: 0wks, 4wks Control: 125 (11), 120 (11), P<0.05 Low fructose: 124 (13), 119 (13), P<0.05 Between groups: NS Clinic DBP Within group, over time: 0wks, 4wks Control: 86 (7), 82 (10), P<0.05 Low fructose: 84 (8), 82 (8), P<0.05 Between groups: NS Global SBP ABPM Within group, over time: 0wks, 4wks Control: NS Low fructose: NS Between groups: NS Global DBP ABPM Within group, over time: 0wks, 4wks Control: NS Low fructose: NS Between groups: NS Day SBP ABPM Within group, over time: 0wks, 4wks Control: NS Low fructose: NS Between groups: NS Day DBP ABPM Within group, over time: 0wks, 4wks Control: NS Low fructose: 83 (8), 81 (8), P<0.05 Between groups: NS <p>Total cholesterol, mg/dL, Mean (SD) Within group, over time: 0wks, 4wks Control: NS Low fructose: NS Between groups: NS</p> <p>Triglycerides, mg/dL, Mean (SD) Within group, over time: 0wks, 4wks Control: NS Low fructose: NS Between groups: NS</p>	<p>TEI adjusted: No (control group significantly increased TEI during intervention; NS with intervention group)</p> <p>Confounders accounted for:</p> <ul style="list-style-type: none"> Key confounders: sex, age, anthropometry Other factors considered: medications <p>Confounders NOT accounted for:</p> <ul style="list-style-type: none"> Key confounders: race/ethnicity, SES, alcohol intake, physical activity, smoking, naturally occurring sugar intake Other factors considered: total energy intake, menopausal status, supplements, sodium, protein, fiber, fat, energy density, family history of CVD, food form (solid/beverage) <p>Additional model adjustments:</p> <ul style="list-style-type: none"> Fructose intake (g/24hr), fructose intake without fruits (g/24hr) <p>Limitations:</p> <ul style="list-style-type: none"> Not all key confounders accounted for No a priori power calculation Trial registry did not include data analysis plan <p>Funding Sources: NR</p>

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	TEI, Confounders, and Study Limitations
<p>Markey, 2016⁸ Crossover RCT, reformulated foods (REFORM) study, UK</p> <p>Baseline N=56, Analytic N=50; Attrition: 1%; Power: n=37 participants to give sufficient power to detect significant changes in our secondary outcome measures including biochemical analysis, if energy compensation did not occur, with P < 0.05 and 80 % power</p> <p>Recruitment: local community of Reading, UK using targeted mailings to volunteers on local participant databases; posters and flyers circulated around university campus and social/community groups in Reading</p> <p>Participant characteristics: healthy normal or overweight adults</p> <ul style="list-style-type: none"> • Sex (female): 68/% • Age: ~ 32y • Race/ethnicity: 80% white • SES: NR • Anthropometrics: BMI ~24 kg/m² • Physical activity: exclude participants of regular vigorous exercise or fitness training (≥20 min × 3 times/week) • Smoking: 100% non-smokers <p>Summary of findings:</p> <p>In healthy normal and overweight adults, compared to a regular diet, substituting at least one food and beverage per day with a reduced-sugar version for 8 weeks did not affect CVD-related outcomes, including systolic and diastolic blood pressure, total cholesterol, HDL, LDL, or triglycerides.</p>	<p>Intervention: Reformulated/sugar-reduced diet: participants exchanged ≥1 beverage and ≥1 food portion per day from their habitual diet <u>with equivalent sugar-reformulated products</u>; foods provided by researchers; n=54</p> <p>Comparator: Regular diet: participants exchanged ≥1 beverage and ≥1 food portion per day from their habitual diet <u>with equivalent sugar-containing products</u>; foods provided by researchers; n=55</p> <p>Intervention duration: 8wk per arm; 4wk washout between arms</p> <p>Intervention compliance: 4d weighted food diaries; As a % EI, carbohydrate (P < 0.001), total sugars (P < 0.001) and NMES (P < 0.001) were lower, whereas fat (P = 0.001) and protein (P = 0.038) were higher on the sugar-reduced diet compared with the regular diet</p> <p>Study added sugars intake: NR</p> <p>Outcome assessment methods/timing:</p> <ul style="list-style-type: none"> • Before and after each arm: 0 and 8wks, 12 and 20wks • Intermediate outcomes measured: total cholesterol (TC), HDL, LDL (calculated), Triglycerides (TG), Blood Pressure (SBP, DBP) 	<p>Intermediate outcomes:</p> <p>Supine SBP, mm Hg, Mean (SD) Within group, over time: 0wks, 8wks Regular diet: NS Reformulated diet: NS Between groups (diet): NS Time*diet: NS</p> <p>Supine DBP, mm Hg, Mean (SD) Within group, over time: 0wks, 8wks Regular diet: NS Reformulated diet: NS Between groups (diet): NS Time*diet: NS</p> <p>TC, mmol/L, Mean (SD) Within group, over time: 0wks, 8wks Regular diet: 4.67 (0.70), 4.59 (0.65) Reformulated diet: 4.57 (0.69), 4.58 (0.67) Between groups (diet): NS Time*diet: P= 0.021</p> <p>HDL-C, mmol/L, Mean (SD) Within group, over time: 0wks, 8wks Regular diet: 1.54 (0.38), 1.51 (0.38) Reformulated diet: 1.50 (0.37), 1.51 (0.34) Between groups (diet): NS Time*diet: P= 0.067</p> <p>LDL-C, mmol/L, Mean (SD) Within group, over time: 0wks, 8wks Regular diet: NS Reformulated diet: NS Between groups (diet): NS Time*diet: NS</p> <p>TG, mmol/L, Mean (SD) Within group, over time: 0wks, 8wks Regular diet: NS Reformulated diet: NS Between groups (diet): NS Time*diet: NS</p>	<p>TEI adjusted: No</p> <p>Confounders accounted for:</p> <ul style="list-style-type: none"> • Key confounders: smoking • Other factors considered: N/A <p>Confounders NOT accounted for:</p> <ul style="list-style-type: none"> • Key confounders: sex, age, race/ethnicity, SES, alcohol intake, physical activity, anthropometry, naturally occurring sugar intake • Other factors considered: total energy intake, menopausal status, medications, supplements, sodium, protein, fiber, fat, energy density, family history of CVD, food form (solid/beverage) <p>Additional model adjustments: N/A</p> <p>Limitations:</p> <ul style="list-style-type: none"> • Trial registry did not include data analysis plan <p>Funding Sources: Sugar Nutrition UK</p>

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	TEI, Confounders, and Study Limitations
<p>Umpleby, 2017⁹ RCT, Crossover design (Control group only – other group all had NAFLD), UK Baseline N=27, Analytic N=25; Attrition: 7.4%; Power: NR (discussion states sample size was originally powered to assess weight-adjusted differences in all outcome variables)</p> <p>Recruitment: NR</p> <p>Participant characteristics: overweight men at increased cardio-metabolic risk</p> <ul style="list-style-type: none"> Sex (female): 0% (100% male) Age: 59y (49-64y) Race/ethnicity: NR SES: NR Anthropometrics: BMI ~28.7 kg/m² (25-30 kg/m²) Physical activity: NR (instructed to maintain normal level) Smoking: 100% non-smokers <p>Summary of findings: In a sample of overweight men at increased cardio-metabolic risk, a 12-wk high- or low-sugar diet did not significantly affect plasma concentrations of total cholesterol, LDL, or HDL. The effect was not significant within group (between the two different diets) or between groups with varying levels of liver fat (NAFLD vs. Control). A high-sugar diet was significantly associated with an increase in plasma TAG in the NAFLD group compared to control.</p>	<p>2-way crossover design: 2, 12-wk dietary interventions High-sugar diet: corresponded to the top 2.5th percentile of non-milk extrinsic sugars (NMES) intake in the UK population (i.e., NMES includes free sugars added to food (including 50% of sugars in tinned and dried fruit), but excludes sugars in whole fruit, and lactose)</p> <p>Low-sugar diet: corresponded to the lower 2.5th percentile of NMES intake</p> <p>Method: diets were achieved by a dietary exchange of sugars for starch using commercially available foods (isoenergetic and equal macronutrient distribution)</p> <p>Control group: n=14</p> <p>Intervention duration: Crossover design: 4wk run in period, 12wk per intervention arm with a 4wk washout period between</p> <p>Intervention compliance: Self-recorded dietary intakes were monitored by regular home visits and indicated compliance was maintained; 3-d diet diaries were also completed during final week of each intervention</p> <p>Outcome assessment methods/timing:</p> <ul style="list-style-type: none"> Measured at beginning and end of each intervention arm Intermediate outcomes measured: Total cholesterol, LDL, HDL, TAG 	<p>Intermediate outcomes: Plasma TAG, mmol/l, Mean (SEM) Within group, High sugar vs. Low sugar: Control (n=14): 1.33 (0.15) vs 1.13 (0.08), NS</p> <p>Plasma cholesterol, mmol/l, Mean (SEM) Within group, High sugar vs. Low sugar: Control (n=14): NS</p> <p>Plasma LDL-C, mmol/l, Mean (SEM) Within group, High sugar vs. Low sugar: Control (n=14): NS</p> <p>Plasma HDL-C, mmol/l, Mean (SEM) Within group, High sugar vs. Low sugar: Control (n=14): NS</p> <p>[Effects of intervention on plasma lipoprotein fraction concentrations, lipoprotein kinetics and de novo lipogenesis, palmitate kinetics, post-heparin lipase, and plasma apoproteins are also provided in paper.]</p>	<p>TEI adjusted: Diets were isocaloric</p> <p>Confounders accounted for:</p> <ul style="list-style-type: none"> Key confounders: no baseline differences in sex, age, or smoking; body weight adjusted in all models Other factors considered: total energy intake, lipid-lowering medication <p>Confounders NOT accounted for:</p> <ul style="list-style-type: none"> Key confounders: race/ethnicity, SES, alcohol intake, physical activity, naturally occurring sugar intake Other factors considered: other medications, supplements, sodium, protein, fiber, fat, energy density, family history of CVD, food form (solid/beverage) <p>Additional model adjustments: N/A</p> <p>Limitations:</p> <ul style="list-style-type: none"> Not all key confounders accounted for No details on power calculation Trial registry did not include data analysis plan <p>Funding Sources: UK government grant from the Biological Biotechnology Scientific Research Council; University of Surrey PhD scholarship; Medical Research Council (body composition measurements); and infrastructure support from the National Institute of Health Research at the Cambridge Biomedical Research Centre.</p>

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	TEI, Confounders, and Study Limitations
Prospective Cohort Studies			
<p>Barrington, 2016¹⁰ Prospective Cohort Study, Vitamins and Lifestyle (VITAL) study, United States Analytic N=69582; Power: NR</p> <p>Recruitment: names of residents in Western Washington State acquired through purchased mailing lists</p> <p>Participant characteristics: older adults</p> <ul style="list-style-type: none"> Sex (female): 51% Age: 47% 50-59y, 35% 60-69y, 18% 70-76y Race/ethnicity: 93% White SES: 43% ≥College graduate Anthropometrics: NR Physical activity: NR Smoking: NR <p>Summary of findings: Among older adults, added sugars from sugar-sweetened drink intake was not significantly associated with risk of CVD-specific mortality</p>	<p>Exposure of interest: Sugar-sweetened drink intake (SSD selected <i>a priori</i> and included servings of sugar-sweetened soda (not diet), fruit drinks not including juice (e.g., Hi-C, Gatorade, lemonade) and cranberry juice, which is highly sweetened)</p> <p>Comparators: SSD intake (categorical, svg/wk)</p> <ul style="list-style-type: none"> Quartile 1: 0-0.1 svg/wk Quartile 2: 0.2-0.4 svg/wk Quartile 3: 0.5-2.7 svg/wk Quartile 4: ≥2.8 svg/wk <p><u>Exposure assessment method and timing:</u></p> <ul style="list-style-type: none"> Semi-quantitative FFQ representing diet over the year previous to baseline At baseline <p>Outcome assessment methods/timing:</p> <ul style="list-style-type: none"> 1yr post-baseline through December 31, 2008 (mean 6.9yr follow-up) Health outcomes measured: death from CVD Cause of death obtained through Washington State death records using codes of the ICD, 10th Revision (CVD codes: I00-I99) 	<p>Endpoint outcomes: Death from CVD (n=1066): By quartiles of SSD drink, Cox proportional hazards, HR (95% CI) Total: P-trend=NS No CVD history (n=192): P-trend=NS CVD history (n=874): P-trend=NS</p> <p>P-interaction=NS</p>	<p>TEI adjusted: Yes</p> <p>Confounders accounted for:</p> <ul style="list-style-type: none"> Key confounders: sex, age, race/ethnicity, SES, alcohol intake, physical activity, smoking Other factors considered: total energy intake, anthropometry, medications, sodium, protein, fiber, fat, energy density, family history of CVD, food form (beverage) <p>Confounders NOT accounted for:</p> <ul style="list-style-type: none"> Key confounders: naturally occurring sugar intake Other factors considered: menopausal status, supplements, sodium, protein, fiber, fat, energy density <p>Additional model adjustments: Self-rated health, mammogram (females), prostate-specific antigen screening (males), sigmoidoscopy, servings of fruits and vegetables, estrogen or estrogen+progestin therapy (females)</p> <p>Limitations:</p> <ul style="list-style-type: none"> Not all key confounders accounted for No information on non-completers Validation of exposure data collection tool unclear Exposure data only measured at baseline No preregistered data analysis plan Generalizability: sample mostly white, educated, older adults <p>Funding sources: NCI; Office of Dietary Supplements</p>

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	TEI, Confounders, and Study Limitations
<p>Collin, 2019¹¹ Prospective Cohort Study, Reasons for Geographic and Racial Differences in Stroke (REGARDS) study, United States Analytic N=13440; Overall cohort attrition: 25%; Power: NR</p> <p>Recruitment: mail and telephone; participants randomly selected using commercially available lists of US residents with goal of recruiting half of study sample from the stroke buckle (coastal North and South Carolina and some parts of Georgia) and the stroke belt (remaining areas of North Carolina, South Carolina, Georgia, Tennessee, Mississippi, Alabama, Louisiana, and Arkansas) and other half from the rest of the United States</p> <p>Participant characteristics: adults</p> <ul style="list-style-type: none"> Sex (female): 41% Age: 63.6 (9.1) y (all >40y) Race/ethnicity: 69% White, 31% Black SES: Education, 31% ≤High school, 41% ≥College Anthropometrics: 71% Overweight or Obesity Physical activity: 30%, 0 times/wk; 31% >4 times/wk Smoking: 48% Never; 38% Former; 13% Current <p>Summary of findings: Among adults, added sugars from sugary beverages, SSBs, and 100% fruit juice intake (combined and separate) was not significantly associated with risk of CHD-related mortality.</p>	<p>Exposure of interest: Sugary beverage intake (including SSBs (sodas, soft drinks, or fruit-flavored drinks) and naturally sweet 100% fruit juices); 12-oz serving</p> <p>Comparators:</p> <ul style="list-style-type: none"> Continuous; 12-oz/svg Categorical; % of TEI intake <ul style="list-style-type: none"> Low: <5% Medium: 5-<10% High: ≥10% <p><u>Exposure assessment method and timing:</u></p> <ul style="list-style-type: none"> Validated semi-quantitative FFQ; represents usual dietary intake over the past year At baseline enrollment (2003-2007) <p>Outcome assessment methods/timing:</p> <ul style="list-style-type: none"> Follow-up every 6mo through 2013 Health outcomes measured: CHD-related mortality Cause of death obtained through medical records, death certificates, National Death Index, Social Security Administration Master Death File, and interviews with family members; adjudication done by clinicians (general internists, cardiologists, and physician assistants) with specific training to identify causes of death 	<p>Endpoint outcomes: CHD-related mortality: Change per 12 oz increase, Cox proportional hazards, HR (95% CI) All sugary beverages: P=NS SSBs: P=NS Fruit juices: P=NS <i>For sugary beverages, SSBs, and fruit juices: NS interaction by age, sex, education, or race/ethnicity</i></p> <p>Change per intake level of sugary beverages, HR (95% CI) <5% TEI (ref) vs 5-<10% TEI: P=NS with TEI unadj and adj ≥10% TEI: P=NS with TEI unadj and adj</p> <p>Examining SSBs and fruit juices separately did not change the results</p>	<p>TEI adjusted: Yes and No</p> <p>Confounders accounted for:</p> <ul style="list-style-type: none"> Key confounders: sex, age, race/ethnicity, SES, alcohol intake, physical activity, smoking Other factors considered: total energy intake, anthropometry, fiber, fat, food form (beverage) <p>Confounders NOT accounted for:</p> <ul style="list-style-type: none"> Key confounders: naturally occurring sugar intake Other factors considered: menopausal status, medications, supplements, sodium, protein, energy density, family history of CVD <p>Additional model adjustments: Diet</p> <p>Limitations:</p> <ul style="list-style-type: none"> Not all key confounders accounted for Non-completers more likely to be female, non-Hispanic black, have overweight/obesity, be former or current smokers, and have less than high school education Exposure data only measured once No preregistered data analysis plan <p>Funding sources: NINDS; NIH; NHLBI</p>

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	TEI, Confounders, and Study Limitations
<p>Kulezic, 2019¹²</p> <p>Prospective Cohort Study, Malmö Diet and Cancer Study (MDCS), Sweden Analytic N=26010; Power: NR</p> <p>Recruitment: community directed (passive) invitation, and a personal letter of invitation (active recruitment)</p> <p>Participant characteristics: middle-aged adults</p> <ul style="list-style-type: none"> Sex (female): 62% Age: ~58y Race/ethnicity: NR SES: University degree ~15% Anthropometrics: BMI~25.6 kg/m² Physical activity: Leisure time physical activity >50 MET-hr/wk, 15% Smoking: 39% Never, 28% Current <p>Summary of findings: In middle-aged Swedish adults, non-adherence to recommended sucrose intake (>10% energy) was not significantly associated with incidence of peripheral artery disease at ~21yr follow-up.</p>	<p>Exposure of interest: Sucrose intake</p> <p>Comparators: categorical (based on adherence to Swedish dietary guidelines and nutrition recommendations for sucrose)</p> <ul style="list-style-type: none"> ≤10% energy (adherence) >10% energy (non-adherence) <p>Exposure assessment method and timing:</p> <ul style="list-style-type: none"> 7-d food diary combined with a food questionnaire and 1hr interview (methods showed good ranking validity when compared to reference method) At baseline <p>Outcome assessment methods/timing:</p> <ul style="list-style-type: none"> At follow-up (median 21.7y, IQR 18.7-23.4y) Health outcomes measured: Peripheral artery disease (PAD) <p>PAD incidence determined using Inpatient and Outpatient Registers, which included information on date of admission and discharge, and diagnostic and procedural codes from all hospitalizations in Sweden; validation of PAD diagnosis done in 100 randomly selected patients, with confirmed diagnosis in 98% of cases</p>	<p>Endpoint outcomes:</p> <p>PAD Incidence, Based on adherence to diet quality index for sucrose, HR (95% CI) Non-adherence (>10% energy): Ref Adherence (≤10% energy): 1.10 (0.96, 1.27)</p> <p><i>Similar results were obtained in sensitivity analysis, which was performed after removing misreporters (n=4799) and dietary-changers (n=5623)</i></p>	<p>TEI adjusted: Yes</p> <p>Confounders accounted for:</p> <ul style="list-style-type: none"> Key confounders: sex, age, SES, alcohol intake, physical activity, smoking Other factors considered: total energy intake, anthropometry, fiber, fat <p>Confounders NOT accounted for:</p> <ul style="list-style-type: none"> Key confounders: race/ethnicity, naturally occurring sugar intake Other factors considered: menopausal status, medications, supplements, sodium, protein, energy density, family history of CVD, food form (solid/beverage) <p>Additional model adjustments: Diet assessment method, season, fish and shellfish, fruit and vegetables</p> <p>Limitations:</p> <ul style="list-style-type: none"> Not all key confounders accounted for Exposure data only measured once No preregistered data analysis plan <p>Funding sources: None</p>

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	TEI, Confounders, and Study Limitations
<p>Liu, 2018¹³</p> <p>Prospective Cohort Study, Mr and Ms OS of Hong Kong, Hong Kong Analytic N=3416; Power: NR</p> <p>Recruitment: notices in senior social centers and housing estates</p> <p>Participant characteristics: Chinese older adults (≥65y)</p> <ul style="list-style-type: none"> Sex (female): 50% Age: ~72.5y Race/ethnicity: 100% Chinese SES: 10% ≥University education Anthropometrics: BMI ~23.5 kg/m² Physical activity: PASE score ~92 Smoking: 7% Current smokers <p>Summary of findings: Among Chinese elderly, compared with those in the lowest quintile of added sugar intake, participants with the highest quintile intake had a significantly lower risk of CVD mortality at ~11yr follow-up. Results were no longer significant after adjustment for adiposity.</p>	<p>Exposure of interest: Added sugar intake (caloric sweeteners, monosaccharides and disaccharides, added to foods/beverages during processing or preparation, including sugars and syrups added at table)</p> <p>Comparators: quintiles (% of energy)</p> <p><u>Exposure assessment method and timing:</u></p> <ul style="list-style-type: none"> Validated FFQ; represents intake (portion size & frequency) during past 12mo At baseline <p>Outcome assessment methods/timing:</p> <ul style="list-style-type: none"> At follow-up (mean 11.1yr) Health outcomes measured: CVD mortality Data on mortality obtained from the Death Registry of the Department of Health of Hong Kong; CVD mortality identified by cause of death on death certificate and classified according to ICD version 10 	<p>Endpoint outcomes: CVD mortality, HR (95% CI) <i>Added sugar intake (% calories)</i> Q1 (ref) Q2: 0.752 (0.307, 1.845) Q3: 0.323 (0.104, 1.006) Q4: 0.445 (0.156, 1.271) Q5: 0.251 (0.070, 0.899) P for trend: 0.011 (P=0.055 after further adjustment for change in body fatness)</p> <p><i>Added sugar from beverages (% calories)</i> Q1 (ref) Q2: 0.923 (0.370, 2.303) Q3: 0.401 (0.127, 1.267) Q4: 0.376 (0.130, 1.085) Q5: 0.344 (0.109, 1.087) P for trend: 0.014 (P=0.074 after further adjustment for change in body fatness)</p> <p><i>Added sugar from cereals (% calories)</i> P for trend: NS (data in paper)</p> <p><i>Added sugar from milk (% calories)</i> P for trend: NS (data in paper)</p> <p><i>Added sugar from sweets (% calories)</i> P for trend: NS (data in paper)</p>	<p>TEI adjusted: Yes</p> <p>Confounders accounted for:</p> <ul style="list-style-type: none"> Key confounders: sex, age, (race/ethnicity), SES, alcohol intake (in adults), physical activity, smoking, Other factors considered: total energy intake, anthropometry, medications, protein, fat, family history of CVD, food form (solid/beverage) <p>Confounders NOT accounted for:</p> <ul style="list-style-type: none"> Key confounders: naturally occurring sugar intake Other factors considered: menopausal status, supplements, sodium, fiber, energy density <p>Additional model adjustments: Fruit and vegetable intake, red or processed meat, total American Heart Association score, coffee, green and Chinese tea, history of cancers</p> <p>Limitations:</p> <ul style="list-style-type: none"> Does not account for all key confounders No information on non-completers Exposure data only measured once No preregistered data analysis plan <p>Funding sources: NIH; Research Grants Council</p>

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	TEI, Confounders, and Study Limitations
<p>Malik, 2019¹⁴ Prospective Cohort Study, Nurses' Health Study (NHS) + Health Professionals Follow-up Study (HPFS), United States Analytic N=118363; Power: NR</p> <p>Recruitment: convenience sample</p> <p>Participant characteristics: adults</p> <ul style="list-style-type: none"> Sex (female): 68% Age: mean ~ 60y, in 1994 Race/ethnicity: ~96% white SES: NR Anthropometrics: BMI ~27 kg/m² Physical activity: NR Smoking: ~12% current smoker, in 1994 <p>Summary of findings: There is a significant association between increased frequency of SSB consumption and risk of CVD mortality.</p>	<p>Exposure of interest: SSBs (caffeinated colas, caffeine-free colas, other (non-cola) carbonated sugar-sweetened beverages, and noncarbonated sugar-sweetened beverages (fruit punches, lemonades, or other fruit drinks); does not include fruit juice</p> <p>Comparators:</p> <ul style="list-style-type: none"> SSB continuous (svg/d) SSB categorical: <ul style="list-style-type: none"> <1/mo 1-4/mo 2-6/wk 1-<2/d ≥2/d <p><u>Exposure assessment method and timing:</u></p> <ul style="list-style-type: none"> FFQ; validated At baseline, every ~4y <p>Outcome assessment methods/timing:</p> <ul style="list-style-type: none"> 34y follow-up for NHS; 28y follow-up for HPFS Endpoint outcome: CVD-related death (ICD codes 390–458 in the NHS and 390–459 in the HPFS) 	<p>CVD mortality, HR (95% CI) Change per 1 svg/d increment: 1.10 (1.06, 1.14)</p> <p>Change by SSB category: <1/mo (ref) vs 1-4/mo: 1.06 (1.00, 1.12) 2-6/wk: 1.10 (1.04, 1.17) 1-<2/d: 1.19 (1.08, 1.31) ≥2/d: 1.31 (1.15, 1.50) P for trend: <0.0001</p> <p><i>Estimates were greater in NHS compared to HPFS but no interaction with sex was observed (P interaction=0.70)</i></p>	<p>TEI adjusted: Yes</p> <p>Confounders accounted for:</p> <ul style="list-style-type: none"> Key confounders: sex, age, race/ethnicity, alcohol, physical activity, smoking Other factors considered: total energy intake, anthropometry, medications (aspirin), supplements, family history of CVD (myocardial infarction), food form (beverage) <p>Confounders NOT accounted for:</p> <ul style="list-style-type: none"> Key confounders: SES, naturally occurring sugar intake Other factors considered: menopausal status, medications, sodium, protein, fiber, fat, energy density <p>Additional model adjustments: Postmenopausal hormone use (NHS), family history of diabetes, family history of cancer, baseline history of hypertension and hypercholesterolemia, intake of whole grains, fruit, vegetables, red and processed meat, artificially sweetened beverages</p> <p>Limitations:</p> <ul style="list-style-type: none"> Not all key confounders accounted for No preregistered data analysis plan <p>Funding sources: NIH</p>

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	TEI, Confounders, and Study Limitations
<p>Mullee, 2019¹⁵ Prospective Cohort Study, European Prospective Investigation into Cancer and Nutrition (EPIC), Denmark, France, Germany, Greece, the Netherlands, Norway, and the United Kingdom Analytic N=202,907; Power: NR</p> <p>Recruitment: convenience sample</p> <p>Participant characteristics: adults</p> <ul style="list-style-type: none"> Sex (female): 71% Age: ~ 51y Race/ethnicity: NR SES: ~25% higher education Anthropometrics: BMI ~24 kg/m² Physical activity: ~20% physically active Smoking: current smokers ~23% <p>Summary of findings: There was not a significant association between sugar-sweetened soft drink consumption and mortality from circulatory diseases or ischemic heart disease.</p>	<p>Exposure of interest: Sugar-sweetened soft drink consumption; 1 glass = 250 mL</p> <p>Comparators: categorical</p> <ul style="list-style-type: none"> <1 glass/mo (ref) 1-4 glasses/mo >1-6 glasses/wk 1-<2 glasses/d ≥2 glasses/d <p><u>Exposure assessment method and timing:</u></p> <ul style="list-style-type: none"> Self-administered questionnaires were used in all centers, except in Greece, Spain, and Ragusa (Italy), where data were collected during personal interviews. In Malmö (Sweden), a combined semi-quantitative food frequency questionnaire and 7-day dietary diary and diet interview was used 4-d dietary record completed by parents; represents dietary intake on both weekdays and weekends; validated for some countries At baseline <p>Outcome assessment methods/timing:</p> <ul style="list-style-type: none"> Mean follow-up time: 16.4y Endpoint outcome: circulatory disease mortality, ischemic heart disease mortality Ischemic heart disease (ICD-10 codes I20-I25) grouped within "Circulatory diseases" (ICD-10 codes I00-I99) 	<p>Circulatory diseases mortality, HR (95% CI), P-trend: Sexes combined: NS Men only: NS Women only: NS</p> <p>Ischemic heart disease mortality, HR (95% CI) P-trend: NS</p> <p><i>Sensitivity analysis excluding BMI from multivariable models are in the paper.</i></p>	<p>TEI adjusted: Yes</p> <p>Confounders accounted for:</p> <ul style="list-style-type: none"> Key confounders: sex, age, SES, alcohol intake, physical activity, smoking Other factors considered: total energy intake, anthropometry, menopausal status <p>Confounders NOT accounted for:</p> <ul style="list-style-type: none"> Key confounders: race/ethnicity, naturally occurring sugar intake Other factors considered: medications, supplements, sodium, protein, fiber, fat, energy density, family history of CVD <p>Additional model adjustments: Use of contraceptive pill, use of menopausal hormone therapy, red and processed meat, fruits and vegetables, coffee, and fruit and vegetable juice, study center, artificially sweetened soft drinks</p> <p>Limitations:</p> <ul style="list-style-type: none"> Not all key confounders accounted for Exposure data collection tool differed between sites, sometimes not validated Exposure data only measured once No preregistered data analysis plan <p>Funding sources: European Commission, the International Agency for Research on Cancer; IARC-Ireland Postdoctoral Research Training Fellowship from the Irish Cancer Society</p>

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	TEI, Confounders, and Study Limitations
<p>Nagata, 2019¹⁶ Prospective Cohort Study, Takayama Study cohort, Japan</p> <p>Analytic N=27079; Power: the sample size and number of total deaths were sufficiently large to detect an HR of 1.2 (or 0.83) for the highest quartile of intake as compared with the lowest, with a statistical power of 80% and significance level of 5%.</p> <p>Participant characteristics: adults</p> <ul style="list-style-type: none"> Sex (female): 58% Age: ~54y <p>Summary of findings:</p> <p>There was a significant association between added sugars intake and increased risk of CVD mortality in men, but not in women.</p>	<p>Exposure of interest: Added sugars; Due to the lack of free sugar values in the database, all sugars in sugar, honey, starch sugar, soft drinks, juices, soya beverages, jams, confectioneries (including traditional confectioneries, cakes, buns, pastries, desserts, biscuits, snacks, candies, chocolates), ice cream, meat and seafood seasoned with sugar, yeast, bread and breakfast cereals were summed up to yield the intake of free sugars. According to the definition by the WHO, '100 % fruit juices' was considered as free sugars. Conversely, naturally occurring sugars in fruit and vegetables or dairy products were not included. Intake of naturally occurring sugars was estimated by subtracting the free sugar intake from the total sugar intake</p> <p>Comparators: categorical, quartiles</p> <p><u>Exposure assessment method and timing:</u></p> <ul style="list-style-type: none"> Validated FFQ At baseline <p>Outcome assessment methods/timing:</p> <ul style="list-style-type: none"> Mean follow-up time: 14.1y Endpoint outcomes: CVD deaths (ICD-10: I00–I99) 	<p>CVD mortality, HR (95% CI) Men: p-trend= 0.0002 Q1: 1.0 Q2: 0.89 (0.72, 1.10) Q3: 1.21 (0.98, 1.50) Q4: 1.37 (1.10, 1.71)</p> <p>Women: NS</p>	<p>TEI adjusted: Yes</p> <p>Confounders accounted for:</p> <ul style="list-style-type: none"> Key confounders: sex, age, (race/ethnicity), SES, alcohol intake, physical activity, smoking, naturally occurring sugar intake Other factors considered: total energy intake, anthropometry, sodium, fiber, fat <p>Confounders NOT accounted for:</p> <ul style="list-style-type: none"> Key confounders: N/A Other factors considered: menopausal status, medications, supplements, protein, energy density, family history of CVD, food form (solid/beverage) <p>Additional model adjustments: Coffee, history of diabetes and hypertension</p> <p>Limitations:</p> <ul style="list-style-type: none"> Exposure data only measured once No preregistered data analysis plan <p>Funding sources: Ministry of Education, Culture, Sports, Science, and Technology, Japan</p>

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	TEI, Confounders, and Study Limitations
<p>Odegaard, 2015¹⁷ Prospective Cohort Study, Singapore Chinese Health Study, Singapore Analytic N=63257; Power: NR</p> <p>Participant characteristics: adults</p> <ul style="list-style-type: none"> Sex (female): ~56% Age: ~ 56y <p>Summary of findings: There was not a significant association between soft drink intake or juice and risk of CVD-related mortality.</p>	<p>Exposure of interest 1: Soft drink intake</p> <p>Exposure of interest 2: Juice intake (unclear if 100%)</p> <p>Comparators: categorical</p> <ul style="list-style-type: none"> None Monthly 1/wk ≥2/wk <p><u>Exposure assessment method and timing:</u></p> <ul style="list-style-type: none"> FFQ interview; intake during past year; focused on frequency not amount; validated At baseline (1993-1998) <p>Outcome assessment methods/timing:</p> <ul style="list-style-type: none"> ~13-18y follow-up Endpoint outcomes: deaths from cardiovascular disease (ICD-9 codes 394.0–459.0) 	<p>CVD Mortality, HR (95% CI), P-trend: Soft drink: NS Juice: NS</p>	<p>TEI adjusted: Yes</p> <p>Confounders accounted for:</p> <ul style="list-style-type: none"> Key confounders: sex, age, SES, physical activity, smoking Other factors considered: total energy intake, anthropometry <p>Confounders NOT accounted for:</p> <ul style="list-style-type: none"> Key confounders: race/ethnicity, alcohol intake, naturally occurring sugar intake Other factors considered: menopausal status, medications, supplements, sodium, protein, fiber, fat, energy density, family history of CVD, food form (solid/beverage) <p>Additional model adjustments: Dialect, year of interview, sleep, hypertension, non-beverage vegetable-fruit-soy-rich dietary pattern score</p> <p>Limitations:</p> <ul style="list-style-type: none"> Not all key confounders accounted for Exposure not well-defined (frequency not amount) Exposure data only measured once No preregistered data analysis plan <p>Funding sources: NIH</p>

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	TEI, Confounders, and Study Limitations
<p>Ogilvie, 2017¹⁸ Prospective Cohort Study, Atherosclerosis Risk in Communities Study (ARIC), United States Analytic N=14082; Power: NR</p> <p>Recruitment: NR</p> <p>Participant characteristics: adults</p> <ul style="list-style-type: none"> Sex (female): 55% Age: ~54y (45-64y) Race/ethnicity: 74% white SES: >high school: ~36% Anthropometrics: NR Physical activity, 1-5 scale: ~2.5 Smoking, current: ~26% 	<p>Exposure of interest: SSBs (regular soda and fruit drinks)</p> <p><u>Exposure assessment method and timing:</u></p> <ul style="list-style-type: none"> FFQ, modification of validated version At baseline only <p>Outcome assessment methods/timing:</p> <ul style="list-style-type: none"> Follow-up visits ~6y & ~9y after baseline Health outcomes measured: Incident peripheral artery disease Defined by a new ABI measure of <0.90 at either visit 3 or 4, or a hospital discharge diagnosis of PAD, a leg amputation, or a leg revascularization procedure (leg endarterectomy, aorto-iliac-femoral bypass surgery, or leg bypass surgery) through 2012 	<p>Peripheral artery disease (PAD), Cox proportional hazard regression, HR (95% CI) (n=events/total participants)</p> <p>SSB, servings:</p> <ul style="list-style-type: none"> Almost never (n=506/4440): Ref 1-3/mo (n=169/1611): 0.87 (0.73, 1.04) 1/wk (233/2069): 0.89 (0.76, 1.05) 2-6/wk (283/2822): 0.74 (0.63, 0.86) ≥1/d (377/3136): 0.86 (0.73, 1.00) <p>P-trend = 0.005</p> <p>The relationship was no longer significant when stratified by diabetes status at baseline</p>	<p>TEI adjusted: Yes</p> <p>Confounders accounted for:</p> <ul style="list-style-type: none"> Key confounders: sex, age, race/ethnicity, SES, physical activity, smoking, naturally occurring sugar intake (as dairy, fruit, refined and whole grains) Other factors considered: total energy intake, anthropometry (health outcomes) <p>Confounders NOT accounted for:</p> <ul style="list-style-type: none"> Key confounders: alcohol intake (in adults), Other factors considered: menopausal status, medications, supplements, sodium, protein, fiber, fat, energy density, family history of CVD, food form (solid/beverage) <p>Additional model adjustments: Field center, intake of meat, dairy, fruits, vegetables, whole grains, and refined grains</p> <p>Limitations:</p> <ul style="list-style-type: none"> Not all key confounders accounted for No information on non-completers Exposure data collection tool not validated Exposure data only measured at baseline No preregistered data analysis plan <p>Funding sources: NHLBI</p>

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	TEI, Confounders, and Study Limitations
<p>Pase, 2017¹⁹ Prospective Cohort Study, Framingham Heart Study offspring cohort, United States Analytic N=2888; Power: NR</p> <p>Participant characteristics: adults</p> <ul style="list-style-type: none"> Sex (female): ~55% Age: ~62y (all >45y) Race/ethnicity: "absence of ethnic minorities" SES: No HS degree ~4% Anthropometrics: BMI: ~27 kg/m² Physical activity: ME, hr/d ~42 Smoking, current: ~12% <p>Summary of findings: In a cohort of US adults over 45y, sugar-sweetened soft drink intake was not significantly associated with greater risk of stroke or risk of ischemic stroke over ~10y.</p>	<p>Exposure of interest: Sugar-sweetened soft drinks (SSSD; high-sugar carbonated beverages such as cola)</p> <p><u>Exposure assessment method and timing:</u></p> <ul style="list-style-type: none"> FFQ assessing avg intake over past year, validated Baseline (1991-1995—5th assessment of overall Framingham Heart Study offspring cohort) Follow ups at ~4y & ~8y (1998-2001), Average of the three assessments <p>Outcome assessment methods/timing:</p> <ul style="list-style-type: none"> Starting at 8y assessment (1998-2001), ~10y follow up Health outcomes self-reported: Incident stroke, defined as the rapid onset of focal neurological symptoms of presumed vascular origin, lasting >24 hours or resulting in death; diagnosis of stroke determined by review committee that adjudicated after reviewing all available medical records, imaging studies, and neurological reports Ischemic stroke proportion also identified 97 cases of stroke (82 ischemic) 	<p>Risk of Stroke, Cox proportional hazards regression, HR (95% CI) SSSD intake at last examination: P=NS</p> <ul style="list-style-type: none"> 0/wk: Ref >0-3/wk: 1.15 (0.71, 1.88) >3/wk: 0.69 (0.29, 1.62) <p>SSSD intake avg of 3 measurements over ~8y: P=NS</p> <ul style="list-style-type: none"> 0/wk: Ref >0-3/wk: 1.17 (0.70, 1.97) >3/wk: 0.61 (0.25, 1.49) <p>Risk of Ischemic Stroke, Cox proportional hazards regression, HR (95% CI) SSSD intake at last examination: P=NS</p> <ul style="list-style-type: none"> 0/wk: Ref >0-3/wk: 1.11 (0.65, 1.89) >3/wk: 0.69 (0.27, 1.73) <p>SSSD intake avg of 3 measurements over ~8y: P=NS</p> <ul style="list-style-type: none"> 0/wk: Ref >0-3/wk: 1.12 (0.63, 1.99) >3/wk: 0.61 (0.23, 1.61) <p>Interactions between beverage consumption and waist to hip ratio, APOE ε4 allele status, and prevalent diabetes: results NS</p> <p>Sensitivity analyses conducted:</p> <ul style="list-style-type: none"> Prevalent hypertension Prevalent CVD Prevalent diabetes Waist to hip ratio Total cholesterol HDL cholesterol <p>None changed significance level of results</p>	<p>TEI adjusted: Yes</p> <p>Confounders accounted for:</p> <ul style="list-style-type: none"> Key confounders: sex, age, physical activity, smoking Other factors considered: total energy intake <p>Confounders NOT accounted for:</p> <ul style="list-style-type: none"> Key confounders: race/ethnicity, SES, naturally occurring sugar intake, alcohol intake (in adults), Other factors considered: menopausal status, medications, supplements, sodium, protein, fiber, fat, energy density, food form (solid/beverage), anthropometry (health outcomes), family history of CVD <p>Additional model adjustments: Diet quality (Dietary guidelines adherence index)</p> <p>Note: Model 3 (not extracted) adjusts for SBP, CVD, Afib, left ventricular hypertrophy, total cholesterol, HDL, diabetes, and waist to hip ratio <i>but does not adjust for</i> diet quality, physical activity, or smoking</p> <p>Limitations:</p> <ul style="list-style-type: none"> Not all key confounders accounted for No information on non-completers No preregistered data analysis plan <p>Funding sources: National Health and Medical Research Council; NHLBI; NIA; NINDS; USDA ARS</p>

Rahman, 2015²⁰

Prospective Cohort Study, Cohort of Swedish Men (COSM), Sweden

Analytic N=42400; Power: NR

Recruitment: All men born 1918-1952 and residing in Örebro and Västmanland counties in Sweden were asked to complete an extensive questionnaire

Participant characteristics: adults

- Sex (female): 0% (100% male)
- Age: ~60y (45-79y)
- Race/ethnicity: NR
- SES: University education ~15%
- Anthropometrics: Obesity: ~47%
- Physical activity: ME, hr/d ~42
- Smoking, ever: ~63%

Summary of findings:

In Swedish men, consuming two or more sweetened beverages per day was associated with a greater risk of heart failure compared to non-consumers over a follow up of ~12 years.

Exposure of interest: Sweetened beverages (defined as soft drinks and sweetened juice drinks; does not include fruit juice); 1 serving = 200mL

Comparators:

Categorization by quartiles for consumers:

- No consumption: Ref
- 0.1-<0.5 svg/d
- 0.5-<1.0 svg/d
- 1.0-<2.0 svg/d
- ≥2.0 svg/d

Exposure assessment method and timing:

- FFQ assessing typical daily/weekly intake, validation unclear
- At baseline only

Added sugars intake at baseline:

- 0 svg/d: 50%
- 0.1-<0.5 svg/d: 17%
- 0.5-<1.0 svg/d: 7%
- 1.0-<2.0 svg/d: 13%
- ≥2.0 svg/d: 13%

Outcome assessment methods/timing:

- Avg follow up ~12y
- Health outcomes measured: Incident heart failure (HF)
- Identified using Swedish National Patient Register and Cause of Death Register using International Classification of Diseases-10 codes I50 and I11.0
- Events identified as either the primary or secondary diagnosis of hospitalization or death were included
- 4113 events occurred (3604 first events HF hospitalizations and 509 HF deaths)

Incident heart failure, Cox proportional hazards ratio, HR (95% CI) (n = number of cases at each intake level)

SSB at baseline:

0 svg/d (n=2123): Ref
0.1-<0.5 svg/d (n=490): 0.98 (0.88, 1.08)
0.5-<1.0 svg/d (n=271): 1.08 (0.95, 1.23)
1.0-<2.0 svg/d (n=572): 1.09 (0.99, 1.20)
≥2.0 svg/d (n=657): 1.23 (1.12, 1.35)
P for trend: <0.001

Smoking status, BMI, age >65y, and diabetes were examined as potential effect modifiers (interactions): Results NS

Sensitivity analyses conducted:

- Excluding HF events occurring in first 5y of follow up (reduce risk of reverse causality)
- Exclude pts with diabetes
- Exclude pts with stroke
- Exclude pts with angina

None changed significance level of results

TEI adjusted: Yes

Confounders accounted for:

- Key confounders: sex, age, SES, alcohol intake (in adults), physical activity, smoking
- Other factors considered: total energy intake, anthropometry (health outcomes), family history of MI

Confounders NOT accounted for:

- Key confounders: race/ethnicity, naturally occurring sugar intake
- Other factors considered: menopausal status, medications, supplements, sodium, protein, fiber, fat, energy density, food form (solid/beverage)

Additional model adjustments:

History of stroke, angina, hypertension, diabetes, intake of coffee, fruit, vegetables, processed meat, and fish

Limitations:

- Not all key confounders accounted for
- No information on non-completers
- Exposure data collection tool not validated
- Exposure data only measured at baseline
- No preregistered data analysis plan

Funding sources:

Swedish Research Council Committee for Medicine and the Swedish Research Council Committee for Infrastructure

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	TEI, Confounders, and Study Limitations
<p>Shah, 2018²¹ Prospective Cohort Study, Cooper Center Longitudinal Study, United States Analytic N=11376; Power: NR</p> <p>Recruitment: patients at the Cooper Clinic medical practice in Dallas, TX ('provides patients an individualized, in-depth picture of their health, an action plan to improve it and their test results in <1 day')</p> <p>Participant characteristics: adults</p> <ul style="list-style-type: none"> Sex (female): 25% Age: ~47y Race/ethnicity: Predominantly non-Hispanic white SES: NR Anthropometrics: BMI: 25.8 kg/m² Physical activity: MET-h/wk ~17.6 Smoking: Current: 12% <p>Summary of findings: In a sample of generally healthy US adults, added sugars intake (examined as a component of the DASH Diet) was not associated with risk of CVD mortality over a follow-up period of ~18y.</p>	<p>Exposure of interest: Added sugar (as a component of the DASH Diet)</p> <p>Comparators: Quintiles of AS intake</p> <p><u>Exposure assessment method and timing:</u></p> <ul style="list-style-type: none"> 3-d diet record At baseline (1987-1999) <p>Added sugars intake:</p> <ul style="list-style-type: none"> <3.5%: 1590 3.5-9.1%: 4782 >9.1%: 3892 <p>Outcome assessment methods/timing:</p> <ul style="list-style-type: none"> Follow up avg: 18y Health outcomes measured: CVD Mortality Mortality assessed via National Death Index; CVD deaths identified using International Classification of Diseases Occurrences: 249 	<p>CVD Mortality, Cox proportional hazard regression, HR (95% CI) Added sugars: NS</p>	<p>TEI adjusted: Yes</p> <p>Confounders accounted for:</p> <ul style="list-style-type: none"> Key confounders: sex, age, alcohol intake, physical activity, smoking Other factors considered: total energy intake, anthropometry <p>Confounders NOT accounted for:</p> <ul style="list-style-type: none"> Key confounders: race/ethnicity, SES, naturally occurring sugar intake Other factors considered: menopausal status, medications, supplements, sodium, protein, fiber, fat, energy density, family history of CVD, food form (solid/beverage) <p>Additional model adjustments: LDL, SBP, glucose, intake of fruit, vegetable, nuts/legumes, dairy, whole grain, sodium, & red/processed meats</p> <p>Limitations:</p> <ul style="list-style-type: none"> Not all key confounders accounted for Exposure data only measured once No information on non-completers No preregistered data analysis plan <p>Funding sources: None</p>

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	TEI, Confounders, and Study Limitations
<p>Sonestedt, 2015²² Prospective Cohort Study, Malmö Diet and Cancer Study (MDCS), Sweden Analytic N=26445; Power: NR</p> <p>Recruitment: all men and women born between 1923 and 1945 (men) or 1950 (women) and living in Malmö were invited to participate (personal letters and ads in newspapers and public areas)</p> <p>Participant characteristics: adults</p> <ul style="list-style-type: none"> Sex (female): 62% Age: ~60y Race/ethnicity: NR SES: NR Anthropometrics: BMI ~26 kg/m² Physical activity: NR Smoking: NR <p>Summary of findings: In a group of Swedish adults, added sugars intake broken down into three food/beverage categories was not related to risk of ischemic CVD events.</p>	<p>Exposure of interest: Sucrose (% TEI), Cookies and cakes (g/d), sugar and sweets (g/d), SSBs (g/d)</p> <p>Comparators: Quintiles of intake; Q1 = REF OR Tertiles if >25% of participants were non-consumers (SSBs)</p> <p><u>Exposure assessment method and timing:</u></p> <ul style="list-style-type: none"> Diet history questionnaire, validated At baseline (1991-'96) only <p>Study added sugars intake: NR</p> <p>Outcome assessment methods/timing:</p> <ul style="list-style-type: none"> Avg follow up ~14y Health outcomes measured: Incident ischemic CVD (iCVD) event (i.e., coronary events and ischemic stroke) Data identified through linkage to the Swedish Hospital Discharge Registry, Cause-of-death Registry, and local stroke registry (STROMA) 	<p>Incident iCVD event, Cox proportional hazard regression, HR (95% CI)</p> <p>Sucrose (% of TEI): Q1 = REF Q2-Q5: NS P-trend = 0.18</p> <p>Cookies & Cakes (g/d): Q1 = REF Q2-Q5: NS P-trend = 0.15</p> <p>Sugar & Sweets (g/d): Q1 = REF Q2-Q5: NS P-trend = 0.46</p> <p>SSBs (g/d): T1 = REF T2-T3: NS P-trend = 0.69</p> <p><i>Excluding participants who reported past dietary changes did not affect results</i></p> <p><i>Excluding BMI from the model did not affect results</i></p>	<p>TEI adjusted: Yes</p> <p>Confounders accounted for:</p> <ul style="list-style-type: none"> Key confounders: sex, age, race/ethnicity, SES, alcohol intake, physical activity, anthropometry, smoking Other factors considered: total energy intake, anthropometry <p>Confounders NOT accounted for:</p> <ul style="list-style-type: none"> Key confounders: race/ethnicity, naturally occurring sugar intake Other factors considered: menopausal status, medications, supplements, sodium, protein, fiber, fat, energy density, family history of CVD, food form (solid/beverage) <p>Additional model adjustments: Season of data collection, diet method version</p> <p>Limitations:</p> <ul style="list-style-type: none"> Not all key confounders accounted for No information on non-completers Exposure data only measured at baseline No preregistered data analysis plan <p>Funding sources: Swedish Medical Research Council; Swedish Society for Medical Research; Swedish Heart and Lung Foundation; Skåne University Hospital; Albert Pahlsson Research Foundation; Crafoord Foundation</p>

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	TEI, Confounders, and Study Limitations
<p>Warfa, 2016²³</p> <p>Prospective Cohort Study, Malmö Diet and Cancer Study (MDCS), Sweden Baseline N=28098, Analytic N=26190; Attrition: NR; Power: NR</p> <p>Recruitment: research invitations in public areas or personal letter sent to population</p> <p>Participant characteristics: adults with no history of CVD or diabetes</p> <ul style="list-style-type: none"> Sex (female): 62% Age: 58y (44-73y) Race/ethnicity: NR SES: Education elementary or less: ~42% Anthropometrics: BMI: ~25.5 kg/m² Physical activity: Lowest: 23% Smoking: Current: 32% <p>Summary of findings: In a sample of Swedish adults, elevated risk of coronary events was observed in participants consuming >15% of their total, non-alcohol energy intake from sucrose. This relationship remained when the reference group was the lowest level of sucrose intake (<5%) and the mid-level of intake (7.5-10%).</p>	<p>Exposure of interest: Total sucrose intake as a percentage of non-alcohol energy intake; calculated for all foods and beverages included in the Swedish Food Database (food groups: sweets, chocolates, sugar and jam, fruit juice, SSBs, cakes and pastries)</p> <p>Comparators: AS as percentage of total, non-alcohol energy intake</p> <ul style="list-style-type: none"> <5% 5-7.5% 7.5-10% 10-15% >15% <p><u>Exposure assessment method and timing:</u></p> <ul style="list-style-type: none"> 7-d food diary Semi-quantitative FFQ Diet history interview At baseline only <p>Outcome assessment methods/timing:</p> <ul style="list-style-type: none"> Assessed from recruitment (1991-'96) until end of follow-up (2013) (avg follow up: 17y) Health outcomes measured: coronary events, defined as a fatal or non-fatal MI or death attributable to ischaemic heart disease Data obtained from Swedish Hospital Discharge Register and the Cause of Death Register 	<p>Incident coronary events (n=2493), Cox proportional hazards regression, HR (95% CI)</p> <p>Categories of sucrose intake by % TEI:</p> <p><5%: REF 5-7.5%: 0.97 (0.85, 1.11) 7.5-10%: 1.02 (0.89, 1.16) 10-15%: 1.00 (0.87, 1.15) >15%: 1.34 (1.11, 1.63) P for trend: 0.01</p> <p>Categories of sucrose intake by % TEI (adjusted for waist circumference):</p> <p><5%: REF 5-7.5%: 0.99 (0.87, 1.13) 7.5-10%: 1.03 (0.90, 1.18) 10-15%: 1.02 (0.89, 1.18) >15%: 1.37 (1.13, 1.66) P for trend: 0.008</p> <p>Middle group as reference (adjusted for waist circumference):</p> <p><5%: 0.97 (0.85, 1.11) 5-7.5%: 0.96 (0.86, 1.07) 7.5-10%: REF 10-15%: 0.99 (0.89, 1.11) >15%: 1.33 (1.12, 1.58)</p> <p>[Data are also available in the paper that:</p> <ul style="list-style-type: none"> Adjust for waist circumference Control for participants who are potential energy misreporters and those who reported past dietary change Show associations between each AS food/bev category and coronary events] 	<p>TEI adjusted: Yes</p> <p>Confounders accounted for:</p> <ul style="list-style-type: none"> Key confounders: sex, age, SES, alcohol intake, physical activity, smoking Other factors considered: total energy intake, anthropometry <p>Confounders NOT accounted for:</p> <ul style="list-style-type: none"> Key confounders: race/ethnicity, naturally occurring sugar intake Other factors considered: menopausal status, medications, supplements, sodium, protein, fiber, fat, energy density, family history of CVD, food form (solid/beverage) <p>Additional model adjustments: Method of data collection, season of data collection, intakes of fruits, vegetables, whole grains, coffee, fermented milk, meat, and fish</p> <p>Limitations:</p> <ul style="list-style-type: none"> Not all key confounders accounted for Exposure assessed at baseline only No preregistered data analysis plan <p>Funding sources: Swedish Research Council; Swedish Society for Medical Research, Albert Pahlsson Foundation; Crawford Foundation; ALF government</p>

Table 5: Risk of bias for randomized controlled trials examining added sugars consumption and risk of cardiovascular disease in adults^{viii, ix}

	Randomization	Deviations from intended interventions	Missing outcome data	Outcome measurement	Selection of the reported result
Bruun, 2015 ⁴	Some concerns	Some concerns	Some concerns	Low	Some concerns
Engel, 2018 ⁵	Some concerns	Low	Low	Low	Some concerns
Hernandez-Cordero, 2014 ⁶	Some concerns	Low	Low	Low	Some concerns
Madero, 2015 ⁷	Low	Low	Low	Low	Some concerns
Markey, 2016, ⁸ Crossover	Some concerns	Low	Low	Low	Some concerns
Umpleby, 2017, ⁹ Crossover	Low	Low	Low	Low	Some concerns

^{viii} A detailed description of the methodology used for assessing risk of bias is available on the NESR website: <https://nesr.usda.gov/2020-dietary-guidelines-advisory-committee-systematic-reviews> and in Part C of the following reference: 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.

^{ix} Possible ratings of low, some concerns, or high determined using the "[Cochrane Risk-of-bias 2.0](#)" (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](https://doi.org/10.1002/14651858.CD201601).)

Table 6: Risk of bias for observational studies examining added sugars consumption and risk of cardiovascular disease in adults^x

	Confounding	Selection of participants	Classification of exposures	Deviations from intended exposures	Missing data	Outcome measurement	Selection of the reported result
Barrington, 2016 ¹⁰	Serious	Low	Moderate	Moderate	Moderate	Low	Moderate
Collin, 2019 ¹¹	Serious	Low	Low	Moderate	Moderate	Low	Moderate
Kulezic, 2019 ¹²	Serious	Low	Low	Moderate	Low	Low	Moderate
Liu, 2018 ¹³	Serious	Low	Low	Moderate	Moderate	Low	Moderate
Malik, 2019 ¹⁴	Serious	Low	Low	Low	Low	Low	Moderate
Mullee, 2019 ¹⁵	Serious	Low	Moderate	Moderate	Low	Low	Moderate
Nagata, 2019 ¹⁶	Moderate	Low	Low	Moderate	Low	Low	Moderate
Odegaard, 2015 ¹⁷	Serious	Low	Moderate	Moderate	Low	Low	Moderate
Ogilvie, 2017 ¹⁸	Serious	Low	Moderate	Moderate	Moderate	Low	Moderate
Pase, 2017 ¹⁹	Serious	Low	Low	Low	Moderate	Low	Moderate
Rahman, 2015 ²⁰	Serious	Low	Moderate	Moderate	Moderate	Low	Moderate
Shah, 2018 ²¹	Serious	Low	Low	Moderate	Moderate	Low	Moderate
Sonestedt, 2015 ²²	Serious	Low	Low	Moderate	Moderate	Low	Moderate
Warfa, 2016 ²³	Serious	Low	Low	Moderate	Low	Low	Moderate

^x Possible ratings of low, moderate, serious, critical, or no information determined 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.)

METHODOLOGY

The NESR team used its rigorous, protocol-driven methodology to support the 2020 Dietary Guidelines Advisory Committee in conducting this systematic review.

NESR's systematic review methodology involves:

- Developing a protocol,
- Searching for and selecting studies,
- Extracting data from and assessing the risk of bias of each included study,
- Synthesizing the evidence,
- Developing conclusion statements,
- Grading the evidence underlying the conclusion statements, and
- Recommending future research.

A detailed description of the methodology used in conducting this systematic review is available on the NESR website: <https://nesr.usda.gov/2020-dietary-guidelines-advisory-committee-systematic-reviews>, and can be found in the 2020 Dietary Guidelines Advisory Committee Report, Part C: Methodology.^{xi} This systematic review was peer reviewed by Federal scientists, and information about the peer review process can also be found in the Committee's Report, Part C. Methodology. Additional information about this systematic review, including a description of and rationale for any modifications made to the protocol can be found in the 2020 Dietary Guidelines Advisory Committee Report, Chapter 12. Added Sugars.

The systematic review described in this document updates an existing systematic review that was conducted by the 2015 Dietary Guidelines Advisory Committee with support from USDA's Nutrition Evidence Systematic Review (NESR) team. Information about the 2015 Dietary Guidelines Advisory Committee's review of the evidence on added sugars and risk of cardiovascular disease can be found in their report, which is available at the following website: <https://nesr.usda.gov/cross-cutting-topics-public-health-importance-subcommittee> and <https://www.dietaryguidelines.gov/current-dietary-guidelines/process-develop-2015-2020-dg/advisory-committee>

Below are details of the final protocol for the systematic review described herein, including the:

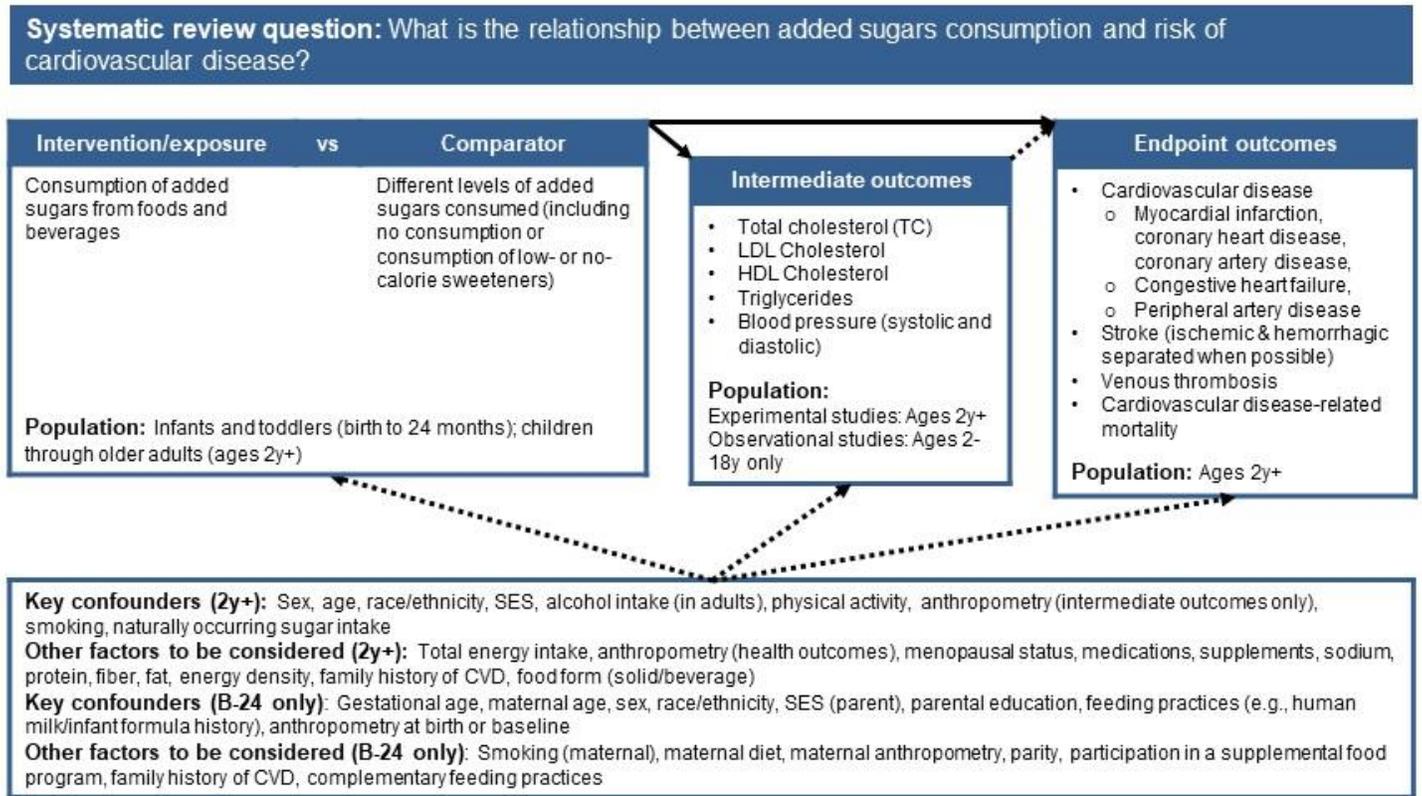
- Analytic framework
- Literature search and screening plan
- Literature search and screening results

^{xi} 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.

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 were defined and operationalized for the review.

Figure 1: Analytic framework



Key definitions

Added sugars: Sugars that are either added during the processing of foods, or are packaged as such (e.g., a bag of sugar). Added sugars include sugars (free, mono- and disaccharides), sugars from syrups and honey, and sugars from concentrated fruit or vegetable juices that are in excess of what would be expected from the same volume of 100 percent fruit or vegetable juice of the same type (FDA, 2016). (Studies that use a different definition of added sugars will also be considered.)

Legend

—————> The relationship of interest in the systematic review
> Factors that may impact the relationship of interest in the systematic review

LITERATURE SEARCH AND SCREENING PLAN

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 were included in or excluded from the systematic review.

Table 7. Inclusion and exclusion criteria

Category	Inclusion Criteria	Exclusion Criteria
Study design	<ul style="list-style-type: none"> • 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 	<ul style="list-style-type: none"> • Uncontrolled trials • Case-control studies • Cross-sectional studies • Uncontrolled before-and-after studies • Narrative reviews • Systematic reviews • Meta-analyses
Study duration	<ul style="list-style-type: none"> • 4-week minimum for experimental studies • No duration cutoff for observational studies 	<ul style="list-style-type: none"> • Experimental studies <4 weeks in duration
Sample size	<ul style="list-style-type: none"> • Observational studies enrolling >1,000 participants 	<ul style="list-style-type: none"> • Observational studies enrolling <1,000 participants
Intervention/exposure	Consumption of added sugars, particularly added sugars from the overall diet or from a food or beverage group that represent a large portion of overall added sugars intake, such as SSBs	Consumption of: <ul style="list-style-type: none"> • Individual types of added sugars (e.g., overall honey intake, which likely does not represent overall added sugars intake) • Experimentally-manipulated foods or beverages • Low- or no-calorie sweeteners • Sugar alcohols
Comparator	<ul style="list-style-type: none"> • Different level of added sugars consumed, including no consumption or consumption of low-calorie sweeteners 	<ul style="list-style-type: none"> • No comparator

Category	Inclusion Criteria	Exclusion Criteria
Outcomes	<p><u>Intermediate outcomes</u> (Experimental studies: Ages 2y+ (Observational studies: 2-18y only):</p> <ul style="list-style-type: none"> • Total Cholesterol (TC) • LDL Cholesterol • HDL Cholesterol • Triglycerides • Blood pressure (systolic and diastolic) <p><u>Health outcomes: (Ages 2y+)</u></p> <ul style="list-style-type: none"> • Cardiovascular disease <ul style="list-style-type: none"> ○ Myocardial infarction, coronary heart disease, coronary artery disease, ○ Congestive heart failure, ○ Peripheral artery disease • Stroke (ischemic & hemorrhagic separated when possible) • Venous thrombosis • Cardiovascular disease-related mortality 	
Date of publication	<ul style="list-style-type: none"> • January 2000 to August 2014 (existing NESR systematic review) • September 2014 – September 2019 (update) 	<ul style="list-style-type: none"> • Articles published prior to September 2014
Publication status	<ul style="list-style-type: none"> • Articles published in peer-reviewed journals 	<ul style="list-style-type: none"> • Articles not published in peer-reviewed journals, including unpublished data, manuscripts, reports, abstracts, pre-prints, and conference proceedings
Language of publication	<ul style="list-style-type: none"> • Articles published in English 	<ul style="list-style-type: none"> • Articles published in languages other than English
Country^{xii}	<ul style="list-style-type: none"> • Studies conducted in Very High or High Human Development Countries 	<ul style="list-style-type: none"> • Studies conducted in Medium or lower Human Development Countries

^{xii} The Human Development classification was 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

Category	Inclusion Criteria	Exclusion Criteria
Study participants	<ul style="list-style-type: none"> • Human participants • Males • Females (including pregnant and lactating women) 	<ul style="list-style-type: none"> • Animal subjects • Hospitalized samples
Age of study participants	<ul style="list-style-type: none"> • Age at intervention or exposure: <ul style="list-style-type: none"> Infants & Toddlers (Birth-24 months) Child (2-5 years) Child (6-12 years) Adolescents (13-18 years) Adults (19-64 years) Older adults (65+ years) • Age at outcome: <ul style="list-style-type: none"> Child (2-5 years) Child (6-12 years) Adolescents (13-18 years) Adults (19-64 years) Older adults (65+ years) 	

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>).

Category	Inclusion Criteria	Exclusion Criteria
Health status of study participants	<ul style="list-style-type: none"> • Studies that enroll participants who are healthy and/or at risk for chronic disease, including those with obesity • Studies that enroll <i>some</i> participants diagnosed with a disease • 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) • Studies that enroll <i>some</i> participants with endpoint outcomes of cardiovascular disease • Studies that enroll infants born full-term (≥ 37 weeks and 0/7 days gestational age) 	<ul style="list-style-type: none"> • 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). • 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) • 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) • Studies that exclusively enroll infants born preterm (gestational age < 37 weeks and 0/7 days), infants with low birth weight (< 2500g), and/or infants born small for gestational age

Electronic databases and search terms

Listed below are the databases searched to identify all potentially relevant articles that have been published to address the update to the existing systematic review.

PubMed

- Provider: U.S. National Library of Medicine
- Date(s) Searched: October 2, 2019
- Date range searched: January 1, 2014-October 2, 2019
- Search Terms:

#1 - "Sweetening Agents"[Mesh] OR "Sweetening Agents"[Pharmacological Action] OR sweeten*[tiab] OR sweets[tw] OR sugary[tw] OR free sugar* OR high sugar* OR sugar substitute* OR table sugar* OR cane sugar* OR cane juice* OR sugar cane* OR sugarcane* OR sugar beet* OR corn sugar* OR sugar intake* OR sugar add* OR raw sugar* OR liquid sugar* OR invert sugar* OR sugar based* OR added sugar* OR sugar added[tw] OR brown sugar* OR white sugar* OR granulated sugar* OR powdered sugar* OR sugar coated* OR sugar sweeten* OR confectioner* OR "Dietary Sugars"[Mesh] OR dietary sugar* OR "Sugar Alcohols"[Mesh] OR sugar alcohol* OR "Nutritive Sweeteners"[Mesh] OR sucrose[tiab] OR sucralose[tw] OR maltose[tiab] OR maltodextrin[tw] OR monosaccharide[tiab] OR "Disaccharides"[Mesh] OR disaccharide[tiab] OR dextrose[tiab] OR "Molasses"[Mesh] OR molasses[tw] OR nectar* OR "Fructose"[Mesh] OR fructose[tiab] OR high-fructose[tw] OR syrup* OR "Honey"[Mesh] OR honey[tw] OR juice concentrat* OR "Lactose"[Mesh] OR lactose[tiab] OR sweetened drink* OR sweet drink* OR sugary drink* OR chocolate drink* OR flavored milk* OR flavoured milk* OR flavored water* OR flavoured water* OR "Candy"[Mesh] OR candy[tw] OR candies[tw] OR pastries[tw] OR "Ice Cream"[Mesh] OR ice cream* OR dairy dessert* OR frozen dessert* OR jello[tw] OR "Yogurt"[Mesh] OR yogurt*[tiab] OR cookies[tw] OR cake*[tw] OR pie[tw] OR pies[tw] OR caramel OR malt barley[tw] OR barley malt* OR chewing gum* OR cereal[tw] OR cereals[tw] OR fruit dessert* OR dried fruit* OR canned fruit* OR processed food* OR granola OR jellies[tiab] OR "Energy Drinks"[Mesh] OR energy drink* OR "Carbonated Beverages"[Mesh] OR carbonated beverage* OR carbonated drink* OR fruit beverage* OR fruit drink* OR fruit punch* OR fruitade* OR soda[tiab] OR soft drink* OR diet beverage* OR sports drink* OR (("Sugars"[Mesh:noexp] OR sugar*[tiab]) AND ("Food and Beverages"[Mesh] OR beverage* OR juice* OR drink* OR food[tiab] OR foods[tiab] OR "Meals"[Mesh] OR meal[tiab] OR snack* OR breakfast* OR "Nutritive Value"[Mesh] OR consumption[tiab] OR intake[tiab] OR "Diet"[Mesh:NoExp] OR diet[tiab]))

#2 - "Cardiovascular Diseases"[Mesh:noexp] OR cardiovascular disease*[tiab] OR coronary artery disease[tiab] OR heart disease*[tiab] OR "Heart Failure"[Mesh] OR heart failure[tiab] OR "Myocardial Infarction"[Mesh] OR myocardial infarction*[tiab] OR "Myocardial Ischemia"[Mesh] OR Myocardial Ischemia*[tiab] OR "Stroke"[Mesh] OR stroke[tiab] OR angina[tiab] OR heart attack[tiab] OR "Venous Thrombosis"[Mesh] OR venous thrombosis[tiab] OR hypertension[tiab] OR high blood pressure[tiab] OR "Lipids/blood"[Mesh] OR "Cholesterol, HDL"[Mesh] OR HDL cholesterol[tiab] OR "Cholesterol, LDL"[Mesh] OR LDL cholesterol[tiab] OR total cholesterol[tiab] OR "Triglycerides"[Mesh] OR triglycerides[tiab]

#3 - (#1 AND #2)

#4 - (#1 AND #2) NOT ("Animals"[Mesh] NOT ("Animals"[Mesh] AND "Humans"[Mesh])) NOT

(editorial[ptyp] OR comment[ptyp] OR news[ptyp] OR letter[ptyp] OR review[ptyp] OR systematic review[ptyp] OR systematic review[ti] OR meta-analysis[ptyp] OR meta-analysis[ti] OR meta-analyses[ti] OR retracted publication[ptyp] OR retraction of publication[ptyp] OR retraction of publication[tiab] OR retraction notice[ti]) Filters: Publication date from 2014/01/01 to 2019/10/02; English

Cochrane Central Register of Controlled Trials (CENTRAL)

- Provider: John Wiley & Sons
- Date(s) Searched: October 2, 2019
- Date range searched: January 1, 2014-October 2, 2019
- Search Terms:

#1 - [mh "Sweetening Agents"] OR [mh "Dietary Sugars"] OR [mh "Sugar Alcohols"] OR [mh "Nutritive Sweeteners"] OR [mh Disaccharides] OR [mh Molasses] OR [mh Fructose] OR [mh Honey] OR [mh Lactose] OR [mh Candy] OR [mh "Ice Cream"] OR [mh Yogurt] OR [mh "Energy Drinks"] OR [mh "Carbonated Beverages"]

#2 - sweeten* OR sweets OR sugary OR "free sugar*" OR "high sugar*" OR "sugar substitute*" OR "table sugar*" OR "cane sugar*" OR "cane juice*" OR "sugar cane*" OR sugarcane* OR "sugar beet*" OR "corn sugar*" OR "sugar intake*" OOR "granulated sugar*" OR "powdered sugar*" OR "sugar coated*" OR "sugar sweeten*" OR "sugar add*" OR "raw sugar*" OR "liquid sugar*" OR "invert sugar*" OR "sugar based" OR "added sugar*" OR "sugar added" OR "brown sugar*" OR "white sugar*" OR "granulated sugar*" OR "powdered sugar*" OR "sugar coated*" OR "sugar sweeten*" OR confectioner* OR "dietary sugar*" OR "sugar alcohol*" OR sucrose OR sucralose OR maltose OR maltodextrin OR monosaccharide OR disaccharide OR dextrose OR molasses OR nectar* OR fructose OR high-fructose OR syrup* OR honey OR "juice concentrat*" OR lactose OR "sweetened drink*" OR "sweet drink*" OR "sugary drink*" "chocolate drink*" OR "flavored milk*" OR "flavoured milk*" OR "flavored water*" OR "flavoured water*" OR candy OR candies OR pastries OR "ice cream*" OR "dairy dessert*" OR "frozen dessert*" OR jello OR yogurt* OR cookies OR cake* OR pie OR pies OR caramel OR "malt barley" OR "barley malt*" OR "chewing gum*" OR cereal OR cereals OR "fruit dessert*" OR "dried fruit*" OR "canned fruit*" OR "processed food*" OR granola OR jellies OR "energy drink*" OR "carbonated beverage*" OR "carbonated drink*" OR "fruit beverage*" OR "fruit drink*" OR "fruit punch*" OR fruitade* OR soda OR "soft drink*" OR "diet beverage*" OR "sports drink*"

#3 - (([mh ^Sugars] OR sugar*) NEAR/6 ([mh "Food and Beverages"] OR beverage* OR juice* OR drink* OR food OR foods OR [mh Meals] OR meal OR snack* OR breakfast* OR [mh "Nutritive Value"] OR consumption OR intake OR [mh ^Diet] OR diet))

#4 - #1 OR #2 OR #3

#5 - [mh ^"Cardiovascular Diseases"] OR [mh "Heart Failure"] OR [mh "Myocardial Infarction"] OR [mh "Myocardial Ischemia"] OR [mh Stroke] OR [mh "Venous Thrombosis"] OR [mh Lipids/BL] OR [mh "Cholesterol, HDL"] OR [mh "Cholesterol, LDL"] OR [mh Triglycerides]

#6 - ("cardiovascular disease*" OR "coronary artery disease" OR "heart disease" OR "heart failure" OR "myocardial infarction*" OR "myocardial ischemia*" OR stroke OR angina OR "heart attack" OR "venous thrombosis" OR "hypertension" OR "high blood pressure" OR "HDL cholesterol" OR "LDL cholesterol" OR "total cholesterol" OR triglycerides):ti,ab,kw

#6 - #5 OR #6

#7 - #4 AND #6" with Publication Year from 2014 to 2019, in Trials (Word variations have been searched)

Embase

- Provider: Elsevier
- Date(s) Searched: October 2, 2019
- Date range searched: January 1, 2014-October 2, 2019
- Search Terms:

#1 - 'sweetening agent'/exp OR 'sugar intake'/exp OR 'sugar alcohol'/exp OR 'nutritive sweetener'/exp OR 'disaccharide'/exp OR 'molasses'/de OR 'fructose'/de OR 'honey'/de OR 'lactose'/de OR 'candy'/de OR 'ice cream'/de OR 'yoghurt'/de OR 'energy drink'/de OR 'carbonated beverage'/de

#2 - sweeten*:ab,ti OR sweets:ab,ti OR sugary:ab,ti OR 'free sugar*':ab,ti OR 'high sugar*':ab,ti OR 'sugar substitute*':ab,ti OR 'table sugar*':ab,ti OR 'cane sugar*':ab,ti OR 'cane juice*':ab,ti OR 'sugar cane*':ab,ti OR sugarcane*:ab,ti OR 'sugar beet*':ab,ti OR 'corn sugar*':ab,ti OR 'sugar intake*':ab,ti OR 'sugar add*':ab,ti OR 'raw sugar*':ab,ti OR 'liquid sugar*':ab,ti OR 'invert sugar*':ab,ti OR 'sugar based*':ab,ti OR 'added sugar*':ab,ti OR 'sugar added':ab,ti OR 'brown sugar*':ab,ti OR 'white sugar*':ab,ti OR 'granulated sugar*':ab,ti OR 'powdered sugar*':ab,ti OR 'sugar coated*':ab,ti OR 'sugar sweeten*':ab,ti OR confectioner*:ab,ti OR 'dietary sugar*':ab,ti OR 'sugar alcohol*':ab,ti OR sucrose:ab,ti OR sucralose:ab,ti OR maltose:ab,ti OR maltodextrin:ab,ti OR monosaccharide:ab,ti OR disaccharide:ab,ti OR dextrose:ab,ti OR molasses:ab,ti OR nectar*:ab,ti OR fructose:ab,ti OR 'high fructose':ab,ti OR syrup*:ab,ti OR honey:ab,ti OR 'juice concentrat*':ab,ti OR lactose:ab,ti OR 'sweetened drink*':ab,ti OR 'sweet drink*':ab,ti OR 'sugary drink*':ab,ti OR 'chocolate drink*':ab,ti OR 'flavored milk*':ab,ti OR 'flavoured milk*':ab,ti OR 'flavored water*':ab,ti OR 'flavoured water*':ab,ti OR candy:ab,ti OR candies:ab,ti OR pastries:ab,ti OR 'ice cream*':ab,ti OR 'dairy dessert*':ab,ti OR 'frozen dessert*':ab,ti OR jello:ab,ti OR yogurt*:ab,ti OR cookies:ab,ti OR cake*:ab,ti OR pie:ab,ti OR pies:ab,ti OR caramel:ab,ti OR 'malt barley':ab,ti OR 'barley malt*':ab,ti OR 'chewing gum*':ab,ti OR cereal:ab,ti OR cereals:ab,ti OR 'fruit dessert*':ab,ti OR 'dried fruit*':ab,ti OR 'canned fruit*':ab,ti OR 'processed food*':ab,ti OR granola:ab,ti OR jellies:ab,ti OR 'energy drink*':ab,ti OR 'carbonated beverage*':ab,ti OR 'carbonated drink*':ab,ti OR 'fruit beverage*':ab,ti OR 'fruit drink*':ab,ti OR 'fruit punch*':ab,ti OR fruitade*:ab,ti OR soda:ab,ti OR 'soft drink*':ab,ti OR 'diet beverage*':ab,ti OR 'sports drink*':ab,ti

#3 - (sugar* NEAR/6 (food OR foods OR beverage* OR juice* OR drink* OR meal OR meals OR snack* OR breakfast*))

#4 - #1 OR #2 OR #3

#5 - 'cardiovascular disease'/de OR 'heart failure'/exp OR 'heart infarction'/exp OR 'heart muscle ischemia'/exp OR 'cerebrovascular accident'/exp OR 'vein thrombosis'/exp OR 'high density lipoprotein cholesterol'/de OR 'low density lipoprotein cholesterol'/de OR 'triacylglycerol'/exp

#6 - 'cardiovascular disease*':ab,ti OR 'coronary artery disease':ab,ti OR 'heart disease':ab,ti OR 'heart failure':ab,ti OR 'myocardial infarction*':ab,ti OR 'myocardial ischemia*':ab,ti OR

stroke:ab,ti OR angina:ab,ti OR 'heart attack':ab,ti OR 'venous thrombosis':ab,ti OR 'hypertension':ab,ti OR 'high blood pressure':ab,ti OR 'hdl cholesterol':ab,ti OR 'ldl cholesterol':ab,ti OR 'total cholesterol':ab,ti OR triglycerides:ab,ti

#7 - #5 OR #6

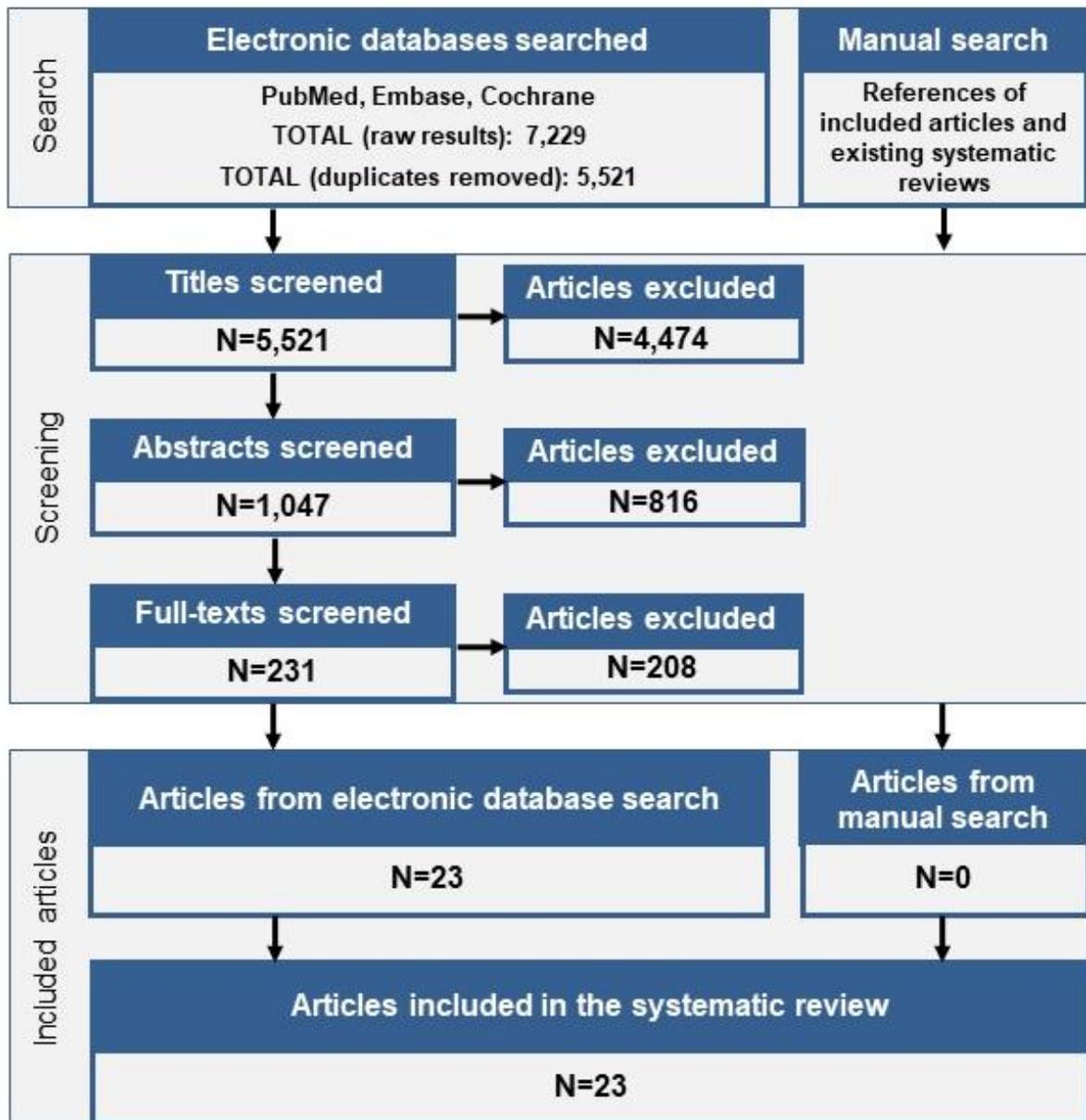
#8 - #4 AND #7

#9 - #4 AND #7 AND ([article]/lim OR [article in press]/lim) AND [humans]/lim AND [english]/lim AND [2014-2019]/py NOT ([conference abstract]/lim OR [conference review]/lim OR [conference paper]/lim OR [editorial]/lim OR [erratum]/lim OR [letter]/lim OR [note]/lim OR [review]/lim OR [systematic review]/lim OR [meta analysis]/lim)

LITERATURE SEARCH AND SCREENING RESULTS

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. Refer to **Table 8** for the rationale for exclusion for each excluded full-text article. 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



Excluded articles

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 for exclusion. Information about articles excluded after title and abstract screening is available upon request.

Table 8. Articles excluded after full text screening with rationale for exclusion

Citation	Rationale
1 . Correction to: Artificially sweetened beverages and stroke, coronary heart disease, and all-cause mortality in the Women's Health Initiative. <i>Stroke</i> . 2019. 50:e176. doi:10.1161/str.000000000000190.	Study design; Intervention/Exposure
2 . No changes in uric acid or blood pressure after 6 months of daily consumption of sugar sweetened or diet beverages. <i>J Am Soc Hypertens</i> . 2016. Conference: 31st Annual Scientific Meeting of the American Society of Hypertension. United States. 10:e56.	Publication status
3 Ab Wahab, SZ, Nik Hussain, NH, Zakaria, R, et al. Long-term effects of honey on cardiovascular parameters and anthropometric measurements of postmenopausal women. <i>Complement Ther Med</i> . 2018. 41:154-160. doi:10.1016/j.ctim.2018.08.015.	Intervention/Exposure
4 Acosta-Navarro JC, Oki AM, Antoniazzi L, et al. Consumption of animal-based and processed food associated with cardiovascular risk factors and subclinical atherosclerosis biomarkers in men. <i>Rev Assoc Med Bras</i> . 2019. 65:43-50. doi:10.1590/1806-9282.65.1.43.	Study design; Intervention/Exposure
5 Adriouch S, Lelong H, Kesse-Guyot E, et al. Compliance with nutritional and lifestyle recommendations in 13,000 patients with a cardiometabolic disease from the Nutrinet-Sante Study. <i>Nutrients</i> . 2017. 9: 546. doi:10.3390/nu9060546.	Intervention/Exposure; Outcome
6 Al Suwaidi, J. Dietary patterns and their association with acute coronary heart disease: Lessons from the REGARDS Study. <i>Glob Cardiol Sci Pract</i> . 2015. 2015:56. doi:10.5339/gcsp.2015.56.	Intervention/Exposure; Publication status
7 AlEssa HB, Cohen R, Malik VS, et al. Carbohydrate quality and quantity and risk of coronary heart disease among US women and men. <i>Am J Clin Nutr</i> . 2018. 107:257-267. doi:10.1093/ajcn/nqx060.	Intervention/Exposure
8 Alvarez-Alvarez I, Toledo E, Lecea O, et al. Adherence to a priori dietary indexes and baseline prevalence of cardiovascular risk factors in the PREDIMED-Plus randomised trial. <i>Eur J Nutr</i> . 2019. 59(3):1219-1232. doi:10.1007/s00394-019-01982-x.	Intervention/Exposure
9 Angelopoulos TJ, Lowndes J, Sinnott S, Rippe, JM. Fructose containing sugars at normal levels of consumption do not effect adversely components of the metabolic syndrome and risk factors for cardiovascular disease. <i>Nutrients</i> . 2016. 8:179. doi:10.3390/nu8040179.	Intervention/Exposure; Comparator
10 Angelopoulos, TJ, Lowndes, J, Sinnott, S, Rippe, JM. Fructose containing sugars do not raise blood pressure or uric acid at normal levels of human consumption. <i>J Clin Hypertens</i> . 2015. 17:87-94. doi:10.1111/jch.12457.	Intervention/Exposure; Comparator

Citation	Rationale
11 Anil, S, Charlton, KE, Tapsell, LC, Probst, Y, Ndanuko, R, Batterham, MJ. Identification of dietary patterns associated with blood pressure in a sample of overweight Australian adults. <i>J Hum Hypertens</i> . 2016. 30:672-678. doi:10.1038/jhh.2016.10.	Intervention/Exposure
12 Anjana, RM, Sudha, V, Nair, DH, et al. Diabetes in Asian Indians-how much is preventable? Ten-year follow-up of the Chennai Urban Rural Epidemiology Study (CURES-142). <i>Diabetes Res Clin Pract</i> . 2015. 109:253-61. doi:10.1016/j.diabres.2015.05.039.	Intervention/Exposure; Country
13 Asadi, Z, Shafiee, M, Sadabadi, F, Heidari-Bakavoli, A, Moohebati, M, Khorrarni, MS, Darroudi, S, Heidari, S, Hoori, T, Tayefi, M, Mohammadi, F, Esmaeily, H, Safarian, M, Ghayour-Mobarhan, M, Ferns, GA. Association of dietary patterns and risk of cardiovascular disease events in the MASHAD cohort study. <i>J Hum Nutr Diet</i> . 2019. 32(6)789-801. doi:10.1111/jhn.12669.	Intervention/Exposure
14 Asghari, G, Yuzbashian, E, Mirmiran, P, Bahadoran, Z, Azizi, F. Prediction of metabolic syndrome by a high intake of energy-dense nutrient-poor snacks in Iranian children and adolescents. <i>Pediatr Res</i> . 2016. 79:697-704. doi:10.1038/pr.2015.270.	Intervention/Exposure
15 Atkins, JL, Whincup, PH, Morris, RW, Lennon, LT, Papacosta, O, Wannamethee, SG. Dietary patterns and the risk of CVD and all-cause mortality in older British men. <i>Br J Nutr</i> . 2016. 116:1246-1255. doi:10.1017/s0007114516003147.	Intervention/Exposure
16 Bahadoran, Z, Mirmiran, P, Tohidi, M, Azizi, F. Longitudinal associations of high-fructose diet with cardiovascular events and potential risk factors: Tehran Lipid and Glucose Study. <i>Nutrients</i> . 2017. 9(8):872. doi:10.3390/nu9080872.	Intervention/Exposure
17 Barbalho SM, Fontana LCS, Finalli EFR, et al. Eating habits and presence of cardiovascular risks in children. <i>Int J Adolesc Med Health</i> . 2016. 30(2). doi:10.1515/ijamh-2016-0045.	Study design
18 Beasley, JM, Yi, SS, Ahn, J, Kwon, SC, Wylie-Rosett, J. Dietary patterns in Chinese Americans are associated with cardiovascular disease risk factors, the Chinese American Cardiovascular Health Assessment (CHA CHA). <i>J Immigr Minor Health</i> . 2019. 21:1061-1069. doi:10.1007/s10903-018-0800-z.	Study design; Intervention/Exposure
19 Bihuniak, JD, Ramos, A, Huedo-Medina, T, Hutchins-Wiese, H, Kerstetter, JE, Kenny, AM. Adherence to a Mediterranean-Style diet and its influence on cardiovascular risk factors in postmenopausal women. <i>J Acad Nutr Diet</i> . 2016. 116:1767-1775. doi:10.1016/j.jand.2016.06.377.	Intervention/Exposure
20 Bonaccio, M, Di Castelnuovo, A, Costanzo, S, et al. Adherence to the traditional Mediterranean diet and mortality in subjects with diabetes. Prospective results from the MOLI-SANI study. <i>Eur J Prev Cardiol</i> . 2016. 23:400-7. doi:10.1177/2047487315569409.	Health status
21 Butler, AA, St-Onge, MP, Siebert, EA, Medici, V, Stanhope, KL, Havel, PJ. Differential responses of plasma adipon concentrations to dietary glucose or fructose consumption in humans. <i>Sci Rep</i> . 2015. 5:14691. doi:10.1038/srep14691.	Comparator; Outcome
22 Campos, V, Despland, C, Brandejsky, V, et al. Metabolic effects of replacing sugar-sweetened beverages with artificially-sweetened beverages in overweight subjects with or without hepatic steatosis: a randomized control clinical trial. <i>Nutrients</i> . 2017. 9(3):202. doi:10.3390/nu9030202.	Outcome

	Citation	Rationale
23	Campos, V, Despland, C, Brandejsky, V, et al. Sugar- and artificially sweetened beverages and intrahepatic fat: A randomized controlled trial. <i>Obesity</i> . 2015. 23:2335-2339. doi:10.1002/oby.21310.	Outcome
24	Campos, V, Despland, C, Schneiter, Ph, Brandejsky, V, Kreis, R, Boesch, Ch, Tappy, L. A randomized control trial of sugar-sweetened and artificially sweetened beverages and intrahepatic fat in overweight subjects. <i>FASEB J</i> . 2015. 29(Suppl 1):602.5.	Publication status
25	Charkiewicz, AE, Jamiolkowski, J, Pedzinski, B, et al. Changes in dietary patterns and the nutritional status in men in the metallurgical industry in poland over a 21-year period. <i>Ann Nutr Metab</i> . 2018. 72:161-171. doi:10.1159/000485389.	Intervention/Exposure; Outcome
26	Charriere, N, Montani, JP, Dulloo, AG. Acute metabolic and cardiovascular responses of healthy young adults to the ingestion of galactose-the forgotten sugar. <i>Obesity facts</i> . 2015. 8:114. doi:10.1159/000382140.	Publication status
27	Cheraghi, Z, Nedjat, S, Mirmiran, P, et al. Effects of food items and related nutrients on metabolic syndrome using Bayesian multilevel modelling using the Tehran Lipid and Glucose Study (TLGS): A cohort study. <i>BMJ Open</i> . 2018. 8:e020642 doi:10.1136/bmjopen-2017-020642.	Study design; Intervention/Exposure; Outcome
28	Chong, ZX, Ho, JH, Hussain, NHN, et al. The effects of Tualang honey versus honey cocktail (HC124) on physiological changes and hormonal profiles among postmenopausal women: a preliminary study. <i>Int J Collab Res Intern Med Public Health</i> . 2015. 7:40-51.	Intervention/Exposure; Comparator
29	Chung S, Ha K, Lee HS, et al. Soft drink consumption is positively associated with metabolic syndrome risk factors only in Korean women: Data from the 2007-2011 Korea National Health and Nutrition Examination Survey. <i>Metabolism</i> . 2015. 64:1477-84. doi:10.1016/j.metabol.2015.07.012.	Study design
30	Dale, MTG, Magnus, P, Leirgul, E, et al. Intake of sucrose-sweetened soft beverages during pregnancy and risk of congenital heart defects (CHD) in offspring: a Norwegian pregnancy cohort study. <i>Eur J Epidemiol</i> . 2019. 34:383-396. doi:10.1007/s10654-019-00480-y.	Outcome
31	de Paula Franco, E, Moraes de Oliveira, GM, Raggio Luiz, R, Rosa, G. Effect of hypoenergetic diet combined with consumption of coconut flour in overweight women. <i>Nutr Hosp</i> . 2015. 32:2012-8. doi:10.3305/nh.2015.32.5.9661.	Intervention/Exposure
32	Dennison, M, Sisson, SB, Stephens, L, Morris, et al. Obesogenic Behaviors and Depressive Symptoms' Influence on Cardiometabolic Risk Factors in American Indian Children. <i>J Allied Health</i> . 2019. 48:100-107.	Study design; Intervention/Exposure
33	Derakhshandeh-Rishehri, SM, Heidari-Beni, M, Feizi, A, Askari, GR, Entezari, MH. Effect of honey vinegar syrup on blood sugar and lipid profile in healthy subjects. <i>Int J Prev Med</i> . 2014. 5:1608-15.	Intervention/Exposure
34	Despland, C, Walther, B, Kast, C, Campos, V, Rey, V, Stefanoni, N, Tappy, L. A randomized-controlled clinical trial of high fructose diets from either Robinia honey or free fructose and glucose in healthy normal weight males. <i>Clin Nutr ESPEN</i> . 2017. 19:16-22. doi:10.1016/j.clnesp.2017.01.009.	Intervention/Exposure; Study duration

Citation	Rationale
35 Dhurandhar, NV, Thomas, D. The link between dietary sugar intake and cardiovascular disease mortality: an unresolved question. <i>JAMA</i> . 2015. 313:959-960. doi:10.1001/jamainternmed.2013.13563.	Study design; Other; Review - article and abstract are different
36 Dushay, JR, Toschi, E, Mitten, EK, Fisher, FM, Herman, MA, Maratos-Flier, E. Fructose ingestion acutely stimulates circulating FGF21 levels in humans. <i>Mol Metab</i> . 2015. 4:51-57. doi:10.1016/j.molmet.2014.09.008.	Intervention/Exposure; Study duration
37 Dusilova, T, Kovar, J, Drobny, M, et al. Different acute effects of fructose and glucose administration on hepatic fat content. <i>Am J Clin Nutr</i> . 2019. 109:1519-1526. doi:10.1093/ajcn/nqy386.	Outcome; Study duration
38 Ebbeling, CB, Feldman, HA, Steltz, SK, Ludwig, DS. Differential effects of sugar-sweetened, artificially sweetened, and unsweetened beverages on taste preference but not CVD risk factors in a 12-month RCT. <i>Circulation</i> . 2019. 139(Suppl 1):AP337. doi:10.1161/circ.139.suppl_1.044.	Publication status
39 Eloranta, AM, Lindi, V, Schwab, U, et al. Dietary factors associated with metabolic risk score in Finnish children aged 6-8 years: the PANIC study. <i>Eur J Nutr</i> . 2014. 53:1431-9. doi:10.1007/s00394-013-0646-z.	Study design; Sample size
40 Enginyurt, O, Cakir, L, Karatas, A, et al. The role of pure honey in the treatment of diabetes mellitus. <i>Biomedical Research</i> . 2017. 28:3305-3312.	Intervention/Exposure; Health status
41 Eren, OC, Ortiz, A, Afsar, B, Covic, A, Kuwabara, M, Lanaspas, MA, Johnson, RJ, Kanbay, M. Multilayered Interplay Between Fructose and Salt in Development of Hypertension. <i>Hypertension</i> . 2019. 73:265-272. doi:10.1161/hypertensionaha.118.12150.	Study design; Intervention/Exposure
42 Ericson, U, Brunkwall, L, Alves Dias, J, Drake, I, Hellstrand, S, Gullberg, B, Sonestedt, E, Nilsson, PM, Wirfält, E, Orho-Melander, M. Food patterns in relation to weight change and incidence of type 2 diabetes, coronary events and stroke in the Malmö Diet and Cancer cohort. <i>European Journal of Nutrition</i> . 2019. 58:1801-1814. doi:10.1007/s00394-018-1727-9.	Intervention/Exposure
43 Esmaili, SS, Fallahi, F, Gholami Fesharaki, M, Noormohammadi, G. A Randomized Trial on the Effect of Razavi's Dietary Pattern on the Components of Metabolic Syndrome. <i>Iran Red Crescent Med J</i> . 2014. 16:e14601. doi:10.5812/ircmj.14601.	Intervention/Exposure
44 Farakla, I, Kouli, E, Arditi, J, Papageorgiou, I, Bartzeliotou, A, Papadopoulos, GE, Mantzou, A, Papathanasiou, C, Dracopoulou, M, Papastamataki, M, Moutsatsou, P, Papassotiriou, I, Chrousos, GP, Charmandari, E. Effect of honey on glucose and insulin concentrations in obese girls. <i>European Journal of Clinical Investigation</i> . 2019. 49. doi:10.1111/eci.13042.	Intervention/Exposure; Comparator
45 Fedacko, J, Vargova, V, Pella, D, Singh, RB, Gupta, AK, Juneja, LR, De Meester, F, Wilson, DW. Sugar and the heart. <i>World Heart Journal</i> . 2014. 6:215-218.	Study design; Publication status; Other; Not primary research

Citation	Rationale
<p>46 Fernandez-Lazaro, CI, Toledo, E, Salas-Salvado, J, Corella, D, Fito, M, Martinez, JA, Buil-Cosiales, P. PREDIMED-Plus trial: one-year changes in the quality of dietary carbohydrate intake and concurrent changes in cardiovascular risk factors. <i>Annals of nutrition & metabolism</i>. 2019. 75:20-21. doi:10.1159/000501441.</p>	Publication status
<p>47 Ferreira-Pego, C, Babio, N, Bes-Rastrollo, M, Corella, D, Estruch, R, Ros, E, Fito, M, Serra-Majem, L, Aros, F, Fiol, M, Santos-Lozano, JM, Munoz-Bravo, C, Pinto, X, Ruiz-Canela, M, Salas-Salvado, J. Frequent Consumption of Sugar- and Artificially Sweetened Beverages and Natural and Bottled Fruit Juices Is Associated with an Increased Risk of Metabolic Syndrome in a Mediterranean Population at High Cardiovascular Disease Risk. <i>J Nutr</i>. 2016. 146:1528-36. doi:10.3945/jn.116.230367.</p>	Outcome
<p>48 Gajda, K, Sulich, A, Hamulka, J, Bialkowska, A. Comparing diabetic with non-diabetic overweight subjects through assessing dietary intakes and key parameters of blood biochemistry and haematology. <i>Rocz Panstw Zakl Hig</i>. 2014. 65:133-8.</p>	Study design; Intervention/Exposure
<p>49 Gallagher, C, Clifton, P, Pedersen, E, Keogh, J. Effect of fructose vs sucrose and sucralose on glucose, insulin and triglyceride levels in a solid mixed meal in healthy people. <i>Circulation</i>. 2015. 132.</p>	Publication status
<p>50 Gardener, H, Caunca, M, Dong, C, Cheung, YK, Alperin, N, Rundek, T, Elkind, MSV, Wright, CB, Sacco, RL. Ideal Cardiovascular Health and Biomarkers of Subclinical Brain Aging: The Northern Manhattan Study. <i>J Am Heart Assoc</i>. 2018. 7:e009544. doi:10.1161/jaha.118.009544.</p>	Intervention/Exposure; Outcome
<p>51 Gonzalez-Granda, A, Damms-Machado, A, Basrai, M, Bischoff, SC. Changes in Plasma Acylcarnitine and Lysophosphatidylcholine Levels Following a High-Fructose Diet: A Targeted Metabolomics Study in Healthy Women. <i>Nutrients</i>. 2018. 10. doi:10.3390/nu10091254.</p>	Outcome; Study duration
<p>52 Gooding, HC, Ning, H, Gillman, MW, Shay, C, Allen, N, Goff, DC, Jr, Lloyd-Jones, D, Chiuve, S. Application of a Lifestyle-Based Tool to Estimate Premature Cardiovascular Disease Events in Young Adults: The Coronary Artery Risk Development in Young Adults (CARDIA) Study. <i>JAMA Intern Med</i>. 2017. 177:1354-1360. doi:10.1001/jamainternmed.2017.2922.</p>	Intervention/Exposure
<p>53 Gopinath, B, Flood, VM, Kifley, A, Louie, JC, Mitchell, P. Association Between Carbohydrate Nutrition and Successful Aging Over 10 Years. <i>J Gerontol A Biol Sci Med Sci</i>. 2016. 71:1335-40. doi:10.1093/gerona/glw091.</p>	Outcome
<p>54 Grasgruber, P, Cacek, J, Hrazdira, E, Hrebickova, S, Sebera, M. Global Correlates of Cardiovascular Risk: A Comparison of 158 Countries. <i>Nutrients</i>. 2018. 10. doi:10.3390/nu10040411.</p>	Study design
<p>55 Guess, N, Wijesuriya, M, Vasantharajah, L, Gulliford, M, Viberti, G, Gnudi, L, Karalliedde, J. The effect of dietary changes on distinct components of the metabolic syndrome in a young Sri Lankan population at high risk of CVD. <i>Br J Nutr</i>. 2016. 116:719-27. doi:10.1017/s0007114516002476.</p>	Intervention/Exposure; Outcome
<p>56 Han, Y, Kwon, EY, Yu, MK, Lee, SJ, Kim, HJ, Kim, SB, Kim, YH, Choi, MS. A Preliminary Study for Evaluating the Dose-Dependent Effect of d-Allulose for Fat Mass Reduction in Adult Humans: A Randomized, Double-Blind, Placebo-Controlled Trial. <i>Nutrients</i>. 2018. 10. doi:10.3390/nu10020160.</p>	Intervention/Exposure

Citation	Rationale
57 Hellstrand, S, Ericson, U, Schulz, CA, Drake, I, Gullberg, B, Hedblad, B, Engstrom, G, Orho-Melander, M, Sonestedt, E. Genetic susceptibility to dyslipidemia and incidence of cardiovascular disease depending on a diet quality index in the Malmö Diet and Cancer cohort. <i>Genes Nutr.</i> 2016. 11:20. doi:10.1186/s12263-016-0536-0.	Intervention/Exposure
58 Hellstrand, S, Ericson, U, Schulz, CA, Drake, I, Gullberg, B, Hedblad, B, Engström, G, Orho-Melander, M, Sonestedt, E. Genetic susceptibility to dyslipidemia and incidence of cardiovascular disease depending on a diet quality index in the Malmö diet and cancer cohort. <i>Genes and Nutrition.</i> 2016. 11. doi:10.1186/s12263-016-0536-0.	Intervention/Exposure
59 Herieka, M, Faraj, TA, Erridge, C. Reduced dietary intake of pro-inflammatory Toll-like receptor stimulants favourably modifies markers of cardiometabolic risk in healthy men. <i>Nutr Metab Cardiovasc Dis.</i> 2016. 26:194-200. doi:10.1016/j.numecd.2015.12.001.	Intervention/Exposure; Study duration
60 Hernandez-Cordero, S, Popkin, BM. Impact of a Water Intervention on Sugar-Sweetened Beverage Intake Substitution by Water: A Clinical Trial in Overweight and Obese Mexican Women. <i>Ann Nutr Metab.</i> 2015. 66 Suppl 3:22-5. doi:10.1159/000381242.	Intervention/Exposure; Comparator
61 Hieronimus, B, Griffen, SC, Keim, NL, Bremer, AA, Berglund, L, Nakajima, K, Havel, PJ, Stanhope, KL. Effects of Fructose or Glucose on Circulating ApoCIII and Triglyceride and Cholesterol Content of Lipoprotein Subfractions in Humans. <i>J Clin Med.</i> 2019. 8. doi:10.3390/jcm8070913.	Intervention/Exposure; Outcome
62 Higgins, KA, Mattes, RD. A randomized controlled trial contrasting the effects of 4 low-calorie sweeteners and sucrose on body weight in adults with overweight or obesity. <i>American Journal of Clinical Nutrition.</i> 2019. 109:1288-1301. doi:10.1093/ajcn/nqy381.	Outcome
63 Hinkle, SN, Rawal, S, Bjerregaard, AA, Halldorsson, TI, Li, M, Ley, SH, Wu, J, Zhu, Y, Chen, L, Liu, A, Grunnet, LG, Rahman, ML, Kampmann, FB, Mills, JL, Olsen, SF, Zhang, C. A prospective study of artificially sweetened beverage intake and cardiometabolic health among women at high risk. <i>Am J Clin Nutr.</i> 2019. doi:10.1093/ajcn/nqz094.	Intervention/Exposure
64 Hochuli, M, Aeberli, I, Weiss, A, Hersberger, M, Troxler, H, Gerber, PA, Spinass, GA, Berneis, K. Sugar-sweetened beverages with moderate amounts of fructose, but not sucrose, induce Fatty Acid synthesis in healthy young men: a randomized crossover study. <i>J Clin Endocrinol Metab.</i> 2014. 99:2164-72. doi:10.1210/jc.2013-3856.	Outcome; Study duration
65 Hooshmand, F, Asghari, G, Yuzbashian, E, Mahdavi, M, Mirmiran, P, Azizi, F. Modified Healthy Eating Index and Incidence of Metabolic Syndrome in Children and Adolescents: Tehran Lipid and Glucose Study. <i>J Pediatr.</i> 2018. 197:134-139.e2. doi:10.1016/j.jpeds.2018.01.080.	Intervention/Exposure; Outcome
66 Hoscan, Y, Yigit, F, Muderrisoglu, H. Adherence to Mediterranean diet and its relation with cardiovascular diseases in Turkish population. <i>Int J Clin Exp Med.</i> 2015. 8:2860-6.	Intervention/Exposure
67 Hu, EA, Steffen, LM, Coresh, J, Appel, LJ, Rebholz, CM. Adherence to the Healthy Eating Index-2015 and Other Dietary Patterns May Reduce Risk of Cardiovascular Disease, Cardiovascular Mortality, and All-Cause Mortality. <i>J Nutr.</i> 2019. doi:10.1093/jn/nxz218.	Intervention/Exposure

Citation	Rationale
<p>68 Huerta-Avila, EE, Ramirez-Silva, I, Torres-Sanchez, LE, Diaz-Benitez, CE, Orbe-Orihuela, YC, Lagunas-Martinez, A, Galvan-Portillo, M, Flores, M, Cruz, M, Burguete-Garcia, AI. High Relative Abundance of Lactobacillus reuteri and Fructose Intake are Associated with Adiposity and Cardiometabolic Risk Factors in Children from Mexico City. <i>Nutrients</i>. 2019. 11. doi:10.3390/nu11061207.</p>	Study design; Intervention/Exposure
<p>69 Hur, YI, Park, H, Kang, JH, Lee, HA, Song, HJ, Lee, HJ, Kim, OH. Associations between Sugar Intake from Different Food Sources and Adiposity or Cardio-Metabolic Risk in Childhood and Adolescence: The Korean Child-Adolescent Cohort Study. <i>Nutrients</i>. 2015. 8. doi:10.3390/nu8010020.</p>	Sample size
<p>70 Ibarra-Reynoso, LDR, Lopez-Lemus, HL, Garay-Sevilla, ME, Malacara, JM. Effect of Restriction of Foods with High Fructose Corn Syrup Content on Metabolic Indices and Fatty Liver in Obese Children. <i>Obes Facts</i>. 2017. 10:332-340. doi:10.1159/000476069.</p>	Study design; Intervention/Exposure; Outcome
<p>71 Iff, S, Wong, G, Webster, AC, Flood, V, Wang, JJ, Mitchell, P, Craig, JC. Relative energy balance, CKD, and risk of cardiovascular and all-cause mortality. <i>Am J Kidney Dis</i>. 2014. 63:437-45. doi:10.1053/j.ajkd.2013.08.026.</p>	Intervention/Exposure
<p>72 Jayadi, Y, Thaha, AR, Hadju, V, Bukhari, A, Dewi, NU, Bohari, . The potential of Indonesian honey to change the lipid profiles of individuals with central obesity. <i>Pakistan Journal of Nutrition</i>. 2019. 18:508-513. doi:10.3923/pjn.2019.508.513.</p>	Intervention/Exposure
<p>73 Jensen, PN, Howard, BV, Best, LG, O'Leary, M, Devereux, RB, Cole, SA, MacCluer, JW, Ali, T, Lee, ET, Yeh, FL, Yeh, J, Umans, JG, Fretts, AM. Associations of diet soda and non-caloric artificial sweetener use with markers of glucose and insulin homeostasis and incident diabetes: the Strong Heart Family Study. <i>Eur J Clin Nutr</i>. 2019. doi:10.1038/s41430-019-0461-6.</p>	Intervention/Exposure; Outcome
<p>74 Jin, R, Welsh, JA, Le, NA, Holzberg, J, Sharma, P, Martin, DR, Vos, MB. Dietary fructose reduction improves markers of cardiovascular disease risk in Hispanic-American adolescents with NAFLD. <i>Nutrients</i>. 2014. 6:3187-201. doi:10.3390/nu6083187.</p>	Intervention/Exposure; Health status
<p>75 Jin, Y, Kanaya, AM, Kandula, NR, Rodriguez, LA, Talegawkar, SA. Vegetarian Diets Are Associated with Selected Cardiometabolic Risk Factors among Middle-Older Aged South Asians in the United States. <i>J Nutr</i>. 2018. 148:1954-1960. doi:10.1093/jn/nxy217.</p>	Intervention/Exposure
<p>76 Julian-Almarcegui, C, Vandevijvere, S, Gottrand, F, Beghin, L, Dallongeville, J, Sjostrom, M, Leclercq, C, Manios, Y, Widhalm, K, Ferreira De Moraes, AC, Gonzalez-Gross, M, Stehle, P, Castillo, MJ, Moreno, LA, Kersting, M, Vyncke, K, De Henauw, S, Huybrechts, I. Association of heart rate and blood pressure among European adolescents with usual food consumption: The HELENA study. <i>Nutr Metab Cardiovasc Dis</i>. 2016. 26:541-8. doi:10.1016/j.numecd.2016.01.014.</p>	Study design; Intervention/Exposure
<p>77 Jurado-Fasoli, L, De-la, OA, Castillo, MJ, Amaro-Gahete, FJ. Dietary differences between metabolically healthy overweight-obese and metabolically unhealthy overweight-obese adults. <i>Br J Nutr</i>. 2019. 1-21. doi:10.1017/s0007114519002071.</p>	Study design; Intervention/Exposure
<p>78 Kang, Y, Kim, J. Soft drink consumption is associated with increased incidence of the metabolic syndrome only in women. <i>Br J Nutr</i>. 2017. 117:315-324. doi:10.1017/s0007114517000046.</p>	Outcome

Citation	Rationale
<p>79 Kaplon, RE, Hill, SD, Bispham, NZ, Santos-Parker, JR, Nowlan, MJ, Snyder, LL, Chonchol, M, LaRocca, TJ, McQueen, MB, Seals, DR. Oral trehalose supplementation improves resistance artery endothelial function in healthy middle-aged and older adults. <i>Aging (Albany NY)</i>. 2016. 8:1167-83. doi:10.18632/aging.100962.</p>	Comparator
<p>80 Karimi, G, Azadbakht, L, Haghghatdoost, F, Esmailzadeh, A. Low energy density diet, weight loss maintenance, and risk of cardiovascular disease following a recent weight reduction program: A randomized control trial. <i>J Res Med Sci</i>. 2016. 21:32. doi:10.4103/1735-1995.181992.</p>	Intervention/Exposure
<p>81 Kassi, EN, Landis, G, Pavlaki, A, Lambrou, G, Mantzou, E, Androulakis, I, Giannakou, A, Papanikolaou, E, Chrousos, GP. Long-term effects of stevia rebaudiana on glucose and lipid profile, adipocytokines, markers of inflammation and oxidation status in patients with metabolic syndrome. <i>Endocrine reviews</i>. 2016. 37. doi:10.1210/endo-meetings.2016.CE.5.SUN-577.</p>	Publication status
<p>82 Katsa, ME, Ioannidis, A, Zyga, S, Tsironi, M, Koutsovitis, P, Chatzipanagiotou, S, Panagiotakos, D, Sachlas, A, Kolovos, P, Routsis, K, Pistikou, AM, Kougioumtzi Dimoliani, DE, Rojas Gil, AP. The Effect of Nutrition and Sleep Habits on Predisposition for Metabolic Syndrome in Greek Children. <i>J Pediatr Nurs</i>. 2018. 40:e2-e8. doi:10.1016/j.pedn.2018.01.012.</p>	Study design; Intervention/Exposure
<p>83 Keller, AC. Sugar-sweetened beverages and cardiovascular diseases. <i>Eur Heart J</i>. 2014. 35:2203-4.</p>	Study design
<p>84 Keller, J, Kahlhofer, J, Peter, A, Bosy-Westphal, A. Effects of Low versus High Glycemic Index Sugar-Sweetened Beverages on Postprandial Vasodilatation and Inactivity-Induced Impairment of Glucose Metabolism in Healthy Men. <i>Nutrients</i>. 2016. 8. doi:10.3390/nu8120802.</p>	Intervention/Exposure; Outcome
<p>85 Khayatzadeh, SS, Moohebati, M, Mazidi, M, Avan, A, Tayefi, M, Parizadeh, SM, Ebrahimi, M, Heidari-Bakavoli, A, Azarpazhooh, MR, Esmaily, H, Ferns, GA, Nematy, M, Safarian, M, Ghayour-Mobarhan, M. Nutrient patterns and their relationship to metabolic syndrome in Iranian adults. <i>Eur J Clin Invest</i>. 2016. 46:840-52. doi:10.1111/eci.12666.</p>	Study design; Intervention/Exposure
<p>86 Kong, LC, Holmes, BA, Cotillard, A, Habi-Rachedi, F, Brazeilles, R, Gougis, S, Gausseres, N, Cani, PD, Fellahi, S, Bastard, JP, Kennedy, SP, Dore, J, Ehrlich, SD, Zucker, JD, Rizkalla, SW, Clement, K. Dietary patterns differently associate with inflammation and gut microbiota in overweight and obese subjects. <i>PLoS One</i>. 2014. 9:e109434. doi:10.1371/journal.pone.0109434.</p>	Intervention/Exposure; Outcome
<p>87 Kromhout, D, Menotti, A, Alberti-Fidanza, A, Puddu, PE, Hollman, P, Kafatos, A, Tolonen, H, Adachi, H, Jacobs, DR, Jr. Comparative ecologic relationships of saturated fat, sucrose, food groups, and a Mediterranean food pattern score to 50-year coronary heart disease mortality rates among 16 cohorts of the Seven Countries Study. <i>Eur J Clin Nutr</i>. 2018. 72:1103-1110. doi:10.1038/s41430-018-0183-1.</p>	Study design
<p>88 Kulezic, A, Bergwall, S, Fatemi, S, Sonestedt, E, Zarrouk, M, Gottsäter, A, Acosta, S. Healthy diet and fiber intake are associated with decreased risk of incident symptomatic peripheral artery disease – A prospective cohort study. <i>Vascular Medicine (United Kingdom)</i>. 2019. doi:10.1177/1358863X19867393.</p>	Duplicate; Other; Duplicate of ref 7287

Citation	Rationale
89 Kuzma, J, Cromer, G, Hagman, D, Breymeyer, K, Roth, C, Foster-Schubert, K, Holte, S, Weigle, D, Kratz, M. No differential effect of beverages sweetened with fructose, high-fructose corn syrup, or glucose on systemic inflammation in healthy, normal weight or obese individuals: a randomized controlled trial. <i>FASEB journal</i> . 2016. 30.	Publication status
90 Kuzma, JN, Cromer, G, Hagman, DK, Breymeyer, KL, Roth, CL, Foster-Schubert, KE, Holte, SE, Weigle, DS, Kratz, M. No differential effect of beverages sweetened with fructose, high-fructose corn syrup, or glucose on systemic or adipose tissue inflammation in normal-weight to obese adults: a randomized controlled trial. <i>Am J Clin Nutr</i> . 2016. 104:306-14. doi:10.3945/ajcn.115.129650.	Outcome; Study duration
91 Kwak, JH, Jo, G, Chung, HK, Shin, MJ. Association between sugar-sweetened beverage consumption and incident hypertension in Korean adults: a prospective study. <i>Eur J Nutr</i> . 2019. 58:1009-1017. doi:10.1007/s00394-018-1617-1.	Outcome
92 Laclaustra, M, Rodriguez-Artalejo, F, Guallar-Castillon, P, Banegas, JR, Graciani, A, Garcia-Esquinas, E, Ordovas, J, Lopez-Garcia, E. Prospective association between added sugars and frailty in older adults. <i>Am J Clin Nutr</i> . 2018. 107:772-779. doi:10.1093/ajcn/nqy028.	Outcome
93 Lara, KM, Levitan, EB, Gutierrez, OM, Shikany, JM, Safford, MM, Judd, SE, Rosenson, RS. Dietary Patterns and Incident Heart Failure in U.S. Adults Without Known Coronary Disease. <i>J Am Coll Cardiol</i> . 2019. 73:2036-2045. doi:10.1016/j.jacc.2019.01.067.	Intervention/Exposure
94 Larsson, SC, Akesson, A, Wolk, A. Sweetened beverage consumption is associated with increased risk of stroke in women and men. <i>J Nutr</i> . 2014. 144:856-60. doi:10.3945/jn.114.190546.	Date
95 Larsson, SC, Wolk, A, Back, M. Dietary patterns, food groups, and incidence of aortic valve stenosis: A prospective cohort study. <i>Int J Cardiol</i> . 2019. 283:184-188. doi:10.1016/j.ijcard.2018.11.007.	Intervention/Exposure; Comparator
96 Leermakers, ETM, Tielemans, MJ, van den Broek, M, Jaddoe, VVW, Franco, OH, Kiefte-de Jong, JC. Maternal dietary patterns during pregnancy and offspring cardiometabolic health at age 6 years: The generation R study. <i>Clin Nutr</i> . 2017. 36:477-484. doi:10.1016/j.clnu.2015.12.017.	Intervention/Exposure; Population
97 Li, Y, Hruby, A, Bernstein, AM, Ley, SH, Wang, DD, Chiuve, SE, Sampson, L, Rexrode, KM, Rimm, EB, Willett, WC, Hu, FB. Saturated Fats Compared With Unsaturated Fats and Sources of Carbohydrates in Relation to Risk of Coronary Heart Disease: A Prospective Cohort Study. <i>J Am Coll Cardiol</i> . 2015. 66:1538-1548. doi:10.1016/j.jacc.2015.07.055.	Intervention/Exposure
98 Li, Y, Wang, DD, Ley, SH, Vasanti, M, Howard, AG, He, Y, Hu, FB. Time Trends of Dietary and Lifestyle Factors and Their Potential Impact on Diabetes Burden in China. <i>Diabetes Care</i> . 2017. 40:1685-1694. doi:10.2337/dc17-0571.	Outcome
99 Lieffers, JRL, Ekwaru, JP, Ohinmaa, A, Veugelers, PJ. The economic burden of not meeting food recommendations in Canada: The cost of doing nothing. <i>PLoS One</i> . 2018. 13:e0196333. doi:10.1371/journal.pone.0196333.	Outcome

	Citation	Rationale
100	Lin, WT, Lee, CY, Tsai, S, Huang, HL, Wu, PW, Chin, YT, Seal, DW, Chen, T, Chao, YY, Lee, CH. Clustering of Metabolic Risk Components and Associated Lifestyle Factors: A Nationwide Adolescent Study in Taiwan. <i>Nutrients</i> . 2019. 11. doi:10.3390/nu11030584.	Study design
101	Loh, DA, Moy, FM, Zaharan, NL, Jalaludin, MY, Mohamed, Z. Sugar-sweetened beverage intake and its associations with cardiometabolic risks among adolescents. <i>Pediatr Obes</i> . 2017. 12:e1-e5. doi:10.1111/ijpo.12108.	Study design
102	Lowndes, J, Sinnett, S, Pardo, S, Nguyen, VT, Melanson, KJ, Yu, Z, Lowther, BE, Rippe, JM. The effect of normally consumed amounts of sucrose or high fructose corn syrup on lipid profiles, body composition and related parameters in overweight/obese subjects. <i>Nutrients</i> . 2014. 6:1128-44. doi:10.3390/nu6031128.	Intervention/Exposure
103	Lowndes, J, Sinnett, S, Yu, Z, Rippe, J. The effects of fructose-containing sugars on weight, body composition and cardiometabolic risk factors when consumed at up to the 90th percentile population consumption level for fructose. <i>Nutrients</i> . 2014. 6:3153-68. doi:10.3390/nu6083153.	Intervention/Exposure
104	Macedo, RCO, Boeno, FP, Farinha, JB, Ramis, TR, Rodrigues-Krause, J, Vieira, AF, Queiroz, J, Moritz, CEJ, Reischak-Oliveira, A. Acute and residual effects of aerobic exercise on fructose-induced postprandial lipemia on lean male subjects. <i>Eur J Nutr</i> . 2019. 58:2293-2303. doi:10.1007/s00394-018-1780-4.	Intervention/Exposure; Outcome; Study duration
105	Macedo, RCO, Boeno, FP, Farinha, JB, Ramis, TR, Rodrigues-Krause, J, Vieira, AF, Queiroz, J, Moritz, CEJ, Reischak-Oliveira, A. Acute and residual effects of aerobic exercise on fructose-induced postprandial lipemia on lean male subjects. <i>European journal of nutrition</i> . 2018. . doi:10.1007/s00394-018-1780-4.	Intervention/Exposure; Comparator
106	Mager, DR, Iniguez, IR, Gilmour, S, Yap, J. The effect of a low fructose and low glycemic index/load (FRAGILE) dietary intervention on indices of liver function, cardiometabolic risk factors, and body composition in children and adolescents with nonalcoholic fatty liver disease (NAFLD). <i>JPEN J Parenter Enteral Nutr</i> . 2015. 39:73-84. doi:10.1177/0148607113501201.	Health status
107	Maki, KC, Nieman, KM, Schild, AL, Kaden, VN, Lawless, AL, Kelley, KM, Rains, TM. Sugar-sweetened product consumption alters glucose homeostasis compared with dairy product consumption in men and women at risk of type 2 diabetes mellitus. <i>J Nutr</i> . 2015. 145:459-66. doi:10.3945/jn.114.204503.	Intervention/Exposure; Comparator
108	Maki, KC, Phillips, AK. Dietary substitutions for refined carbohydrate that show promise for reducing risk of type 2 diabetes in men and women. <i>Journal of Nutrition</i> . 2015. 145:159S-163S. doi:10.3945/jn.114.195149.	Study design; Intervention/Exposure
109	Mandalazi, E, Drake, I, Wirfält, E, Orho-Melander, M, Sonestedt, E. A high diet quality based on dietary recommendations is not associated with lower incidence of type 2 diabetes in the malmö diet and cancer cohort. <i>International Journal of Molecular Sciences</i> . 2016. 17. doi:10.3390/ijms17060901.	Intervention/Exposure; Outcome

Citation	Rationale
110 Martin, CL, Siega-Riz, AM, Sotres-Alvarez, D, Robinson, WR, Daniels, JL, Perrin, EM, Stuebe, AM. Maternal Dietary Patterns are Associated with Lower Levels of Cardiometabolic Markers during Pregnancy. <i>Paediatr Perinat Epidemiol.</i> 2016. 30:246-55. doi:10.1111/ppe.12279.	Intervention/Exposure
111 Maruyama, C, Nakano, R, Shima, M, Mae, A, Shijo, Y, Nakamura, E, Okabe, Y, Park, S, Kameyama, N, Hirai, S, Nakanishi, M, Uchida, K, Nishiyama, H. Effects of a Japan Diet Intake Program on Metabolic Parameters in Middle-Aged Men. <i>J Atheroscler Thromb.</i> 2017. 24:393-401. doi:10.5551/jat.36780.	Intervention/Exposure
112 Matikainen, N, Soderlund, S, Bjornson, E, Bogl, LH, Pietilainen, KH, Hakkarainen, A, Lundbom, N, Eliasson, B, Rasanen, SM, Rivellese, A, Patti, L, Prinster, A, Riccardi, G, Despres, JP, Almeras, N, Holst, JJ, Deacon, CF, Boren, J, Taskinen, MR. Fructose intervention for 12 weeks does not impair glycemic control or incretin hormone responses during oral glucose or mixed meal tests in obese men. <i>Nutr Metab Cardiovasc Dis.</i> 2017. 27:534-542. doi:10.1016/j.numecd.2017.03.003.	Study design; Intervention/Exposure; Comparator
113 Matthews, LA, Rovio, SP, Jaakkola, JM, Niinikoski, H, Lagstrom, H, Jula, A, Viikari, JSA, Ronnema, T, Simell, O, Raitakari, OT, Pahkala, K. Longitudinal effect of 20-year infancy-onset dietary intervention on food consumption and nutrient intake: the randomized controlled STRIP study. <i>Eur J Clin Nutr.</i> 2019. 73:937-949. doi:10.1038/s41430-018-0350-4.	Outcome
114 Meier, T, Gräfe, K, Senn, F, Sur, P, Stangl, GI, Dawczynski, C, März, W, Kleber, ME, Lorkowski, S. Cardiovascular mortality attributable to dietary risk factors in 51 countries in the WHO European Region from 1990 to 2016: a systematic analysis of the Global Burden of Disease Study. <i>European Journal of Epidemiology.</i> 2019. 34:37-55. doi:10.1007/s10654-018-0473-x.	Study design; Intervention/Exposure
115 Mellendick, K, Shanahan, L, Wideman, L, Calkins, S, Keane, S, Lovelady, C. Diets Rich in Fruits and Vegetables Are Associated with Lower Cardiovascular Disease Risk in Adolescents. <i>Nutrients.</i> 2018. 10. doi:10.3390/nu10020136.	Study design; Outcome
116 Meng, H, Matthan, NR, Benitez, SB, Fried, SK, Lichtenstein, AH. Effect of dietary carbohydrate type on serum lipid profile, adipose tissue macrophage infiltration and inflammatory status, and peripheral macrophage cholesterol efflux. <i>Circulation.</i> 2018. 137.	Publication status
117 Mertens, E, Markey, O, Geleijnse, JM, Givens, DI, Lovegrove, JA. Dietary Patterns in Relation to Cardiovascular Disease Incidence and Risk Markers in a Middle-Aged British Male Population: Data from the Caerphilly Prospective Study. <i>Nutrients.</i> 2017. 9. doi:10.3390/nu9010075.	Intervention/Exposure
118 Mirmiran, P, Yuzbashian, E, Asghari, G, Hosseinpour-Niazi, S, Azizi, F. Consumption of sugar sweetened beverage is associated with incidence of metabolic syndrome in Tehranian children and adolescents. <i>Nutr Metab (Lond).</i> 2015. 12:25. doi:10.1186/s12986-015-0021-6.	Sample size
119 Monge, A, Lajous, M, Ortiz-Panozo, E, Rodríguez, BL, Góngora, JJ, López-Ridaura, R. Western and Modern Mexican dietary patterns are directly associated with incident hypertension in Mexican women: A prospective follow-up study. <i>Nutrition Journal.</i> 2018. 17. doi:10.1186/s12937-018-0332-3.	Study design; Intervention/Exposure; Outcome

Citation	Rationale
<p>120 Moreira, PV, Hyseni, L, Moubarac, JC, Martins, APB, Baraldi, LG, Capewell, S, O'Flaherty, M, Guzman-Castillo, M. Effects of reducing processed culinary ingredients and ultra-processed foods in the Brazilian diet: a cardiovascular modelling study. <i>Public Health Nutr.</i> 2018. 21:181-188. doi:10.1017/s1368980017002063.</p>	Study design; Intervention/Exposure
<p>121 Mousavi, SM, Milajerdi, A, Pouraram, H, Saadatnia, M, Shakeri, F, Keshteli, AH, Tan, SC, Esmailzadeh, A. Adherence to Alternative Healthy Eating Index (AHEI-2010) is not associated with risk of stroke in Iranian adults: a case-control study. <i>Int J Vitam Nutr Res.</i> 2019. 1-8. doi:10.1024/0300-9831/a000603.</p>	Study design; Intervention/Exposure
<p>122 Mustafa, N, Abd Majid, H, Toumpakari, Z, Carroll, HA, Yazid Jalaludin, M, Al Sadat, N, Johnson, L. The Association of Breakfast Frequency and Cardiovascular Disease (CVD) Risk Factors among Adolescents in Malaysia. <i>Nutrients.</i> 2019. 11. doi:10.3390/nu11050973.</p>	Study design; Intervention/Exposure
<p>123 Mytton, OT, Forouhi, NG, Scarborough, P, Lentjes, M, Luben, R, Rayner, M, Khaw, KT, Wareham, NJ, Monsivais, P. Association between intake of less-healthy foods defined by the United Kingdom's nutrient profile model and cardiovascular disease: A population-based cohort study. <i>PLoS Med.</i> 2018. 15:e1002484. doi:10.1371/journal.pmed.1002484.</p>	Intervention/Exposure
<p>124 Nazari, SSH, Mokhayeri, Y, Mansournia, MA, Khodakarim, S, Soori, H. Associations between dietary risk factors and ischemic stroke: a comparison of regression methods using data from the Multi-Ethnic Study of Atherosclerosis. <i>Epidemiol Health.</i> 2018. 40:e2018021. doi:10.4178/epih.e2018021.</p>	Intervention/Exposure
<p>125 Nazeminezhad, R, Tajfard, M, Latiff, LA, Mouhebati, M, Esmaeily, H, Ferns, GA, Ghayour-Mobarhan, M, Rahimi, HR. Dietary intake of patients with angiographically defined coronary artery disease and that of healthy controls in Iran. <i>Eur J Clin Nutr.</i> 2014. 68:109-13. doi:10.1038/ejcn.2013.205.</p>	Study design; Intervention/Exposure
<p>126 Ndanuko, R, Tapsell, L, Charlton, K, Neale, E, Batterham, M. Dietary patterns associated with blood pressure in a clinical sample of overweight adults volunteering for a weight loss trial. <i>Revista espanola de nutricion humana y dietetica.</i> 2016. 20:460-461.</p>	Publication status
<p>127 Nickols-Richardson, SM, Piehowski, KE, Metzgar, CJ, Miller, DL, Preston, AG. Changes in body weight, blood pressure and selected metabolic biomarkers with an energy-restricted diet including twice daily sweet snacks and once daily sugar-free beverage. <i>Nutr Res Pract.</i> 2014. 8:695-704. doi:10.4162/nrp.2014.8.6.695.</p>	Intervention/Exposure; Comparator
<p>128 Nobbs, HM, Yaxley, A, Thomas, J, Delaney, C, Koczwara, B, Luszcz, M, Miller, M. Do dietary patterns in older age influence the development of cancer and cardiovascular disease: A longitudinal study of ageing. <i>Clin Nutr.</i> 2016. 35:528-535. doi:10.1016/j.clnu.2015.04.003.</p>	Intervention/Exposure
<p>129 Nobili, V, Mosca, A, De Vito, R, Raponi, M, Scorletti, E, Byrne, CD. Liver zonation in children with non-alcoholic fatty liver disease: Associations with dietary fructose and uric acid concentrations. <i>Liver International.</i> 2018. 38:1102-1109. doi:10.1111/liv.13661.</p>	Health status

Citation	Rationale
130 Novotny, JA, Baer, DJ, Khoo, C, Gebauer, SK, Charron, CS. Cranberry juice consumption lowers markers of cardiometabolic risk, including blood pressure and circulating C-reactive protein, triglyceride, and glucose concentrations in adults. <i>J Nutr.</i> 2015. 145:1185-93. doi:10.3945/jn.114.203190.	Intervention/Exposure
131 Olofsson, C, Anderstam, B, Bragfors-Helin, AC, Eriksson, M, Qureshi, AR, Lindholm, B, Hilding, A, Wiczowski, W, Orsini, N, Stenvinkel, P, Rajamand Ekberg, N. Effects of acute fructose loading on levels of serum uric acid-a pilot study. <i>Eur J Clin Invest.</i> 2019. 49:e13040. doi:10.1111/eci.13040.	Outcome; Study duration
132 O'Neil, CE, Nicklas, TA, Liu, Y, Berenson, GS. Candy consumption in childhood is not predictive of weight, adiposity measures or cardiovascular risk factors in young adults: the Bogalusa Heart Study. <i>J Hum Nutr Diet.</i> 2015. 28 Suppl 2:59-69. doi:10.1111/jhn.12200.	Sample size
133 Padilla-Camberos, E, Barragan-Alvarez, CP, Diaz-Martinez, NE, Rathod, V, Flores-Fernandez, JM. Effects of Agave fructans (Agave tequilana Weber var. azul) on Body Fat and Serum Lipids in Obesity. <i>Plant Foods Hum Nutr.</i> 2018. 73:34-39. doi:10.1007/s11130-018-0654-5.	Intervention/Exposure
134 Papoutsou, S, Briassoulis, G, Hadjigeorgiou, C, Savva, SC, Solea, T, Hebestreit, A, Pala, V, Sieri, S, Kourides, Y, Kafatos, A, Tornaritis, M. The combination of daily breakfast consumption and optimal breakfast choices in childhood is an important public health message. <i>Int J Food Sci Nutr.</i> 2014. 65:273-9. doi:10.3109/09637486.2013.854750.	Intervention/Exposure
135 Parnell, JA, Klancic, T, Reimer, RA. Oligofructose decreases serum lipopolysaccharide and plasminogen activator inhibitor-1 in adults with overweight/obesity. <i>Obesity (Silver Spring).</i> 2017. 25:510-513. doi:10.1002/oby.21763.	Intervention/Exposure; Outcome
136 Pase, MP, Grima, N, Cockerell, R, Pipingas, A. Habitual intake of fruit juice predicts central blood pressure. <i>Appetite.</i> 2015. 84:68-72. doi:10.1016/j.appet.2014.09.019.	Study design; Intervention/Exposure
137 Patel, L, Alicandro, G, La Vecchia, C. Low-Calorie Beverage Consumption, Diet Quality and Cardiometabolic Risk Factors in British Adults. <i>Nutrients.</i> 2018. 10. doi:10.3390/nu10091261.	Study design; Intervention/Exposure
138 Payab, M, Kelishadi, R, Qorbani, M, Motlagh, ME, Ranjbar, SH, Ardalan, G, Zahedi, H, Chinian, M, Asayesh, H, Larijani, B, Heshmat, R. Association of junk food consumption with high blood pressure and obesity in Iranian children and adolescents: the CASPIAN-IV Study. <i>J Pediatr (Rio J).</i> 2015. 91:196-205. doi:10.1016/j.jped.2014.07.006.	Study design; Intervention/Exposure
139 Perez-Heras, A, Ros, E, Serra-Mir, M, Vinyas, C, Mestre, C, Alegret, M, Laguna, JC. Intake of simple sugar-S from sweetened beverages is associated with cancer incidence and mortality in the predimed study cohort. <i>Revista espanola de nutricion humana y dietetica.</i> 2016. 20:425-426.	Publication status
140 Price, CA, Argueta, DA, Medici, V, Bremer, AA, Lee, V, Nunez, MV, Chen, GX, Keim, NL, Havel, PJ, Stanhope, KL, DiPatrizio, NV. Plasma fatty acid ethanolamides are associated with postprandial triglycerides, ApoCIII, and ApoE in humans consuming a high-fructose corn syrup-sweetened beverage. <i>Am J Physiol Endocrinol Metab.</i> 2018. 315:E141-e149. doi:10.1152/ajpendo.00406.2017.	Outcome; Study duration

Citation	Rationale
141 Raatz, SK, Johnson, LK, Picklo, MJ. Consumption of Honey, Sucrose, and High-Fructose Corn Syrup Produces Similar Metabolic Effects in Glucose-Tolerant and -Intolerant Individuals. <i>J Nutr</i> . 2015. 145:2265-72. doi:10.3945/jn.115.218016.	Intervention/Exposure; Comparator; Study duration
142 Ramírez-Vélez, R, Ojeda, ML, Tordecilla, MA, Peña, JC, Meneses, JF. Regular consumption of sugar-sweetened beverages increases the lipid-metabolic profile and adiposity among university students from Colombia. <i>Revista Colombiana de Cardiología</i> . 2016. 23:11-18. doi:10.1016/j.rccar.2015.04.006.	Study design
143 Rasad, H, Entezari, MH, Ghadiri, E, Mahaki, B, Pahlavani, N. The effect of honey consumption compared with sucrose on lipid profile in young healthy subjects (randomized clinical trial). <i>Clin Nutr ESPEN</i> . 2018. 26:8-12. doi:10.1016/j.clnesp.2018.04.016.	Intervention/Exposure
144 Rashid, MR, Nor Aripin, KN, Syed Mohideen, FB, Baharom, N, Omar, K, Md Taujuddin, NMS, Mohd Yusof, HH, Addnan, FH. The Effect of Kelulut Honey on Fasting Blood Glucose and Metabolic Parameters in Patients with Impaired Fasting Glucose. <i>J Nutr Metab</i> . 2019. 2019:3176018. doi:10.1155/2019/3176018.	Intervention/Exposure
145 Rauber, F, Campagnolo, PD, Hoffman, DJ, Vitolo, MR. Consumption of ultra-processed food products and its effects on children's lipid profiles: a longitudinal study. <i>Nutr Metab Cardiovasc Dis</i> . 2015. 25:116-22. doi:10.1016/j.numecd.2014.08.001.	Intervention/Exposure
146 Rebholz, CM, Young, BA, Katz, R, Tucker, KL, Carithers, TC, Norwood, AF, Correa, A. Patterns of Beverages Consumed and Risk of Incident Kidney Disease. <i>Clin J Am Soc Nephrol</i> . 2019. 14:49-56. doi:10.2215/cjn.06380518.	Outcome
147 Rezende, LF, Azeredo, CM, Canella, DS, Luiz Odo, C, Levy, RB, Eluf-Neto, J. Coronary heart disease mortality, cardiovascular disease mortality and all-cause mortality attributable to dietary intake over 20years in Brazil. <i>Int J Cardiol</i> . 2016. 217:64-8. doi:10.1016/j.ijcard.2016.04.176.	Intervention/Exposure
148 Roberge, JB, Van Hulst, A, Barnett, TA, Drapeau, V, Benedetti, A, Tremblay, A, Henderson, M. Lifestyle Habits, Dietary Factors, and the Metabolically Unhealthy Obese Phenotype in Youth. <i>Journal of Pediatrics</i> . 2019. 204:46-52.e1. doi:10.1016/j.jpeds.2018.08.063.	Outcome
149 Rodriguez-Cano, A, Mier-Cabrera, J, Balas-Nakash, M, Munoz-Manrique, C, Legorreta-Legorreta, J, Perichart-Perera, O. Dietary changes associated with improvement of metabolic syndrome components in postmenopausal women receiving two different nutrition interventions. <i>Menopause</i> . 2015. 22:758-64. doi:10.1097/gme.0000000000000400.	Intervention/Exposure; Outcome
150 Rompay, MIV, McKeown, NM, Goodman, E, Eliasziw, M, Chomitz, VR, Gordon, CM, Economos, CD, Sacheck, JM. Sugar-Sweetened Beverage Intake Is Positively Associated with Baseline Triglyceride Concentrations, and Changes in Intake Are Inversely Associated with Changes in HDL Cholesterol over 12 Months in a Multi-Ethnic Sample of Children 1-3. <i>Journal of Nutrition</i> . 2015. 145:2389-2395. doi:10.3945/jn.115.212662.	Sample size
151 Ross, SM. Cardiovascular disease mortality: the deleterious effects of excess dietary sugar intake. <i>Holist Nurs Pract</i> . 2015. 29:53-7. doi:10.1097/hnp.0000000000000066.	Study design; Publication status

Citation	Rationale
152 Ryman, TK, Boyer, BB, Hopkins, S, Philip, J, Beresford, SA, Thompson, B, Heagerty, PJ, Pomeroy, JJ, Thummel, KE, Austin, MA. Associations between diet and cardiometabolic risk among Yup'ik Alaska Native people using food frequency questionnaire dietary patterns. <i>Nutr Metab Cardiovasc Dis.</i> 2015. 25:1140-5. doi:10.1016/j.numecd.2015.08.003.	Study design; Intervention/Exposure
153 Sakurai, K, Fujiwara, N, Takahashi, K, Nakayashiro, M. Excessive soft drink may induce pulmonary hypertension via thiamine deficiency. <i>Pediatr Int.</i> 2019. 61:823-824. doi:10.1111/ped.13913.	Study design; Intervention/Exposure
154 Sanjeevi, N, Lipsky, LM, Nansel, TR. Cardiovascular Biomarkers in Association with Dietary Intake in a Longitudinal Study of Youth with Type 1 Diabetes. <i>Nutrients.</i> 2018. 10. doi:10.3390/nu10101552.	Health status
155 Santiago, S, Zazpe, I, Gea, A, de la Rosa, PA, Ruiz-Canela, M, Martinez-Gonzalez, MA. Healthy-eating attitudes and the incidence of cardiovascular disease: the SUN cohort. <i>Int J Food Sci Nutr.</i> 2017. 68:595-604. doi:10.1080/09637486.2016.1265100.	Intervention/Exposure
156 Saritas, A, Dikici, S, Gunes, H. Adverse effects of energy drinks. <i>The American journal of emergency medicine.</i> 2015. 33:461-462. doi:10.1016/j.ajem.2014.11.054.	Intervention/Exposure; Publication status
157 Sayon-Orea, C, Martinez-Gonzalez, MA, Gea, A, Alonso, A, Pimenta, AM, Bes-Rastrollo, M. Baseline consumption and changes in sugar-sweetened beverage consumption and the incidence of hypertension: The SUN project. <i>Clin Nutr.</i> 2015. 34:1133-40. doi:10.1016/j.clnu.2014.11.010.	Study design; Outcome
158 Schumacher, TL, Burrows, TL, Cliff, DP, Jones, RA, Okely, AD, Baur, LA, Morgan, PJ, Callister, R, Boggess, MM, Collins, CE. Dietary Intake Is Related to Multifactor Cardiovascular Risk Score in Obese Boys. <i>Healthcare (Basel).</i> 2014. 2:282-98. doi:10.3390/healthcare2030282.	Outcome
159 Schwarz, JM, Noworolski, SM, Erkin-Cakmak, A, Korn, NJ, Wen, MJ, Tai, VW, Jones, GM, Palii, SP, Velasco-Alin, M, Pan, K, Patterson, BW, Gugliucci, A, Lustig, RH, Mulligan, K. Effects of Dietary Fructose Restriction on Liver Fat, De Novo Lipogenesis, and Insulin Kinetics in Children With Obesity. <i>Gastroenterology.</i> 2017. 153:743-752. doi:10.1053/j.gastro.2017.05.043.	Intervention/Exposure; Outcome; Study duration
160 Schwingshackl, L, Knüppel, S, Michels, N, Schwedhelm, C, Hoffmann, G, Iqbal, K, De Henauw, S, Boeing, H, Devleeschauwer, B. Intake of 12 food groups and disability-adjusted life years from coronary heart disease, stroke, type 2 diabetes, and colorectal cancer in 16 European countries. <i>European Journal of Epidemiology.</i> 2019. 34:765-775. doi:10.1007/s10654-019-00523-4.	Intervention/Exposure; Outcome
161 Seferidi, P, Millett, C, Lavery, AA. Sweetened beverage intake in association to energy and sugar consumption and cardiometabolic markers in children. <i>Pediatr Obes.</i> 2018. 13:195-203. doi:10.1111/ijpo.12194.	Study design
162 Setayeshgar, S, Ekwaru, JP, Maximova, K, Majumdar, SR, Storey, KE, McGavock, J, Veugelers, PJ. Dietary intake and prospective changes in cardiometabolic risk factors in children and youth. <i>Appl Physiol Nutr Metab.</i> 2017. 42:39-45. doi:10.1139/apnm-2016-0215.	Sample size

Citation	Rationale
163 Setayeshgar, S, Whiting, SJ, Pahwa, P, Vatanparast, H. Predicted 10-year risk of cardiovascular disease among Canadian adults using modified Framingham Risk Score in association with dietary intake. <i>Appl Physiol Nutr Metab.</i> 2015. 40:1068-74. doi:10.1139/apnm-2015-0074.	Study design
164 Shams, N, Niaz, F, Motwani, R, Shaikh, Z, Saleem, F. Obesity and hypertension in female medical students; frequency and risk factors. <i>Journal of the Liaquat University of Medical and Health Sciences.</i> 2015. 14:26-32.	Study design; Intervention/Exposure
165 Sharafi, M, Duffy, VB, Miller, RJ, Winchester, SB, Huedo-Medina, TB, Sullivan, MC. Dietary behaviors of adults born prematurely may explain future risk for cardiovascular disease. <i>Appetite.</i> 2016. 99:157-167. doi:10.1016/j.appet.2016.01.007.	Study design; Intervention/Exposure; Outcome
166 Shehab, A, Elkilany, GEN, Singh, RB, Hristova, K, Chaves, H, Cornélissen, G, Otsuka, K. Coronary risk factors in South West Asia. <i>World Heart Journal.</i> 2015. 7:21-29.	Study design; Other; Not primary research (review)
167 Shi, Z, Ruel, G, Dal Grande, E, Pilkington, R, Taylor, AW. Soft drink consumption and multimorbidity among adults. <i>Clin Nutr ESPEN.</i> 2015. 10:e71-e76. doi:10.1016/j.clnesp.2015.01.001.	Study design
168 Shikany, JM, Judd, SE, Letter, AJ, Ard, JD, Newby, PK. Dietary contributors to glycemic load in the REasons for Geographic and Racial Differences in Stroke study. <i>Nutrition.</i> 2015. 31:708-15. doi:10.1016/j.nut.2014.11.017.	Intervention/Exposure; Outcome
169 Shikany, JM, Safford, MM, Bryan, J, Newby, PK, Richman, JS, Durant, RW, Brown, TM, Judd, SE. Dietary Patterns and Mediterranean Diet Score and Hazard of Recurrent Coronary Heart Disease Events and All-Cause Mortality in the REGARDS Study. <i>J Am Heart Assoc.</i> 2018. 7. doi:10.1161/jaha.117.008078.	Intervention/Exposure
170 Shikany, JM, Safford, MM, Newby, PK, Durant, RW, Brown, TM, Judd, SE. Southern Dietary Pattern is Associated With Hazard of Acute Coronary Heart Disease in the Reasons for Geographic and Racial Differences in Stroke (REGARDS) Study. <i>Circulation.</i> 2015. 132:804-14. doi:10.1161/circulationaha.114.014421.	Intervention/Exposure
171 Shim, JS, Kang, NH, Lee, JS, Kim, KN, Chung, HK, Chung, HR, Kim, HJ, Ahn, YS, Chang, MJ. Socioeconomic burden of sugar-sweetened beverages consumption in Korea. <i>Nutr Res Pract.</i> 2019. 13:134-140. doi:10.4162/nrp.2019.13.2.134.	Study design; Outcome
172 Shin, Y, Lee, S, Kim, Y. Sweet Preference Associated with the Risk of Hypercholesterolemia Among Middle-Aged Women in Korea. <i>J Atheroscler Thromb.</i> 2018. 25:1215-1221. doi:10.5551/jat.43000.	Intervention/Exposure
173 Siervo, M, Montagnese, C, Mathers, JC, Soroka, KR, Stephan, BC, Wells, JC. Sugar consumption and global prevalence of obesity and hypertension: an ecological analysis. <i>Public Health Nutr.</i> 2014. 17:587-96. doi:10.1017/s1368980013000141.	Study design
174 Simpson, EJ, Mendis, B, Macdonald, IA. Orange juice consumption and its effect on blood lipid profile and indices of the metabolic syndrome; a randomised, controlled trial in an at-risk population. <i>Food Funct.</i> 2016. 7:1884-91. doi:10.1039/c6fo00039h.	Intervention/Exposure

Citation	Rationale
175 Sonestedt, E, Hellstrand, S, Drake, I, Schulz, CA, Ericson, U, Hlebowicz, J, Persson, MM, Gullberg, B, Hedblad, B, Engstrom, G, Orho-Melander, M. Diet Quality and Change in Blood Lipids during 16 Years of Follow-up and Their Interaction with Genetic Risk for Dyslipidemia. <i>Nutrients</i> . 2016. 8. doi:10.3390/nu8050274.	Study design; Intervention/Exposure; Outcome
176 Soto, R, Guilloty, N, Anzalota, L, Rosario, Z, Cordero, JF, Palacios, C. Association between maternal diet factors and hemoglobin levels, glucose tolerance, blood pressure and gestational age in a Hispanic population. <i>Arch Latinoam Nutr</i> . 2015. 65:86-96.	Study design; Intervention/Exposure; Outcome
177 Sotos-Prieto, M, Mattei, J, Cook, NR, Hu, FB, Willett, WC, Chiuve, SE, Rimm, EB, Sesso, HD. Association Between a 20-Year Cardiovascular Disease Risk Score Based on Modifiable Lifestyles and Total and Cause-Specific Mortality Among US Men and Women. <i>J Am Heart Assoc</i> . 2018. 7:e010052. doi:10.1161/jaha.118.010052.	Intervention/Exposure
178 Srour, B, Fezeu, LK, Kesse-Guyot, E, Alles, B, Mejean, C, Andrianasolo, RM, Chazelas, E, Deschasaux, M, Hercberg, S, Galan, P, Monteiro, CA, Julia, C, Touvier, M. Ultra-processed food intake and risk of cardiovascular disease: prospective cohort study (NutriNet-Sante). <i>Bmj</i> . 2019. 365:l1451. doi:10.1136/bmj.l1451.	Intervention/Exposure
179 Srour, B, Fezeu, LK, Kesse-Guyot, E, Allès, B, Méjean, C, Andrianasolo, RM, Chazelas, E, Deschasaux, M, Hercberg, S, Galan, P, Monteiro, CA, Julia, C, Touvier, M. Ultra-processed food intake and risk of cardiovascular disease: Prospective cohort study (NutriNet-Santé). <i>BMJ (Online)</i> . 2019. 365. doi:10.1136/bmj.l1451.	Intervention/Exposure
180 Stańczyk, M, Tomczyk, D, Grzelak, M, Topolska-Kusiak, J, Raczyński, P, Tkaczyk, M. Metabolic profile and dietary fructose intake in prehypertensive and hypertensive adolescents. <i>Pediatrica i Medycyna Rodzinna</i> . 2016. 12:428-435. doi:10.15557/PiMR.2016.0043.	Study design; Intervention/Exposure
181 Stanhope, KL, Medici, V, Bremer, AA, Lee, V, Lam, HD, Nunez, MV, Chen, GX, Keim, NL, Havel, PJ. A dose-response study of consuming high-fructose corn syrup-sweetened beverages on lipid/lipoprotein risk factors for cardiovascular disease in young adults. <i>Am J Clin Nutr</i> . 2015. 101:1144-54. doi:10.3945/ajcn.114.100461.	Study duration
182 Stewart, RA, Wallentin, L, Benatar, J, Danchin, N, Hagstrom, E, Held, C, Husted, S, Lonn, E, Stebbins, A, Chiswell, K, Vedin, O, Watson, D, White, HD. Dietary patterns and the risk of major adverse cardiovascular events in a global study of high-risk patients with stable coronary heart disease. <i>Eur Heart J</i> . 2016. 37:1993-2001. doi:10.1093/eurheartj/ehw125.	Intervention/Exposure
183 Streppel, MT, Sluik, D, van Yperen, JF, Geelen, A, Hofman, A, Franco, OH, Witteman, JC, Feskens, EJ. Nutrient-rich foods, cardiovascular diseases and all-cause mortality: the Rotterdam study. <i>Eur J Clin Nutr</i> . 2014. 68:741-7. doi:10.1038/ejcn.2014.35.	Intervention/Exposure
184 Svendsen, K, Henriksen, HB, Ostengen, B, Jacobs, DR, Jr, Telle-Hansen, VH, Carlsen, MH, Retterstol, K. Evaluation of a short Food Frequency Questionnaire to assess cardiovascular disease-related diet and lifestyle factors. <i>Food Nutr Res</i> . 2018. 62. doi:10.29219/fnr.v62.1370.	Study design; Intervention/Exposure; Outcome
185 Tasevska, N, Park, Y, Jiao, L, Hollenbeck, A, Subar, AF, Potischman, N. Sugars and risk of mortality in the NIH-AARP Diet and Health Study. <i>Am J Clin Nutr</i> . 2014. 99:1077-88. doi:10.3945/ajcn.113.069369.	Date

Citation	Rationale
<p>186 Tasevska, N, Pettinger, M, Kipnis, V, Midthune, D, Tinker, LF, Potischman, N, Neuhouser, ML, Beasley, JM, Van Horn, L, Howard, BV, Liu, S, Manson, JE, Shikany, JM, Thomson, CA, Prentice, RL. Associations of Biomarker-Calibrated Intake of Total Sugars With the Risk of Type 2 Diabetes and Cardiovascular Disease in the Women's Health Initiative Observational Study. <i>Am J Epidemiol</i>. 2018. 187:2126-2135. doi:10.1093/aje/kwy115.</p>	Intervention/Exposure
<p>187 Taskinen, MR, Soderlund, S, Bogl, LH, Hakkarainen, A, Matikainen, N, Pietilainen, KH, Rasanen, S, Lundbom, N, Bjornson, E, Eliasson, B, Mancina, RM, Romeo, S, Almeras, N, Pepa, GD, Vetrani, C, Prinster, A, Annuzzi, G, Rivellese, A, Despres, JP, Boren, J. Adverse effects of fructose on cardiometabolic risk factors and hepatic lipid metabolism in subjects with abdominal obesity. <i>J Intern Med</i>. 2017. 282:187-201. doi:10.1111/joim.12632.</p>	Study design; Intervention/Exposure
<p>188 Telford, RD, Cunningham, RB, Waring, P, Telford, RM, Potter, JM, Hickman, PE, Abhayaratna, WP. Sensitivity of blood lipids to changes in adiposity, exercise, and diet in children. <i>Med Sci Sports Exerc</i>. 2015. 47:974-82. doi:10.1249/mss.0000000000000493.</p>	Intervention/Exposure
<p>189 Thornley, S, Marshall, RJ, Bach, K, Koopu, P, Reynolds, G, Sundborn, G, Ei, WL. Sugar, dental caries and the incidence of acute rheumatic fever: a cohort study of Maori and Pacific children. <i>J Epidemiol Community Health</i>. 2017. 71:364-370. doi:10.1136/jech-2016-208219.</p>	Intervention/Exposure; Outcome
<p>190 Ulven, SM, Leder, L, Elind, E, Ottestad, I, Christensen, JJ, Telle-Hansen, VH, Skjetne, AJ, Raael, E, Sheikh, NA, Holck, M, Torvik, K, Lamglait, A, Thyholt, K, Byfuglien, MG, Granlund, L, Andersen, LF, Holven, KB. Exchanging a few commercial, regularly consumed food items with improved fat quality reduces total cholesterol and LDL-cholesterol: a double-blind, randomised controlled trial. <i>Br J Nutr</i>. 2016. 116:1383-1393. doi:10.1017/s0007114516003445.</p>	INCLUDE: CVD (2y and older); Intervention/Exposure
<p>191 Umpleby, M, Shojaee-Moradie, F, Fielding, B, Li, X, Isherwood, C, Jackson, N, Wilinska, G, Hovorka, R, Bell, J, Thomas, EL, etal, . A diet low in sugar reduces the production of atherogenic lipoproteins in men with high liver fat. <i>Atherosclerosis</i>.. 2015. 241:e46.</p>	Publication status
<p>192 Varsamis, P, Formosa, MF, Larsen, RN, Reddy-Luthmoodoo, M, Jennings, GL, Cohen, ND, Grace, M, Hawley, JA, Devlin, BL, Owen, N, etal, . Between-meal sucrose-sweetened beverage consumption impairs glycaemia and lipid metabolism during prolonged sitting: a randomized controlled trial. <i>Clinical nutrition (edinburgh, scotland)</i>. 2018. doi:10.1016/j.clnu.2018.08.021.</p>	Outcome; Study duration
<p>193 Viester, L, Verhagen, Ealm, Bongers, PM, van der Beek, AJ. Effectiveness of a Worksite Intervention for Male Construction Workers on Dietary and Physical Activity Behaviors, Body Mass Index, and Health Outcomes: Results of a Randomized Controlled Trial. <i>Am J Health Promot</i>. 2018. 32:795-805. doi:10.1177/0890117117694450.</p>	Intervention/Exposure; Outcome
<p>194 Vitale, M, Masulli, M, Cocozza, S, Anichini, R, Babini, AC, Boemi, M, Bonora, E, Buzzetti, R, Carpinteri, R, Caselli, C, Ceccarelli, E, Cignarelli, M, Citro, G, Clemente, G, Consoli, A, Corsi, L, De Gregorio, A, Di Bartolo, P, Di Cianni, G, Fontana, L, Garofolo, M, Giorda, CB, Giordano, C, Grioni, S, Iovine, C, Longhitano, S, Mancastroppa, G, Mazzucchelli, C, Montani, V, Mori, M, Perriello, G, Rinaldi, ME, Ruffo, MC, Salvi, L, Sartore, G, Scaranna, C, Tonutti, L, Zamboni, C, Zogheri, A, Krogh, V, Cappellini, F, Signorini, S, Riccardi, G, Vaccaro, O. Sex differences in food choices, adherence to dietary recommendations and plasma lipid profile in type 2 diabetes - The TOSCA.IT study. <i>Nutr Metab Cardiovasc Dis</i>. 2016. 26:879-85. doi:10.1016/j.numecd.2016.04.006.</p>	Health status

Citation	Rationale
195 Voortman, T, Kiefte-de Jong, JC, Ikram, MA, Stricker, BH, van Rooij, FJA, Lahousse, L, Tiemeier, H, Brusselle, GG, Franco, OH, Schoufour, JD. Adherence to the 2015 Dutch dietary guidelines and risk of non-communicable diseases and mortality in the Rotterdam Study. <i>Eur J Epidemiol.</i> 2017. 32:993-1005. doi:10.1007/s10654-017-0295-2.	Intervention/Exposure
196 Vorster, HH, Kruger, A, Wentzel-Viljoen, E, Kruger, HS, Margetts, BM. Added sugar intake in South Africa: findings from the Adult Prospective Urban and Rural Epidemiology cohort study. <i>Am J Clin Nutr.</i> 2014. 99:1479-86. doi:10.3945/ajcn.113.069005.	Outcome; Country
197 Vyas, A, Rubenstein, L, Robinson, J, Seguin, RA, Vitolins, MZ, Kazlauskaitė, R, Shikany, JM, Johnson, KC, Snetselaar, L, Wallace, R. Diet drink consumption and the risk of cardiovascular events: a report from the Women's Health Initiative. <i>J Gen Intern Med.</i> 2015. 30:462-8. doi:10.1007/s11606-014-3098-0.	Intervention/Exposure
198 Warfa, K, Drake, I, Wallström, P, Engström, G, Sonestedt, E. Association between sucrose intake and acute coronary event risk and effect modification by lifestyle factors: Malmö Diet and Cancer Cohort Study. <i>British Journal of Nutrition.</i> 2016. 116:1611-1620. doi:10.1017/S0007114516003561.	Other; Duplicate of Ref 8852
199 Whitfield, P, Parry-Strong, A, Walsh, E, Weatherall, M, Krebs, JD. The effect of a cinnamon-, chromium- and magnesium-formulated honey on glycaemic control, weight loss and lipid parameters in type 2 diabetes: an open-label cross-over randomised controlled trial. <i>Eur J Nutr.</i> 2016. 55:1123-31. doi:10.1007/s00394-015-0926-x.	Intervention/Exposure; Health status
200 Williams, EJ, Baines, KJ, Berthon, BS, Wood, LG. Effects of an Encapsulated Fruit and Vegetable Juice Concentrate on Obesity-Induced Systemic Inflammation: A Randomised Controlled Trial. <i>Nutrients.</i> 2017. 9. doi:10.3390/nu9020116.	Intervention/Exposure
201 Winkvist, A, Klingberg, S, Nilsson, LM, Wennberg, M, Renstrom, F, Hallmans, G, Boman, K, Johansson, I. Longitudinal 10-year changes in dietary intake and associations with cardio-metabolic risk factors in the Northern Sweden Health and Disease Study. <i>Nutr J.</i> 2017. 16:20. doi:10.1186/s12937-017-0241-x.	Study design; Outcome
202 Xu, X, Byles, J, Shi, Z, McElduff, P, Hall, J. Dietary pattern transitions, and the associations with BMI, waist circumference, weight and hypertension in a 7-year follow-up among the older Chinese population: a longitudinal study. <i>BMC Public Health.</i> 2016. 16:743. doi:10.1186/s12889-016-3425-y.	Intervention/Exposure
203 Yang, H, Kim, H, Kim, JM, Chung, HW, Chang, N. Associations of dietary intake and metabolic syndrome risk parameters in Vietnamese female marriage immigrants in South Korea: The KoGES follow-up study. <i>Nutr Res Pract.</i> 2016. 10:313-20. doi:10.4162/nrp.2016.10.3.313.	Study design; Intervention/Exposure; Outcome
204 Yang, Q, Zhang, Z, Gregg, EW, Flanders, WD, Merritt, R, Hu, FB. Added sugar intake and cardiovascular diseases mortality among US adults. <i>JAMA Intern Med.</i> 2014. 174:516-24. doi:10.1001/jamainternmed.2013.13563.	Date
205 Yau, AM, McLaughlin, J, Gilmore, W, Maughan, RJ, Evans, GH. The Acute Effects of Simple Sugar Ingestion on Appetite, Gut-Derived Hormone Response, and Metabolic Markers in Men. <i>Nutrients.</i> 2017. 9. doi:10.3390/nu9020135.	Outcome; Study duration

Citation	Rationale
206 Zheng, Y, Li, Y, Huang, T, Cheng, HL, Campos, H, Qi, L. Sugar-sweetened beverage intake, chromosome 9p21 variants, and risk of myocardial infarction in Hispanics. <i>Am J Clin Nutr.</i> 2016. 103:1179-84. doi:10.3945/ajcn.115.107177.	Study design; Outcome
207 Zhou, L, Feng, Y, Yang, Y, Zhao, X, Fan, Y, Rong, J, Liu, D, Zhao, L, Yu, Y. Diet behaviours and hypertension in US adults: the National Health and Nutrition Examination Survey 2013-2014. <i>J Hypertens.</i> 2019. 37:1230-1238. doi:10.1097/hjh.0000000000002037.	Study design; Intervention/Exposure
208 Zoellner, J, Connell, C, Madson, MB, Thomson, JL, Landry, AS, Fontenot Molaison, E, Blakely Reed, V, Yadrick, K. HUB city steps: a 6-month lifestyle intervention improves blood pressure among a primarily African-American community. <i>J Acad Nutr Diet.</i> 2014. 114:603-12. doi:10.1016/j.jand.2013.11.020.	Intervention/Exposure