# 2015 Dietary Guidelines Advisory Committee:

# Systematic Reviews of the Cross-Cutting Topics of Public Health Importance Subcommittee

USDA's Nutrition Evidence Library supported the 2015 Dietary Guidelines Advisory Committee as it conducted systematic reviews on diet and health. This document includes archives from www.NEL.gov of the complete evidence portfolios for all NEL systematic reviews conducted by the Cross-Cutting Topics of Public Health Importance Subcommittee. The *Scientific Report of the 2015 Dietary Guidelines Advisory Committee* summarizes these systematic review findings and provides interpretations and implications related to these reviews.

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# CHAPTER 1. SUBCOMMITTEE OVERVIEW

## OVERVIEW

The *Dietary Guidelines for Americans, 2010* included guidance on sodium, saturated fat, and added sugars, and the 2015 Dietary Guidelines Advisory Committee determined that a reexamination of the evidence on these topics was necessary to evaluate whether revisions to the guidance were warranted. These topics were considered to be of public health importance because each has been associated with negative health outcomes when over-consumed. As the Committee considered it essential to address these topics across two or more Subcommittees, Working Groups were formed with representatives from the relevant Subcommittees to ensure that the topics were thoroughly addressed in a coordinated way. Additionally, the Committee acknowledged that a potential unintended consequence of a recommendation on added sugars might be that consumers and manufacturers replace added sugars with low-calorie sweeteners. As a result, the Committee also examined evidence on low-calorie sweeteners to inform statements on this topic. The updated findings in this chapter will help inform recommendations on these topics for the *2015 Dietary Guidelines for Americans*.

Although sodium, saturated fat, and added sugars are receiving particular focus here, it is important to consider these aspects of the diet in the context of a healthy dietary pattern. A healthy dietary pattern has little room for sodium, saturated fat, and added sugars. That said, these components of the diet are modifiable, and strategies at various levels of the socio-ecologic model, ranging from policy to consumer education, can promote shifts in intake to support healthy dietary patterns.

For additional information, see: ***Scientific Report of the 2015 Dietary Guidelines Advisory Committee, Part D. Chapter 6: Cross-Cutting Topics of Public Health Importance***. Information in the report was vetted by the full committee and presented at public meetings; however, more detailed supporting information on each specific systematic review is available on the NEL website. Below are links to the questions answered using a NEL systematic review approach.

For 2015 Dietary Guidelines Advisory Subcommittee work structure and member organization, see ***Scientific Report of the 2015 Dietary Guidelines Advisory Committee Appendix E-9.***

For 2015 Dietary Guidelines Advisory Committee and support staff membership and acknowledgments lists, see: ***Membership*** and ***Appendix E-10: Dietary Guidelines Advisory Committee Report Acknowledgments.***

## NEL SYSTEMATIC REVIEW QUESTIONS

### Sodium

- What is the relationship between sodium intake and blood pressure in children?
- What is the relationship between sodium intake and cardiovascular disease?

### Added Sugars

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



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# CHAPTER 2. SODIUM – BLOOD PRESSURE IN CHILDREN

## WHAT IS THE RELATIONSHIP BETWEEN SODIUM INTAKE AND BLOOD PRESSURE IN CHILDREN FROM TWO TO 18 YEARS OF AGE?

## TECHNICAL ABSTRACT


### Background

The goal of this systematic review was to determine whether sodium intake is associated with blood pressure in children from two to 18 years. In order to answer this question, the 2015 Dietary Guidelines Advisory Committee (DGAC) updated a systematic review done on this topic by the 2010 DGAC.

### Conclusion statement

The 2015 DGAC concurs with the 2010 DGAC that "a moderate body of evidence has documented that as sodium intake decreases, so does blood pressure in children, birth to age 18 years."

2015 DGAC Grade: Moderate

### Methods

To update the 2010 DGAC systematic review on this topic, literature searches were conducted using PubMed, Embase, Navigator (BIOSIS, CAB Abstracts and Food Science and Technology Abstracts) and Cochrane databases to identify studies that evaluated the association between sodium and blood pressure. Studies that met the following criteria were included in the review: randomized controlled trials (RCTs), non-randomized controlled trials, or prospective cohort studies; human subjects aged two years to 18 years who were healthy or at elevated chronic disease risk; subjects from countries with high or very high human development (2012 Human Development Index); and published in English in peer-reviewed journals. The date range was from January 2009 to January 2014, as the 2010 DGAC review include studies published between January 1970 and May 2009. The intervention or exposure was sodium intake, and the outcome was blood pressure.

Data from each included article were extracted, and risk of bias was assessed. The evidence was qualitatively synthesized, a conclusion statement was developed and the strength of the evidence (grade) was assessed using pre-established criteria including evaluation of the quality and risk of bias, quantity, consistency, magnitude of effect and generalizability of available evidence. The 2015 DGAC then considered the studies published since 2010 on sodium and blood pressure in children, and determined whether the 2010 DGAC Conclusion Statement or Grade needed to be modified.

### Findings

- The 2010 DGAC conducted a systematic review to examine the relationship between sodium intake and blood pressure in children from birth to age 18 years, examining studies published from January 1970 to May 2009. That systematic review included 19 articles from 15 intervention studies and four prospective cohort studies
- The 2015 DGAC updated this systematic review and identified two additional articles published since May 2009, including one RCT and one prospective cohort study
- The 2015 DGAC considered the evidence reviewed by the 2010 DGAC related to dietary sodium intake and blood pressure in children, and determined that, based on the two new studies identified in the updated search, changes were not warranted to the conclusion statement or grade. In aggregate, the data reviewed by the 2010




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DGAC indicated that sodium reduction modestly lowers BP in infants and children. Neither of the two studies identified in the update found a relationship between dietary sodium intake and blood pressure in healthy, normotensive children.

### Limitations

The ability to draw strong conclusions was limited by the following issues:

- A lack of rigorous intervention studies in children and adolescents, particularly controlled feeding studies that measure blood pressure multiple times over several days to account for variability in blood pressure and obtain measures of 24-hour urinary sodium excretion to determine levels of sodium before, during and after the intervention, rather than relying on estimates drawn from dietary intake assessment
- Studies are generally conducted in health children and adolescents with normal blood pressure, who are not likely to experience a benefit from sodium reduction.

## FULL REVIEW

## Conclusion statement

The 2015 DGAC concurs with the 2010 DGAC that “a moderate body of evidence has documented that as sodium intake decreases, so does blood pressure in children, birth to age 18 years.”

## Grade

Moderate

## Key findings

1. The 2010 DGAC conducted a systematic review to examine the relationship between sodium intake and blood pressure in children from birth to age 18 years, examining studies published from January 1970 to May 2009. That systematic review included 19 articles from 15 intervention studies and four prospective cohort studies
2. The 2015 DGAC updated this systematic review and identified two additional articles published since May 2009, including one RCT and one prospective cohort study
3. The 2015 DGAC considered the evidence reviewed by the 2010 DGAC related to dietary sodium intake and blood pressure in children, and determined that, based on the two new studies identified in the updated search, changes were not warranted to the conclusion statement or grade. In aggregate, the data reviewed by the 2010 DGAC indicated that sodium reduction modestly lowers blood pressure in infants and children. Neither of the two studies identified in the update found a relationship between dietary sodium intake and blood pressure in healthy, normotensive children.

## Evidence summary

### Description of the Evidence

#### *2010 Dietary Guidelines Advisory Committee Systematic Review*

The 2010 Dietary Guidelines Advisory Committee (DGAC) conducted a systematic review to examine the relationship between sodium (Na) intake and blood pressure (BP) in children from birth to age 18 years, examining studies published from January 1970 to May 2009.

Briefly, that systematic review included 19 articles from 15 intervention studies and four prospective cohort studies. Of the 15 trials, 14 were randomized controlled clinical trials (RCTs) and one was a non-randomized controlled trial. Five of the RCTs and the non-RCT were positive quality, seven RCTs were neutral quality and two RCTs were negative quality.



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Two of the prospective cohort studies were positive quality, one was neutral quality and one was negative quality.

### *2015 Dietary Guidelines Advisory Committee Update*

The 2015 DGAC updated the systematic review done by the 2010 DGAC, and identified two additional articles published since May 2009. This includes one RCT (Cotter, 2013) and one prospective cohort study (Shi, 2014) that examined the relationship between sodium and BP in children and adolescents. The included articles had moderate risk of bias ratings [eight of 28 (Cotter, 2013) and zero of 26 (Shi, 2014)].

**Table 1. Summary of studies published since May 2009 examining the relationship between sodium and blood pressure in children from age 2 to 18 years.**



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**Table 1.** Summary of studies published since May 2009 examining the relationship between sodium and blood pressure in children from age 2 to 18 years

| Author, Year<br><br>Study Design; Location (Trial or Cohort Name)<br><br>Risk of Bias* | Sample Size (Gender; Age)<br><br>Duration of Follow-up | Description of Study<br><br>Sodium Assessment Method | Results | Summary of Findings |
|---|---|---|---|---|
| **Cotter, 2013**<br><br>**Randomized Controlled Trial (RCT); Portugal**<br><br>**Risk of Bias: 8/28** | N=127 (55% female); Age=10.9y<br><br>6 months | **To examine the influence of educational interventions on salt intake and blood pressure:**<br><br>• *Control students (CTR):* Students from the same classes that received no intervention<br>• *Theoretical (THEOR) students:* Attended regular lectures on the potential dangers of excessive salt intake<br>• *Practical (PRACT) students:* Attended the same lectures, and during the second half of the school year they worked on a practical project for 2h a week in the school gardening club, cultivating a garden of plants (Aromas), from which they took home herbs as a salt substitute for food preparation.<br><br>24-h urinary samples were collected at baseline and 6 months to determine sodium content. Estimated salt intake was derived from 24-h urinary sodium excretion as 1mEq/24h sodium=0.058g per day salt. | **MM Estimated salt intake at baseline/follow-up (g/day):**<br><br>• *CTR:* 7.7±2g/7.4±3g<br>• *THEOR:* 8.1±3g/7.5±3g<br>• *PRACT:* 7.5±2.4g/6.4±2.2g<br><br>There were no significant correlations between changes in blood pressure and changes in salt intake from baseline to the end of the study for either the whole sample or for each intervention group (NS). | No correlation was found between blood pressure (SBP or DBP) and sodium excretion (salt intake). |
| **Shi, 2014**<br><br>**Prospective Cohort Study (PCS); Germany (DOrtmund Nutritional and Anthropometric Longitudinally Designed Study DONALD Study)** | N=435 (49% women; Age=~6y)<br><br>10y | To examine the relationship between salt and fruit and vegetable intakes and blood pressure.<br><br>24-h urinary samples were collected yearly to determine sodium excretion. | **Estimated median salt intake at baseline/last assessment (10y later) (g/day):**<br><br>• *Boys:* 3.9g/7.7g<br>• *Girls:* 3.4g/6.3g<br><br>**Pre-Pubertal:** No significant association between Na excretion and BP, either between-person or within-person (NS).<br><br>**Pubertal:** No significant association between | There were no significant associations between sodium excretion (salt intake) and blood pressure. |

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**Table 1.** Summary of studies published since May 2009 examining the relationship between sodium and blood pressure in children from age 2 to 18 years

| Author, Year<br><br>Study Design; Location (Trial or Cohort Name)<br><br>Risk of Bias* | Sample Size (Gender; Age)<br><br>Duration of Follow-up | Description of Study<br><br>Sodium Assessment Method | Results | Summary of Findings |
|---|---|---|---|---|
| **Risk of Bias: 0/26** | | | Na excretion and BP, either between-person or within-person (NS) *(**Note:** results for the within-person effect were almost significant, P<0.06 for SBP and P<0.09 for DBP).* | |

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Both studies were conducted in generally healthy children. Cotter, 2013 tested an intervention in children from Portugal (N=127; mean age of approximately 11 years), while Shi, 2014 followed children from Germany (N=435; mean age of approximately six years) for 10 years. Neither article provided much demographic data about subjects, such as race/ethnicity or socioeconomic status (SES).

In both studies, 24-hour urinary samples were used to assess sodium excretion as a biomarker of salt intake. Also, in both studies blood pressure was measured after five minutes of rest in the right arm, using two (Shi, 2014) or three (Cotter, 2013) measurements to determine systolic blood pressure (SBP) and diastolic blood pressure (DBP) values.

## Evidence Synthesis

The 2015 DGAC considered the evidence reviewed by the 2010 DGAC related to dietary sodium intake and BP in children, and determined that, based on the two new studies identified in the updated search, changes were not warranted to the conclusion statement or grade. In evaluating this evidence, important considerations included the study design, the intensity of the intervention and the baseline values of BP of the study participants. A discussion of the evidence considered by the 2010 DGAC and the two new studies published since is below.

### *2010 Dietary Guidelines Advisory Committee Systematic Review*

In aggregate, the data reviewed by the 2010 DGAC indicated that sodium reduction modestly lowers BP in infants and children. While the degree of BP lowering was usually small, in the range of -1mmHg to -5mmHg, such an effect, if sustained over time, could translate into reduced BP in adults, as well as reduced prevalence of hypertension. Furthermore, if a reduced sodium intake blunts the age-related rise in BP in children, then the effects of sodium reduction will be greater than projected from these studies.

Ten of the 14 RCTs achieved contrasts in sodium intake of 40% or more between treatment groups or periods, two RCTs achieved contrasts of 7% to 12% and two achieved less then 2% difference between groups. Although sodium reduction often appeared large, the data often came from dietary recalls and histories, rather than 24-hour urine collections. Twelve of the 15 intervention studies showed a decrease in SBP and DBP on the low sodium diet. In eight of those 12 intervention studies, the decrease was statistically significant for all, or a subset, of the study population. Three studies reported no change in BP on a low sodium diet.

Results from three of the four prospective cohort studies tend to support the results of the intervention trials. Two studies involved prospective cohorts that were followed for seven years, and found that higher sodium intake was associated increased BP over time; in a third prospective cohort study, a 15-year follow-up study found that SBP and DBP were lower among children initially assigned to the low sodium diet during infancy. The fourth study found a non-significant trend toward a dose-related response between salt intake and BP.

Most of the studies had methodological limitations, particularly small sample size (and consequently inadequate statistical power), brief duration (typically less than one month) and inadequate or uncertain contrast in sodium intake.

### *2015 Dietary Guidelines Advisory Committee Update*

Neither of the two studies identified in the update found a relationship between dietary sodium intake and BP in children. In the clinical trial (Cotter, 2013), an educational intervention was done to reduce dietary sodium intake. The study included 127 healthy children, with a mean age of 11 years. The authors reported no significant correlations between changes in BP and changes in salt intake from baseline to the end of the study for either the whole sample or for



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each intervention group. However, the ability of an intervention to influence BP typically depends on the level of the baseline BP. In the case of the Cotter, 2013 study, subjects were normotensive at baseline, and therefore it was not likely that their BP would be lowered by the intervention. The prospective cohort study (Shi, 2014) included 435 healthy, normotensive children. Over the 10 years of follow up, significant increases in sodium intake were observed. However, there was no significant association found between sodium excretion and BP, either between-person or within-person among prepubertal subjects. In pubertal subjects, there was also no significant association between sodium excretion and BP, either between-person or within-person. However, results for the within-person effect approached significance ($P<0.06$ for SBP and $P<0.09$ for DBP).

## Research recommendations

In order to better assess the relationship between dietary sodium intake and blood pressure in children from birth to age 18 years, additional research is needed, including:

- More rigorous intervention studies in children and adolescents, particularly controlled feeding studies
- Study populations that include children and adolescents who are in the upper percentiles of measured blood pressure, and thus may benefit from sodium reduction
- Studies that measure blood pressure multiple times over several days to account for variability in blood pressure
- Studies that obtain measures of 24-hour urinary sodium excretion to determine levels of sodium before, during and after the intervention, rather than relying on estimates drawn from dietary intake assessment
- Consideration of potassium intakes before, during and after the intervention.

## Search plan and results

### Inclusion criteria

TBD Inclusion criteria for the systematic review included the following:

- Human subjects
- Subject populations from countries with high or very high human development, according to the 2012 Human Development Index [1]
- Children and adolescents from two to 18 years of age
- Subjects who were healthy or at elevated chronic disease risk
- Randomized (RCT) or non-randomized controlled trial, or prospective cohort studies
- The independent variable/exposure was sodium intake, and the comparator was different levels of sodium intake
- The outcome was blood pressure.

In addition, articles were included if they were published in English in a peer-reviewed journal between January 2009 and June 2014. If an author is included on more than one primary research article that is similar in content, the paper with the most pertinent data and endpoints was included. If data and endpoints from both papers are appropriate, it was made clear that results are from the same intervention.

[1] United Nations Development Programme. Human Development Report 2013, The Rise of the South: Human Progress in a Diverse World 2013. Available from: http://hdr.undp.org/sites/default/files/reports/14/hdr2013_en_complete.pdf.

### Exclusion criteria

- Animals and *in vitro* models
- Subject populations from countries with medium or low human development, according to



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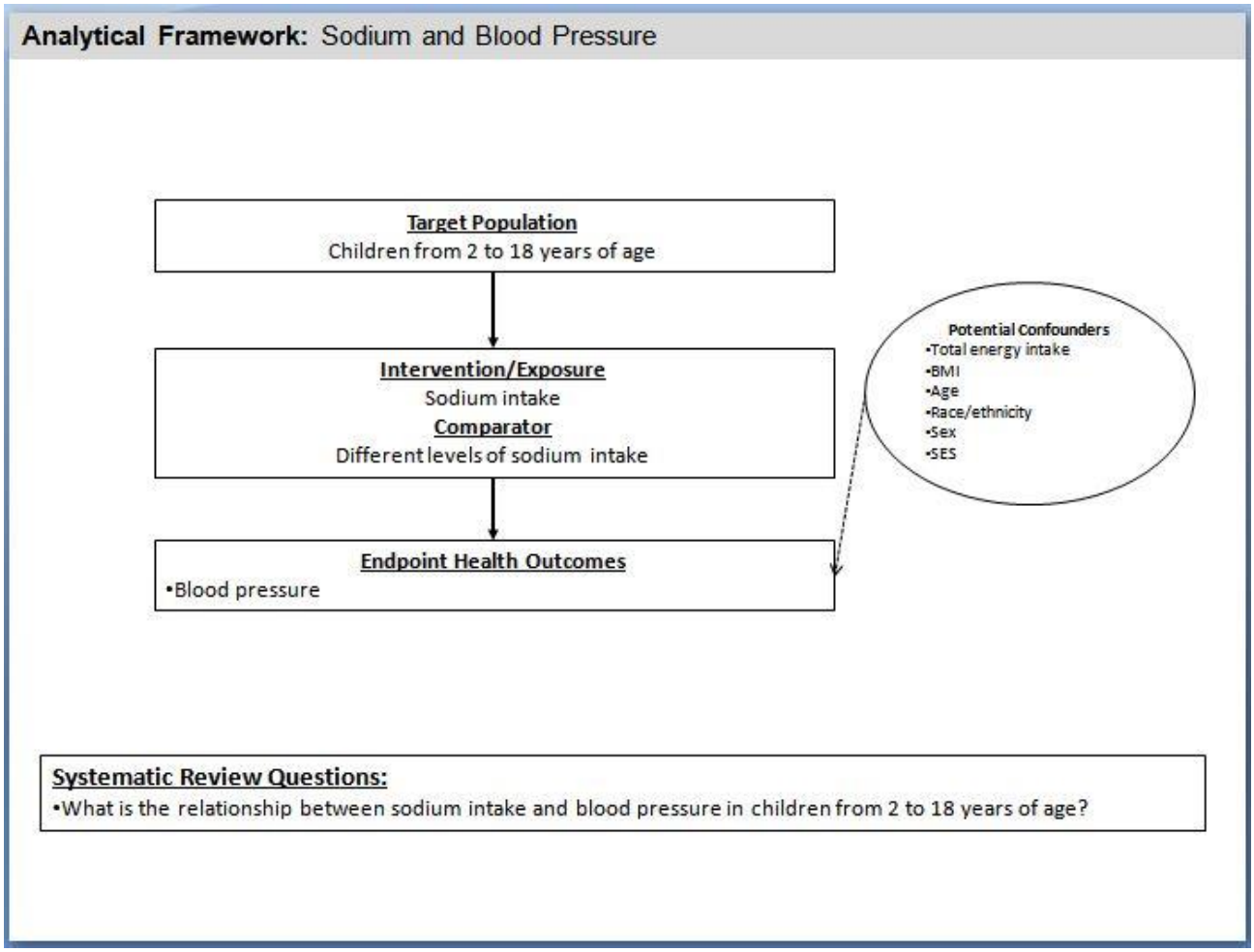
the Human Development Index
- Infants and toddlers ages two years and younger; adults older than 18 years of age
- Subjects who were hospitalized, diagnosed with disease and receiving medical treatment
- Systematic review, meta-analysis, narrative review, before-and-after, uncontrolled, cross-sectional, ecological study designs.

Articles were excluded if they were not published in English, or were published before January 2009. Articles, abstracts and presentations not published in peer-reviewed journals (e.g., websites, magazine articles, Federal reports) were also excluded. Finally, if an author was included on more than one review article or primary research article that is similar in content, the paper with the most pertinent data and endpoints was included; others were excluded.

### Analytic framework




### Search terms and electronic databases used

- ***Pubmed***
  - *Date(s) Searched:* ***June 2014***
  - *Search Terms: ("Hypertension"[mesh] OR "blood pressure"[MeSH Terms] OR hypertension[tiab] OR "blood pressure"[tiab]) AND ("Sodium, Dietary"[Mesh] OR "sodium"[MeSH Terms] OR "sodium chloride"[mesh] OR sodium[tiab] OR salt[tiab]) AND (child* OR youth* OR adolesc* OR teen* OR preteen* OR pre-teen* OR*



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*pre-adolesc* OR preadolesc* OR preschool* OR pediatric* OR paediatric* OR boy OR boys or girl OR girls OR schoolchild* OR high school* OR college* OR juvenile[tiab] OR pubescent[tiab] OR kid[tiab] OR kids[tiab])*

- *Limiters: All Child: zero to 18 years, Publication Date from 2009 AND "english and humans"[Filter]*

- ***Cochrane***
  - *Date(s) Searched:* ***June 2014***
  - *Search Terms: ("blood pressure":ti, kw OR hypertension:ti, ab, kw) AND (sodium OR salt):ti, ab, kw (child* OR youth* OR adolesc* OR teen* OR preteen* OR pre-teen* OR pre-adolesc* OR preadolesc* OR preschool* OR pediatric* OR paediatric* OR boy OR boys or girl OR girls OR schoolchild* OR high school* OR college* OR juvenile OR pubescen* OR kid OR kids)*

- ***EMBASE***
  - *Date(s) Searched:* ***June 2014***
  - *Search Terms: 'hypertension'/exp OR hypertension OR 'blood pressure'/exp OR 'blood pressure' OR hypertension:ab, ti OR 'blood pressure':ab, ti AND ('sodium'/exp OR sodium OR 'electrolyte intake'/exp OR 'electrolyte intake' OR 'electrolyte blood level'/exp OR 'electrolyte blood level' OR 'sodium chloride'/exp OR 'sodium chloride' OR salt:ti, ab OR sodium:ti, ab) NOT [medline]/lim AND ([article]/lim OR [article in press]/lim OR [review]/lim) AND [english]/lim AND ([child]/lim OR [preschool]/lim OR [school]/lim OR [adolescent]/lim) AND [embase]/lim AND [2009-2014]/py*

- ***CINAHL***
  - *Date(s) Searched:* ***July 2014***
  - *Search Terms: (MH "Hypertension") OR (MH "Blood Pressure") AND (MH "Sodium, Dietary") OR (MH "Sodium") OR (MH "Sodium Chloride") NOT medline ALL child*

**Date range:** January 2014 to July 2014

**Summary of articles identified to review**

- Total hits from all electronic database searches: 530
- Total articles identified to review from electronic databases: 80
- Articles identified via handsearch or other means: 0
- Number of Primary Articles Identified: 2
- Number of Review Articles Identified: 0
- Total Number of Articles Identified: 2
- Number of Articles Reviewed but Excluded: 78



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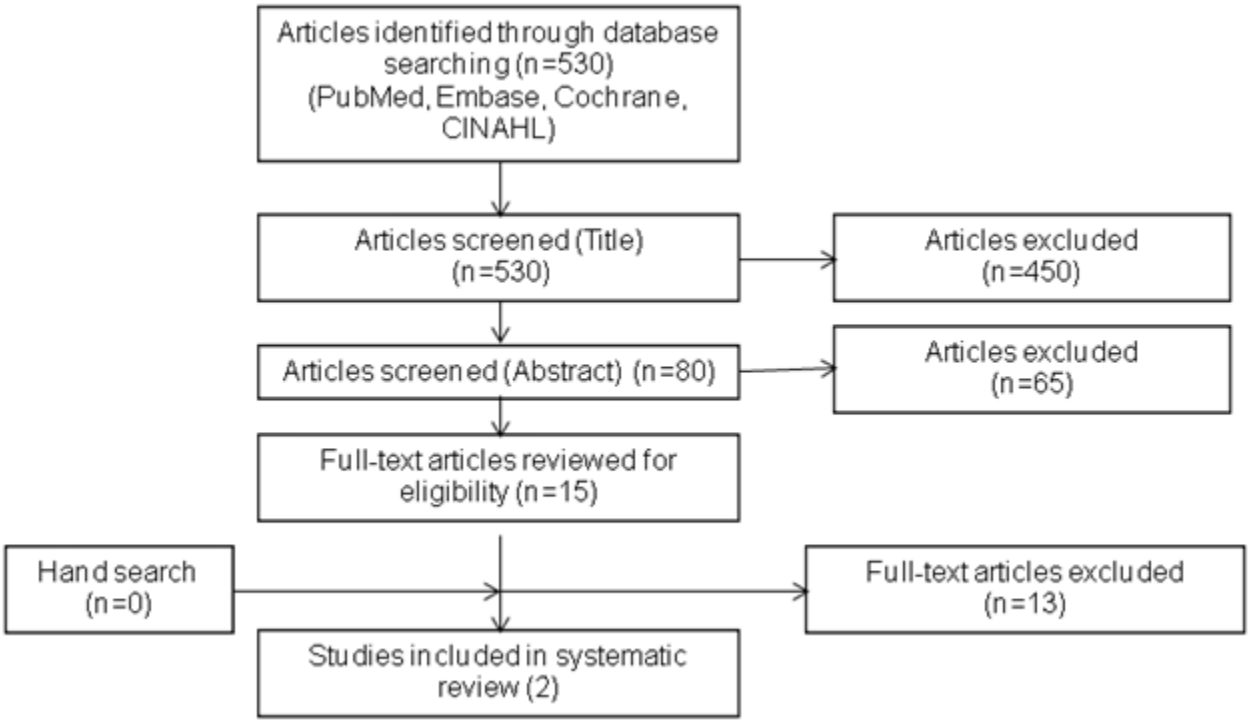


### Included articles (References)

- Cotter J, Cotter MJ, Oliveira P, Cunha P, Polonia J. Salt intake in children 10-12 years old and its modification by active working practices in a school garden. *J Hypertens.* 2013;31(10):1966-71. PMID:24107730. http://www.ncbi.nlm.nih.gov/pubmed/24107730
- Shi L, Krupp D, Remer T. Salt, fruit and vegetable consumption and blood pressure development: a longitudinal investigation in healthy children. *Br J Nutr.* 2014;111(4):662-71. PMID:24326147. http://www.ncbi.nlm.nih.gov/pubmed/24326147

### Excluded articles

See Appendix A for a full list of excluded articles with reason.



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# CHAPTER 3. SODIUM – CARDIOVASCULAR DISEASE

## WHAT IS THE RELATIONSHIP BETWEEN SODIUM INTAKE AND RISK OF CARDIOVASCULAR DISEASE?

## TECHNICAL ABSTRACT

### Background

The goal of this systematic review was to determine whether sodium intake is associated with risk of cardiovascular disease (CVD). In order to answer this question, the 2015 Dietary Guidelines Advisory Committee (DGAC) updated systematic reviews done on this topic by the Institute of Medicine (IOM) and the National Heart, Lung, and Blood Institute (NHLBI) in 2013.

### Conclusion statement

The DGAC concurs with the IOM review, which concluded that "although the reviewed evidence on associations between sodium intake and direct health outcomes has methodological flaws and limitations, when considered collectively, it indicates a positive relationship between higher levels of sodium intake and risk of CVD. This evidence is consistent with existing evidence on blood pressure as a surrogate indicator of CVD risk."

IOM Grade: Grade not determined, outside the statement of task
2015 DGAC Grade: Moderate

The DGAC concurs with the IOM conclusion that "evidence from studies on direct health outcomes is inconsistent and insufficient to conclude that lowering sodium intakes below 2,300mg per day either increases or decreases risk of CVD outcomes (including stroke and CVD mortality) or all-cause mortality in the general US population."

IOM Grade: Grade not determined, outside the statement of task
2015 DGAC Grade: Not Assignable

The DGAC concurs with the NHLBI review, which concluded that "a reduction in sodium intake by approximately 1,000mg per day reduces CVD events by about 30%" and that "higher dietary sodium intake is associated with a greater risk for fatal and nonfatal stroke and CVD."

NHLBI Strength of Evidence: Low
2015 DGAC Grade: Limited

The DGAC concurs with the NHLBI conclusion that "evidence is not sufficient to determine the association between sodium intake and the development of heart failure."

NHLBI Strength of Evidence: Not assigned due to insufficient evidence
2015 DGAC Grade: Not Assignable

### Methods

To update the 2013 IOM and NHLBI systematic reviews on this topic, literature searches were conducted using PubMed, Embase, Navigator (BIOSIS, CAB Abstracts and Food Science and Technology Abstracts) and Cochrane databases to identify studies that evaluated the association between sodium and cardiovascular disease. Studies that met the following criteria were included in the review: randomized controlled trials (RCTs), non-randomized controlled trials or prospective cohort studies; human subjects who were healthy or at elevated chronic disease risk; subjects from countries with high or very high human development (2012 Human Development Index) (if a study included subjects from multiple countries with differing Human Development Index ratings, the study was included); and



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published in English in peer-reviewed journals. The date range was from January 2013 to September 2014. The intervention or exposure was sodium intake, and the outcome was myocardial infarction (MI), stroke, coronary heart disease (CHD), CVD-related mortality, incidence of hypertension and congestive heart failure.

Data from each included article were extracted, and risk of bias was assessed. The evidence was qualitatively synthesized, a conclusion statement was developed and the strength of the evidence (grade) was assessed using pre-established criteria including evaluation of the quality and risk of bias, quantity, consistency, magnitude of effect and generalizability of available evidence. The 2015 DGAC then considered the studies published since 2010 on sodium and cardiovascular, and determined whether the conclusions reached by the IOM and NHLBI needed to be modified.

### Findings

- The DGAC updated systematic reviews done in 2013 by the IOM and NHLBI, and identified four additional articles published since 2013, all of which were prospective cohort studies
- The evidence reviewed for the 2013 IOM report was published between 2003 and December 2012
- The DGAC considered the conclusions reached by the IOM and NHLBI related to dietary sodium intake and risk of CVD, and determined that the findings from the four new studies identified in the updated search did not warrant changes to the conclusion statements. In aggregate, the data indicate a relationship between higher sodium intake and higher risk of CVD.

### Limitations

The ability to draw strong conclusions was limited by the following issues:

- A small number of well-conducted studies evaluating sodium intake and direct health outcomes
- Inconsistency in findings across the published literature, possibly due to methodological factors
- Lack of comparability in sodium intake levels across studies, particularity in international studies
- Absence of strong data related to sodium goals and direct health outcomes, not including hypertension.

## FULL REVIEW

## Conclusion statement

The DGAC concurs with the IOM Report: *Sodium Intake in Populations*, which concluded that “although the reviewed evidence on associations between sodium intake and direct health outcomes has methodological flaws and limitations, when considered collectively, it indicates a positive relationship between higher levels of sodium intake and risk of CVD. This evidence is consistent with existing evidence on blood pressure as a surrogate indicator of CVD risk.”

IOM Grade: Grade not determined, outside the statement of task
2015 DGAC Grade: Moderate

The DGAC concurs with the IOM Report: *Sodium Intake in Populations* that “evidence from studies on direct health outcomes is inconsistent and insufficient to conclude that lowering sodium intakes below 2,300mg per day either increases or decreases risk of CVD outcomes (including stroke and CVD mortality) or all-cause mortality in the general US population.”



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IOM Grade: Grade not determined, outside the statement of task
2015 DGAC Grade: Not Assignable

The DGAC concurs with the NHLBI Lifestyle Report, which concluded that "a reduction in sodium intake by approximately 1,000mg per day reduces CVD events by about 30%" and that "higher dietary sodium intake is associated with a greater risk for fatal and nonfatal stroke and CVD."

NHLBI Strength of Evidence: Low
2015 DGAC Grade: Limited

The DGAC concurs with the NHLBI Lifestyle Report that "evidence is not sufficient to determine the association between sodium intake and the development of heart failure."

NHLBI Strength of Evidence: Not assigned due to insufficient evidence
2015 DGAC Grade: Not Assignable

## Grade

See above.

## Key findings

- The DGAC updated systematic reviews done in 2013 by the IOM and NHLBI, and identified four additional articles published since 2013, all of which were prospective cohort studies
- The evidence reviewed for the 2013 IOM report was published between 2003 and December 2012
- The DGAC concluded that the reviewed evidence on associations between sodium intake and direct health outcomes has methodological flaws and limitations, including: a small number of well-conducted studies evaluating sodium intake and direct health outcomes; inconsistency in findings across the published literature, possibly due to methodological factors; lack of comparability in sodium intake levels across studies, particularity in international studies; and absence of strong data related to sodium goals and direct health outcomes, not including hypertension
- The DGAC considered the conclusions reached by the IOM and NHLBI related to dietary sodium intake and risk of CVD, and determined that the findings from the four new studies identified in the updated search did not warrant changes to the conclusion statements. In aggregate, the data indicate a relationship between higher sodium intake and higher risk of CVD.

## Evidence summary

### Description of the evidence

Three sources of evidence were considered in addressing this question, including a 2013 Institute of Medicine (IOM) systematic review (IOM, 2013), a 2013 National Heart Lung and Blood Institute (NHLBI) systematic review (NHLBI, 2013) and an NEL systematic review update done to identify studies published since the completion of the reviews done by IOM and NHLBI.

#### *IOM*

The IOM's review of evidence included studies (randomized controlled trials (RCTs), cohort studies and case-control studies) published from 2003 to 2012. For the general US population, there were two main findings and conclusions reached.

First, the committee found that the results from studies linking dietary sodium intake with direct health outcomes were highly variable in methodological quality, particularly in assessing



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sodium intake. The range of limitations included over-reporting or underreporting of intakes or incomplete collection of urine samples. In addition, variability in data collection methodologies limited the committee's ability to compare results across studies.

- *Conclusion 1:* Although the reviewed evidence on associations between sodium intake and direct health outcomes has methodological flaws and limitations, the committee concluded that, when considered collectively, it indicates a positive relationship between higher levels of sodium intake and risk of cardiovascular disease (CVD). This evidence is consistent with existing evidence on blood pressure as a surrogate indicator of CVD risk.

Second, the committee found that the evidence from studies on direct health outcomes was insufficient and inconsistent regarding an association between sodium intake below 2,300mg per day and benefit or risk of CVD outcomes (including stroke and CVD mortality) or all-cause mortality in the general US population.

- *Conclusion 2:* The committee determined that evidence from studies on direct health outcomes is inconsistent and insufficient to conclude that lowering sodium intakes below 2,300mg per day either increases or decreases risk of CVD outcomes (including stroke and CVD mortality) or all-cause mortality in the general US population.

### *NHLBI*

The NHLBI's systematic review included RCTs and observational studies published from 1997 to 2010. The following evidence statements and associated strength of evidence ratings were reached:

- *Evidence Statement 8:* A reduction in sodium intake by approximately 1,000mg per day reduces CVD events by about 30%. (Strength of evidence: Low)
- *Evidence Statement 9:* Higher dietary sodium intake is associated with a greater risk for fatal and nonfatal stroke and CVD. (Strength of evidence: Low)
- *Evidence Statement 10:* Evidence is not sufficient to determine the association between sodium intake and the development of heart failure (HF).

### *2015 Dietary Guidelines Advisory Committee NEL Systematic Review Update*

This NEL systematic review update included four articles, all from prospective cohort studies (Cook, 2014; Joosten, 2014; O'Donnell, 2014; Pfister, 2014) published since 2013 that examined the relationship between sodium and risk of CVD. The included articles had low to moderate and high risk of bias ratings.

**Table 1. Summary of studies examining the relationship between sodium and risk of cardiovascular disease (CVD)**



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**Table 1.** Summary of studies examining the relationship between sodium and risk of cardiovascular disease (CVD)

| Author, Year<br><br>Study Design; Location (Trial or Cohort Name)<br><br>Risk of Bias* | Sample Size (Gender; Age)<br><br>Duration of Follow-up | Description of Sodium Assessment and Intake | Results | Summary of Findings |
|---|---|---|---|---|
| **Cook, 2014**<br><br>**Prospective Cohort Study (PCS); US (Trials of Hypertension Prevention)**<br><br>**Risk of Bias: 0/28** | N=2,275 (31% female); Age =~43y<br><br>10-15y<br><br>**Cases:** 193 cardiovascular events or deaths | 24-hour urine collections (3-7 times) were used to calculate estimated mean sodium excretion.<br><br>Mean sodium excretion was 3,630mg/d.<br><br>**Subjects were categorized as:**<br><br><2,300mg<br>2,300-3,600mg<br>3,600-4,800mg (referent category)<br>>4,800mg | There were no significant differences in CVD risk based on category of sodium intake (NS).<br><br>When sodium was considered as a continuous term, there was a 17% increase in CVD risk per 1,000mg/d increase in sodium (P=0.054). | Higher sodium intake was associated with increased risk of CVD. |
| **Joosten, 2014**<br><br>**PCS; The Netherlands (Prevention of Renal and Vascular End-stage Disease (PREVEND) Study)**<br><br>**Risk of Bias: 4/28** | N=7,543 (51% women; Age=~48y)<br><br>10.5y<br><br>**Cases:** 452 coronary heart disease (CHD) events | 24-hour urine collections (2 consecutive days) were used to estimate sodium excretion.<br><br>Mean sodium excretion was 137mmol (~3,360mg).<br><br>**Subjects categorized as (women/men):**<br><br><95/<122mmol (<2,185/<2,806mg)<br>95-121/122-154mmol (2,185-2,783/2,806-3,542mg)<br>122-151/155-190mmol (2,806-3,473/3,565-4,370mg)<br>>151/>190mmol (>3,473/>4,370mg) | There were no significant associations between sodium excretion and CHD risk in the full sample (NS).<br><br>Increased sodium excretion (as a continuous variable) was associated with increased CHD risk among hypertensives (per 1g/d increase, HR=1.14, 95% CI=1.01-1.28, P=0.03), but not in normotensives or when analyzed as a categorical variable.<br><br>Increased sodium excretion (as a continuous variable) was associated with increased CHD risk in those with NT-proBNP among the sex-specific median (per 1g/d increase, HR=1.16, 95% CI=1.03-1.30, P=0.01), but not in those below the median. | Overall, there was no association between sodium excretion and risk of CHD. However, higher sodium excretion was associated with higher CHD risk among hypertensives and those with elevate NT-proBNP. |
| **O'Donnell, 2014**<br><br>**PCS; Argentina, Bangladesh,** | N=101,945 (58% women; Age=~51y) | A fasting morning urine sample was collected at baseline, and used to estimate 24-hour urinary sodium excretion (using the Kawasaki formula). | **7g/d vs. 4-5.99 g/d Sodium Excretion**<br><br>**7g/d was associated with increased risks of:** | An estimated sodium intake between 3-6g/d was associated with a lower risk of death and cardiovascular |

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**Table 1.** Summary of studies examining the relationship between sodium and risk of cardiovascular disease (CVD)

| Author, Year<br><br>Study Design; Location (Trial or Cohort Name)<br><br>Risk of Bias* | Sample Size (Gender; Age)<br><br>Duration of Follow-up | Description of Sodium Assessment and Intake | Results | Summary of Findings |
|---|---|---|---|---|
| **Brazil, Canada, Chile, China, Colombia, India, Iran, Malaysia, Pakistan, Poland, South Africa, Sweden, Turkey, United Arab Emirates, Zimbabwe (Prospective Urban Rural Epidemiology Study)**<br><br>**Risk of Bias: 12/26** | 3.7y<br><br>**Cases:** 3,317 CVD events or death (650 CVD deaths, 857 myocardial infarctions, 872 strokes, 261 with heart failure) | Mean sodium excretion was 4.93g/d.<br><br>**Subject categorized as:**<br><br><3g/d<br>3-3.99g/d<br>4-5.99g/d (referent category)<br>6-6.99g/d<br>>7g/d | • *Primary composite CVD:* (OR=1.15; 95% CI: 1.02-1.30)<br>• *Death, any cause:* (OR=1.25; 95% CI: 1.07-1.48)<br>• *A major cardiovascular event:* (OR=1.16; 95% CI: 1.01-1.34)<br>• *Death from CVD:* (OR=1.54; 95% CI: 1.21-1.95)<br>• *Stroke (death or hospitalization):* (OR=1.29; 95% CI: 1.02-1.63)<br><br>The associations for composite CVD, major cardiovascular events, and stroke resulting in death or hospitalization were not significant after adjusting for blood pressure or prior hypertension, but death from any cause remained significant.<br><br>**3g/d vs. 4-5.99 g/d Sodium Excretion**<br><br>**3g/d was associated with increased risks of:**<br><br>• *Primary composite CVD:* (OR=1.27; 95% CI: 1.12-1.44)<br>• *Death, any cause:* (OR=1.38; 95% CI: 1.15-1.66)<br>• *A major cardiovascular event:* (OR=1.30; 95% CI: 1.13-1.50)<br>• *Death from CVD:* (OR=1.77; 95% CI: 1.36-2.31)<br>• *Stroke (death or hospitalization)*: (OR=1.37; 95% CI: 1.07-1.76)<br><br>These associations remained significant after adjusting for blood pressure or prior hypertension. | events than was either a higher (>7g/d) or lower (3g/d) estimated level of intake. |
| **Pfister, 2014** | N=19,857 | Casual urine specimen at baseline; formula | **Risk of heart failure was highest in the lowest and** | Risk of heart failure was |

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**Table 1.** Summary of studies examining the relationship between sodium and risk of cardiovascular disease (CVD)

| Author, Year<br><br>Study Design; Location (Trial or Cohort Name)<br><br>Risk of Bias* | Sample Size (Gender; Age)<br><br>Duration of Follow-up | Description of Sodium Assessment and Intake | Results | Summary of Findings |
|---|---|---|---|---|
| **PCS; UK (European Prospective Investigation into Cancer and Nutrition EPIC-Norfolk)**<br><br>**Risk of Bias: 6/26** | (55% female); Age=~58y<br><br>12.9y<br><br>**Cases:** 1,210 (137 fatal, 1,073 non-fatal) incident cases of heart | (from the Japanese Society of Hypertension) was used to estimate 24-h urinary sodium excretion<br><br>M**edian estimated 24-h urinary sodium excretion:** 158mmol/d (~3,634mg)<br><br>**Subjects were categorized by quintiles of estimated 24-h urinary sodium excretion:**<br><br>115mmol/d (~2,645mg)<br>145mmol/d (~3,335mg) (Referent category)<br>163mmol/d (~3,749mg)<br>182mmol/d (~4,186mg)<br>218mmol/d (~5,014mg) | **highest quintiles of estimated urinary sodium excretion:**<br><br>• *Q1:* 115mmol/d (~2,645mg): HR=1.30 (95% CI=1.08-1.55)<br>• *Q2:* 145mmol/d (~3,335mg): HR=1.00 (reference)<br>• *Q3:* 163mmol/d (~3,749mg): HR=1.03 (95% CI=0.85-1.24)<br>• *Q4:* 182mmol/d (~4,186mg): HR=0.99 (95% CI=0.82-1.19)<br>• *Q5:* 218mmol/d (~5,014mg): HR=1.22 (95% CI=1.02-1.46) | highest in the lowest (~2,645mg) and highest quintiles (~5,014mg) of estimated urinary sodium excretion, compared to the reference category (~3,335mg). |

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One study each was conducted in the United States (Cook, 2014), the Netherlands (Joosten, 2014) and the United Kingdom (Pfister, 2014), and one included subjects from 17 countries (O'Donnell, 2014: Argentina, Bangladesh, Brazil, Canada, Chile, China, Colombia, India, Iran, Malaysia, Pakistan, Poland, South Africa, Sweden, Turkey, United Arab Emirates, Zimbabwe). Studies were conducted in adult men and women. Two of the studies included generally healthy adults (Joosten, 2014; Pfister, 2014), one study included adults with high normal blood pressure and elevated body mass index (BMI) (Cook, 2014) and one study included adults, regardless of health status (O'Donnell, 2014). Subject age ranged from 30 years to 79 years; mean age was approximately 43 years to 58 years.

Two studies used multiple 24-hour urinary samples to estimate sodium excretion as a biomarker of salt intake (Cook, 2014; Joosten, 2014) and two used a single urine sample to estimate 24-hour sodium excretion (O'Donnell, 2014; Pfister, 2014). A range of CVD outcomes were examined, all based on self-report by subjects, and verification using medical and death records. Three studies assessed multiple CVD outcomes [including myocardial infarction (MI), stroke, coronary artery bypass graft, percutaneous transluminal coronary angioplasty, ischemic heart disease, CVD mortality and congestive heart failure (CHF)] (Cook, 2014; Joosten, 2014; O'Donnell, 2014) and one examined HF (Pfister, 2014).

### Evidence Synthesis

The 2015 DGAC considered the conclusions reached in the IOM and NHLBI reviews related to dietary sodium intake and risk of CVD, and determined that based on the four new studies identified in the updated search, changes were not warranted to the conclusions and grades. Two of the four studies are consistent with previous findings from both the IOM and NHLBI, that concluded higher levels of sodium intake are associated with higher risk of CVD, particularly when sodium was analyzed as a continuous variable and not as a categorical variable. The other two studies suggest either no association or an inverse association between low sodium intake and risk of CVD. However, both of these studies had limitations that make interpretation of the results challenging, including inclusion of study subjects from countries of lower development that may not be generalizable to the US population and use less reliable measures for estimating sodium intake.

## Research recommendations

In order to better assess the relationship between dietary sodium intake and risk of CVD, additional research is needed, including:

- Studies primarily designed to evaluate the relationship of sodium intake and CVD and the impact of changes in sodium intake (especially lowering) on CVD using 24-hour urinary excretion as the assessment of sodium intake
- Studies to validate biochemical markers of dietary sodium intake (i.e., casual, spot and 24-hour urine measures and sodium/creatine ratios) and determine how well these biochemical markers estimate actual sodium intake among varied populations and a wide range of sodium intakes, including those with different health conditions (e.g., heart failure, chronic kidney disease).

## Search plan and results

### Inclusion criteria

- Human subjects
- Subject populations from countries with high or very high human development, according to the 2012 Human Development Index [1]
- Children and adults, ages two years and above



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- Subjects who were healthy or at elevated chronic disease risk
- Randomized (RCT) or non-randomized controlled trial, or prospective cohort studies
- The independent variable/exposure was sodium intake, and the comparator was different levels of sodium intake
- The outcomes were myocardial infarction (MI), stroke, coronary heart disease (CHD), cardiovascular disease (CVD)-related mortality, incidence of hypertension, and congestive heart failure (CHF).

In addition, articles were included if they were published in English in a peer-reviewed journal between January 2013 and September 2014. If an author is included on more than one primary research article that is similar in content, the paper with the most pertinent data and endpoints was included. If data and endpoints from both papers are appropriate, it was made clear that results are from the same intervention.

[1] United Nations Development Programme. Human Development Report 2013, The Rise of the South: Human Progress in a Diverse World 2013. Available from: http://hdr.undp.org/sites/default/files/reports/14/hdr2013_en_complete.pdf.

## Exclusion criteria

Exclusion criteria for the systematic review included:

- Animals and in vitro models
- Exclusively enroll subject populations from countries with medium or low human development, according to the Human Development Index
- Infants and toddlers ages 2 years and younger
- Subjects who were hospitalized, diagnosed with disease, and/or receiving medical treatment
- Systematic review, meta-analysis, narrative review, before and after, uncontrolled, cross-sectional, ecological designs
- Articles were excluded if they were not published in English, or were published before January 2013. Articles, abstracts, and presentations not published in peer-reviewed journals (e.g., websites, magazine articles, federal reports) were also excluded. Finally, if an author was included on more than one review article or primary research article that is similar in content, the paper with the most pertinent data/endpoints was included, and others were excluded.

## Analytic framework



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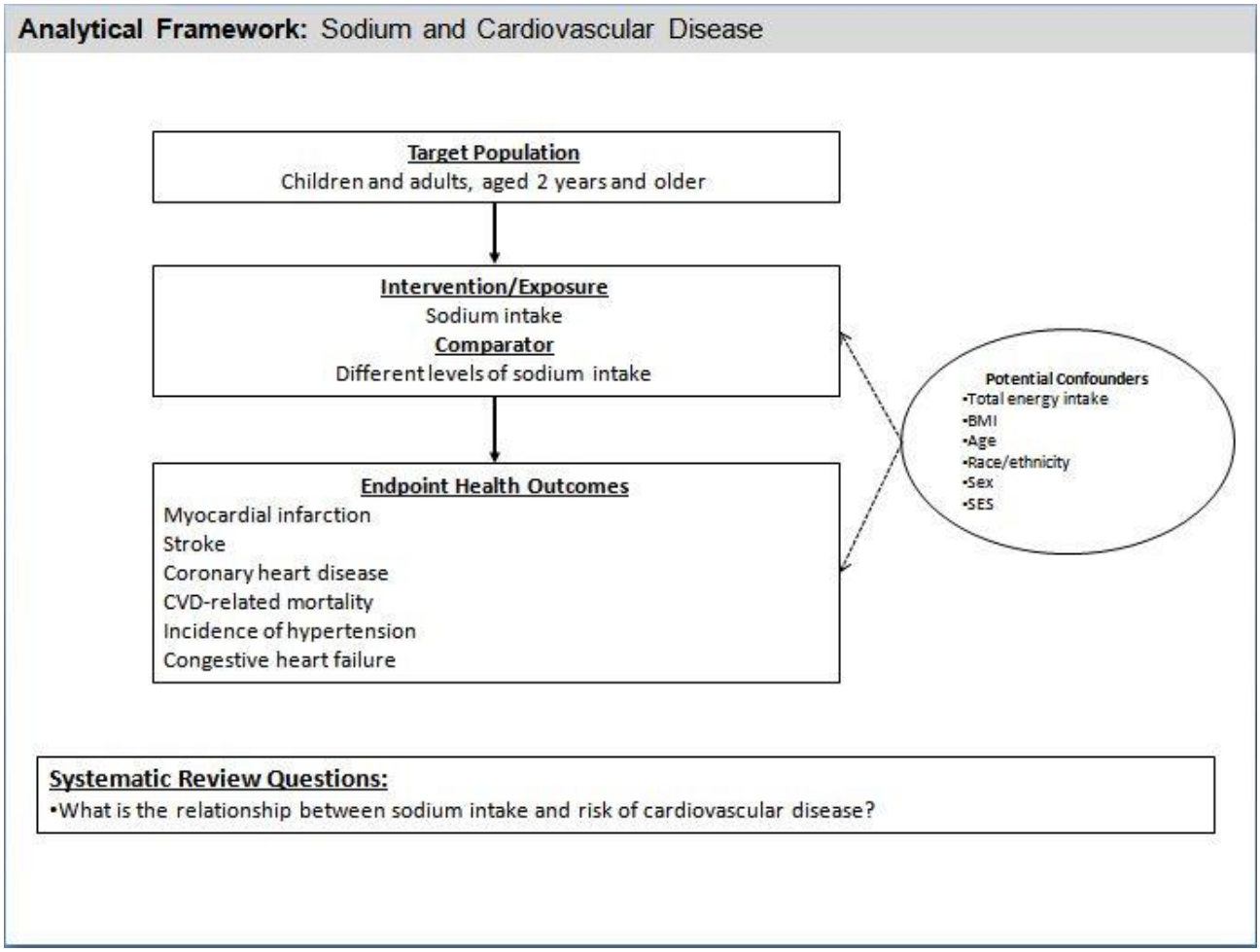


**Search terms and electronic databases used**

- ***PubMed***
  - *Date(s) Searched:* ***September 2014***
  - *Search Terms: "Mortality"[Mesh] OR mortality[tiab] OR "blood pressure"[tiab] OR "blood pressure"[mesh] OR "cardiovascular diseases"[mh:noexp] OR "Heart Diseases"[Mesh:NoExp] OR Heart Disease*[tiab] OR "Heart Diseases"[Major] OR cardiovascular disease*[tiab] OR cardiovascular event*[tiab] OR hypertension[tiab] OR "Myocardial Infarction"[Mesh] OR "Myocardial Infarction"[tiab] OR "Heart Failure"[Mesh] OR "Heart Arrest"[Mesh] OR "Myocardial Ischemia"[Mesh] OR heart failure*[tiab] OR "heart arrest"[tiab] OR "Myocardial Ischemia"[tiab] OR hypertension[mh] OR stroke[tiab] OR "stroke"[Mesh] OR (coronary[tiab] AND disease*[tiab])*
  - *AND*
  - *("Sodium, Dietary"[Mesh] OR "sodium"[MeSH Terms] OR "sodium chloride"[mesh] OR sodium[tiab] OR salt[tiab])*
- ***Cochrane***
  - *Date(s) Searched:* ***September 2014***



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- *Search Terms: mortality OR "blood pressure" OR (cardiovascular NEXT (event OR disease*)) OR (heart NEXT disease*) OR ((cholesterol OR lipid*) NEAR/2 blood) OR (Cholesterol NEAR/2 HDL) OR cholesterol OR (Cholesterol NEAR/2 Dietary) OR triglyceride*:ti, ab OR "Myocardial Infarction" OR "Heart Arrest" OR "Myocardial Ischemia" OR (heart NEXT failure*) OR hypertension OR stroke:ti, ab OR hypercholesterol* :ti, ab OR hypercholesterolemia*:ti, ab OR (heart NEXT infarction*):ti, ab*
- *AND (sodium OR salt):ti, ab, kw*

- ***EMBASE***
  - *Date(s) Searched:* ***September 2014***
  - *Search Terms: ('cardiovascular disease'/de OR 'heart arrhythmia'/de OR 'heart atrium fibrillation'/de OR 'heart failure'/de OR 'heart infarction'/de OR 'hypertension'/de) AND [adult]/lim ([article]/lim OR [article in press]/lim) AND [humans]/lim AND [english]/lim AND [embase]/lim AND [2013-2014]/py NOT [medline]/lim*
  - *AND*
  - *(Sodium OR 'sodium blood level'/exp OR 'sodium chloride'/exp OR salt OR 'high sodium intake'/exp OR 'salt intake'/exp OR 'sodium intake'/exp OR 'sodium restriction'/exp)*

- ***CINAHL***
  - *Date(s) Searched:* ***September 2014***
  - *Search Terms: (MH "Stroke+") OR (MH "Heart Diseases+") OR (MM "Cardiovascular Diseases") AND (MH "Sodium, Dietary") OR (MH "Sodium") OR (MH "Sodium Chloride")*
  - *Limiters: Adults; 2013, non-Medline*

**Date range:** September 2014 to September 2014

**Summary of articles identified to review**

- Total hits from all electronic database searches: 1111
- Total articles identified to review from electronic databases: 55
- Articles identified via handsearch or other means: 0
- Number of Primary Articles Identified: 4
- Number of Review Articles Identified: 0
- Total Number of Articles Identified: 4
- Number of Articles Reviewed but Excluded: 51



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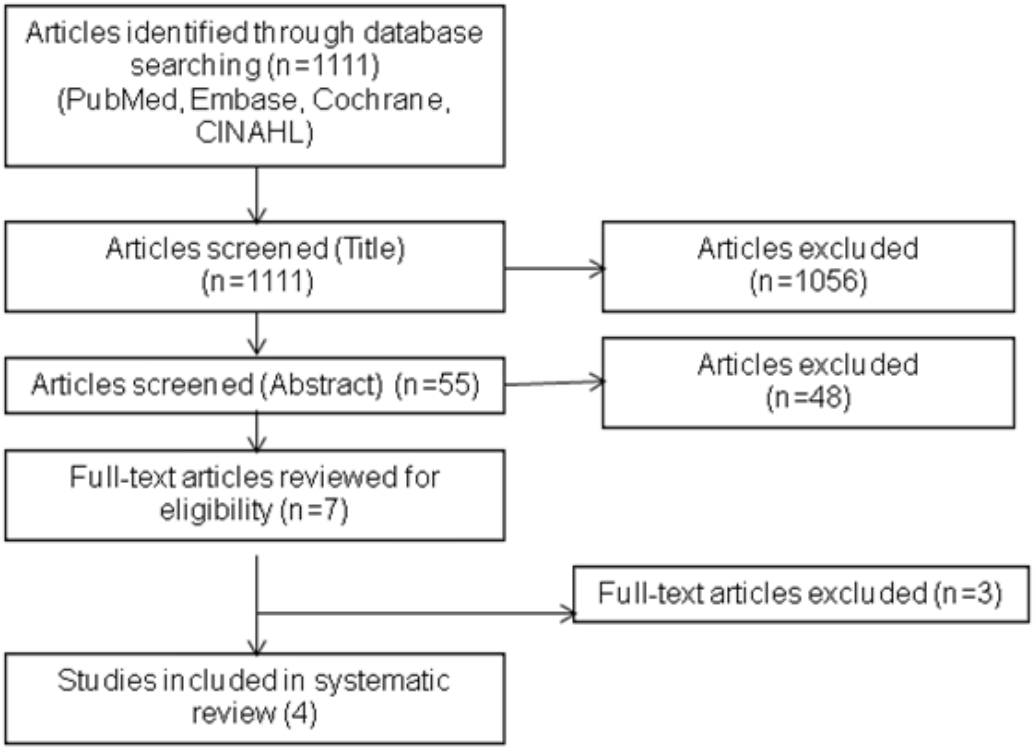


## Included articles (References)

### *Systematic reviews included for review*


1. IOM (Institute of Medicine). *Sodium Intake in Populations: Assessment of Evidence.* Washington, DC: The National Academies Press, 2013.
2. U.S. Department of Health and Human Services, National Institutes of Health, NHLBI (National Heart Lung and Blood Institute). *Lifestyle Interventions to Reduce Cardiovascular Risk: Systematic Evidence Review from the Lifestyle Work Group*. Bethesda, MD, 2013.


### *Primary articles included in systematic review*


1. Cook NR, Appel LJ, Whelton PK. Lower levels of sodium intake and reduced cardiovascular risk. *Circulation.* 2014;129(9):981-9. PMID:24415713. http://www.ncbi.nlm.nih.gov/pubmed/24415713
2. Joosten MM, Gansevoort RT, Mukamal KJ, Lambers Heerspink HJ, Geleijnse JM, Feskens EJ, Navis G, Bakker SJ. Sodium excretion and risk of developing coronary heart disease. *Circulation.* 2014;129(10):1121-8. PMID:24425751. http://www.ncbi.nlm.nih.gov/pubmed/24425751
3. O'Donnell M, Mente A, Rangarajan S, McQueen MJ, Wang X, Liu L, Yan H, Lee SF, Mony P, Devanath A, Rosengren A, Lopez-Jaramillo P, Diaz R, Avezum A, Lanas F, Yusoff K, Iqbal R, Ilow R, Mohammadifard N, Gulec S, Yusufali AH, Kruger L, Yusuf R, Chifamba J, Kabali C, Dagenais G, Lear SA, Teo K, Yusuf S. Urinary sodium and potassium excretion, mortality, and cardiovascular events. *N Engl J Med.* 2014;371(7):612-23. PMID:25119607. http://www.ncbi.nlm.nih.gov/pubmed/25119607
4. Pfister R, Michels G, Sharp SJ, Luben R, Wareham NJ, Khaw KT. Estimated urinary sodium excretion and risk of heart failure in men and women in the EPIC-Norfolk study. *Eur J Heart Fail.* 2014. PMID: 24464931. http://www.ncbi.nlm.nih.gov/pubmed/24464931




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## Excluded articles

See Appendix B for a full list of excluded articles with reason.



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# CHAPTER 4. ADDED SUGARS – CARDIOVASCULAR DISEASE

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

## TECHNICAL ABSTRACT


### Background

The goal of this systematic review was to determine whether intake of added sugars is associated with risk of cardiovascular disease (CVD). Added sugars were defined as sugars that are either added during the processing of foods, or are packaged as such, and include sugars (free, monosaccharides- and disaccharides), syrups, naturally occurring sugars that are isolated from a whole food and concentrated so that sugar is the primary component (e.g., fruit juice concentrates) and other caloric sweeteners.

### Conclusion statement

Moderate evidence from prospective cohort studies indicates that higher intake of added sugars, especially in the form of sugar-sweetened beverages, is consistently associated with increased risk of hypertension, stroke, and coronary heart disease (CHD) in adults. Observational and intervention studies indicate a consistent relationship between higher added sugars intake and higher blood pressure and serum triglycerides.

2015 DGAC Grade: Moderate

### Methods

Literature searches were conducted using PubMed, Embase, Navigator (BIOSIS, CAB Abstracts and Food Science and Technology Abstracts) and Cochrane databases to identify studies that evaluated the association between added sugars and risk of cardiovascular disease. Studies that met the following criteria were included in the review: randomized controlled trials (RCTs), non-randomized controlled trials, prospective cohort studies, or nested case-control studies; adults who were healthy or at elevated chronic disease risk; subjects from countries with high or very high human development (2012 Human Development Index); and published in English in peer-reviewed journals. The date range was from January 2000 to August 2014. The intervention or exposure was intake of added sugars and sugar-sweetened beverages, compared to different levels of intake of added sugars and sugar-sweetened beverages. The outcomes were cholesterol (low-density lipoprotein (LDL), high-density lipoprotein (HDL), total cholesterol (TC):HDL and LDL:HDL ratios), triglycerides, blood pressure and incidence of hypertension, incidence of myocardial infarction (MI), incidence of stroke, incidence of CHD, CVD-related mortality.

Data from each included article were extracted, and risk of bias was assessed. The evidence was qualitatively synthesized, a conclusion statement was developed and the strength of the evidence (grade) was assessed using pre-established criteria including evaluation of the quality and risk of bias, quantity, consistency, magnitude of effect and generalizability of available evidence.

### Findings

- This NEL systematic review included 23 articles published since 2000 that examined the relationship between added sugars and risk of CVD or CVD risk factors such as blood lipids and blood pressure. This literature included 11 intervention studies and 12




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prospective cohort studies.

- The majority of intervention and observational studies included in this systematic review provide some evidence among adults in support of an association between higher intake of added sugars, especially in the form of sugar-sweetened beverages, and higher risk of CVD or increased CVD risk factors:
    - More consistent associations were seen between added sugars and elevated serum triglycerides, blood pressure, and increased risk of hypertension, stroke, or CHD
    - Evidence for associations between added sugars and dyslipidemia (i.e., low HDL, high LDL and high TC) was not as consistent, especially among intervention studies.

### Limitations

The ability to draw strong conclusions was limited by the following issues:

- The intervention studies had extensive heterogeneity in terms of the types and forms of sugars used (i.e., fructose, glucose, sucrose, sugar-sweetened beverages, sweetened milk) and the type of control and isocaloric condition used
- Most intervention studies had a short duration of the intervention and a small sample size
- Most of the observational studies assessed dietary intake only at baseline, and did not take assessments during follow-up
- Residual confounding by other dietary and lifestyle factors in observational analyses could not be completely ruled out.

## FULL REVIEW

## Conclusion statement

Moderate evidence from prospective cohort studies indicates that higher intake of added sugars, especially in the form of sugar-sweetened beverages, is consistently associated with increased risk of hypertension, stroke and CHD in adults. Observational and intervention studies indicate a consistent relationship between higher added sugars intake and higher blood pressure and serum triglycerides.

## Grade

Moderate

## Key findings

- This NEL systematic review included 23 articles published since 2000 that examined the relationship between added sugars and risk of CVD or CVD risk factors such as blood lipids and blood pressure. This literature included 11 intervention studies and 12 prospective cohort studies.
- The majority of intervention and observational studies included in this systematic review provide some evidence among adults in support of an association between higher intake of added sugars, especially in the form of sugar-sweetened beverages, and higher risk of CVD or increased CVD risk factors
    - More consistent associations were seen between added sugars and elevated serum triglycerides, blood pressure and increased risk of hypertension, stroke or CHD
    - Evidence for associations between added sugars and dyslipidemia (i.e., low HDL, high LDL and high TC) was not as consistent, especially among intervention studies.



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- The body of evidence examined in this systematic review had a number of limitations. For example, the intervention studies had extensive heterogeneity in terms of the types and forms of sugars used (i.e., fructose, glucose, sucrose, sugar-sweetened beverages, sweetened milk) and the type of control and isocaloric condition used. In addition, most intervention studies had a short duration of the intervention and a small sample size. Most of the observational studies assessed dietary intake only at baseline, and did not take assessments during follow-up. Residual confounding by other dietary and lifestyle factors in observational analyses could not be completely ruled out.

## Evidence summary

### Description of the Evidence

This systematic review included 23 articles that examined the relationship between added sugars and risk of cardiovascular disease (CVD).

**Table 1. Summary of studies examining the relationship between added sugars and risk of cardiovascular disease**



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**Table 1.** Summary of studies examining the relationship between added sugars and risk of cardiovascular disease

| Author, Year<br><br>Study Design; Location<br><br>Risk of Bias* | Sample Size<br><br>Age<br><br>Gender | Added Sugars Intervention or Exposure<br><br>Study Duration | Results | Summary of Findings |
|---|---|---|---|---|
| **Intervention Studies** | | | | |
| **Aeberli, 2011**<br><br>**Randomized Controlled Trial (RCT) (crossover)**<br><br>**Switzerland**<br><br>**Risk of Bias: 4/28** | Initial N=29<br>Final N=29<br>Attrition=0%<br><br>26y (SD=7)<br><br>0% female | **Participants received 600ml beverages daily with either:**<br><br>1. *Medium fructose:* 40g/d fructose<br>2. *High fructose:* 80g/d fructose<br>3. *Medium glucose:* 40g/d glucose<br>4. *High glucose:* 80g/d glucose<br>5. *High sucrose:* 80g/d sucrose<br>6. *Control:* Received advice to decrease fructose<br><br>**Study Duration:** 3-week interventions, 4-week washout | **Triglycerides, Total cholesterol, HDL, LDL, Blood pressure**: No differences between interventions (NS). | There were no differences in total cholesterol, LDL, HDL, triglycerides, or blood pressure after consuming 600ml/d sugar-sweetened beverages with either 40g/d (fructose or glucose) or 80g/d (fructose, glucose, or sucrose) for 3 weeks. |
| **Aeberli, 2013**<br><br>**RCT (crossover)**<br><br>**Switzerland**<br><br>**Risk of Bias: 2/28** | Initial N=9<br>Final N=9<br>Attrition=0%<br><br>23y (SD=2)<br><br>0% female | **Participants received 600ml beverages daily with either:**<br><br>1. *Medium fructose:* 40g/d fructose<br>2. *High fructose:* 80g/d fructose<br>3. *High glucose:* 80g/d glucose<br>4. *High sucrose:* 80g/d sucrose<br><br>**Study Duration:** 3-week interventions, 4-week washout | **Total Cholesterol, LDL:** Total and LDL cholesterol were higher after the medium fructose compared to high glucose (P<0.05).<br><br>**Triglycerides, HDL:** No differences between groups (NS). | Consuming SSBs (600ml/d) with medium fructose (40g/d), high fructose (80g/d), and high sucrose (80g/d) raised total cholesterol and LDL compared to high glucose. There were no differences in HDL or triglycerides. |
| **Black, 2006**<br><br>**RCT (crossover)**<br><br>**UK** | Initial N=14<br>Final N=13<br>Attrition=7%<br><br>33y (SD=3) | **Participants received two isocaloric diets (55% energy from CHO, 30-35% energy from fat, 10-15% energy from protein, and 18g/d fiber), with either:**<br><br>1. *Low sucrose:* 10% sucrose | **Total cholesterol:** Total cholesterol was higher after the high vs. low sucrose diet (4.62±0.8 vs. 4.01±0.8; P<0.01).<br><br>**LDL:** LDL cholesterol was higher after the high vs. low sucrose diet (2.25±0.25 vs. 2.78±0.3; | Consuming a high sucrose diet (25% sucrose) increased total and LDL cholesterol, but had no effect on HDL cholesterol or triglycerides. |

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**Table 1.** Summary of studies examining the relationship between added sugars and risk of cardiovascular disease

| Author, Year<br><br>Study Design; Location<br><br>Risk of Bias* | Sample Size<br><br>Age<br><br>Gender | Added Sugars Intervention or Exposure<br><br>Study Duration | Results | Summary of Findings |
|---|---|---|---|---|
| **Risk of Bias: 7/28** | 0% female | 2. *High sucrose:* 25% sucrose<br><br>**Study Duration:** 6-week interventions, 4-week washout | P<0.01).<br><br>**HDL, Triglycerides:** No differences between groups (NS). | |
| **Faeh, 2005**<br><br>**RCT (crossover)**<br><br>**Switzerland**<br><br>**Risk of Bias: 6/28** | Initial N=7<br>Final N=7<br>Attrition=0%<br><br>22-31y<br><br>0% female | **Participants received four diets:**<br><br>1. *Fish oil:* 7.2g/d for 28 days<br>2. *High fructose:* 3g/kg/d (~+25% energy requirement)<br>3. *Fish-oil + High fructose:* 7.2g/d fish oil + high fructose diet<br>*4. Control*<br><br>**Study Duration:** 28-day interventions, 12 week washout | **Triglycerides:** Triglycerides were lower after the fish oil+ high fructose diet compared to the high fructose diet alone (37%, P<0.05), but both were higher than the fish oil and control conditions (P<0.05). | Triglycerides were higher after consumption of a high fructose diet (3g/kg/d or ~25% extra kcal, with or without fish oil supplementation) compared to the fish oil supplement alone and the control condition. |
| **Le, 2009**<br><br>**RCT (crossover)**<br><br>**Switzerland**<br><br>**Risk of Bias: 6/28** | Initial N=24<br>Final N=24<br>Attrition=0%<br><br>25y (SD=1)<br><br>0% female | **Participants received two diets:**<br><br>1. *Isocaloric diet:* 55% carbohydrate, 30% fat, 15% protein<br>2. High fructose diet: Isocaloric diet +3.5g/kg fructose (+35% energy requirement)<br><br>**Study Duration:** 1-week interventions, 4 to 5-week washout | **Triglycerides:** Triglycerides increased following the high fructose vs. the isocaloric diet (+35% in the control group, +73% in the group of participants who had a parent with diabetes). | A high fructose (and higher calorie) (3/5g/kg/d or +35% kcal) diet increased triglycerides compared to a control diet. |
| **Lewis, 2013**<br><br>**RCT (crossover)**<br><br>**UK** | Initial N=17<br>Final N=13<br>Attrition=24%<br><br>46y (SD=2) | **Participants received two isocaloric diets (55% energy from CHO, 30-35% energy from fat, 10-15% energy from protein, and 18 g/d fiber), with either:** | **Total Cholesterol, LDL, HDL, Triglycerides, Blood pressure:** No differences between groups (NS). | There were no differences in blood pressure, total cholesterol, LDL, HDL, or triglycerides after consuming a high (15% sucrose) - vs. low-sucrose (5% sucrose) diet. |

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**Table 1.** Summary of studies examining the relationship between added sugars and risk of cardiovascular disease

| Author, Year<br><br>Study Design; Location<br><br>Risk of Bias* | Sample Size<br><br>Age<br><br>Gender | Added Sugars Intervention or Exposure<br><br>Study Duration | Results | Summary of Findings |
|---|---|---|---|---|
| **Risk of Bias: 10/28** | 29% female | 1. *Low sucrose:* 5% sucrose<br>2. *High sucrose:* 15% sucrose<br><br>**Study Duration:** 6-week interventions, 4-week washout | | |
| **Lowndes, 2014a**<br><br>**RCT**<br><br>**US**<br><br>**Risk of Bias: 8/28** | Initial N=86<br>Final N=65<br>Attrition=25%<br><br>39y (SD=12)<br>(25-60y)<br><br>52% female | **Participants received a 1% sweetened milk beverage daily with either:**<br><br>1. *HFCS 10%:* 10% of calories from high-fructose corn syrup (HFCS)<br>2. *HFCS 20%:* 20% of calories from HFCS<br>3. *Sucrose 10%:* 10% of calories from sucrose<br>4. *Sucrose 20%:* 20% of calories from sucrose<br><br>**Study Duration:** 10 weeks | **HDL, Total Cholesterol:HDL ratio**: Sweetened milk consumption decreased HDL (P<0.01) and increased the TC:HDL ratio (P<0.01), but there were no differences between groups.<br><br>**Total Cholesterol, LDL; Blood Pressure, Triglycerides**: No differences between groups (NS). | Drinking sweetened milk decreased HDL and increased the TC:HDL ratio. Drinking 20% sucrose milk significantly reduced total and LDL cholesterol compared to drinking 20% HFCS milk. However, no differences were seen in blood pressure or triglycerides. |
| **Lowndes, 2014b**<br><br>**RCT**<br><br>**US**<br><br>**Risk of Bias: 6/28** | Initial N=465<br>Final N=355<br>Attrition=26%<br><br>40y (SD=12)<br>(20-60y)<br><br>54% female | **Participants received a 1% sweetened milk beverage daily with either:**<br><br>1. *Low sucrose:* 8% of calories from sucrose<br>2. *Low HFCS:* 8% of calories from HFCS<br>3. *Moderate sucrose:* 18% of calories from sucrose<br>4. *Moderate HFCS:* 18% of calories from HFCS<br>5. *High sucrose:* 30% of calories from sucrose<br>6. *High HFCS:* 30% of calories from HFCS<br><br>**Study Duration:** 10 weeks | **Systolic Blood Pressure:** There was a Time x Sugar Type x Sugar Level interaction, such that a decrease was observed in the 8% sucrose group (P<0.01).<br><br>**Diastolic blood pressure, total Cholesterol, LDL, HDL, Triglycerides:** No differences between groups (NS).<br><br>**Pooled Analyses:** In the entire cohort, drinking sugar-sweetened low-fat milk produced increased triglycerides (P<0.001) and decreased HDL (P<0.05). | Drinking sweetened milk increased triglycerides and decreased HDL, and the 8% sucrose drink decreased systolic blood pressure. However, no differences were seen in the other outcomes, or in the other intervention conditions. |

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**Table 1.** Summary of studies examining the relationship between added sugars and risk of cardiovascular disease

| Author, Year<br><br>Study Design; Location<br><br>Risk of Bias* | Sample Size<br><br>Age<br><br>Gender | Added Sugars Intervention or Exposure<br><br>Study Duration | Results | Summary of Findings |
|---|---|---|---|---|
| **Maersk, 2012**<br><br>**RCT**<br><br>**Denmark**<br><br>**Risk of Bias: 9/28** | Initial N=60<br>Final N=47<br>Attrition=21.7 %<br><br>38y (SD=9)<br><br>64% female | **Participants received a 1 liter/day of either:**<br><br>1. Regular cola<br>2. Aspartame-sweetened cola<br>3. Semi-skim milk<br>4. Still mineral water<br><br>**Study Duration:** 6 months | **Total cholesterol**: Regular cola increased total cholesterol by 11.4% (SD 3.2) compared to milk 0.634% (SD 3.0, P<0.01), diet cola -5.89% (SD 3.0, P=0.05), and water -0.159% (SD 2.8, NS) (P for trend 0.004).<br><br>**Triglycerides**: Regular cola increased triglycerides by 32.7% (SD 8.6) compared to milk -0.301% (SD 8.1, P=0.05), diet cola -14.1% (SD 8.1, P<0.01), water -14.2% (SD 7.7, P<0.01) (P for trend 0.001).<br><br>**Systolic Blood Pressure**: Regular cola increased SBP by ~4% compared to milk (~-7%, P<0.05), diet cola (~-7%, P<0.05), and water (NS).<br><br>**HDL, Diastolic Blood Pressure**: No significant differences between groups (NS; DBP: P<0.057). | Intake of 1 liter/d of sucrose-sweetened cola (compared to milk, diet soda, and water) increased total cholesterol, triglycerides, and systolic blood pressure, but had no effect on HDL cholesterol or diastolic blood pressure. |
| **Raben, 2002**<br><br>**RCT**<br><br>**Denmark**<br><br>**Risk of Bias: 5/28** | Initial N=42<br>Final N=41<br>Attrition=2.4%<br><br>35y (SD=2)<br><br>88% female | **Participants were instructed to consume their usual diet with either:**<br>• Sucrose (~2g/kg body weight/d, or ~23% of calories)<br>• Artificial sweeteners<br><br>**Study Duration:** 10 weeks | **Blood pressure:** Systolic and diastolic blood pressure increased in the sucrose group and decreased in the artificial sweetener group (*Difference between groups: SBP:* 6.9 (95% CI 2-11.9), P<0.01; *DBP:* 5.3 (95% CI 1.1-9.6), P<0.05).<br><br>Change in SBP was correlated with change in sucrose (r=0.43, P<0.01).<br>Change in DBP was correlated with change in sucrose (r=0.39, P<0.05). | Consuming a diet higher in sucrose containing foods and drinks for 10 weeks increased blood pressure compared to consuming foods and drinks with artificial sweeteners. (~2g/kg/d or ~23% energy) |

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**Table 1.** Summary of studies examining the relationship between added sugars and risk of cardiovascular disease

| Author, Year<br><br>Study Design; Location<br><br>Risk of Bias* | Sample Size<br><br>Age<br><br>Gender | Added Sugars Intervention or Exposure<br><br>Study Duration | Results | Summary of Findings |
|---|---|---|---|---|
| **Yu, 2013**<br><br>**RCT**<br>**US**<br><br>**Risk of Bias: 6/28** | Initial N=465<br>Final N=138<br>Attrition=70%<br><br>38y (SD=11)<br>(20-60y)<br><br>43% female | **Participants received a 1% sweetened milk beverage daily with either:**<br><br>1. *Low sucrose:* 8% of calories from sucrose<br>2. *Low HFCS:* 8% of calories from HFCS<br>3. *Moderate sucrose:* 18% of calories from sucrose<br>4. *Moderate HFCS:* 18% of calories from HFCS<br>5. *High sucrose:* 30% of calories from sucrose<br>6. *High HFCS:* 30% of calories from HFCS<br><br>**Study Duration:** 10 weeks | **Triglycerides:** Triglycerides increased following all sweetened milk interventions (P<0.01), but there were no differences between groups. | Drinking sweetened milk increased triglycerides regardless of type of sweetener (sucrose vs. HFCS) or amount (8%, 18%, 30% of energy). |
| **Observational Studies** | | | | |
| **Barrio-Lopez, 2013**<br><br>**PCS (Seguimiento University of Navarra (SUN) cohort)**<br><br>**Spain**<br><br>**Risk of Bias: 2/26** | N=8,157<br><br>~36y<br><br>65% female | Sugar-sweetened carbonated colas and fruit-flavored carbonated sugar soft drinks (non-100% fruit juice excluded).<br><br>**Study Duration:** 6 years | **Triglycerides:** Increasing sugar-sweetened beverage intake was associated with a higher risk of high triglycerides (Q5 vs. Q1; OR 1.7 (95% CI=1.1-2.6); P=0.015).<br><br>**Blood pressure:** Increasing sugar-sweetened beverage intake was associated with a higher risk of high blood pressure (Q5 vs. Q1; OR 1.6 (95% CI=1.3-2.1); P=<0.001).<br><br>**HDL cholesterol:** No significant association with change in sugar-sweetened beverage intake (NS). | Compared to those who did not change their sugar-sweetened beverage intake, those who increased intake of sugar-sweetened beverage (increase of >33ml/d) had an increased risk of having elevated triglycerides and blood pressure, but no difference in risk of reduced HDL cholesterol levels. |

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**Table 1.** Summary of studies examining the relationship between added sugars and risk of cardiovascular disease

| Author, Year<br><br>Study Design; Location<br><br>Risk of Bias* | Sample Size<br><br>Age<br><br>Gender | Added Sugars Intervention or Exposure<br><br>Study Duration | Results | Summary of Findings |
|---|---|---|---|---|
| **Bernstein, 2012**<br><br>**PCS (Nurses' Health Study; Health Professionals Follow-up Study)**<br><br>**US**<br><br>**Risk of Bias: 2/26** | N=127,456<br><br>~58y females), ~62y (males)<br><br>66% female | Soda, including low-calorie with caffeine, other low-calorie carbonated beverages, sugar-sweetened cola caffeine, sugar-sweetened cola without caffeine).<br><br>**Study Duration:** 28 years (women), 22 years (men) | **Total Stroke**:<br><br>*Men:* No significant association with sugar-sweetened soda intake (NS)<br>*Women:* Increased sugar-sweetened soda intake was associated with a higher risk of total stroke (P<0.02) (RR for 1 serving/day=1.14 (95% CI=1.02-1.27)<br><br>*Total Sample:* Increased sugar-sweetened soda intake was associated with a higher risk of total stroke (P<0.02) (RR for 1 serving/day=1.12 (95% CI=1.02-1.24).<br><br>**Ischemic Stroke, Hemorrhagic Stroke**:<br>*Men, Women, Total Sample:* No significant associated with sugar-sweetened soda intake (NS). | Increased sugar-sweetened soda intake (1 serving/d) was associated with increased risk of total stroke in women, and in women and men combined, but not in men alone. There were no significant associations seen between sugar-sweetened soda intake and ischemic stroke and hemorrhagic stroke. |

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**Table 1.** Summary of studies examining the relationship between added sugars and risk of cardiovascular disease

| Author, Year<br><br>Study Design; Location<br><br>Risk of Bias* | Sample Size<br><br>Age<br><br>Gender | Added Sugars Intervention or Exposure<br><br>Study Duration | Results | Summary of Findings |
|---|---|---|---|---|
| **Chen, 2010**<br><br>**PCS (PREMIER)**<br><br>**US**<br><br>**Risk of Bias: 2/26** | N=801<br><br>50y (SD=9)<br><br>61.5% female | Sugar-sweetened beverages (SSB), including carbonated or non-carbonated drinks that were sweetened with sugars (sucrose or high-fructose corn syrup), such as regular soft drinks, fruit drinks, lemonade, fruit punch, and other sweetened beverages (diet drinks excluded).<br><br>**Study Duration:** 18 months | **Systolic Blood Pressure**:<br><br>Reducing SSB intake by 1 serving/d decreased SBP in:<br><br>• *All participants:* (0.7 (95% CI=0.15-1.25), P=0.01)<br>• *Whites:* (0.7 (95% CI=0.15-1.25), P=0.01)<br>• *Men:* (0.78 (95% CI=0.09-1.47), P=0.03)<br>• *Women:* (0.61 (95% CI=-0.27-1.48), P=0.01)<br>*Non-hypertensives, Blacks:* No significant relationship between SSB intake and SBP (NS).<br><br>**Diastolic Blood Pressure**:<br><br>Reducing SSB intake by 1 serving/d decreased DBP in:<br><br>• *All participants*: (0.38 (95% CI =0.02-0.75), P=0.04)<br>• *Whites:* (0.38 (95% CI=0.02-0.75), P=0.04)<br>• *Men:* (0.50 (95% CI=0.01-1.00), P=0.05)<br>*Blacks, Women, Non-hypertensives:* No significant relationship between SSB intake and DBP (NS). | There were some modest associations between reduced consumption of sugar-sweetened beverages (by 1 serving/d) and decreased systolic and diastolic blood pressure. |

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**Table 1.** Summary of studies examining the relationship between added sugars and risk of cardiovascular disease

| Author, Year<br><br>Study Design; Location<br><br>Risk of Bias* | Sample Size<br><br>Age<br><br>Gender | Added Sugars Intervention or Exposure<br><br>Study Duration | Results | Summary of Findings |
|---|---|---|---|---|
| **Cohen, 2012**<br><br>**PCS (Nurses' Health Study; Health Professionals Follow-up Study)**<br><br>**US**<br><br>**Risk of Bias: 4/26** | N=223,891<br><br>~45y<br>(38-53y)<br><br>83% female | Sugar-sweetened beverages, including sugar-sweetened cola, sugar-sweetened caffeine-free cola, sugar-sweetened non-cola, and fruit punch or other sugar-sweetened fruit drinks.<br><br>**Study Duration:** NHS I-38 years, NHS II-16 years, HPSF-22 years | **Incident Hypertension**<br><br>*NHS I, NHS II:* Higher intake of SSB was associated with increased risk of hypertension (>1 SSB/month vs. ≥1 SSB/d), *NHS I:* HR=1.12 (95% CI 1.08-1.17) in NHS I; *NHS II:* HR=1.17 (95% CI 1.1-1.23).<br><br>*HPFS:* NS<br><br>*Cola vs. non-cola:* The association between SSB intake and hypertension incidence was stronger for cola vs. non-cola beverages in NHS I (P-interactions <0.001) and HPFS (P-interactions <0.04).<br><br>*Carbonated vs. non-carbonated:* The association between SSB intake and hypertension incidence was stronger for carbonated vs. non-carbonated beverages in NHS I (P-interactions <0.001) and NHS II (P-interactions <0.03).<br><br>*Fructose from SSB:* Fructose intake derived from SSBs is associated with increased risk of hypertension in NHS I (P=0.001) and NHS II (P=0.001). | Higher intake of sugar-sweetened beverages (>1 SSB/month vs. ≥1 SSB/d) was associated with increased risk of hypertension, particularly for colas and carbonated beverages. |

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**Table 1.** Summary of studies examining the relationship between added sugars and risk of cardiovascular disease

| Author, Year<br><br>Study Design; Location<br><br>Risk of Bias* | Sample Size<br><br>Age<br><br>Gender | Added Sugars Intervention or Exposure<br><br>Study Duration | Results | Summary of Findings |
|---|---|---|---|---|
| **de Koning, 2012**<br><br>**PCS (Health Professionals Follow-up Study)**<br><br>**US**<br><br>**Risk of Bias: 0/26** | N=42,883<br><br>40-75y<br><br>0% female | Sugar-sweetened beverages, including caffeinated colas, non-caffeinated colas, other carbonated sugar-sweetened beverages, non-carbonated sugar-sweetened beverages, and artificially sweetened beverages.<br><br>**Study Duration:** 22 years | **Coronary Heart Disease:** Increased sugar-sweetened beverage intake was associated with higher risk of CHD (Never vs. 3.7/wk-9/d; HR: 1.18 (95% CI=1.06-1.31), P<0.01). | Consumption of sugar-sweetened beverages (Never vs. 3.7/wk to 9/d) was associated with a significantly increased risk of CHD. |
| **Dhingra, 2007**<br><br>**PCS (Framingham Heart Study)**<br><br>**US**<br><br>**Risk of Bias: 2/26** | N=6,039<br><br>53y (SD=10)<br><br>58% female | Soft drinks (regular and diet)<br><br>**Study Duration:** 4 years | **Triglycerides**: Increasing soft drink intake was associated with a higher risk of high triglycerides (>1 serving/day; OR 1.25 (95% CI=1.04-1.51); P<0.05).<br><br>**Blood pressure**: No significant association with soft drink intake (NS).<br><br>**HDL cholesterol**: Increasing soft drink intake was associated with a higher risk of low HDL (>1 serving/day; OR 1.32 (95% CI=1.06-1.64); P<0.05) | Increased soft drink intake (>1 serving/day) was associated with increased risk of elevated triglycerides and reduced HDL cholesterol. |
| **Duffey, 2010**<br><br>**PCS (CARDIO Study)**<br><br>**US**<br><br>**Risk of Bias: 2/26** | N=2774<br><br>25y (SD=4) (18-30y)<br><br>54% female | Sugar-sweetened soda and fruit drinks<br><br>**Study Duration:** 20 years | **Triglycerides:** Higher sugar-sweetened beverage intake (according to quartile average of years 0 and 7) was associated with increased risk of high triglycerides (RR=1.06 (95% CI=1.01-1.13), P<0.033).<br><br>**LDL:** Higher sugar-sweetened beverage intake was associated with increased risk of high LDL (RR=1.18 (95% CI=1.02-1.36), P<0.018).<br><br>**Hypertension:** Higher sugar-sweetened | Higher intake of sugar-sweetened beverages was associated with increased risk of high triglycerides, high LDL, and hypertension, but not with HDL levels. |

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**Table 1.** Summary of studies examining the relationship between added sugars and risk of cardiovascular disease

| Author, Year<br><br>Study Design; Location<br><br>Risk of Bias* | Sample Size<br><br>Age<br><br>Gender | Added Sugars Intervention or Exposure<br><br>Study Duration | Results | Summary of Findings |
|---|---|---|---|---|
| | | | beverage intake was associated with increased risk of hypertension (RR=1.06 (95% CI=1.01-1.12), P<0.023).<br><br>**HDL:** No significant associations (NS). | |
| **Eshak, 2012**<br><br>**PCS**<br><br>**Japan**<br><br>**Risk of Bias: 2/26** | N=39,786<br><br>~57y (SD=7) (40-59y)<br><br>53% female | Soft drinks that contained added caloric sweeteners, including cola-type beverages, flavored juices, and non-100% fruit juices.<br><br>**Study Duration:** 18 years | **Stroke**:<br><br>*Men:* No association between soft drink intake and risk of total stroke, hemorrhagic stroke, or ischemic stroke (NS)<br>*Women:* Increased soft drink intake was associated with increased risk of total stroke (never/rarely vs. every day), (HR=1.21 (95% CI=0.88-1.68), P<0.02) and ischemic stroke (HR=1.83 (95% CI=1.22-2.75), P<0.001). There was no association between soft drink intake and hemorrhagic stroke (NS).<br><br>**Ischemic Heart Disease**: *Men, Women:* No significant associations (NS). | Increased soft drink intake (never/rarely vs. every day) was associated with increased risk of total stroke and ischemic stroke in women. |

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**Table 1.** Summary of studies examining the relationship between added sugars and risk of cardiovascular disease

| Author, Year<br><br>Study Design; Location<br><br>Risk of Bias* | Sample Size<br><br>Age<br><br>Gender | Added Sugars Intervention or Exposure<br><br>Study Duration | Results | Summary of Findings |
|---|---|---|---|---|
| **Fung, 2009**<br><br>**PCS (Nurses' Health Study)**<br><br>**US**<br><br>**Risk of Bias: 0/26** | N=88,520<br><br>30-55y<br><br>100% female | Sugar-sweetened beverages, including caffeinated and non-caffeinated colas, other carbonated beverages with sugar, non-carbonated sweetened beverages.<br><br>**Study Duration:** 24 years | **Coronary Heart Disease**: Increased sugar-sweetened beverage intake was associated with a greater risk of CHD (<1/mo vs. >2/d, HR=1.35 (95% CI=1.07-1.69), P<0.001).<br><br>*Total SSBs:* A 2-serving increase in sugar-sweetened beverage intake was associated with a greater risk of CHD (HR=1.28 (95% CI=1.14-1.44), P<0.001)<br>*Colas:* A 2-serving increase in cola intake was associated with a greater risk of CHD (HR=1.35 (95% CI=1.15-1.57), P<0.001)<br>*Fruit drinks and punch:* A 2-serving increase in fruit drink/punch intake was associated with a greater risk of CHD (HR=1.33 (95% CI=1.03-1.71), P=0.03)<br>*Carbonated noncola:* No significant association with CHD (NS). | Increased sugar-sweetened beverage intake (<1/mo vs. >2/d) was associated with a greater risk of CHD. |
| **Larsson, 2014**<br><br>**PCS (Swedish Mammography Cohort, Cohort of Swedish Men)**<br><br>**Sweden**<br><br>**Risk of Bias: 2/26** | N=68,459<br><br>~60y<br>(45-83y)<br><br>48% female | Soft drinks or sweetened juice drinks, including both sugar-sweetened and low-calorie drinks.<br><br>**Study Duration:** 10 years | **Total Stroke**: Increased sugar-sweetened beverage intake was associated with a higher risk of total stroke (0 vs. >2 servings/day; OR 1.19 (95% CI=1.04-1.36); P<0.01).<br><br>**Cerebral Infarction**: Increased sugar-sweetened beverage intake was associated with a higher risk of cerebral infarction (0 vs. >2 servings/day; OR 1.22 (95% CI=1.04-1.42); P<0.01).<br><br>**Hemorrhagic Stroke:** No significant associations (NS). | Increased intake of sugar-sweetened beverages (0 vs. >2 servings/d) was associated with increased total stroke risk and increased risk of cerebral infarction, but not with hemorrhagic stroke. |

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**Table 1.** Summary of studies examining the relationship between added sugars and risk of cardiovascular disease

| Author, Year<br><br>Study Design; Location<br><br>Risk of Bias* | Sample Size<br><br>Age<br><br>Gender | Added Sugars Intervention or Exposure<br><br>Study Duration | Results | Summary of Findings |
|---|---|---|---|---|
| **Tasevska, 2014**<br><br>**PCS (NIH-AARP Diet and Health Study)**<br><br>**Risk of Bias: 2/26** | N=353,751<br><br>~61y<br>(50-71y)<br><br>42% female | Added sugars included all mono- and disaccharides used as ingredients in processed and prepared foods, soft and alcoholic drinks, jams and jellies, candies, and ice cream, and sugars eaten separately. Added sucrose and fructose was the sum of sucrose and fructose from added sugars, plus sucrose and fructose from fruit juice, and half of sucrose and fructose from apple sauce and dried fruit (due to cellular disruption during processing).<br><br>**Study Duration:** 13 years | **CVD Mortality**: Added sugars, added fructose, and added sucrose were not associated with CVD mortality in either women or men (NS). | Consumption of added sugars (total, as well as added sucrose and added fructose) was not associated with CVD mortality. |
| **Yang, 2014**<br><br>**PCS (National Health and Nutrition Examination Survey (NHANES) Linked Mortality Cohort)**<br><br>**US**<br><br>**Risk of Bias: 3/26** | N=11,733<br><br>20y and older<br><br>Gender not reported | Added sugars included all sugars used in processed or prepared foods, such as sugar-sweetened beverages, grain-based desserts, fruit drinks, dairy desserts, candy, ready-to-eat cereals, and yeast breads (naturally occurring sugar excluded).<br><br>**Study Duration:** 14.6 years | **CVD Mortality**: Increased added sugars intake was associated with higher risk of CVD mortality (0-10% vs. >25% calories from added sugars; HR: 2.75 (95% CI=1.40-5.42), P=0.004). | Increase intake of added sugars (0-10% vs. >25% energy) was associated with increased risk of CVD mortality. |

*Risk of Bias as determined using the Nutrition Evidence Library Bias Assessment Tool

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**Intervention Studies**

Eleven studies included in this systematic review were intervention studies that examined the effects of added sugars intake on CVD risk factors, seven of which were randomized crossover trials (Aeberli, 2011; Aeberli, 2013; Black, 2066; Faeh, 2005; Le, 2009; Lewis, 2013) and five were randomized controlled trials (RCT) (Lowndes, 2014a; Lowndes, 2014b; Maersk, 2012; Raben, 2002; Yu, 2013). The included articles had moderate risk of bias ratings (scores ranged from two to 10 out of 28).

Studies were conducted in a number of different countries, including four in the United States (Lowndes, 2014a; Lowndes, 2014a; Yu, 2013), four in Switzerland (Aeberli, 2011; Aeberli, 2013; Faeh, 2005; Le, 2009), two in Denmark (Maersk, 2012; Raben, 2002) and two in the United Kingdom (Black, 2006; Lewis, 2013). All of the articles included generally healthy adults (mean age ranged from 23 years to 46 years). Five articles included only men (Aeberli, 2011; Aeberli, 2013; Black, 2006; Faeh, 2005; Le, 2009) and the others included both men and women. Sample size ranged from seven to 355 participants (six articles had less than 30 participants, three articles had 30 to 65 participants, one study had 138 participants and one had 355 participants). Little information was provided about participants' race/ethnicity or socioeconomic status (SES).

*Added Sugars*

The 12 intervention studies included in this review used a variety of approaches to compare different levels of added sugars, varying in the types and amounts of sugars tested. The studies ranged in duration from one week to six months, though most interventions were carried out for fewer than ten weeks. Table 2 provides a brief summary of the interventions tested.

**Table 2. Type and Amount of Added Sugars Tested in Intervention Studies Designed to Test the Effects of Added Sugars on Cardiovascular Disease Risk**

| Article | Type and Amount of Added Sugars Tested |
|---|---|
| Aeberli, 2011 | *Medium fructose:* 40g per day fructose<br>*High fructose:* 80g per day fructose<br>*Medium glucose:* 40g per day glucose<br>*High glucose:* 80g per day glucose<br>*High sucrose:* 80g per day sucrose<br>*Control:* Received advice to decrease fructose |
| Aeberli, 2013 | *Medium fructose:* 40g per day fructose<br>*High fructose:* 80g per day fructose<br>*High glucose:* 80g per day glucose<br>*High sucrose:* 80g per day sucrose. |
| Black, 2006 | *Low sucrose diet:* 10% sucrose<br>*High sucrose diet:* 25% sucrose. |



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| | |
|---|---|
| Faeh, 2005 | *Fish oil:* 7.2g per day for 28 days<br>*High fructose:* 3g per kg per day (approximately +25% energy requirement)<br>Fish-oil + High fructose: 7.2g per day fish oil + high fructose diet<br>*Control.* |
| Le, 2009 | *Isocaloric diet:* 55% carbohydrate, 30% fat, 15% protein<br>*High fructose diet:* Isocaloric diet +3.5g per kg fructose (+35% energy requirement). |
| Lewis, 2013 | *Low sucrose diet:* 5% sucrose<br>*High sucrose diet:* 15% sucrose. |
| Lowndes, 2014a | *HFCS 10%:* 10% of calories from high-fructose corn syrup (HFCS)<br>*HFCS 20%:* 20% of calories from high-fructose corn syrup<br>*Sucrose 10%:* 10% of calories from sucrose<br>*Sucrose 20%:* 20% of calories from sucrose. |
| Lowndes, 2014b | *Low sucrose:* 8% of calories from sucrose<br>*Low HFCS:* 8% of calories from HFCS<br>*Moderate sucrose:* 18% of calories from sucrose<br>*Moderate HFCS:* 18% of calories from HFCS<br>*High sucrose:* 30% of calories from sucrose<br>*High HFCS:* 30% of calories from HFCS. |
| Maersk, 2012 | *Regular cola:* 1L per day<br>*Aspartame-sweetened cola:* 1L per day<br>*Semi-skim milk:* 1L per day<br>*Still mineral water:* 1L per day. |
| Raben, 2002 | *Sucrose group* (approximately 2g per kg body weight per day, or approximately 23% of calories)<br>*Artificial sweetener group.* |



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| | |
|---|---|
| Yu, 2013 | *Low sucrose:* 8% of calories from sucrose<br>*Low HFCS:* 8% of calories from HFCS<br>*Moderate sucrose:* 18% of calories from sucrose<br>*Moderate HFCS:* 18% of calories from HFCS<br>*High sucrose:* 30% of calories from sucrose<br>*High HFCS:* 30% of calories from HFCS. |

### *Outcomes*

All included articles measured one or more intermediate cardiovascular disease risk outcomes, including triglycerides, total cholesterol, LDL cholesterol, HDL cholesterol, total cholesterol:HDL ratio, and blood pressure (Table 3).

**Table 3. Cardiovascular Disease Outcomes Examined in Intervention Studies Designed to Test the Effects of Added Sugars on Cardiovascular Disease Risk Factors**

| Article | Outcomes |
|---|---|
| Aeberli, 2011 | Total cholesterol, LDL cholesterol, HDL cholesterol, triglycerides, blood pressure |
| Aeberli, 2013 | Total cholesterol, LDL cholesterol, HDL cholesterol, triglycerides |
| Black, 2006 | Total cholesterol, LDL cholesterol, HDL cholesterol, triglycerides |
| Faeh, 2005 | Triglycerides |
| Le, 2009 | Triglycerides |
| Lewis, 2013 | Total cholesterol, LDL cholesterol, HDL cholesterol, triglycerides, blood pressure |
| Lowndes, 2014a | Total cholesterol, LDL cholesterol, HDL cholesterol, triglycerides, blood pressure, total cholesterol:HDL ratio |
| Lowndes, 2014b | Total cholesterol, LDL cholesterol, HDL cholesterol, triglycerides, blood pressure |
| Maersk, 2012 | Total cholesterol, HDL cholesterol, triglycerides, blood pressure |
| Raben, 2002 | Blood pressure |



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| | |
|---|---|
| Yu, 2013 | Triglycerides |

### *Observational Studies*

Twelve articles included in this systematic review were prospective cohort studies that examined the relationship between added sugars (mostly in the form of SSBs) and risk of cardiovascular disease (Barrio-Lopez, 2013; Bernstein, 2012; Chen, 2010; Cohen, 2012; de Koning, 2012; Dhingra, 2007; Duffey, 2010; Eshak, 2012; Fung, 2009; Larsson, 2014; Tasevska, 2014; Yang, 2014). The 12 articles used data from ten different cohorts, with three articles each using data from the Health Professionals Follow-up Study (Bernstein, 2012; Cohen, 2012; de Koning, 2012) and the Nurses' Health Study (Bernstein, 2012; Cohen, 2012; Fung, 2009). The included articles had low risk of bias ratings (Scores ranged from zero to four out of 26.

Nine of the observational studies used participants from the United States (Bernstein, 2012; Chen, 2010; Cohen, 2012; de Koning, 2012; Dhingra, 2007; Duffey, 2010; Fung, 2009; Tasevska, 2014; Yang, 2014) and one each were done in Spain (Barrio-Lopez, 2013), Japan (Eshak, 2012) and Sweden (Larsson, 2024).

All of the articles included generally healthy adults (mean age ranged from 25 to 61 years). One article included only women (Fung, 2009), one included only men (de Koning, 2012) Aeberli, 2011; Aeberli, 2013; Black, 2006; Faeh, 2005; Le, 2009), and the others included both men and women. Sample size ranged from 801 to 353,751 participants. Only a few studies provided information about participants' SES, and in those articles that provided information about race/ethnicity, participants were primarily non-Hispanic white.

#### *Added Sugars*

The 12 observational articles included in this review used a variety of approaches to assessing intake of added sugars. In many cases, sugar-sweetened beverages were examined, while in others, total added sugars intake from all foods and beverages was calculated. The articles ranged in duration from 18 months to 38 years of follow up, with most cohorts being followed for over 10 years. Six out of the 12 articles assessed added sugars intake several times over the course of follow-up and used cumulative intakes in analyses (Barrio-Lopez, 2013; Bernstein, 2012; Chen, 2010; de Koning, 2012; Eshak, 2012; Fung, 2009), while six articles assessed added sugars at a single time point, usually at baseline (Cohen, 2012; Dhingra, 2007; Duffey, 2010; Larsson, 2014; Tasevska, 2014; Yang, 2014). Table 4 provides a summary of how added sugars were defined and examined in this group of articles.

**Table 4. Definitions of Added Sugars Examined in Observational Studies Examining the Relationship Between Added Sugars and Risk of Cardiovascular Disease**

| Article | Added Sugars Definition |
|---|---|
| Barrio-Lopez, 2013 | Sugar-sweetened carbonated colas and fruit-flavored carbonated sugar soft drinks (non-100% fruit juice excluded) |
| Bernstein, 2012 | Soda, including low-calorie with caffeine, other low-calorie carbonated beverages, sugar-sweetened cola with caffeine, sugar-sweetened cola without caffeine |



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| | |
|---|---|
| Chen, 2010 | Sugar-sweetened beverages, including carbonated or non-carbonated drinks that were sweetened with sugars (sucrose or HFCS), such as regular soft drinks, fruit drinks, lemonade, fruit punch and other sweetened beverages (diet drinks excluded) |
| Cohen, 2012 | SSBs, including sugar-sweetened cola, sugar-sweetened caffeine-free cola, sugar-sweetened non-cola and fruit punch or other sugar-sweetened fruit drinks |
| de Koning, 2012 | SSBs, including caffeinated colas, non-caffeinated colas, other carbonated sugar-sweetened beverages, non-carbonated SSBs and artificially sweetened beverages |
| Dhingra, 2007 | Soft drinks (regular and diet) |
| Duffey, 2010 | Sugar-sweetened soda and fruit drinks |
| Eshak, 2012 | Soft drinks that contained added caloric sweeteners, including cola-type beverages, flavored juices and non-100% fruit juices |
| Fung, 2009 | SSBs, including caffeinated and non-caffeinated colas, other carbonated beverages with sugar, non-carbonated sweetened beverages |
| Larsson, 2014 | Soft drinks or sweetened juice drinks, including both sugar-sweetened and low-calorie drinks |
| Tasevska, 2014 | Added sugars included all monosaccharides and disaccharides used as ingredients in processed and prepared foods, soft and alcoholic drinks, jams and jellies, candies, ice cream and sugars eaten separately. Added sucrose and fructose was the sum of sucrose and fructose from added sugars, plus sucrose and fructose from fruit juice, and half of sucrose and fructose from apple sauce and dried fruit (due to cellular disruption during processing) |
| Yang, 2014 | Added sugars included all sugars used in processed or prepared foods, such as SSBs, grain-based desserts, fruit drinks, dairy desserts, candy, ready-to-eat cereals and yeast breads (naturally occurring sugar excluded) |

### *Outcomes*

The observational studies included in this review examined a range of both intermediate and endpoint cardiovascular disease outcomes. Table 5 provides a summary of the outcomes considered by these articles.



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| Table 5. Cardiovascular Disease Outcomes Examined in Observational Studies Examining the Relationship Between Added Sugars and Risk of Cardiovascular Disease | |
|---|---|
| **Article** | **Outcomes** |
| Barrio-Lopez, 2013 | Triglycerides, HDL cholesterol, blood pressure |
| Bernstein, 2012 | Incidence of stroke |
| Chen, 2010 | Blood pressure |
| Cohen, 2012 | Incidence of hypertension |
| de Koning, 2012 | Incidence of coronary heart disease [fatal and non-fatal myocardial infarction (MI)] |
| Dhingra, 2007 | Triglycerides, HDL cholesterol, blood pressure |
| Duffey, 2010 | Triglycerides, LDL cholesterol, HDL cholesterol, incidence of hypertension |
| Eshak, 2012 | Ischemic heart disease (MI), stroke |
| Fung, 2009 | Nonfatal myocardial infarction, fatal CHD |
| Larsson, 2014 | Incidence of stroke |
| Tasevska, 2014 | CVD mortality |
| Yang, 2014 | CVD mortality |

### Evidence Synthesis

The majority of intervention and observational studies included in this systematic review provide some evidence in support of an association between intake of added sugars, especially in the form of SSBs and elevated risk of CVD or increased CVD risk factors. In particular, more consistent associations were seen with elevated triglycerides and increased risk of stroke, CHD and hypertension. However, evidence for associations between added sugars and dyslipidemia (HDL, LDL and total cholesterol) and blood pressure was not as consistent from intervention studies.

Thirteen studies examined added sugars and triglycerides, including ten RCTs (Aeberli, 2011; Aeberli, 2013; Black, 2006; Faeh, 2005; Le, 2009; Lewis, 2013; Lowndes, 2014a; Lowndes, 2014b; Maersk, 2012; Yu, 2013) and three prospective cohort studies (Barrio-Lopez, 2013; Dhingra, 2007; Duffey, 2010). Eight of the 13 studies found that consuming added sugars was associated with increased triglycerides, including five of the RCTs and all three cohort studies (Barrio-Lopez, 2013; Dhingra, 2007; Duffey, 2010; Faeh, 2005; Le, 22009; Lowndes, 2014b; Maerks, 2012; Yu, 2013). The remaining five RCTs found no differences between interventions groups in terms of triglycerides.



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Five cohort studies examined added sugars and risk of stroke or CHD (Bernstein, 2012; de Koning, 2012; Eshak, 2012; Fung, 2009; Larsson, 2014). All three of the articles that examined stroke reported an association between higher intake of added sugars in the form of SSBs and increased risk of stroke (Bernstein, 2012; Eshak, 2012; Larsson, 2014), particularly among women (Bernstein, 2012; Eshak, 2012). Both studies that examined risk of CHD reported that increased SSB intake was associated with increased risk of CHD (de Koning, 2012; Fung, 2009).

Ten studies examined blood lipids (i.e., total cholesterol, LDL cholesterol, and HDL cholesterol) in relation to added sugars intake, including seven RCTs (Aeberli, 2011; Aeberli, 2013; Black, 2006; Lewis, 2013; Lowndes, 2014a; Lowndes, 2014b; Maersk, 2012) and three prospective cohort studies (Barrio-Lopez- 2013; Dhingra, 2007; Duffey, 2010). The results of these studies were mixed. Three studies found that total cholesterol or the total cholesterol:HDL ratio increased with added sugars intake (Black, 2006; Lowndes, 2014a; Maersk, 2012). One found that 40g of fructose increased total cholesterol compared to 80g of glucose (Aeberli, 2013), while three found no relationship between added sugars intake and total cholesterol (Aeberli, 2011; Lewis, 2013; Lowndes, 2014b). Similarly, two studies found that LDL was higher after increased added sugar intake (Black 2006; Duffey, 2010) and one found that 40g of fructose increased total cholesterol compared to 80g of glucose (Aeberli, 2013), while four studies showed no relationship between amount of added sugars consumed and LDL cholesterol levels (Aeberli, 2011; Lewis, 2013; Lowndes, 2014a; Lowndes, 2014b). Finally, three studies reported that increased added sugars intake decreased HDL cholesterol (Lowndes, 2014a; Lowndes, 2014b; Dhingra, 2007), while seven studies reported no relationship between added sugars and HDL cholesterol (Aeberli, 2011; Aeberli, 2013; Barrio-Lopez, 2013; Black, 2006; Duffey, 2010; Lewis, 2013; Maersk, 2012).

Eleven studies examined the relationship between added sugars consumption and blood pressure or risk of hypertension, including six RCTS (Aeberli, 2011; Lewis, 2013; Lowndes, 2014a; Lowndes, 2014b; Maersk, 2012; Raben, 2002) and five cohort studies (Barrio-Lopez, 2013; Chen, 2010; Chen, 2012; Dhingra, 2007; Duffey, 2010). Several of these studies found no relationship between added sugars intake and blood pressure or hypertension [Aeberli, 2011; Lewis, 2013; Lowndes, 2014a; Lowndes, 2014b (diastolic only); Maersk, 2012 (diastolic only); Dhingra, 2007], though a number of large prospective cohort studies and intervention studies did provide some evidence that increased added sugars intake was associated with higher blood pressure or increased risk of hypertension [Barrio-Lopez, 2013; Chen, 2010; Cohen, 2012; Duffey, 2010; Lowndes, 2014b (systolic only); Maersk, 2012 (systolic only), Raben, 2002].

Only two studies, both prospective cohort studies, examined the relationship between added sugars intake and mortality from cardiovascular disease (Tasevka, 2014; Yang, 2014), and results were mixed. Tasevka, 2014 found no relationship between added sugars and CVD mortality, while Yang, 2014 reported that increased added sugars intake (more than 25% of calories vs. zero to 10% of calories) was associated with higher risk of CVD mortality. Of note, a single food frequency questionnaire (FFQ) used in Tasevka, 2014 was unlikely to capture total added sugar intake reliably, whereas in the National Health and Nutrition Examination Survey (NHANES) follow-up study (Yang, 2014), usual intake of added sugar was estimated based on two 24-hour recalls. In the NHANES study, higher consumption of SSBs (more than one serving per day) was associated with 30% increased risk of CVD mortality.

Generalizability of this body of evidence to the US population is somewhat limited. Most studies included predominantly white participants, although a few used samples that included various race and ethnic groups represented in the US population (Eshak, 2012; Yang, 2014). Most of the intervention studies were conducted in younger adults (mean age of 20 years to 30 years). Several intervention studies and one cohort study included only male participants (Aeberli, 2011; Aeberli, 2013; Black, 2006; de Koning, 2012; Faeh, 2005; Le, 2009), while one



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of the cohort studies included only women (Fung, 2009).

The body of evidence examined in this systematic review had a number of limitations. The intervention studies had extensive heterogeneity in terms of the types, amounts and forms of added sugars tested (fructose, glucose, sucrose, SSB, sweetened milk), as well as the type of control and isocaloric condition used. Several interventions, which were isocaloric and held carbohydrate content constant, substituted the sugar with starch, which may not be a realistic substitution model of free-living dietary practice, especially for beverages. The intervention studies also tended to be short in duration (from one week to six months), the sample sizes were relatively small (seven to 355 subjects), and participant retention was an issue. Many of the intervention studies did not control for other aspects of the diet, such as salt intake, and so it is possible that differences in these other dietary components could have impacted results. Most of the observational studies only assessed dietary intake at baseline and did not take assessments during follow-up, which would not capture changes in diet or other health conditions over time. In addition, the dietary intake assessment methods used, in most cases an FFQ, may not have adequately captured the total amount of added sugars intake. Finally, the potential for residual confounding in the observational studies cannot be ruled out.

## Research recommendations

In order to better assess the relationship between added sugars and CVD, additional research is needed:

- To examine, in well-designed RCTs, the effects of added sugars over longer time periods. It is particularly important to test interventions that can be implemented in free-living populations.
- That obtains more precise exposure measurements of added sugars in long-term prospective observation studies with repeated measures of exposure
- That includes diverse populations, especially women, children and adolescents, as well as non-white race/ethnic groups.

## Search plan and results

### Inclusion criteria

- Human subjects
- Subject populations from countries with high or very high human development, according to the 2012 Human Development Index [1]
- Adults aged 18 years and older
- Subjects who were healthy or at elevated chronic disease risk
- Randomized or non-randomized controlled trial, prospective cohort study or a nested case-control study
- The intervention or exposure was added sugars, including studies on sugar-sweetened beverages. The definition of added sugars used for the purpose of this review was “Sugars that are either added during the processing of foods, or are packaged as such, and include sugars (free, monosaccharides and disaccharides), syrups, naturally occurring sugars that are isolated from a whole food and concentrated so that sugar is the primary component (e.g., fruit juice concentrates) and other caloric sweeteners. This would include single-ingredient foods such as individually packaged table sugar. Sugar alcohols are not considered to be added sugars. Names for added sugars include brown sugar, corn sweetener, corn syrup, dextrose, fructose, fruit juice concentrates, glucose, high-fructose corn syrup, honey, invert sugar, lactose, maltose, malt sugar, molasses, raw sugar, turbinado sugar, trehalose and sucrose.”
- The comparator was different levels of intake of added sugars or sugar-sweetened



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beverages
- The outcomes were cholesterol (LDL, HDL, TC:HDL and LDL:HDL ratios), triglycerides, blood pressure and incidence of hypertension, incidence of myocardial infarction, incidence of stroke, incidence of CHD and CVD-related mortality.

Articles were included if they were published in English in a peer-reviewed journal between January 2000 and August 2014. If an author is included on more than one primary research article that is similar in content, the paper with the most pertinent data and endpoints was included. If data and endpoints from both papers are appropriate, it was made clear that results are from the same intervention.

[1] United Nations Development Programme. Human Development Report 2013, The Rise of the South: Human Progress in a Diverse World 2013. Available from: http://hdr.undp.org/sites/default/files/reports/14/hdr2013_en_complete.pdf.

### Exclusion criteria

- Animals and *in vitro* models
- Subject populations from countries with medium or low human development, according to the Human Development Index
- Children under the age of two years
- Subjects who were hospitalized, diagnosed with disease and receiving medical treatment
- Systematic review, meta-analysis, narrative review, before-and-after studies, uncontrolled studies, cross-sectional studies, case-control studies, ecological designs.

Articles were excluded if they were not published in English or were published before January 2000. Articles, abstracts and presentations not published in peer-reviewed journals (e.g., websites, magazine articles, Federal reports) were also excluded. Finally, if an author was included on more than one review article or primary research article that is similar in content, the paper with the most pertinent data and endpoints was included and others were excluded.

### Analytic framework



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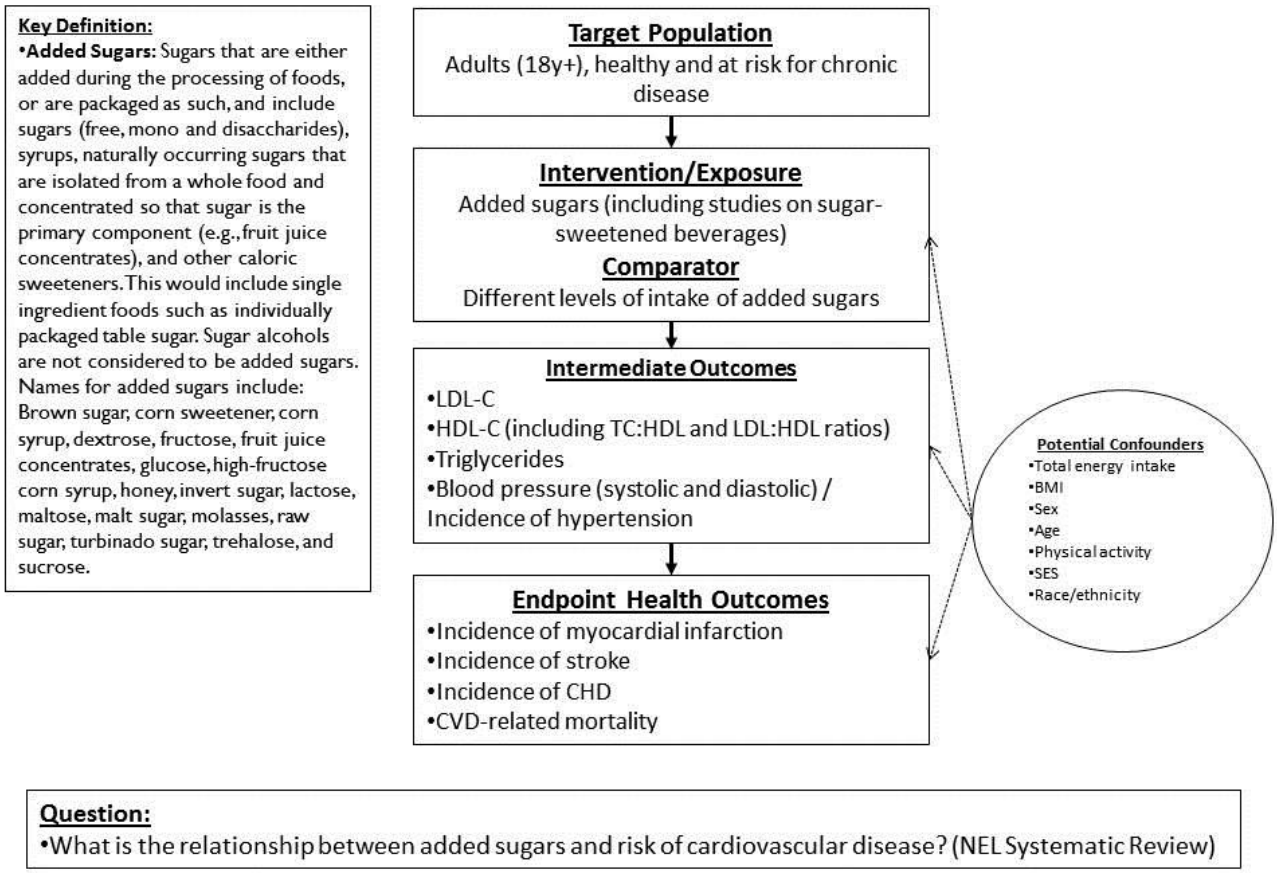
**Analytical Framework:** Added Sugars and Cardiovascular Disease




## Search terms and electronic databases used

- ***PubMed***
  - *Date(s) Searched:* ***August 2014***
  - *Search Terms:* Added Sugar* OR brown sugar*[tiab] OR white sugar*[tiab] OR raw sugar* OR syrup*[tiab] OR dextrose OR fructose OR fruit juice concentrate* OR glucose OR honey[mh] OR honey[tiab] OR jam[tiab] OR invert sugar* OR malt sugar* OR maltose[tiab] OR maltodextrin OR molasses OR turbinado sugar* OR cane sugar*[tiab] OR cane juice*[tiab] OR “sugar cane”[tiab] OR sugar beet*[tiab] OR trehalose[tiab] OR sucrose[tiab] OR sweetene* OR table sugar*[tiab] OR "Monosaccharides"[Mesh] OR Monosaccharide*[tiab] OR disaccharide*[tiab] OR "Disaccharides"[Mesh] OR "Sweetening Agents"[Mesh:noexp] OR "Nutritive Sweeteners"[Mesh] OR "Dietary Sucrose"[tiab] OR sugar based* OR sugar-based* OR HFCS OR candy[tiab] OR "Candy"[Mesh] OR “Carbonated beverages”[mh] OR Soft drink* OR Liquid sugar* OR Soda pop* OR soda[tiab] OR Carbonated drink*[tiab] OR dessert*[tiab] OR pastries[tiab] OR ice cream*[tiab] OR cookies[tiab] OR cake*[tiab] OR pie[tiab] OR pies[tiab] OR gelatin*[tiab] OR jello[tiab] OR fruit punch*[tiab] OR fruitade*[tiab] OR sugary[tiab] OR sweets[tiab] OR sugar-sweetene*[tiab] OR caramel OR "malt barley" OR "barley malt" OR "Sweetening Agents" [Pharmacological Action] (done; w/ food/diet terms 30; none selected; 8/7/2014) OR sugar-coated[tiab] OR sugar coated*[tiab] OR sugar*[ti] OR sugar sweeten*[tiab] OR dietary sugar*[tiab] OR confectioner*[tiab] OR fizzy drink*[tiab] OR chewing gum*[tiab]



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- AND
- "Mortality"[Mesh] OR mortality[tiab] OR "blood pressure"[tiab] OR "blood pressure"[mesh] OR "cardiovascular diseases"[mh:noexp] OR cardiovascular disease*[tiab] OR cardiovascular event*[tiab] OR hypertension[tiab] OR "Myocardial Infarction"[Mesh] OR "Myocardial Infarction"[tiab] OR "Heart Failure"[Mesh] OR "Heart Arrest"[Mesh] OR "Myocardial Ischemia"[Mesh] OR "heart failure"[tiab] OR "heart arrest"[tiab] OR "Myocardial Ischemia"[tiab] OR hypertension[mh] OR stroke[tiab] OR "stroke"[Mesh] OR mortality[sh] OR (coronary[tiab] AND disease*[tiab]) OR
- "cholesterol/blood"[mh] OR "Cholesterol, Dietary"[Mesh] OR "Cholesterol"[Mesh] OR "Cholesterol, HDL"[Mesh] OR "Cholesterol, LDL"[Mesh] OR "Cholesterol, VLDL"[Mesh] OR cholesterol[tiab] OR "Cholesterol, Dietary"[Mesh] OR triglyceride* OR "Lipids/blood"[Mesh] OR hypercholesterolemia[mh] OR hypercholesterol*[tiab] OR hypercholesterolemia[tiab]
  AND (food[tiab] OR beverage*[tiab] OR drink* OR "Food and Beverages"[Mesh] OR diet[tiab] OR diets[tiab] OR dietary[tiab] OR nutrition* OR dietetic* OR diet[mh])
- ("Study Characteristics" [Publication Type] OR “clinical trial”[ptyp] OR "Epidemiologic Studies"[Mesh] OR "Support of Research"[ptyp] OR cohort[tiab] OR observational[tiab] OR retrospective[tiab] OR longitudinal[tiab]) NOT (editorial[ptyp] OR comment[ptyp] OR news[ptyp] OR letter[ptyp] OR review[ptyp] OR systematic[sb])

- ***Cochrane***
  - *Date(s) Searched:* ***August 2014***
  - *Search Terms:* (Added NEXT Sugar*) OR (brown NEXT sugar*) OR (white NEXT sugar*) OR (raw NEXT sugar*) OR syrup*:ti, kw OR dextrose:ti OR fructose:ti OR (fruit NEXT juice NEXT concentrate*) OR glucose:ti OR honey:ti OR jam:ti OR (invert NEXT sugar*) OR (malt NEXT sugar*) OR maltose:ti OR maltodextrin:ti OR molasses OR (turbinado NEXT sugar*) OR (cane NEXT sugar*) OR (cane NEXT juice*) OR “sugar cane”:ti, ab OR (sugar NEXT beet*):ti, ab OR trehalose:ti OR sucrose:ti OR sweetene* OR (table NEXT sugar*) OR Monosaccharide*:ti OR disaccharide*:ti OR "Dietary Sucrose":ti, ab OR (sugar NEXT based*) OR sugar-based* OR HFCS OR candy:ti, ab OR candies:ti, ab OR (Carbonated NEAR beverage*) OR (Carbonated NEAR drink*) OR (Soft NEXT drink*) OR (Liquid NEXT sugar*) OR (Soda NEXT pop*) OR popsicle* OR soda:ti OR dessert*:ti, ab OR pastries:ti, ab OR (ice NEAR/1 cream*) OR cookies:ti, ab OR cake*:ti OR pie:ti OR pies:ti OR gelatin*:ti OR jello:ti OR “fruit punch”:ti, ab OR fruitade*:ti, ab OR sugar*:ti OR sweets:ti OR (sugar-sweetene*:ti, kw, ab) OR caramel:ti, ab OR (malt* NEAR/1 barley) OR 'syrup':ti, ab, kw OR (dietary NEXT sugar*):ti, ab OR sugary:ti, ab OR sugar*:ti OR (sugar NEAR/3 sweet*):ti, ab OR (sugar NEAR/3 coat*):ti, ab OR (dietary NEXT/1 sugar*):ti, ab OR confectioner*:ti, ab OR (fizzy NEXT/1 drink*):ti, ab OR chewing gum*:ti, ab

    AND

    mortality OR "blood pressure" OR (cardiovascular NEXT (event OR disease*)) OR (coronary NEXT heart NEXT disease*) OR ((cholesterol OR lipid*) NEAR/2 blood) OR (Cholesterol NEAR/2 HDL) OR cholesterol OR (Cholesterol NEAR/2 Dietary) OR triglyceride*:ti, ab OR "Myocardial Infarction" OR "Heart Arrest" OR "Myocardial Ischemia" OR (heart NEXT failure*) OR hypertension OR stroke:ti, ab OR hypercholesterol* :ti, ab OR hypercholesterolemia*:ti, ab



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- ***EMBASE***
  - *Date(s) Searched:* ***August 2014***
  - *Search Terms:* (added NEXT/1 sugar*):ti, ab OR (raw NEXT/1 sugar*):ti, ab OR (white NEXT/1 sugar*):ti, ab OR (brown NEXT/1 sugar*):ti, ab OR 'sugar intake'/exp OR 'sucrose'/exp OR 'sweetening agent'/de OR 'fructose'/exp OR 'monosaccharide'/exp OR 'sugarcane'/exp OR 'lactose'/exp OR (milk NEXT/2 sugar*):ti, ab OR 'sugar beet'/exp OR 'sugar'/exp/mj OR (sugar NEXT/1 beet*):ti, ab OR sugarcane:ti, ab OR (sugar NEXT/1 cane):ti, ab OR dextrose:ti, ab OR 'glucose'/exp OR (corn NEXT/1 syrup*):ti, ab OR (maple NEXT/1 syrup*):ti, ab OR 'honey'/exp OR 'invert sugar'/exp OR (invert NEXT/1 sugar*):ti, ab OR 'maltose'/exp OR (malt NEXT/1 sugar*):ti, ab OR 'maltodextrin'/exp OR 'molasses'/exp OR (turbinado NEXT/1 sugar*):ti, ab OR 'disaccharide'/exp OR disaccharide*:ti, ab OR trehalose*:ti, ab OR (sugar NEXT/1 based*):ti, ab OR HFCS*:ti, ab OR candy:ti, ab OR candies:ti, ab OR 'carbonated beverage'/exp OR (carbonated NEXT/1 beverage*):ti, ab OR (Soft NEXT/1 drink*):ti, ab OR (Liquid NEXT/1 sugar*):ti, ab OR (Soda NEXT/1 pop*):ti, ab OR popsicle*:ti, ab OR (soda NEAR/10 (drink* OR beverage*)) OR (Carbonated NEXT/1 drink*):ti, ab OR 'soft drink'/exp OR dessert*:ti, ab OR pastries:ti, ab OR (ice NEXT/1 cream*):ti, ab OR 'ice cream'/exp OR cookies:ti, ab OR cake*:ti OR pie:ti, ab OR pies:ti, ab OR gelatin*:ti, ab OR jello:ti, ab OR (fruit NEXT/1 punch*):ti, ab OR fruitade*:ti, ab OR (('fruit juice'/exp OR (fruit NEXT/1 juice*)) AND concentrate) OR sweets:ti, ab OR caramel:ti, ab OR (malt* NEAR/1 barley) OR ('syrup'/exp OR syrup*:ti, ab) OR sugary:ti, ab OR sugar*:ti OR (sugar NEAR/3 sweet*):ti, ab OR (sugar NEAR/3 coat*):ti, ab OR (dietary NEXT/1 sugar*):ti, ab OR confectioner*:ti, ab OR (fizzy NEXT/1 drink*):ti, ab OR chewing gum*:ti, ab OR 'chewing gum'/exp

    AND

    'cardiovascular disease'/de OR (cardiovascular NEXT/1 disease*):ti, ab OR 'hypertension'/exp OR 'blood pressure'/exp OR 'mortality'/exp OR 'triacylglycerol'/exp OR triglyceride*:ab, ti OR (cholesterol NEAR/2 (hdl OR ldl)) OR 'low density lipoprotein'/exp OR 'high density lipoprotein cholesterol'/exp OR 'cholesterol intake'/exp OR 'stroke'/exp OR stroke*:ti, ab OR 'heart failure'/exp OR (heart NEXT/1 failure*):ti, ab OR 'heart infarction'/exp OR (heart infarction*):ti, ab OR 'heart disease'/exp OR (heart NEXT/1 disease*):ti, ab OR lipid/exp OR lipid*:ti, ab OR 'cholesterol'/exp OR cholesterol*:ti, ab OR 'meat'/exp OR hyperlipidemia*:ti, ab OR hypercholesterolem*:ti, ab OR hypertriglyeridem*:ti, ab
- ***Naviagator (Food Science & Technology Abstracts/BIOSIS/CAB Abstracts)***
  - *Date(s) Searched:* ***August 2014***
  - *Search Terms:* ((Added NEXT Sugar*) OR (brown NEAR/1 sugar*) OR (white NEAR/1 sugar*) OR (raw NEAR/1 sugar*) OR title:syrup* OR title:dextrose OR title:fructose OR (fruit NEAR/1 juice NEAR/1 concentrate*) OR title:glucose OR title:honey OR title:jam OR (invert NEAR/1 sugar*) OR (malt NEAR/1 sugar*) OR title:maltose OR title:maltodextrin OR title:molasses OR (turbinado NEAR/1 sugar*) OR (cane NEAR/1 sugar*) OR (cane NEAR/1 juice*) OR “sugar cane” OR (sugar NEAR/1 beet*) OR title:trehalose OR title:sucrose OR title:sweetene* OR (table NEAR/1 sugar*) OR title:Monosaccharide* OR title:disaccharide* OR "Dietary Sucrose" OR (sugar NEAR/1 based*) OR sugar-based* OR HFCS OR title:candy OR title:candie* OR (Carbonated NEAR beverage*) OR (Carbonated NEAR drink*) OR (Soft NEAR/1 drink*) OR (Liquid NEAR/1 sugar*) OR (Soda NEAR/1 pop*) OR popsicle* OR title:soda OR title:dessert* OR title:pastries OR (ice NEAR/1 cream*)



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OR title:cookies OR title:cake* OR title:pie OR pies:ti OR title:gelatin* OR title:jello OR “fruit punch” OR title:fruitade* OR title:sweets OR (sugar-sweetene*) OR title:caramel OR (malt* NEAR/1 barley) OR (dietary NEAR/1 sugar*) OR title:sugar* OR (sugar NEAR/3 sweet*) OR (sugar NEAR/3 coat*) OR (dietary NEAR/1/1 sugar*) OR title:confectioner* OR (fizzy NEAR/1 drink*) OR chewing NEAR/1 gum*)

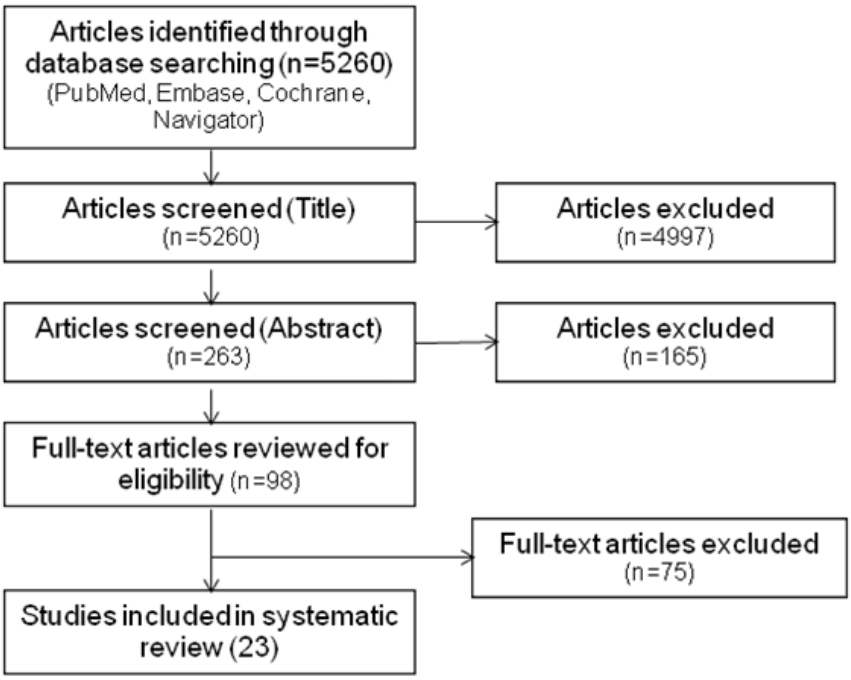
AND

(title:mortality OR abstract:mortality OR “blood pressure” OR “cardiovascular diseases” OR ((blood OR dietary OR “high density” OR “low density” OR hdl OR ldl) near/2 cholesterol) OR title:cholesterol OR abstract:cholesterol
OR title:triglyceride* OR abstract:triglyceride* OR title:stroke OR abstract:stroke OR (blood near/2 lipid*) OR title:hypertension OR abstract:hypertension OR "Myocardial Infarction” OR "Heart Failure" OR "Heart Arrest" OR "Myocardial Ischemia")
Limit: doc-type:"Medical Trials & Studies" (database:biosis OR database:cab)

**Date range: August 2014 to August 2014**

**Summary of articles identified to review**

- Total hits from all electronic database searches: 5260
- Total articles identified to review from electronic databases: 263
- Articles identified via handsearch or other means: 0
- Number of Primary Articles Identified: 23
- Number of Review Articles Identified: 0
- Total Number of Articles Identified: 23
- Number of Articles Reviewed but Excluded: 240




**Included articles (References)**



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1. Aeberli I, Gerber PA, Hochuli M, Kohler S, Haile SR, Gouni-Berthold I, Berthold HK, Spinas GA, Berneis K. Low to moderate sugar-sweetened beverage consumption impairs glucose and lipid metabolism and promotes inflammation in healthy young men: a randomized controlled trial. *Am J Clin Nutr.* 2011;94(2):479-85. PMID:21677052. http://www.ncbi.nlm.nih.gov/pubmed/21677052
2. Aeberli I, Hochuli M, Gerber PA, Sze L, Murer SB, Tappy L, Spinas GA, Berneis K. Moderate amounts of fructose consumption impair insulin sensitivity in healthy young men: a randomized controlled trial. *Diabetes Care.* 2013;36(1):150-6. PMID:22933433. http://www.ncbi.nlm.nih.gov/pubmed/22933433
3. Barrio-Lopez MT, Martinez-Gonzalez MA, Fernandez-Montero A, Beunza JJ, Zazpe I, Bes-Rastrollo M. Prospective study of changes in sugar-sweetened beverage consumption and the incidence of the metabolic syndrome and its components: the SUN cohort. *Br J Nutr.* 2013;110(9):1722-31. PMID:23534417. http://www.ncbi.nlm.nih.gov/pubmed/23534417
4. Bernstein AM, de Koning L, Flint AJ, Rexrode KM, Willett WC. Soda consumption and the risk of stroke in men and women. *Am J Clin Nutr.* 2012;95(5):1190-9. PMID:22492378. http://www.ncbi.nlm.nih.gov/pubmed/22492378
5. Black RN, Spence M, McMahon RO, Cuskelly GJ, Ennis CN, McCance DR, Young IS, Bell PM, Hunter SJ. Effect of eucaloric high- and low-sucrose diets with identical macronutrient profile on insulin resistance and vascular risk: a randomized controlled trial. *Diabetes.* 2006;55(12):3566-72. PMID:17130505. http://www.ncbi.nlm.nih.gov/pubmed/17130505
6. Chen L, Caballero B, Mitchell DC, Loria C, Lin PH, Champagne CM, Elmer PJ, Ard JD, Batch BC, Anderson CA, Appel LJ. Reducing consumption of sugar-sweetened beverages is associated with reduced blood pressure: a prospective study among United States adults. *Circulation.* 2010;121(22):2398-406. PMID:20497980. http://www.ncbi.nlm.nih.gov/pubmed/20497980
7. Cohen L, Curhan G, Forman J. Association of sweetened beverage intake with incident hypertension. *J Gen Intern Med.* 2012;27(9):1127-34. PMID:22539069. http://www.ncbi.nlm.nih.gov/pubmed/22539069
8. de Koning L, Malik VS, Kellogg MD, Rimm EB, Willett WC, Hu FB. Sweetened beverage consumption, incident coronary heart disease, and biomarkers of risk in men. *Circulation.* 2012;125(14):1735-41, s1. PMID:22412070. http://www.ncbi.nlm.nih.gov/pubmed/22412070
9. Dhingra R, Sullivan L, Jacques PF, Wang TJ, Fox CS, Meigs JB, D'Agostino RB, Gaziano JM, Vasan RS. Soft drink consumption and risk of developing cardiometabolic risk factors and the metabolic syndrome in middle-aged adults in the community. *Circulation.* 2007;116(5):480-8. PMID:17646581. http://www.ncbi.nlm.nih.gov/pubmed/17646581
10. Duffey KJ, Gordon-Larsen P, Steffen LM, Jr. Jacobs DR, Popkin BM. Drinking caloric beverages increases the risk of adverse cardiometabolic outcomes in the Coronary Artery Risk Development in Young Adults (CARDIA) Study. *Am J Clin Nutr.* 2010;92(4):954-9. PMID:20702604. http://www.ncbi.nlm.nih.gov/pubmed/20702604
11. Eshak ES, Iso H, Kokubo Y, Saito I, Yamagishi K, Inoue M, Tsugane S. Soft drink intake in relation to incident ischemic heart disease, stroke, and stroke subtypes in Japanese men and women: the Japan Public Health Centre-based study cohort I. *Am J Clin Nutr.* 2012;96(6):1390-7. PMID:23076619. http://www.ncbi.nlm.nih.gov/pubmed/23076619
12. Faeh D, Minehira K, Schwarz JM, Periasamy R, Park S, Tappy L. Effect of fructose overfeeding and fish oil administration on hepatic de novo lipogenesis and insulin sensitivity in healthy men. *Diabetes.* 2005;54(7):1907-13. PMID:15983189. http://www.ncbi.nlm.nih.gov/pubmed/15983189
13. Fung TT, Malik V, Rexrode KM, Manson JE, Willett WC, Hu FB. Sweetened beverage



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consumption and risk of coronary heart disease in women. *Am J Clin Nutr.* 2009;89(4):1037-42. PMID:19211821. http://www.ncbi.nlm.nih.gov/pubmed/19211821

14. Larsson SC, Akesson A, Wolk A. Sweetened beverage consumption is associated with increased risk of stroke in women and men. *J Nutr.* 2014;144(6):856-60. PMID:24717367. http://www.ncbi.nlm.nih.gov/pubmed/24717367
15. Le KA, Ith M, Kreis R, Faeh D, Bortolotti M, Tran C, Boesch C, Tappy L. Fructose overconsumption causes dyslipidemia and ectopic lipid deposition in healthy subjects with and without a family history of type 2 diabetes. *Am J Clin Nutr.* 2009;89(6):1760-5. PMID:19403641. http://www.ncbi.nlm.nih.gov/pubmed/19403641
16. Lewis AS, McCourt HJ, Ennis CN, Bell PM, Courtney CH, McKinley MC, Young IS, Hunter SJ. Comparison of 5% versus 15% sucrose intakes as part of a eucaloric diet in overweight and obese subjects: effects on insulin sensitivity, glucose metabolism, vascular compliance, body composition and lipid profile. A randomised controlled trial. *Metabolism.* 2013;62(5):694-702. PMID:23363580. http://www.ncbi.nlm.nih.gov/pubmed/23363580
17. 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. *Nutrients.* 2014;6(3):1128-44. PMID:24642950. http://www.ncbi.nlm.nih.gov/pubmed/24642950 ("a")
18. 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. *Nutrients.* 2014;6(8):3153-68. PMID:25111121. http://www.ncbi.nlm.nih.gov/pubmed/25111121 ("b")
19. Maersk M, Belza A, Stodkilde-Jorgensen H, Ringgaard S, Chabanova E, Thomsen H, Pedersen SB, Astrup A, Richelsen B. Sucrose-sweetened beverages increase fat storage in the liver, muscle, and visceral fat depot: a 6-mo randomized intervention study. *Am J Clin Nutr.* 2012;95(2):283-9. PMID:22205311. http://www.ncbi.nlm.nih.gov/pubmed/22205311
20. Raben A, Vasilaras TH, Moller AC, Astrup A. Sucrose compared with artificial sweeteners: different effects on ad libitum food intake and body weight after 10 wk of supplementation in overweight subjects. *Am J Clin Nutr.* 2002;76(4):721-9. PMID:12324283. http://www.ncbi.nlm.nih.gov/pubmed/12324283
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22. Yang Q, Zhang Z, Gregg EW, Flanders WD, Merritt R, Hu FB. Added sugar intake and cardiovascular diseases mortality among US adults. *JAMA Intern Med.* 2014;174(4):516-24. PMID:24493081. http://www.ncbi.nlm.nih.gov/pubmed/24493081
23. Yu Z, Lowndes J, Rippe J. High-fructose corn syrup and sucrose have equivalent effects on energy-regulating hormones at normal human consumption levels. *Nutr Res.* 2013;33(12):1043-52. PMID:24267044. http://www.ncbi.nlm.nih.gov/pubmed/24267044

## Excluded articles

See Appendix C for a full list of excluded articles with reason.



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# APPENDIX A. SODIUM AND BLOOD PRESSURE IN CHILDREN – EXCLUDED ARTICLES LIST



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## Excluded Articles: Sodium Intake & Blood Pressure in Children from Birth to Age 18 Years

The table below lists the excluded articles with at least one reason for exclusion, but may not reflect all possible reasons.

| | Excluded Citations | Reason for Exclusion |
|---|---|---|
| 1. | Adair LS,Gordon-Larsen P,Du SF,Zhang B,Popkin BM. The emergence of cardiometabolic disease risk in Chinese children and adults: consequences of changes in diet, physical activity and obesity. Obes Rev. 2014;15 Suppl 1(#number#):49-59. PMID:24341758. | Study Design |
| 2. | Ahn S,Park S,Kim JN,Han SN,Jeong SB,Kim HK. Salt content of school meals and comparison of perception related to sodium intake in elementary, middle, and high schools. Nutr Res Pract. 2013;7(1):59-65. PMID:23424102. | Study Design,Outcome |
| 3. | Alderman MH,Cohen H. Lower sodium intake reduces blood pressure in adults and children, but is not associated with a reduced risk of all CVD or all cause mortality. Evid Based Med. 2014;19(1):33-4. PMID:23873817. | Study Design |
| 4. | Alkhunaizi AM,Al JH,Al SZ. Salt intake in Eastern Saudi Arabia. East Mediterr Health J. 2013;19(11):915-8. PMID:24673081. | Study Design |
| 5. | Anyaegbu EI,Dharnidharka VR. Hypertension in the teenager. Pediatr Clin North Am. 2014;61(1):131-51. PMID:24267462. | Study Design,Independent Variable |
| 6. | Baciu A. Essential arterial hypertension occurring in children and teenagers anthropological correlations. International Journal of Collaborative Research on Internal Medicine and Public Health. 2012;4(6):1017-1039. PMID:#accession number#. | Study Design |
| 7. | Bhagatwala J,Harris RA,Parikh SJ,Zhu H,Huang Y,Kotak I,Seigler N,Pierce GL,Egan BM,Dong Y. Epithelial sodium channel inhibition by amiloride on blood pressure and cardiovascular disease risk in young prehypertensives. J Clin Hypertens (Greenwich). 2014;16(1):47-53. PMID:24410943. | Independent Variable |
| 8. | Bi Z,Liang X,Xu A,Wang L,Shi X,Zhao W,Ma J,Guo X,Zhang X,Zhang J,Ren J,Yan L,Lu Z,Wang H,Tang J,Cai X,Dong J,Zhang J,Chu J,Engelgau M,Yang Q,Hong Y,Wang Y. Hypertension Prevalence, Awareness, Treatment, and Control and Sodium Intake in Shandong Province, China: Baseline Results From Shandong-Ministry of Health Action on Salt Reduction and Hypertension (SMASH), 2011. Prev Chronic Dis. 2014;11(#number#):E88. PMID:24854239. | Study Design |
| 9. | Bucher BS,Ferrarini A,Weber N,Bullo M,Bianchetti MG,Simonetti GD. Primary hypertension in childhood. Curr Hypertens Rep. 2013;15(5):444-52. PMID:23897423. | Study Design |
| 10. | Campagnoli T,Gonzalez L,Santa Cruz F. Salt intake and blood pressure in the University of Asuncion-Paraguay youths: a preliminary study. J Bras Nefrol. 2012;34(4):361-8. PMID:23318825. | Study Design |

## Excluded Articles: Sodium Intake & Blood Pressure in Children from Birth to Age 18 Years

The table below lists the excluded articles with at least one reason for exclusion, but may not reflect all possible reasons.

| | Excluded Citations | Reason for Exclusion |
|---|---|---|
| 11. | Campbell NR,Willis KJ,L'Abbe M,Strang R,Young E. Canadian initiatives to prevent hypertension by reducing dietary sodium. Nutrients. 2011;3(8):756-64. PMID:22254122. | Study Design |
| 12. | Chandar J,Zilleruelo G. Hypertensive crisis in children. Pediatr Nephrol. 2012;27(5):741-51. PMID:21773822. | Study Design |
| 13. | Chang A,Van Horn L, Jr. Jacobs DR,Liu K,Muntner P,Newsome B,Shoham DA,Durazo-Arvizu R,Bibbins-Domingo K,Reis J,Kramer H. Lifestyle-related factors, obesity, and incident microalbuminuria: the CARDIA (Coronary Artery Risk Development in Young Adults) study. Am J Kidney Dis. 2013;62(2):267-75. PMID:23601954. | Age |
| 14. | Chateau-Degat ML,Ferland A,Dery S,Dewailly E. Dietary sodium intake deleteriously affects blood pressure in a normotensive population. Eur J Clin Nutr. 2012;66(4):533-5. PMID:22333870. | Age |
| 15. | Chen J,Gu D,Huang J,Rao DC,Jaquish CE,Hixson JE,Chen CS,Chen J,Lu F,Hu D,Rice T,Kelly TN,Hamm LL,Whelton PK,He J,GenSalt Collaborative Research G. Metabolic syndrome and salt sensitivity of blood pressure in non-diabetic people in China: a dietary intervention study. Lancet. 2009;373(9666):829-35. PMID:19223069. | Country,Age |
| 16. | Colin-Ramirez E,Castillo-Martinez L,Orea-Tejeda A,Villa Romero AR,Vergara Castaneda A,Asensio Lafuente E. Waist circumference and fat intake are associated with high blood pressure in Mexican children aged 8 to 10 years. J Am Diet Assoc. 2009;109(6):996-1003. PMID:19465181. | Study Design |
| 17. | Covelli MM. A review of long-term effects of low sodium diet versus high sodium diet on blood pressure, renin, aldosterone, catecholamines, cholesterol and triglyceride. Evid Based Nurs. 2012;15(3):70-1. PMID:22411159. | Study Design |
| 18. | Defago MD,Gu D,Hixson JE,Shimmin LC,Rice TK,Gu CC,Jaquish CE,Liu DP,He J,Kelly TN. Common genetic variants in the endothelial system predict blood pressure response to sodium intake: the GenSalt study. Am J Hypertens. 2013;26(5):643-56. PMID:23443727. | Comparator,Age |
| 19. | Feber J,Ahmed M. Hypertension in children: new trends and challenges. Clin Sci (Lond). 2010;119(4):151-61. PMID:20477751. | Study Design |
| 20. | Feig DI. The role of uric acid in the pathogenesis of hypertension in the young. J Clin Hypertens (Greenwich). 2012;14(6):346-52. PMID:22672087. | Study Design |
| 21. | Fischer ME,Cruickshanks KJ,Pinto A,Schubert CR,Klein BE,Klein R,Nieto FJ,Pankow JS,Snyder DJ,Keating BJ. Intensity of Salt Taste and Prevalence of Hypertension Are Not Related in the Beaver Dam Offspring Study. Chemosens Percept. 2012;5(2):139-145. PMID:22745848. | Study Design |
| 22. | Garg R,Williams GH,Hurwitz S,Brown NJ,Hopkins PN,Adler GK. Low-salt diet increases insulin | Age |

## Excluded Articles: Sodium Intake & Blood Pressure in Children from Birth to Age 18 Years

The table below lists the excluded articles with at least one reason for exclusion, but may not reflect all possible reasons.

| | Excluded Citations | Reason for Exclusion |
|---|---|---|
| | resistance in healthy subjects. Metabolism. 2011;60(7):965-8. PMID:21036373. | |
| 23. | Goel R,Misra A,Agarwal SK,Vikram N. Correlates of hypertension among urban Asian Indian adolescents. Arch Dis Child. 2010;95(12):992-7. PMID:20705721. | Study Design |
| 24. | Gopinath B,Louie JC,Flood VM,Rochtchina E,Baur LA,Mitchell P. Parental history of hypertension and dietary intakes in early adolescent offspring: a population-based study. J Hum Hypertens. 2014;#volume#(#number#):#pages#. PMID:24573132. | Study Design |
| 25. | Grimes CA,Riddell LJ,Campbell KJ,Nowson CA. Dietary salt intake, sugar-sweetened beverage consumption, and obesity risk. Pediatrics. 2013;131(1):14-21. PMID:23230077. | Study Design,Outcome |
| 26. | Gu D,Zhao Q,Chen J,Chen JC,Huang J,Bazzano LA,Lu F,Mu J,Li J,Cao J,Mills K,Chen CS,Rice T,Hamm LL,He J. Reproducibility of blood pressure responses to dietary sodium and potassium interventions: the GenSalt study. Hypertension. 2013;62(3):499-505. PMID:23897070. | Country,Age |
| 27. | Guallar-Castillon P,Munoz-Pareja M,Aguilera MT,Leon-Munoz LM,Rodriguez-Artalejo F. Food sources of sodium, saturated fat and added sugar in the Spanish hypertensive and diabetic population. Atherosclerosis. 2013;229(1):198-205. PMID:23642731. | Study Design |
| 28. | Haga M,Sakata T. Daily salt intake of healthy Japanese infants of 3-5 years based on sodium excretion in 24-hour urine. J Nutr Sci Vitaminol (Tokyo). 2010;56(5):305-10. PMID:21228501. | Outcome |
| 29. | Hajna S,Liu J,LeBlanc PJ,Faught BE,Merchant AT,Cairney J,Hay J. Association between body composition and conformity to the recommendations of Canada's Food Guide and the Dietary Approaches to Stop Hypertension (DASH) diet in peri-adolescence. Public Health Nutr. 2012;15(10):1890-6. PMID:22717343. | Independent Variable,Outcome |
| 30. | Hanevold CD. Sodium intake and blood pressure in children. Curr Hypertens Rep. 2013;15(5):417-25. PMID:23949320. | Study Design |
| 31. | Hari P,Sinha A. Hypertensive emergencies in children. Indian J Pediatr. 2011;78(5):569-75. PMID:21271305. | Study Design |
| 32. | Harrington JM,Fitzgerald AP,Kearney PM,McCarthy VJ,Madden J,Browne G,Dolan E,Perry IJ. DASH Diet Score and Distribution of Blood Pressure in Middle-Aged Men and Women. Am J Hypertens. 2013;#volume#(#number#):#pages#. PMID:23920282. | Study Design |
| 33. | He FJ,MacGregor GA. A comprehensive review on salt and health and current experience of worldwide salt reduction programmes. J Hum Hypertens. 2009;23(6):363-84. PMID:19110538. | Study Design |
| 34. | He FJ,Wu Y,Ma J,Feng X,Wang H,Zhang J,Lin CP,Yuan J,Ma Y,Yang Y,Yan LL,Jan S,Nowson C,Macgregor GA. A school-based education programme to reduce salt intake in children and their families (School-EduSalt): protocol of a cluster randomised controlled trial. BMJ Open. | Study Design,Country |

## Excluded Articles: Sodium Intake & Blood Pressure in Children from Birth to Age 18 Years

The table below lists the excluded articles with at least one reason for exclusion, but may not reflect all possible reasons.

| | Excluded Citations | Reason for Exclusion |
|---|---|---|
| | 2013;3(7):#pages#. PMID:23864214. | |
| 35. | Hendriksen MA,Hoogenveen RT,Hoekstra J,Geleijnse JM,Boshuizen HC,van Raaij JM. Potential effect of salt reduction in processed foods on health. Am J Clin Nutr. 2014;99(3):446-53. PMID:24335058. | Study Design |
| 36. | Katona E,Zrinyi M,Komonyi E,Lengyel S,Paragh G,Zatik J,Fulesdi B,Pall D. Factors influencing adolescent blood pressure: the Debrecen Hypertension Study. Kidney Blood Press Res. 2011;34(3):188-95. PMID:21502767. | Study Design,Comparator |
| 37. | Kelishadi R,Gheisari A,Zare N,Farajian S,Shariatinejad K. Salt intake and the association with blood pressure in young Iranian children: first report from the middle East and north Africa. Int J Prev Med. 2013;4(4):475-83. PMID:23671781. | Study Design |
| 38. | Khang YH,Lynch JW. Exploring determinants of secular decreases in childhood blood pressure and hypertension. Circulation. 2011;124(4):397-405. PMID:21730305. | Study Design |
| 39. | Kho M,Lee JE,Song YM,Lee K,Kim K,Yang S,Joung H,Sung J. Genetic and environmental influences on sodium intake determined by using half-day urine samples: the Healthy Twin Study. Am J Clin Nutr. 2013;98(6):1410-6. PMID:24088720. | Outcome |
| 40. | Kokanovic A,Mandic ML,Banjari I. Does individual dietary intervention have any impact on adolescents with cardiovascular health risks?. Med Glas (Zenica). 2014;11(1):234-7. PMID:24496370. | Independent Variable,Comparator |
| 41. | Krikken JA,Dallinga-Thie GM,Navis G,Dullaart RP. Short term dietary sodium restriction decreases HDL cholesterol, apolipoprotein A-I and high molecular weight adiponectin in healthy young men: relationships with renal hemodynamics and RAAS activation. Nutr Metab Cardiovasc Dis. 2012;22(1):35-41. PMID:20678904. | Age |
| 42. | Krupp D,Shi L,Remer T. Longitudinal relationships between diet-dependent renal acid load and blood pressure development in healthy children. Kidney Int. 2014;85(1):204-10. PMID:24025638. | Independent Variable |
| 43. | Kumar J,Deshmukh PR,Garg BS. Prevalence and correlates of sustained hypertension in adolescents of rural Wardha, central India. Indian J Pediatr. 2012;79(9):1206-12. PMID:22203427. | Study Design |
| 44. | Lawlor DA,Macdonald-Wallis C,Fraser A,Nelson SM,Hingorani A,Davey Smith G,Sattar N,Deanfield J. Cardiovascular biomarkers and vascular function during childhood in the offspring of mothers with hypertensive disorders of pregnancy: findings from the Avon Longitudinal Study of Parents and Children. Eur Heart J. 2012;33(3):335-45. PMID:21862461. | Independent Variable |
| 45. | Lee WJ,Kim HC,Oh SM,Choi DP,Cho J,Suh I. Factors Associated with a Low-sodium Diet: The | Study Design |

## Excluded Articles: Sodium Intake & Blood Pressure in Children from Birth to Age 18 Years

The table below lists the excluded articles with at least one reason for exclusion, but may not reflect all possible reasons.

| | Excluded Citations | Reason for Exclusion |
|---|---|---|
| | Fourth Korean National Health and Nutrition Examination Survey. Epidemiol Health. 2013;35(#number#):e2013005. PMID:23807908. | |
| 46. | Liu F,Zheng S,Mu J,Chu C,Wang L,Wang Y,Xiao H,Wang D,Cao Y,Ren K,Liu E,Yuan Z. Common variation in with no-lysine kinase 1 (WNK1) and blood pressure responses to dietary sodium or potassium interventions- family-based association study. Circ J. 2013;77(1):169-74. PMID:23059770. | Country,Age |
| 47. | Lucas L,Riddell L,Liem G,Whitelock S,Keast R. The influence of sodium on liking and consumption of salty food. J Food Sci. 2011;76(1):S72-6. PMID:21535718. | Outcome |
| 48. | Magriplis E,Farajian P,Pounis GD,Risvas G,Panagiotakos DB,Zampelas A. High sodium intake of children through 'hidden' food sources and its association with the Mediterranean diet: the GRECO study. J Hypertens. 2011;29(6):1069-76. PMID:21451420. | Study Design |
| 49. | Morinaga Y,Tsuchihashi T,Ohta Y,Matsumura K. Salt intake in 3-year-old Japanese children. Hypertens Res. 2011;34(7):836-9. PMID:21593740. | Study Design |
| 50. | Morrison AC,Ness RB. Sodium intake and cardiovascular disease. Annu Rev Public Health. 2011;32(#number#):71-90. PMID:21219163. | Study Design |
| 51. | Mu J,Liu Z,Liu F,Xu X,Liang Y,Zhu D. Family-based randomized trial to detect effects on blood pressure of a salt substitute containing potassium and calcium in hypertensive adolescents. Am J Hypertens. 2009;22(9):943-7. PMID:19661927. | Country,Subject Health |
| 52. | Mu J,Zheng S,Lian Q,Liu F,Liu Z. Evolution of blood pressure from adolescents to youth in salt sensitivies: a 18-year follow-up study in Hanzhong children cohort. Nutr J. 2012;11(#number#):70. PMID:22978814. | Country,Age |
| 53. | Niinikoski H,Jula A,Viikari J,Ronnemaa T,Heino P,Lagstrom H,Jokinen E,Simell O. Blood pressure is lower in children and adolescents with a low-saturated-fat diet since infancy: the special turku coronary risk factor intervention project. Hypertension. 2009;53(6):918-24. PMID:19364991. | Independent Variable,Comparator |
| 54. | O'Brien F,Walker IA. Fluid homeostasis in the neonate. Paediatr Anaesth. 2014;24(1):49-59. PMID:24299660. | Study Design |
| 55. | Oikonen M,Tikkanen E,Juhola J,Tuovinen T,Seppala I,Juonala M,Taittonen L,Mikkila V,Kahonen M,Ripatti S,Viikari J,Lehtimaki T,Havulinna AS,Kee F,Newton-Cheh C,Peltonen L,Schork NJ,Murray SS,Berenson GS,Chen W,Srinivasan SR,Salomaa V,Raitakari OT. Genetic variants and blood pressure in a population-based cohort: the Cardiovascular Risk in Young Finns study. Hypertension. 2011;58(6):1079-85. PMID:22025373. | Independent Variable,Comparator |

## Excluded Articles: Sodium Intake & Blood Pressure in Children from Birth to Age 18 Years

The table below lists the excluded articles with at least one reason for exclusion, but may not reflect all possible reasons.

| | Excluded Citations | Reason for Exclusion |
|---|---|---|
| 56. | Palacios C,Wigertz K,Martin BR,Braun M,Pratt JH,Peacock M,Weaver CM. Racial differences in potassium homeostasis in response to differences in dietary sodium in girls. Am J Clin Nutr. 2010;91(3):597-603. PMID:20007307. | Drop-out Rate |
| 57. | Raj M,Krishnakumar R. Hypertension in children and adolescents: epidemiology and pathogenesis. Indian J Pediatr. 2013;80 Suppl 1(#number#):S71-6. PMID:22941155. | Study Design |
| 58. | Raj M. Essential hypertension in adolescents and children: Recent advances in causative mechanisms. Indian J Endocrinol Metab. 2011;15 Suppl 4(#number#):S367-73. PMID:22145141. | Study Design |
| 59. | Rebacz-Maron E,Baranowska-Bosiacka I,Gutowska I,Chlubek D. Blood pressure and levels of Fe, Ca, Mg, Zn, Cu, Na and K in the hair of young bantu men from Tanzania. Biological Trace Element Research. 2013;151(3):350-359. PMID:#accession number#. | Country |
| 60. | Reddy D,Kushwaha AS,Kotwal CA,Basannar DR,Mahen A. Study of blood pressure profile of school children 6-15 years in a rural setting of Maharashtra. Medical Journal Armed Forces India. 2012;68(3):222-225. | Study Design |
| 61. | Riley M,Bluhm B. High blood pressure in children and adolescents. Am Fam Physician. 2012;85(7):693-700. PMID:22534345. | Study Design |
| 62. | Shim E,Ryu HJ,Hwang J,Kim SY,Chung EJ. Dietary sodium intake in young Korean adults and its relationship with eating frequency and taste preference. Nutr Res Pract. 2013;7(3):192-8. PMID:23766880. | Age |
| 63. | Simonetti GD,Farese S,Aregger F,Uehlinger D,Frey FJ,Mohaupt MG. Nocturnal dipping behaviour in normotensive white children and young adults in response to changes in salt intake. J Hypertens. 2010;28(5):1027-33. PMID:20173652. | Sample Size |
| 64. | Spagnolo A,Giussani M,Ambruzzi AM,Bianchetti M,Maringhini S,Matteucci MC,Menghetti E,Salice P,Simionato L,Strambi M,Virdis R,Genovesi S. Focus on prevention, diagnosis and treatment of hypertension in children and adolescents. Ital J Pediatr. 2013;39(#number#):20. PMID:23510329. | Study Design |
| 65. | Stabouli S,Papakatsika S,Kotsis V. The role of obesity, salt and exercise on blood pressure in children and adolescents. Expert Rev Cardiovasc Ther. 2011;9(6):753-61. PMID:21714606. | Study Design |
| 66. | Stein LJ,Cowart BJ,Beauchamp GK. The development of salty taste acceptance is related to dietary experience in human infants: a prospective study. Am J Clin Nutr. 2012;95(1):123-9. PMID:22189260. | Outcome |
| 67. | Strazzullo P,Campanozzi A,Avallone S. Does salt intake in the first two years of life affect the development of cardiovascular disorders in adulthood?. Nutr Metab Cardiovasc Dis. | Study Design |

## Excluded Articles: Sodium Intake & Blood Pressure in Children from Birth to Age 18 Years

The table below lists the excluded articles with at least one reason for exclusion, but may not reflect all possible reasons.

| | Excluded Citations | Reason for Exclusion |
|---|---|---|
| | 2012;22(10):787-92. PMID:22749679. | |
| 68. | Tanase CM,Koski KG,Laffey PJ,Cooper MJ,Cockell KA. Canadians continue to consume too much sodium and not enough potassium. Can J Public Health. 2011;102(3):164-8. PMID:21714312. | Outcome |
| 69. | Tayel DI,El-Sayed NA,El-Sayed NA. Dietary pattern and blood pressure levels of adolescents in Sohag, Egypt. J Egypt Public Health Assoc. 2013;88(2):97-103. PMID:23963089. | Study Design,Country |
| 70. | Taylor S,Tibbett T,Patel D,Bishop E. Use of environmental change strategies to facilitate sodium reduction: a case study in a rural California school district. J Public Health Manag Pract. 2014;20(1 Suppl 1):S38-42. PMID:24322814. | Study Design,Independent Variable |
| 71. | Thrift AG,Srikanth V,Fitzgerald SM,Kalyanram K,Kartik K,Hoppe CC,Walker KZ,Evans RG. Potential roles of high salt intake and maternal malnutrition in the development of hypertension in disadvantaged populations. Clin Exp Pharmacol Physiol. 2010;37(2):e78-90. PMID:19650789. | Study Design |
| 72. | Trajkovic-Pavlovic L,Martinov-Cvejin M,Novakovic B,Bijelovic S,Torovic L. Analysis of salt content in meals in kindergarten facilities in Novi Sad. Srp Arh Celok Lek. 2010;138(9-10):619-23. PMID:21179911. | Outcome |
| 73. | Vitolo MR,da Costa Louzada ML,Rauber F,Campagnolo PD. Risk factors for high blood pressure in low income children aged 3-4 years. Eur J Pediatr. 2013;172(8):1097-103. PMID:23636283. | Study Design |
| 74. | Yang Q,Zhang Z,Kuklina EV,Fang J,Ayala C,Hong Y,Loustalot F,Dai S,Gunn JP,Tian N,Cogswell ME,Merritt R. Sodium intake and blood pressure among US children and adolescents. Pediatrics. 2012;130(4):611-9. PMID:22987869. | Study Design |
| 75. | Yuan WL,Kakinami L,Gray-Donald K,Czernichow S,Lambert M,Paradis G. Influence of dairy product consumption on children's blood pressure: results from the QUALITY cohort. J Acad Nutr Diet. 2013;113(7):936-41. PMID:23684662. | Study Design,Independent Variable |
| 76. | Zhang J,Xu AQ,Ma JX,Shi XM,Guo XL,Engelgau M,Yan LX,Li Y,Li YC,Wang HC,Lu ZL,Zhang JY,Liang XF. Dietary sodium intake: knowledge, attitudes and practices in Shandong Province, China, 2011. PLoS One. 2013;8(3):e58973. PMID:23527061. | Study Design,Age |
| 77. | Zhang Z,Kris-Etherton PM,Hartman TJ. Birth Weight and Risk Factors for Cardiovascular Disease and Type 2 Diabetes in US Children and Adolescents: 10 Year Results from NHANES. Matern Child Health J. 2013;#volume#(#number#):#pages#. PMID:24241968. | Study Design,Independent Variable |
| 78. | Zhu X,Lin J,Song Y,Liu H,Zhang R,Fan M,Li Y,Tian R,Fang D. A high-carbohydrate diet lowered blood pressure in healthy Chinese male adolescents. Biosci Trends. 2014;8(2):132-7. PMID:24815391. | Independent Variable,Country |

## Excluded Articles: Sodium Intake & Blood Pressure in Children from Birth to Age 18 Years

The table below lists the excluded articles with at least one reason for exclusion, but may not reflect all possible reasons.

# APPENDIX B. SODIUM AND CARDIOVASCULAR DISEASE – EXCLUDED ARTICLES LIST



Archived from www.NEL.gov on March 21, 2017

## Excluded Articles: Sodium Intake & Risk of Cardiovascular Disease

The table below lists the excluded articles with at least one reason for exclusion, but may not reflect all possible reasons.

| Reference | Excluded Citations | Reason for Exclusion |
|---|---|---|
| 1. | Adrogue HJ,Madias NE. The impact of sodium and potassium on hypertension risk. Semin Nephrol. 2014;34(3):257-72. PMID:25016398. | Study Design |
| 2. | Alderman MH,Cohen H. Lower sodium intake reduces blood pressure in adults and children, but is not associated with a reduced risk of all CVD or all cause mortality. Evid Based Med. 2014;19(1):33-4. PMID:23873817. | Study Design |
| 3. | Allison SJ. Hypertension: Urinary sodium and potassium excretion: association with blood pressure and clinical outcomes. Nat Rev Nephrol. 2014;#volume#(#number#):#pages#. PMID:25157836. | Study Design |
| 4. | Batis C,Gordon-Larsen P,Cole SR,Du S,Zhang B,Popkin B. Sodium intake from various time frames and incident hypertension among Chinese adults. Epidemiology. 2013;24(3):410-8. PMID:23466527. | Country, Unhealthy Subjects |
| 5. | Baudrand R,Campino C,Carvajal CA,Olivieri O,Guidi G,Faccini G,Vohringer PA,Cerda J,Owen G,Kalergis AM,Fardella CE. High sodium intake is associated with increased glucocorticoid production, insulin resistance and metabolic syndrome. Clinical Endocrinology. 2014;80(5):677-684. | Outcome |
| 6. | Bertoia ML,Triche EW,Michaud DS,Baylin A,Hogan JW,Neuhouser ML,Tinker LF,Van Horn L,Waring ME,Li W,Shikany JM,Eaton CB. Mediterranean and Dietary Approaches to Stop Hypertension dietary patterns and risk of sudden cardiac death in postmenopausal women. Am J Clin Nutr. 2014;99(2):344-51. PMID:24351877. | Independent Variable |
| 7. | Bi Z,Liang X,Xu A,Wang L,Shi X,Zhao W,Ma J,Guo X,Zhang X,Zhang J,Ren J,Yan L,Lu Z,Wang H,Tang J,Cai X,Dong J,Zhang J,Chu J,Engelgau M,Yang Q,Hong Y,Wang Y. Hypertension prevalence, awareness, treatment, and control and sodium intake in Shandong Province, China: baseline results from Shandong-Ministry of Health Action on Salt Reduction and Hypertension (SMASH), 2011. Int J Vasc Med. 2014;11(#number#):E88. PMID:24854239. | Study Design, Country |
| 8. | Brown IJ,Dyer AR,Chan Q,Cogswell ME,Ueshima H,Stamler J,Elliott P. Estimating 24-hour urinary sodium excretion from casual urinary sodium concentrations in Western populations: the INTERSALT study. Am J Epidemiol. 2013;177(11):1180-92. PMID:23673246. | Outcome |
| 9. | Cotugna N,Fanelli-Kuczmarski M,Clymer J,Hotchkiss L,Zonderman AB,Evans MK. Sodium intake of special populations in the Healthy Aging in Neighborhoods of Diversity Across the Life Span (HANDLS) study. Prev Med. 2013;57(4):334-8. PMID:23769900. | Study Design, Outcome |
| 10. | Coxson PG,Cook NR,Joffres M,Hong Y,Orenstein D,Schmidt SM,Bibbins-Domingo K. Mortality benefits from US population-wide reduction in sodium consumption: projections from 3 modeling approaches. Hypertension. 2013;61(3):564-70. PMID:23399718. | Study Design, Outcome |
| 11. | Domenech M,Roman P,Lapetra J,Garcia de la Corte FJ,Sala-Vila A,de la Torre R,Corella D,Salas-Salvado | Independent |

## Excluded Articles: Sodium Intake & Risk of Cardiovascular Disease

The table below lists the excluded articles with at least one reason for exclusion, but may not reflect all possible reasons.

| Reference | Excluded Citations | Reason for Exclusion |
|---|---|---|
| | J,Ruiz-Gutierrez V,Lamuela-Raventos RM,Toledo E,Estruch R,Coca A,Ros E. Mediterranean diet reduces 24-hour ambulatory blood pressure, blood glucose, and lipids: one-year randomized, clinical trial. Hypertension. 2014;64(1):69-76. PMID:24799608. | Variable, Outcome |
| 12. | Donfrancesco C,Ippolito R,Lo Noce C,Palmieri L,Iacone R,Russo O,Vanuzzo D,Galletti F,Galeone D,Giampaoli S,Strazzullo P. Excess dietary sodium and inadequate potassium intake in Italy: results of the MINISAL study. Nutr Metab Cardiovasc Dis. 2013;23(9):850-6. PMID:22835983. | Study Design, Outcome |
| 13. | Franco V. Modest salt intake reduction for 4 weeks or longer decreases blood pressure. Evid Based Nurs. 2014;17(3):92. PMID:24170820. | Study Design |
| 14. | Graudal N,Jurgens G,Baslund B,Alderman MH. Compared with usual sodium intake, low- and excessive-sodium diets are associated with increased mortality: a meta-analysis. Am J Hypertens. 2014;27(9):1129-37. PMID:24651634. | Study Design |
| 15. | Gu D,Zhao Q,Chen J,Chen JC,Huang J,Bazzano LA,Lu F,Mu J,Li J,Cao J,Mills K,Chen CS,Rice T,Hamm LL,He J. Reproducibility of blood pressure responses to dietary sodium and potassium interventions: the GenSalt study. Hypertension. 2013;62(3):499-505. PMID:23897070. | Country |
| 16. | Ha SK. Dietary salt intake and hypertension. Electrolyte Blood Press. 2014;12(1):7-18. PMID:25061468. | Study Design |
| 17. | Haghighatdoost F,Sarrafzadegan N,Khosravi A,Noori F,Boshtam M,Mohammadifard N,Abdollhi Z,Azadbakht L. Is the association between salt intake and blood pressure mediated by body mass index and central adiposity?. Arch Iran Med. 2013;16(3):167-71. PMID:23432169. | Outcome |
| 18. | Jablonski KL,Fedorova OV,Racine ML,Geolfos CJ,Gates PE,Chonchol M,Fleenor BS,Lakatta EG,Bagrov AY,Seals DR. Dietary sodium restriction and association with urinary marinobufagenin, blood pressure, and aortic stiffness. Clin J Am Soc Nephrol. 2013;8(11):1952-9. PMID:23929930. | Outcome |
| 19. | Jablonski KL,Racine ML,Geolfos CJ,Gates PE,Chonchol M,McQueen MB,Seals DR. Dietary sodium restriction reverses vascular endothelial dysfunction in middle-aged/older adults with moderately elevated systolic blood pressure. J Am Coll Cardiol. 2013;61(3):335-43. PMID:23141486. | Outcome |
| 20. | Jun M,Neal B. Low dietary sodium in heart failure: a need for scientific rigour. Heart. 2013;#volume#(#number#):#pages#. PMID:23213171. | Study Design |
| 21. | Konerman MC,Hummel SL. Sodium restriction in heart failure: benefit or harm?. Curr Treat Options Cardiovasc Med. 2014;16(2):286. PMID:24398803. | Study Design |
| 22. | Laffer CL,Elijovich F. Differential predictors of insulin resistance in nondiabetic salt-resistant and salt-sensitive subjects. Hypertension. 2013;61(3):707-15. PMID:23283360. | Outcome |

## Excluded Articles: Sodium Intake & Risk of Cardiovascular Disease

The table below lists the excluded articles with at least one reason for exclusion, but may not reflect all possible reasons.

| Reference | Excluded Citations | Reason for Exclusion |
|---|---|---|
| 23. | Lee SG,Lee W,Kwon OH,Kim JH. Association of urinary sodium/creatinine ratio and urinary sodium/specific gravity unit ratio with blood pressure and hypertension: KNHANES 2009-2010. Clinica Chimica Acta. 2013;424(#number#):168-173. PMID:#accession number#. | Study Design, Independent Variable |
| 24. | McMahon EJ,Bauer JD,Hawley CM,Isbel NM,Stowasser M,Johnson DW,Campbell KL. A randomized trial of dietary sodium restriction in CKD. J Am Soc Nephrol. 2013;24(12):2096-103. PMID:24204003. | Outcome, Unhealthy Subjects |
| 25. | Mendes Tde A,Goldbaum M,Segri NJ,Barros MB,Cesar CL,Carandina L. Factors associated with the prevalence of hypertension and control practices among elderly residents of Sao Paulo city, Brazil. Cad Saude Publica. 2013;29(11):2275-86. PMID:24233042. | Study Design, Outcome |
| 26. | Mente A,O'Donnell MJ,Rangarajan S,McQueen MJ,Poirier P,Wielgosz A,Morrison H,Li W,Wang X,Di C,Mony P,Devanath A,Rosengren A,Oguz A,Zatonska K,Yusufali AH,Lopez-Jaramillo P,Avezum A,Ismail N,Lanas F,Puoane T,Diaz R,Kelishadi R,Iqbal R,Yusuf R,Chifamba J,Khatib R,Teo K,Yusuf S. Association of urinary sodium and potassium excretion with blood pressure. N Engl J Med. 2014;371(7):601-11. PMID:25119606. | Outcome |
| 27. | Messerli FH,Bangalore S. Dietary salt reduction; further lowering of target lowers blood pressure but may increase risk. Evid Based Med. 2014;19(1):22. PMID:24001453. | Study Design, Outcome |
| 28. | Mezue K. The increasing burden of hypertension in Nigeria - can a dietary salt reduction strategy change the trend?. Perspect Public Health. 2013;#volume#(#number#):#pages#. PMID:24002906. | Study Design |
| 29. | Mozaffarian D,Fahimi S,Singh GM,Micha R,Khatibzadeh S,Engell RE,Lim S,Danaei G,Ezzati M,Powles J. Global sodium consumption and death from cardiovascular causes. N Engl J Med. 2014;371(7):624-34. PMID:25119608. | Study Design |
| 30. | Oh HY,Kim MK,Lee M,Kim YO. Macronutrient composition and sodium intake of diet are associated with risk of metabolic syndrome and hypertension in Korean women. PLoS One. 2013;8(10):e78088. PMID:24205105. | Study Design, Outcome |
| 31. | Poggio R,Gutierrez L,Matta MG,Elorriaga N,Irazola V,Rubinstein A. Daily sodium consumption and CVD mortality in the general population: systematic review and meta-analysis of prospective studies. Public Health Nutr. 2014;#volume#(#number#):1-10. PMID:24848764. | Study Design |
| 32. | Polonia J,Martins L,Pinto F,Nazare J. Prevalence, awareness, treatment and control of hypertension and salt intake in Portugal: changes over a decade. The PHYSA study. J Hypertens. 2014;32(6):1211-21. PMID:24675681. | Study Design, Outcome |
| 33. | Rodrigues SL,Baldo MP,Machado RC,Forechi L,Molina Mdel C,Mill JG. High potassium intake blunts the effect of elevated sodium intake on blood pressure levels. J Am Soc Hypertens. 2014;8(4):232-8. PMID:24524886. | Independent Variable, Outcome |

## Excluded Articles: Sodium Intake & Risk of Cardiovascular Disease

The table below lists the excluded articles with at least one reason for exclusion, but may not reflect all possible reasons.

| Reference | Excluded Citations | Reason for Exclusion |
|---|---|---|
| 34. | Sakaki M,Tsuchihashi T,Arakawa K,Fukui H,Kameda W,Tominaga M. Long-term variability of urinary salt excretion and blood pressure in hypertensive patients. Hypertens Res. 2014. PMID:25007766. | Unhealthy Subjects |
| 35. | Sampson UKA,Edwards TL,Jahangir E,Munro H,Wariboko M,Wassef MG,Fazio S,Mensah GA,Kabagambe EK,Blot WJ,Lipworth L. Factors associated with the prevalence of hypertension in the southeastern united states insights from 69 211 blacks and whites in the southern community cohort study. Circulation: Cardiovascular Quality and Outcomes. 2014;7(1):33-54. | Independent Variable |
| 36. | Sharma S,McFann K,Chonchol M,Kendrick J. Dietary sodium and potassium intake is not associated with elevated blood pressure in US adults with no prior history of hypertension. J Clin Hypertens (Greenwich). 2014;16(6):418-23. PMID:24720647. | Study Design, Outcome |
| 37. | Singer P,Cohen H,Alderman M. Assessing the Associations of Sodium Intake With Long-Term All-Cause and Cardiovascular Mortality in a Hypertensive Cohort. Am J Hypertens. 2014;#volume#(#number#):#pages#. PMID:25159082. | Unhealthy Subjects |
| 38. | Sison JA. Does dietary salt intake correlate with regional differences in the prevalence of hypertension in the Philippines?. Phillippine Journal of Internal Medicine. 2013;51(4). | Outcome, Country |
| 39. | Song EK,Moser DK,Dunbar SB,Pressler SJ,Lennie TA. Dietary sodium restriction below 2 g per day predicted shorter event-free survival in patients with mild heart failure. Eur J Cardiovasc Nurs. 2013;#volume#(#number#):#pages#. PMID:24366983. | Unhealthy Subjects |
| 40. | Teo K,Mente A. Blood pressure reduction by reducing sodium intake in the population: one shoe fits all?. Curr Opin Cardiol. 2014;29(4):331-5. PMID:25029451. | Study Design |
| 41. | Umesawa M,Kitamura A,Kiyama M,Okada T,Shimizu Y,Imano H,Ohira T,Nakamura M,Maruyama K,Iso H. Association between dietary behavior and risk of hypertension among Japanese male workers. Hypertens Res. 2013;36(4):374-80. PMID:23303292. | Independent Variable, Outcome |
| 42. | Welsh D,Lennie TA,Marcinek R,Biddle MJ,Abshire D,Bentley B,Moser DK. Low-sodium diet self-management intervention in heart failure: pilot study results. Eur J Cardiovasc Nurs. 2013;12(1):87-95. PMID:22492785. | Outcome, Unhealthy Subjects |
| 43. | Westrick SC,Garza KB,Stevenson TL,Oliver WD. Association of blood pressure with sodium-related knowledge and behaviors in adults with hypertension. J Am Pharm Assoc (2003). 2014;54(2):154-8. PMID:24562633. | Study Design, Outcome, Unhealthy Subjects |
| 44. | Whelton PK. Sodium, potassium, blood pressure, and cardiovascular disease in humans. Curr Hypertens Rep. 2014;16(8):465. PMID:24924995. | Study Design |
| 45. | Woodruff SJ,Fryer K,Campbell T,Cole M. Associations among blood pressure, salt consumption and body | Study Design, |

## Excluded Articles: Sodium Intake & Risk of Cardiovascular Disease

The table below lists the excluded articles with at least one reason for exclusion, but may not reflect all possible reasons.

| Reference | Excluded Citations | Reason for Exclusion |
|---|---|---|
| | weight status of students from south-western Ontario. Public Health Nutr. 2014;17(5):1114-9. PMID:23453007. | Outcome |
| 46. | Yi SS,Kansagra SM. Associations of sodium intake with obesity, body mass index, waist circumference, and weight. American Journal of Preventive Medicine. 2014;46(6):e53-e55. | Study Design |
| 47. | Yu D,Zhang X,Xiang YB,Yang G,Li H,Gao YT,Zheng W,Shu XO. Adherence to dietary guidelines and mortality: A report from prospective cohort studies of 134,000 Chinese adults in urban Shanghai. American Journal of Clinical Nutrition. 2014;100(2):693-700. | Independent Variable, Country |
| 48. | Zhang Z,Cogswell ME,Gillespie C,Fang J,Loustalot F,Dai S,Carriquiry AL,Kuklina EV,Hong Y,Merritt R,Yang Q. Association between usual sodium and potassium intake and blood pressure and hypertension among U.S. adults: NHANES 2005-2010. PLoS One. 2013;8(10):e75289. PMID:24130700. | Study Design, Outcome |
| 49. | Zhao Q,Gu D,Chen J,Li J,Cao J,Lu F,Guo D,Wang R,Shen J,Chen J,Chen CS,Mills KT,Schwander K,Rao DC,He J. Blood pressure responses to dietary sodium and potassium interventions and the cold pressor test: the GenSalt replication study in rural North China. Am J Hypertens. 2014;27(1):72-80. PMID:24004934. | Outcome |
| 50. | Zhao X,Yang X,Zhang X,Li Y,Zhao X,Ren L,Wang L,Gu C,Zhu Z,Han Y. Dietary Salt Intake and Coronary Atherosclerosis in Patients With Prehypertension. Journal of Clinical Hypertension. 2014;16(8):575-580. | Country |
| 51. | Zhou B,Wang HL,Wang WL,Wu XM,Fu LY,Shi JP. Long-term effects of salt substitution on blood pressure in a rural north Chinese population. J Hum Hypertens. 2013;27(7):427-33. PMID:23254595. | Country |

# APPENDIX C. SUGARS AND CARDIOVASCULAR DISEASE – EXCLUDED ARTICLES LIST



Archived from www.NEL.gov on March 21, 2017

## Excluded Articles: Added Sugars & Risk of Cardiovascular Disease

The table below lists the excluded articles with at least one reason for exclusion, but may not reflect all possible reasons.

| | Excluded Citations | Reason for Exclusion |
|---|---|---|
| 1. | How sweet it's not: sugary drinks take a toll on health. Harv Mens Health Watch. 2013;17(11):1, 8. PMID:24000425. http://www.ncbi.nlm.nih.gov/pubmed/24000425 | Study Design |
| 2. | Reducing sugary beverage consumption in childhood may lessen chronic disease risk. J Am Dent Assoc. 2007;138(2):160. PMID:17272370. http://www.ncbi.nlm.nih.gov/pubmed/17272370 | Study Design |
| 3. | Soft drinks found to increase stroke risk. Study implicates both diet and sugar-sweetened sodas. Harv Heart Lett. 2012;22(10):7. PMID:22764402. http://www.ncbi.nlm.nih.gov/pubmed/22764402 | Study Design |
| 4. | Abdel-Sayed A,Binnert C,Le KA,Bortolotti M,Schneiter P,Tappy L. A high-fructose diet impairs basal and stress-mediated lipid metabolism in healthy male subjects. Br J Nutr. 2008;100(2):393-9. PMID:18205992. http://www.ncbi.nlm.nih.gov/pubmed/18205992 | Independent Variable, Outcomes |
| 5. | Aeberli I,Zimmermann MB,Molinari L,Lehmann R,l'Allemand D,Spinas GA,Berneis K. Fructose intake is a predictor of LDL particle size in overweight schoolchildren. Am J Clin Nutr. 2007;86(4):1174-8. PMID:17921399. http://www.ncbi.nlm.nih.gov/pubmed/17921399 | Study Design |
| 6. | Ali A,Yazaki Y,Njike VY,Ma Y,Katz DL. Effect of fruit and vegetable concentrates on endothelial function in metabolic syndrome: a randomized controlled trial. Nutr J. 2011;10(#number#):72. PMID:21714890. http://www.ncbi.nlm.nih.gov/pubmed/21714890 | Independent Variable |
| 7. | Althuis MD,Weed DL. Evidence mapping: methodologic foundations and application to intervention and observational research on sugar-sweetened beverages and health outcomes. Am J Clin Nutr. 2013;98(3):755-68. PMID:23824722. http://www.ncbi.nlm.nih.gov/pubmed/23824722 | Study Design |
| 8. | Al-Waili NS,Boni NS. Natural honey lowers plasma prostaglandin concentrations in normal individuals. J Med Food. 2003;6(2):129-33. PMID:12935324. http://www.ncbi.nlm.nih.gov/pubmed/12935324 | Outcomes |
| 9. | Al-Waili NS. Natural honey lowers plasma glucose, C-reactive protein, homocysteine, and blood lipids in healthy, diabetic, and hyperlipidemic subjects: comparison with dextrose and sucrose. J Med Food. 2004;7(1):100-7. PMID:15117561. http://www.ncbi.nlm.nih.gov/pubmed/15117561 | Independent Variable |
| 10. | Angelopoulos TJ,Lowndes J,Zukley L,Melanson KJ,Nguyen V,Huffman A,Rippe JM. The effect of high-fructose corn syrup consumption on triglycerides and uric acid. J Nutr. 2009;139(6):1242s-1245s. PMID:19403709. http://www.ncbi.nlm.nih.gov/pubmed/19403709 | Study Design |
| 11. | Ashidate K,Kawamura M,Tohda H,Miyazaki S,Hirata Y. Soft drink ketosis associated with type III hyperlipidemia and diabetic xanthoma, case report. Journal of the Japan Diabetes Society. 2004;47(12):939-943. PMID:#accession number#. http://www.embase.com/search/results?subaction=viewrecord&from=export&id=L40215897 | Study Design |
| 12. | Aune D. Soft drinks, aspartame, and the risk of cancer and cardiovascular disease. Am J Clin Nutr. 2012;96(6):1249-51. PMID:23134894. http://www.ncbi.nlm.nih.gov/pubmed/23134894 | Study Design |
| 13. | Austin GL,Krueger PM. Increasing the percentage of energy from dietary sugar, fats, and alcohol in adults is associated with increased energy intake but has minimal association with biomarkers of cardiovascular risk. J | Study Design |

## Excluded Articles: Added Sugars & Risk of Cardiovascular Disease

The table below lists the excluded articles with at least one reason for exclusion, but may not reflect all possible reasons.

| | Excluded Citations | Reason for Exclusion |
|---|---|---|
| | Nutr. 2013;143(10):1651-8. PMID:23946345. http://www.ncbi.nlm.nih.gov/pubmed/23946345 | |
| 14. | Azizi F,Emami H,Salehi P,Ghanbarian A,Mirmiran P,Mirbolooki M,Azizi T. Cardiovascular risk factors in the elderly: the Tehran Lipid and Glucose Study. J Cardiovasc Risk. 2003;10(1):65-73. PMID:12569239. http://www.ncbi.nlm.nih.gov/pubmed/12569239 | Study Design |
| 15. | Azizi F,Rahmani M,Emami H,Mirmiran P,Hajipour R,Madjid M,Ghanbili J,Ghanbarian A,Mehrabi Y,Saadat N,Salehi P,Mortazavi N,Heydarian P,Sarbazi N,Allahverdian S,Saadati N,Ainy E,Moeini S. Cardiovascular risk factors in an Iranian urban population: Tehran lipid and glucose study (phase 1). Soz Praventivmed. 2002;47(6):408-26. PMID:12643001. http://www.ncbi.nlm.nih.gov/pubmed/12643001 | Study Design |
| 16. | Bakker LE,van Schinkel LD,Guigas B,Streefland TC,Jonker JT,van Klinken JB,van der Zon GC,Lamb HJ,Smit JW,Pijl H,Meinders AE,Jazet IM. A 5-day high-fat, high-calorie diet impairs insulin sensitivity in healthy, young South Asian men but not in Caucasian men. Diabetes. 2014;63(1):248-58. PMID:24357702. http://www.ncbi.nlm.nih.gov/pubmed/24357702 | Independent Variable |
| 17. | Banaschak S,Bajanowski T,Brinkmann B. Suicide of a diabetic by inducing hyperglycemic coma. Int J Legal Med. 2000;113(3):162-3. PMID:10876988. http://www.ncbi.nlm.nih.gov/pubmed/10876988 | Study Design |
| 18. | Bantle JP,Raatz SK,Thomas W,Georgopoulos A. Effects of dietary fructose on plasma lipids in healthy subjects. Am J Clin Nutr. 2000;72(5):1128-34. PMID:11063439. http://www.ncbi.nlm.nih.gov/pubmed/11063439 | Independent Variable |
| 19. | Bantle JP. Dietary fructose and metabolic syndrome and diabetes. J Nutr. 2009;139(6):1263s-1268s. PMID:19403723. http://www.ncbi.nlm.nih.gov/pubmed/19403723 | Study Design |
| 20. | Bantle JP. Is fructose the optimal low glycemic index sweetener?. Nestle Nutr Workshop Ser Clin Perform Programme. 2006;11(#number#):83-91; discussion 92-5. PMID:16820733. http://www.ncbi.nlm.nih.gov/pubmed/16820733 | Study Design |
| 21. | Basaranoglu M,Basaranoglu G,Sabuncu T,Senturk H. Fructose as a key player in the development of fatty liver disease. World J Gastroenterol. 2013;19(8):1166-72. PMID:23482247. http://www.ncbi.nlm.nih.gov/pubmed/23482247 | Study Design |
| 22. | Basciano H,Federico L,Adeli K. Fructose, insulin resistance, and metabolic dyslipidemia. Nutr Metab (Lond). 2005;2(1):5. PMID:15723702. http://www.ncbi.nlm.nih.gov/pubmed/15723702 | Study Design |
| 23. | Beulens JW,de Bruijne LM,Stolk RP,Peeters PH,Bots ML,Grobbee DE,van der Schouw YT. High dietary glycemic load and glycemic index increase risk of cardiovascular disease among middle-aged women: a population-based follow-up study. J Am Coll Cardiol. 2007;50(1):14-21. PMID:17601539. http://www.ncbi.nlm.nih.gov/pubmed/17601539 | Independent Variable |
| 24. | Bobridge KS,Haines GL,Mori TA,Beilin LJ,Oddy WH,Sherriff J,O'Sullivan TA. Dietary fructose in relation to blood pressure and serum uric acid in adolescent boys and girls. J Hum Hypertens. 2013;27(4):217-24. PMID:22971754. http://www.ncbi.nlm.nih.gov/pubmed/22971754 | Study Design |
| 25. | Bomback AS,Katz R,He K,Shoham DA,Burke GL,Klemmer PJ. Sugar-sweetened beverage consumption and | Outcomes, Unhealthy |

## Excluded Articles: Added Sugars & Risk of Cardiovascular Disease

The table below lists the excluded articles with at least one reason for exclusion, but may not reflect all possible reasons.

| | Excluded Citations | Reason for Exclusion |
|---|---|---|
| | the progression of chronic kidney disease in the Multi-Ethnic Study of Atherosclerosis (MESA). Am J Clin Nutr. 2009;90(5):1172-8. PMID:19740973. http://www.ncbi.nlm.nih.gov/pubmed/19740973 | Subjects |
| 26. | Bopp M,Wilcox S,Laken M,Hooker SP,Parra-Medina D,Saunders R,Butler K,Fallon EA,McClorin L. 8 Steps to Fitness: a faith-based, behavior change physical activity intervention for African Americans. J Phys Act Health. 2009;6(5):568-77. PMID:19953833. http://www.ncbi.nlm.nih.gov/pubmed/19953833 | Independent Variable |
| 27. | Botezelli JD,Dalia RA,Reis IM,Barbieri RA,Rezende TM,Pelarigo JG,Codogno J,Goncalves R,Mello MA. Chronic consumption of fructose rich soft drinks alters tissue lipids of rats. Diabetol Metab Syndr. 2010;2(#number#):43. PMID:20573247. http://www.ncbi.nlm.nih.gov/pubmed/20573247 | Unhealthy Subjects |
| 28. | Boyko EJ,Barr EL,Zimmet PZ,Shaw JE. Two-hour glucose predicts the development of hypertension over 5 years: the AusDiab study. J Hum Hypertens. 2008;22(3):168-76. PMID:18046430. http://www.ncbi.nlm.nih.gov/pubmed/18046430 | Independent Variable |
| 29. | Bravo S,Lowndes J,Sinnett S,Yu Z,Rippe J. Consumption of sucrose and high-fructose corn syrup does not increase liver fat or ectopic fat deposition in muscles. Appl Physiol Nutr Metab. 2013;38(6):681-8. PMID:23724887. http://www.ncbi.nlm.nih.gov/pubmed/23724887 | Outcomes |
| 30. | Bray GA,Popkin BM. Calorie-sweetened beverages and fructose: what have we learned 10 years later. Pediatr Obes. 2013;8(4):242-8. PMID:23625798. http://www.ncbi.nlm.nih.gov/pubmed/23625798 | Study Design |
| 31. | Bray GA,Popkin BM. Dietary sugar and body weight: have we reached a crisis in the epidemic of obesity and diabetes?: health be damned! Pour on the sugar. Diabetes Care. 2014;37(4):950-6. PMID:24652725. http://www.ncbi.nlm.nih.gov/pubmed/24652725 | Study Design |
| 32. | Bray GA. Energy and fructose from beverages sweetened with sugar or high-fructose corn syrup pose a health risk for some people. Adv Nutr. 2013;4(2):220-5. PMID:23493538. http://www.ncbi.nlm.nih.gov/pubmed/23493538 | Study Design |
| 33. | Bray GA. Fructose and risk of cardiometabolic disease. Curr Atheroscler Rep. 2012;14(6):570-8. PMID:22949106. http://www.ncbi.nlm.nih.gov/pubmed/22949106 | Study Design |
| 34. | Bray GA. Fructose: pure, white, and deadly? Fructose, by any other name, is a health hazard. J Diabetes Sci Technol. 2010;4(4):1003-7. PMID:20663467. http://www.ncbi.nlm.nih.gov/pubmed/20663467 | Study Design |
| 35. | Bray GA. Fructose: should we worry?. Int J Obes (Lond). 2008;32 Suppl 7(#number#):S127-31. PMID:19136981. http://www.ncbi.nlm.nih.gov/pubmed/19136981 | Study Design |
| 36. | Bray GA. How bad is fructose?. Am J Clin Nutr. 2007;86(4):895-6. PMID:17921361. http://www.ncbi.nlm.nih.gov/pubmed/17921361 | Study Design |
| 37. | Bray GA. Soft drink consumption and obesity: it is all about fructose. Curr Opin Lipidol. 2010;21(1):51-7. PMID:19956074. http://www.ncbi.nlm.nih.gov/pubmed/19956074 | Study Design |
| 38. | Bremer AA,Auinger P,Byrd RS. Sugar-Sweetened Beverage Intake Trends in US Adolescents and Their Association with Insulin Resistance-Related Parameters. J Nutr Metab. 2010;2010(#number#):#pages#. | Study Design |

## Excluded Articles: Added Sugars & Risk of Cardiovascular Disease

The table below lists the excluded articles with at least one reason for exclusion, but may not reflect all possible reasons.

| | Excluded Citations | Reason for Exclusion |
|---|---|---|
| | PMID:20700405. http://www.ncbi.nlm.nih.gov/pubmed/20700405 | |
| 39. | Brown CM,Dulloo AG,Montani JP. Sugary drinks in the pathogenesis of obesity and cardiovascular diseases. Int J Obes (Lond). 2008;32 Suppl 6(#number#):S28-34. PMID:19079277. http://www.ncbi.nlm.nih.gov/pubmed/19079277 | Study Design |
| 40. | Brown CM,Dulloo AG,Yepuri G,Montani JP. Fructose ingestion acutely elevates blood pressure in healthy young humans. Am J Physiol Regul Integr Comp Physiol. 2008;294(3):R730-7. PMID:18199590. http://www.ncbi.nlm.nih.gov/pubmed/18199590 | Independent Variable |
| 41. | Brown IJ,Stamler J,Van Horn L,Robertson CE,Chan Q,Dyer AR,Huang CC,Rodriguez BL,Zhao L,Daviglus ML,Ueshima H,Elliott P. Sugar-sweetened beverage, sugar intake of individuals, and their blood pressure: international study of macro/micronutrients and blood pressure. Hypertension. 2011;57(4):695-701. PMID:21357284. http://www.ncbi.nlm.nih.gov/pubmed/21357284 | Study Design |
| 42. | Brunner S,Holub I,Theis S,Gostner A,Melcher R,Wolf P,Amann-Gassner U,Scheppach W,Hauner H. Metabolic effects of replacing sucrose by isomaltulose in subjects with type 2 diabetes: a randomized double-blind trial. Diabetes Care. 2012;35(6):1249-51. PMID:22492584. http://www.ncbi.nlm.nih.gov/pubmed/22492584 | Unhealthy Subjects |
| 43. | Brynes AE,Mark Edwards C,Ghatei MA,Dornhorst A,Morgan LM,Bloom SR,Frost GS. A randomised four-intervention crossover study investigating the effect of carbohydrates on daytime profiles of insulin, glucose, non-esterified fatty acids and triacylglycerols in middle-aged men. Br J Nutr. 2003;89(2):207-18. PMID:12575905. http://www.ncbi.nlm.nih.gov/pubmed/12575905 | Independent Variable |
| 44. | Chan TF,Lin WT,Huang HL,Lee CY,Wu PW,Chiu YW,Huang CC,Tsai S,Lin CL,Lee CH. Consumption of sugar-sweetened beverages is associated with components of the metabolic syndrome in adolescents. Nutrients. 2014;6(5):2088-103. PMID:24858495. http://www.ncbi.nlm.nih.gov/pubmed/24858495 | Study Design |
| 45. | Chen L,Appel LJ,Loria C,Lin PH,Champagne CM,Elmer PJ,Ard JD,Mitchell D,Batch BC,Svetkey LP,Caballero B. Reduction in consumption of sugar-sweetened beverages is associated with weight loss: the PREMIER trial. Am J Clin Nutr. 2009;89(5):1299-306. PMID:19339405. http://www.ncbi.nlm.nih.gov/pubmed/19339405 | Outcomes |
| 46. | Chiavaroli L,Mirrahimi A,de Souza RJ,Sievenpiper JL. Meta-analysis of fructose and cholesterol: a concern regarding missing data. J Nutr. 2014;144(4):538-9. PMID:24652188. http://www.ncbi.nlm.nih.gov/pubmed/24652188 | Study Design |
| 47. | Chong MF,Fielding BA,Frayn KN. Metabolic interaction of dietary sugars and plasma lipids with a focus on mechanisms and de novo lipogenesis. Proc Nutr Soc. 2007;66(1):52-9. PMID:17343772. http://www.ncbi.nlm.nih.gov/pubmed/17343772 | Study Design |
| 48. | Claesson AL,Holm G,Ernersson A,Lindstrom T,Nystrom FH. Two weeks of overfeeding with candy, but not peanuts, increases insulin levels and body weight. Scand J Clin Lab Invest. 2009;69(5):598-605. PMID:19396658. http://www.ncbi.nlm.nih.gov/pubmed/19396658 | Independent Variable |
| 49. | Cooper RA,Fehily AM,Pickering JE,Erusalimsky JD,Elwood PC. Honey, health and longevity. Curr Aging Sci. | Study Design, Outcomes |

## Excluded Articles: Added Sugars & Risk of Cardiovascular Disease

The table below lists the excluded articles with at least one reason for exclusion, but may not reflect all possible reasons.

| | Excluded Citations | Reason for Exclusion |
|---|---|---|
| | 2010;3(3):239-41. PMID:20735343. http://www.ncbi.nlm.nih.gov/pubmed/20735343 | |
| 50. | Couch SC,Crandell JL,Shah AS,Dolan LM,Merchant AT,Liese AD,Lawrence JM,Pihoker C,Mayer-Davis EJ. Fructose intake and cardiovascular risk factors in youth with type 1 diabetes: SEARCH for diabetes in youth study. Diabetes Res Clin Pract. 2013;100(2):265-71. PMID:23540682. http://www.ncbi.nlm.nih.gov/pubmed/23540682 | Study Design, Unhealthy Subjects |
| 51. | Coulston AM,Johnson RK. Sugar and sugars: myths and realities. J Am Diet Assoc. 2002;102(3):351-3. PMID:11902367. http://www.ncbi.nlm.nih.gov/pubmed/11902367 | Study Design |
| 52. | Curhan GC,Forman JP. Sugar-sweetened beverages and chronic disease. Kidney Int. 2010;77(7):569-70. PMID:20224584. http://www.ncbi.nlm.nih.gov/pubmed/20224584 | Study Design |
| 53. | Damiao R,Castro TG,Cardoso MA,Gimeno SG,Ferreira SR. Dietary intakes associated with metabolic syndrome in a cohort of Japanese ancestry. Br J Nutr. 2006;96(3):532-8. PMID:16925859. http://www.ncbi.nlm.nih.gov/pubmed/16925859 | Independent Variable |
| 54. | Daniels SR. How could sugar-sweetened beverages cause blood pressure elevation?. J Pediatr. 2009;154(6):A3. PMID:19446091. http://www.ncbi.nlm.nih.gov/pubmed/19446091 | Study Design |
| 55. | David Wang D,Sievenpiper JL,de Souza RJ,Cozma AI,Chiavaroli L,Ha V,Mirrahimi A,Carleton AJ,Di Buono M,Jenkins AL,Leiter LA,Wolever TM,Beyene J,Kendall CW,Jenkins DJ. Effect of fructose on postprandial triglycerides: a systematic review and meta-analysis of controlled feeding trials. Atherosclerosis. 2014;232(1):125-33. PMID:24401226. http://www.ncbi.nlm.nih.gov/pubmed/24401226 | Study Design |
| 56. | de Castro UG,dos Santos RA,Silva ME,de Lima WG,Campagnole-Santos MJ,Alzamora AC. Age-dependent effect of high-fructose and high-fat diets on lipid metabolism and lipid accumulation in liver and kidney of rats. Lipids Health Dis. 2013;12(#number#):136. PMID:24044579. http://www.ncbi.nlm.nih.gov/pubmed/24044579 | Unhealthy Subjects |
| 57. | de Koning L,Malik VS,Rimm EB,Willett WC,Hu FB. Sugar-sweetened and artificially sweetened beverage consumption and risk of type 2 diabetes in men. Am J Clin Nutr. 2011;93(6):1321-7. PMID:21430119. http://www.ncbi.nlm.nih.gov/pubmed/21430119 | Outcomes |
| 58. | Denova-Gutierrez E,Talavera JO,Huitron-Bravo G,Mendez-Hernandez P,Salmeron J. Sweetened beverage consumption and increased risk of metabolic syndrome in Mexican adults. Public Health Nutr. 2010;13(6):835-42. PMID:20144256. http://www.ncbi.nlm.nih.gov/pubmed/20144256 | Study Design |
| 59. | Dohadwala MM,Hamburg NM,Holbrook M,Kim BH,Duess MA,Levit A,Titas M,Chung WB,Vincent FB,Caiano TL,Frame AA, Jr. Keaney JF,Vita JA. Effects of Concord grape juice on ambulatory blood pressure in prehypertension and stage 1 hypertension. Am J Clin Nutr. 2010;92(5):1052-9. PMID:20844075. http://www.ncbi.nlm.nih.gov/pubmed/20844075 | Independent Variable |
| 60. | Ellingsen I,Hjerkinn EM,Seljeflot I,Arnesen H,Tonstad S. Consumption of fruit and berries is inversely associated with carotid atherosclerosis in elderly men. Br J Nutr. 2008;99(3):674-81. PMID:17894919. http://www.ncbi.nlm.nih.gov/pubmed/17894919 | Independent Variable |

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The table below lists the excluded articles with at least one reason for exclusion, but may not reflect all possible reasons.

| | Excluded Citations | Reason for Exclusion |
|---|---|---|
| 61. | Erkkila AT,Schwab US,Agren JJ,Hallikainen M,Gylling H,Uusitupa MI. Moderate increase in dietary sucrose does not influence fasting or postprandial serum lipids regardless of the presence of apolipoprotein E2 allele in healthy subjects. Eur J Clin Nutr. 2007;61(9):1094-101. PMID:17228342. http://www.ncbi.nlm.nih.gov/pubmed/17228342 | Independent Variable |
| 62. | Feig DI. Sour notes on sweet drinks. J Pediatr. 2009;154(6):783-4. PMID:19446093. http://www.ncbi.nlm.nih.gov/pubmed/19446093 | Study Design |
| 63. | Feig DI. Sugar-sweetened beverages and hypertension. Future Cardiol. 2010;6(6):773-6. PMID:21142633. http://www.ncbi.nlm.nih.gov/pubmed/21142633 | Study Design |
| 64. | Feinman RD,Fine EJ. Fructose in perspective. Nutr Metab (Lond). 2013;10(1):45. PMID:23815799. http://www.ncbi.nlm.nih.gov/pubmed/23815799 | Study Design |
| 65. | Ferder L,Ferder MD,Inserra F. The role of high-fructose corn syrup in metabolic syndrome and hypertension. Curr Hypertens Rep. 2010;12(2):105-12. PMID:20424937. http://www.ncbi.nlm.nih.gov/pubmed/20424937 | Study Design |
| 66. | Fernandes J,Arts J,Dimond E,Hirshberg S,Lofgren IE. Dietary factors are associated with coronary heart disease risk factors in college students. Nutr Res. 2013;33(8):647-52. PMID:23890354. http://www.ncbi.nlm.nih.gov/pubmed/23890354 | Study Design |
| 67. | Fernandez JM,Da Silva-Grigoletto ME,Ruano-Ruiz JA,Caballero-Villarraso J,Moreno-Luna R,Tunez-Finana I,Tasset-Cuevas I,Perez-Martinez P,Lopez-Miranda J,Perez-Jimenez F. Fructose modifies the hormonal response and modulates lipid metabolism during aerobic exercise after glucose supplementation. Clin Sci (Lond). 2009;116(2):137-45. PMID:18533896. http://www.ncbi.nlm.nih.gov/pubmed/18533896 | Independent Variable |
| 68. | Fisher-Wellman KH,Bloomer RJ. Lack of effect of a high-calorie dextrose or maltodextrin meal on postprandial oxidative stress in healthy young men. Int J Sport Nutr Exerc Metab. 2010;20(5):393-400. PMID:20975107. http://www.ncbi.nlm.nih.gov/pubmed/20975107 | Independent Variable |
| 69. | Forman JP,Choi H,Curhan GC. Fructose and vitamin C intake do not influence risk for developing hypertension. J Am Soc Nephrol. 2009;20(4):863-71. PMID:19144761. http://www.ncbi.nlm.nih.gov/pubmed/19144761 | Independent Variable |
| 70. | Francini-Pesenti F,Beltramolli D,Dall'acqua S,Brocadello F. Effect of sugar cane policosanol on lipid profile in primary hypercholesterolemia. Phytother Res. 2008;22(3):318-22. PMID:18167048. http://www.ncbi.nlm.nih.gov/pubmed/18167048 | Independent Variable |
| 71. | Francis DK,Van den Broeck J,Younger N,McFarlane S,Rudder K,Gordon-Strachan G,Grant A,Johnson A,Tulloch-Reid M,Wilks R. Fast-food and sweetened beverage consumption: association with overweight and high waist circumference in adolescents. Public Health Nutr. 2009;12(8):1106-14. PMID:19243675. http://www.ncbi.nlm.nih.gov/pubmed/19243675 | Study Design, Outcomes |
| 72. | Franz M. High-fructose corn syrup. What's all the fuss about?. Diabetes Self Manag. 2011;28(3):33-4, 36-7. PMID:21661508. http://www.ncbi.nlm.nih.gov/pubmed/21661508 | Study Design |
| 73. | Fuchs MA,Sato K,Niedzwiecki D,Ye X,Saltz LB,Mayer RJ,Mowat RB,Whittom R,Hantel A,Benson A,Atienza | Outcomes |

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The table below lists the excluded articles with at least one reason for exclusion, but may not reflect all possible reasons.

| Excluded Citations | | Reason for Exclusion |
|---|---|---|
| | D,Messino M,Kindler H,Venook A,Ogino S,Wu K,Willett WC,Giovannucci EL,Meyerhardt JA. Sugar-sweetened beverage intake and cancer recurrence and survival in CALGB 89803 (Alliance). PLoS One. 2014;9(6):e99816. PMID:24937507. http://www.ncbi.nlm.nih.gov/pubmed/24937507 | |
| 74. | Gao X,Qi L,Qiao N,Choi HK,Curhan G,Tucker KL,Ascherio A. Intake of added sugar and sugar-sweetened drink and serum uric acid concentration in US men and women. Hypertension. 2007;50(2):306-12. PMID:17592072. http://www.ncbi.nlm.nih.gov/pubmed/17592072 | Study Design |
| 75. | Gersch MS,Mu W,Cirillo P,Reungjui S,Zhang L,Roncal C,Sautin YY,Johnson RJ,Nakagawa T. Fructose, but not dextrose, accelerates the progression of chronic kidney disease. Am J Physiol Renal Physiol. 2007;293(4):F1256-61. PMID:17670904. http://www.ncbi.nlm.nih.gov/pubmed/17670904 | Unhealthy Subjects |
| 76. | Gibson S,Gunn P,Wittekind A,Cottrell R. The effects of sucrose on metabolic health: a systematic review of human intervention studies in healthy adults. Crit Rev Food Sci Nutr. 2013;53(6):591-614. PMID:23627502. http://www.ncbi.nlm.nih.gov/pubmed/23627502 | Study Design |
| 77. | Grasser EK,Dulloo A,Montani JP. Cardiovascular responses to the ingestion of sugary drinks using a randomised cross-over study design: does glucose attenuate the blood pressure-elevating effect of fructose?. Br J Nutr. 2014;112(2):183-92. PMID:24780643. http://www.ncbi.nlm.nih.gov/pubmed/24780643 | Independent Variable |
| 78. | Green AK,Jacques PF,Rogers G,Fox CS,Meigs JB,McKeown NM. Sugar-sweetened beverages and prevalence of the metabolically abnormal phenotype in the Framingham Heart Study. Obesity (Silver Spring). 2014;22(5):E157-63. PMID:24550031. http://www.ncbi.nlm.nih.gov/pubmed/24550031 | Study Design |
| 79. | Greenwood DC,Threapleton DE,Evans CE,Cleghorn CL,Nykjaer C,Woodhead C,Burley VJ. Association between sugar-sweetened and artificially sweetened soft drinks and type 2 diabetes: systematic review and dose-response meta-analysis of prospective studies. Br J Nutr. 2014;#volume#(#number#):1-10. PMID:24932880. http://www.ncbi.nlm.nih.gov/pubmed/24932880 | Study Design |
| 80. | Grimes CA,Riddell LJ,Campbell KJ,Nowson CA. Dietary salt intake, sugar-sweetened beverage consumption, and obesity risk. Pediatrics. 2013;131(1):14-21. PMID:23230077. http://www.ncbi.nlm.nih.gov/pubmed/23230077 | Study Design |
| 81. | Ha V,Jayalath VH,Cozma AI,Mirrahimi A,de Souza RJ,Sievenpiper JL. Fructose-containing sugars, blood pressure, and cardiometabolic risk: a critical review. Curr Hypertens Rep. 2013;15(4):281-97. PMID:23793849. http://www.ncbi.nlm.nih.gov/pubmed/23793849 | Study Design |
| 82. | Ha V,Sievenpiper JL,de Souza RJ,Chiavaroli L,Wang DD,Cozma AI,Mirrahimi A,Yu ME,Carleton AJ,Dibuono M,Jenkins AL,Leiter LA,Wolever TM,Beyene J,Kendall CW,Jenkins DJ. Effect of fructose on blood pressure: a systematic review and meta-analysis of controlled feeding trials. Hypertension. 2012;59(4):787-95. PMID:22331380. #URL# | Study Design |
| 83. | He FJ,MacGregor GA. Salt intake, sugar-sweetened soft drink consumption, and blood pressure. Am J Cardiol. 2014;114(3):499-500. PMID:25017662. http://www.ncbi.nlm.nih.gov/pubmed/25017662 | Study Design |

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The table below lists the excluded articles with at least one reason for exclusion, but may not reflect all possible reasons.

| | Excluded Citations | Reason for Exclusion |
|---|---|---|
| 84. | He FJ,Marrero NM,MacGregor GA. Salt intake is related to soft drink consumption in children and adolescents: a link to obesity?. Hypertension. 2008;51(3):629-34. PMID:18287345. http://www.ncbi.nlm.nih.gov/pubmed/18287345 | Study Design |
| 85. | Hecker PA,Galvao TF,O'Shea KM,Brown BH, Jr. Henderson R,Riggle H,Gupte SA,Stanley WC. High-sugar intake does not exacerbate metabolic abnormalities or cardiac dysfunction in genetic cardiomyopathy. Nutrition. 2012;28(5):520-6. PMID:22304857. http://www.ncbi.nlm.nih.gov/pubmed/22304857 | Unhealthy Subjects |
| 86. | Heden TD,Liu Y,Park YM,Nyhoff LM,Winn NC,Kanaley JA. Moderate amounts of fructose- or glucose-sweetened beverages do not differentially alter metabolic health in male and female adolescents. Am J Clin Nutr. 2014;#volume#(#number#):#pages#. PMID:25030782. http://www.ncbi.nlm.nih.gov/pubmed/25030782 | Independent Variable |
| 87. | Hooshmand S,Holloway B,Nemoseck T,Cole S,Petrisko Y,Hong MY,Kern M. Effects of Agave Nectar Versus Sucrose on Weight Gain, Adiposity, Blood Glucose, Insulin, and Lipid Responses in Mice. J Med Food. 2014;#volume#(#number#):#pages#. PMID:25011004. http://www.ncbi.nlm.nih.gov/pubmed/25011004 | Unhealthy Subjects |
| 88. | Hosseini-Esfahani F,Bahadoran Z,Mirmiran P,Hosseinpour-Niazi S,Hosseinpanah F,Azizi F. Dietary fructose and risk of metabolic syndrome in adults: Tehran Lipid and Glucose study. Nutr Metab (Lond). 2011;8(1):50. PMID:21749680. http://www.ncbi.nlm.nih.gov/pubmed/21749680 | Study Design |
| 89. | Hostmark AT. The Oslo Health Study: a Dietary Index estimating high intake of soft drinks and low intake of fruits and vegetables was positively associated with components of the metabolic syndrome. Appl Physiol Nutr Metab. 2010;35(6):816-25. PMID:21164553. http://www.ncbi.nlm.nih.gov/pubmed/21164553 | Independent Variable |
| 90. | Hostmark AT. The Oslo health study: soft drink intake is associated with the metabolic syndrome. Appl Physiol Nutr Metab. 2010;35(5):635-42. PMID:20962919. http://www.ncbi.nlm.nih.gov/pubmed/20962919 | Study Design |
| 91. | Hu FB,Malik VS. Sugar-sweetened beverages and risk of obesity and type 2 diabetes: epidemiologic evidence. Physiol Behav. 2010;100(1):47-54. PMID:20138901. http://www.ncbi.nlm.nih.gov/pubmed/20138901 | Study Design |
| 92. | Hu FB. Resolved: there is sufficient scientific evidence that decreasing sugar-sweetened beverage consumption will reduce the prevalence of obesity and obesity-related diseases. Obes Rev. 2013;14(8):606-19. PMID:23763695. http://www.ncbi.nlm.nih.gov/pubmed/23763695 | Study Design |
| 93. | Hu Y,Costenbader KH,Gao X,Al-Daabil M,Sparks JA,Solomon DH,Hu FB,Karlson EW,Lu B. Sugar-sweetened soda consumption and risk of developing rheumatoid arthritis in women. Am J Clin Nutr. 2014;#volume#(#number#):#pages#. PMID:25030783. http://www.ncbi.nlm.nih.gov/pubmed/25030783 | Outcomes |
| 94. | Huang C,Huang J,Tian Y,Yang X,Gu D. Sugar sweetened beverages consumption and risk of coronary heart disease: a meta-analysis of prospective studies. Atherosclerosis. 2014;234(1):11-6. PMID:24583500. http://www.ncbi.nlm.nih.gov/pubmed/24583500 | Study Design |
| 95. | Huang D,Dhawan T,Young S,Yong WH,Boros LG,Heaney AP. Fructose impairs glucose-induced hepatic triglyceride synthesis. Lipids Health Dis. 2011;10(#number#):20. PMID:21261970. http://www.ncbi.nlm.nih.gov/pubmed/21261970 | Study Design |

## Excluded Articles: Added Sugars & Risk of Cardiovascular Disease

The table below lists the excluded articles with at least one reason for exclusion, but may not reflect all possible reasons.

| | Excluded Citations | Reason for Exclusion |
|---|---|---|
| 96. | Hudgins LC,Parker TS,Levine DM,Hellerstein MK. A dual sugar challenge test for lipogenic sensitivity to dietary fructose. J Clin Endocrinol Metab. 2011;96(3):861-8. PMID:21252253. http://www.ncbi.nlm.nih.gov/pubmed/21252253 | Independent Variable, Outcomes |
| 97. | Huffman MD. Association or causation of sugar-sweetened beverages and coronary heart disease: recalling Sir Austin Bradford Hill. Circulation. 2012;125(14):1718-20. PMID:22412071. http://www.ncbi.nlm.nih.gov/pubmed/22412071 | Study Design |
| 98. | Huttunen JK,Makinen KK,Scheinin A. Turku sugar studies XI. Effects of sucrose, fructose and xylitol diets on glucose, lipid and urate metabolism. Acta odontologica Scandinavica. 1976;34(6):#pages#. PMID:CN-00229192. http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/192/CN-00229192/frame.html | Study Design |
| 99. | Iles JD. Dietary sugar and myocardial infarction. Can Med Assoc J. 1971;104(11):986. PMID:20311786. http://www.ncbi.nlm.nih.gov/pubmed/20311786 | Study Design |
| 100. | Jacob LM. Diet based on meat, milk and sugar: Up to 27 times higher prostate cancer mortality. Deutsche Zeitschrift fur Onkologie. 2013;45(4):152-162. PMID:#accession number#. http://www.embase.com/search/results?subaction=viewrecord&from=export&id=L370553017 | Study Design, Independent Variable, Outcomes |
| 101. | Jalal DI,Smits G,Johnson RJ,Chonchol M. Increased fructose associates with elevated blood pressure. J Am Soc Nephrol. 2010;21(9):1543-9. PMID:20595676. http://www.ncbi.nlm.nih.gov/pubmed/20595676 | Study Design |
| 102. | Janket SJ,Manson JE,Sesso H,Buring JE,Liu S. A prospective study of sugar intake and risk of type 2 diabetes in women. Diabetes Care. 2003;26(4):1008-15. PMID:12663565. http://www.ncbi.nlm.nih.gov/pubmed/12663565 | Outcomes |
| 103. | Jia G,Aroor AR,Whaley-Connell AT,Sowers JR. Fructose and uric acid: is there a role in endothelial function?. Curr Hypertens Rep. 2014;16(6):434. PMID:24760443. http://www.ncbi.nlm.nih.gov/pubmed/24760443 | Study Design |
| 104. | Johnson RJ,Nakagawa T,Sanchez-Lozada LG,Shafiu M,Sundaram S,Le M,Ishimoto T,Sautin YY,Lanaspa MA. Sugar, uric acid, and the etiology of diabetes and obesity. Diabetes. 2013;62(10):3307-15. PMID:24065788. http://www.ncbi.nlm.nih.gov/pubmed/24065788 | Study Design |
| 105. | Johnson RJ,Sanchez-Lozada LG,Nakagawa T. The effect of fructose on renal biology and disease. J Am Soc Nephrol. 2010;21(12):2036-9. PMID:21115612. http://www.ncbi.nlm.nih.gov/pubmed/21115612 | Study Design |
| 106. | Johnson RJ,Segal MS,Sautin Y,Nakagawa T,Feig DI,Kang DH,Gersch MS,Benner S,Sanchez-Lozada LG. Potential role of sugar (fructose) in the epidemic of hypertension, obesity and the metabolic syndrome, diabetes, kidney disease, and cardiovascular disease. Am J Clin Nutr. 2007;86(4):899-906. PMID:17921363. http://www.ncbi.nlm.nih.gov/pubmed/17921363 | Study Design |
| 107. | Johnson RK,Appel LJ,Brands M,Howard BV,Lefevre M,Lustig RH,Sacks F,Steffen LM,Wylie-Rosett J. Dietary sugars intake and cardiovascular health: a scientific statement from the American Heart Association. Circulation. 2009;120(11):1011-20. PMID:19704096. http://www.ncbi.nlm.nih.gov/pubmed/19704096 | Study Design |
| 108. | Johnston RD,Stephenson MC,Crossland H,Cordon SM,Palcidi E,Cox EF,Taylor MA,Aithal GP,Macdonald IA. No difference between high-fructose and high-glucose diets on liver triacylglycerol or biochemistry in healthy | Independent Variable |

## Excluded Articles: Added Sugars & Risk of Cardiovascular Disease

The table below lists the excluded articles with at least one reason for exclusion, but may not reflect all possible reasons.

| | Excluded Citations | Reason for Exclusion |
|---|---|---|
| | overweight men. Gastroenterology. 2013;145(5):1016-1025.e2. PMID:23872500. http://www.ncbi.nlm.nih.gov/pubmed/23872500 | |
| 109. | Jones JM. Dietary sweeteners containing fructose: overview of a workshop on the state of the science. J Nutr. 2009;139(6):1210s-1213s. PMID:19386822. http://www.ncbi.nlm.nih.gov/pubmed/19386822 | Study Design |
| 110. | Kanazawa M,Xue CY,Kageyama H,Suzuki E,Ito R,Namba Y,Osaka T,Kimura S,Inoue S. Effects of a high-sucrose diet on body weight, plasma triglycerides, and stress tolerance. Nutr Rev. 2003;61(5 Pt 2):S27-33. PMID:12828189. http://www.ncbi.nlm.nih.gov/pubmed/12828189 | Unhealthy Subjects |
| 111. | Karalius VP,Shoham DA. Dietary sugar and artificial sweetener intake and chronic kidney disease: a review. Adv Chronic Kidney Dis. 2013;20(2):157-64. PMID:23439375. http://www.ncbi.nlm.nih.gov/pubmed/23439375 | Study Design |
| 112. | Kassis AN,Kubow S,Jones PJ. Sugar cane policosanols do not reduce LDL oxidation in hypercholesterolemic individuals. Lipids. 2009;44(5):391-6. PMID:19337769. http://www.ncbi.nlm.nih.gov/pubmed/19337769 | Independent Variable |
| 113. | Kavey RE. How sweet it is: sugar-sweetened beverage consumption, obesity, and cardiovascular risk in childhood. J Am Diet Assoc. 2010;110(10):1456-60. PMID:20869483. http://www.ncbi.nlm.nih.gov/pubmed/20869483 | Study Design |
| 114. | Kelishadi R,Mansourian M,Heidari-Beni M. Association of fructose consumption and components of metabolic syndrome in human studies: a systematic review and meta-analysis. Nutrition. 2014;30(5):503-10. PMID:24698343. http://www.ncbi.nlm.nih.gov/pubmed/24698343 | Study Design |
| 115. | Kell KP,Cardel MI,Bohan Brown MM,Fernandez JR. Added sugars in the diet are positively associated with diastolic blood pressure and triglycerides in children. Am J Clin Nutr. 2014;100(1):46-52. PMID:24717340. http://www.ncbi.nlm.nih.gov/pubmed/24717340 | Study Design |
| 116. | Keller AC. Added sugars and cardiovascular diseases. Eur Heart J. 2014;35(23):1500-1. PMID:25075405. http://www.ncbi.nlm.nih.gov/pubmed/25075405 | Study Design |
| 117. | Khalil MI,Sulaiman SA. The potential role of honey and its polyphenols in preventing heart diseases: a review. Afr J Tradit Complement Altern Med. 2010;7(4):315-21. PMID:21731163. http://www.ncbi.nlm.nih.gov/pubmed/21731163 | Study Design |
| 118. | Khosravi-Boroujeni H,Sarrafzadegan N,Mohammadifard N,Alikhasi H,Sajjadi F,Asgari S,Esmaillzadeh A. Consumption of sugar-sweetened beverages in relation to the metabolic syndrome among Iranian adults. Obes Facts. 2012;5(4):527-37. PMID:22854602. http://www.ncbi.nlm.nih.gov/pubmed/22854602 | Study Design |
| 119. | Kim YH,Abris GP,Sung MK,Lee JE. Consumption of sugar-sweetened beverages and blood pressure in the United States: the national health and nutrition examination survey 2003-2006. Clin Nutr Res. 2012;1(1):85-93. PMID:23430313. http://www.ncbi.nlm.nih.gov/pubmed/23430313 | Study Design |
| 120. | Knuth ND,Remias DB,Horowitz JF. Adding carbohydrate to a high-fat meal blunts postprandial lipemia in women and reduces meal-derived fatty acids in systemic circulation. Appl Physiol Nutr Metab. 2008;33(2):315-25. PMID:18347687. http://www.ncbi.nlm.nih.gov/pubmed/18347687 | Independent Variable |

## Excluded Articles: Added Sugars & Risk of Cardiovascular Disease

The table below lists the excluded articles with at least one reason for exclusion, but may not reflect all possible reasons.

| | Excluded Citations | Reason for Exclusion |
|---|---|---|
| 121. | Kosova EC,Auinger P,Bremer AA. The relationships between sugar-sweetened beverage intake and cardiometabolic markers in young children. J Acad Nutr Diet. 2013;113(2):219-27. PMID:23351625. http://www.ncbi.nlm.nih.gov/pubmed/23351625 | Study Design |
| 122. | Lagerpusch M,Enderle J,Eggeling B,Braun W,Johannsen M,Pape D,Muller MJ,Bosy-Westphal A. Carbohydrate quality and quantity affect glucose and lipid metabolism during weight regain in healthy men. J Nutr. 2013;143(10):1593-601. PMID:23946346. http://www.ncbi.nlm.nih.gov/pubmed/23946346 | Independent Variable |
| 123. | Le KA,Faeh D,Stettler R,Ith M,Kreis R,Vermathen P,Boesch C,Ravussin E,Tappy L. A 4-wk high-fructose diet alters lipid metabolism without affecting insulin sensitivity or ectopic lipids in healthy humans. Am J Clin Nutr. 2006;84(6):1374-9. PMID:17158419. http://www.ncbi.nlm.nih.gov/pubmed/17158419 | Independent Variable |
| 124. | Le KA,Tappy L. Fructose consumption, lipid matabolism and the metabolic syndrome. Current Nutrition and Food Science. 2006;2(3):221-229. PMID:#accession number#. http://www.embase.com/search/results?subaction=viewrecord&from=export&id=L44237220 http://dx.doi.org/10.2174/157340106778017823 | Study Design |
| 125. | Le MT,Frye RF,Rivard CJ,Cheng J,McFann KK,Segal MS,Johnson RJ,Johnson JA. Effects of high-fructose corn syrup and sucrose on the pharmacokinetics of fructose and acute metabolic and hemodynamic responses in healthy subjects. Metabolism. 2012;61(5):641-51. PMID:22152650. http://www.ncbi.nlm.nih.gov/pubmed/22152650 | Independent Variable |
| 126. | Lee AK,Binongo JN,Chowdhury R,Stein AD,Gazmararian JA,Vos MB,Welsh JA. 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. PMID:24572253. http://www.ncbi.nlm.nih.gov/pubmed/24572253 | Unhealthy Subjects |
| 127. | Liese AD,Gilliard T,Schulz M, Jr. D'Agostino RB,Wolever TM. Carbohydrate nutrition, glycaemic load, and plasma lipids: the Insulin Resistance Atherosclerosis Study. Eur Heart J. 2007;28(1):80-7. PMID:17132647. http://www.ncbi.nlm.nih.gov/pubmed/17132647 | Independent Variable |
| 128. | Lin WT,Huang HL,Huang MC,Chan TF,Ciou SY,Lee CY,Chiu YW,Duh TH,Lin PL,Wang TN,Liu TY,Lee CH. Effects on uric acid, body mass index and blood pressure in adolescents of consuming beverages sweetened with high-fructose corn syrup. Int J Obes (Lond). 2013;37(4):532-9. PMID:22890489. http://www.ncbi.nlm.nih.gov/pubmed/22890489 | Study Design |
| 129. | Liu S,Willett WC,Stampfer MJ,Hu FB,Franz M,Sampson L,Hennekens CH,Manson JE. A prospective study of dietary glycemic load, carbohydrate intake, and risk of coronary heart disease in US women. Am J Clin Nutr. 2000;71(6):1455-61. PMID:10837285. http://www.ncbi.nlm.nih.gov/pubmed/10837285 | Independent Variable |
| 130. | Livesey G,Taylor R. Fructose consumption and consequences for glycation, plasma triacylglycerol, and body weight: meta-analyses and meta-regression models of intervention studies. Am J Clin Nutr. 2008;88(5):1419-37. PMID:18996880. http://www.ncbi.nlm.nih.gov/pubmed/18996880 | Study Design |

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The table below lists the excluded articles with at least one reason for exclusion, but may not reflect all possible reasons.

| | Excluded Citations | Reason for Exclusion |
|---|---|---|
| 131. | Lopez-Molina R,Parra-Cabrera S,Lopez-Ridaura R,Gonzalez-Villalpando ME,Ferrannini E,Gonzalez-Villalpando C. Sweetened beverages intake, hyperuricemia and metabolic syndrome: the Mexico City Diabetes Study. Salud Publica Mex. 2013;55(6):557-63. PMID:24715008. http://www.ncbi.nlm.nih.gov/pubmed/24715008 | Study Design |
| 132. | Ma J,Sloan M,Fox CS,Hoffmann U,Smith CE,Saltzman E,Rogers GT,Jacques PF,McKeown NM. Sugar-sweetened beverage consumption is associated with abdominal fat partitioning in healthy adults. J Nutr. 2014;144(8):1283-90. PMID:24944282. http://www.ncbi.nlm.nih.gov/pubmed/24944282 | Study Design |
| 133. | Madero M,Perez-Pozo SE,Jalal D,Johnson RJ,Sanchez-Lozada LG. Dietary fructose and hypertension. Curr Hypertens Rep. 2011;13(1):29-35. PMID:20957458. http://www.ncbi.nlm.nih.gov/pubmed/20957458 | Study Design |
| 134. | Malhotra A. The dietary advice on added sugar needs emergency surgery. Bmj. 2013;346(#number#):f3199. PMID:23694809. http://www.ncbi.nlm.nih.gov/pubmed/23694809 | Study Design |
| 135. | Malik AH,Akram Y,Shetty S,Malik SS,Yanchou Njike V. Impact of sugar-sweetened beverages on blood pressure. Am J Cardiol. 2014;113(9):1574-80. PMID:24630785. http://www.ncbi.nlm.nih.gov/pubmed/24630785 | Study Design |
| 136. | Malik VS,Popkin BM,Bray GA,Despres JP,Hu FB. Sugar-sweetened beverages, obesity, type 2 diabetes mellitus, and cardiovascular disease risk. Circulation. 2010;121(11):1356-64. PMID:20308626. http://www.ncbi.nlm.nih.gov/pubmed/20308626 | Study Design |
| 137. | Malik VS,Popkin BM,Bray GA,Despres JP,Willett WC,Hu FB. Sugar-sweetened beverages and risk of metabolic syndrome and type 2 diabetes: a meta-analysis. Diabetes Care. 2010;33(11):2477-83. PMID:20693348. http://www.ncbi.nlm.nih.gov/pubmed/20693348 | Study Design |
| 138. | Mattei J,Malik V,Hu FB,Campos H. Substituting homemade fruit juice for sugar-sweetened beverages is associated with lower odds of metabolic syndrome among Hispanic adults. J Nutr. 2012;142(6):1081-7. PMID:22551801. http://www.ncbi.nlm.nih.gov/pubmed/22551801 | Study Design |
| 139. | McCarthy M. Higher sugar intake linked to raised risk of cardiovascular mortality, study finds. Bmj. 2014;348(#number#):g1352. PMID:24501228. http://www.ncbi.nlm.nih.gov/pubmed/24501228 | Study Design |
| 140. | Memon MQ,Kumar A. The fructose mystery: how bad or good is it?. Pak J Pharm Sci. 2013;26(6):1241-5. PMID:24191333. http://www.ncbi.nlm.nih.gov/pubmed/24191333 | Study Design |
| 141. | Merchant AT,Anand SS,Kelemen LE,Vuksan V,Jacobs R,Davis B,Teo K,Yusuf S. Carbohydrate intake and HDL in a multiethnic population. Am J Clin Nutr. 2007;85(1):225-30. PMID:17209200. http://www.ncbi.nlm.nih.gov/pubmed/17209200 | Study Design |
| 142. | Milei J,Otero Losada M,Gomez Llambi H,Grana DR,Suarez D,Azzato F,Ambrosio G. Chronic cola drinking induces metabolic and cardiac alterations in rats. World J Cardiol. 2011;3(4):111-6. PMID:21526048. http://www.ncbi.nlm.nih.gov/pubmed/21526048 | Unhealthy Subjects |
| 143. | Miller PE,McKinnon RA,Krebs-Smith SM,Subar AF,Chriqui J,Kahle L,Reedy J. Sugar-sweetened beverage consumption in the U.S.: novel assessment methodology. Am J Prev Med. 2013;45(4):416-21. PMID:24050417. http://www.ncbi.nlm.nih.gov/pubmed/24050417 | Study Design |

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The table below lists the excluded articles with at least one reason for exclusion, but may not reflect all possible reasons.

| | Excluded Citations | Reason for Exclusion |
|---|---|---|
| 144. | Mitka M. AHA: added sugar not so sweet. Jama. 2009;302(16):1741-2. PMID:19861662. http://www.ncbi.nlm.nih.gov/pubmed/19861662 | Study Design |
| 145. | Mucci L,Santilli F,Cuccurullo C,Davi G. Cardiovascular risk and dietary sugar intake: is the link so sweet?. Intern Emerg Med. 2012;7(4):313-22. PMID:21544534. http://www.ncbi.nlm.nih.gov/pubmed/21544534 | Study Design |
| 146. | Murphy MM,Barraj LM,Bi X,Stettler N. Body weight status and cardiovascular risk factors in adults by frequency of candy consumption. Nutr J. 2013;12(1):53. PMID:23631725. http://www.ncbi.nlm.nih.gov/pubmed/23631725 | Study Design |
| 147. | Na J,Musselman LP,Pendse J,Baranski TJ,Bodmer R,Ocorr K,Cagan R. A Drosophila model of high sugar diet-induced cardiomyopathy. PLoS Genet. 2013;9(1):e1003175. PMID:23326243. http://www.ncbi.nlm.nih.gov/pubmed/23326243 | Unhealthy Subjects |
| 148. | Nguyen S,Choi HK,Lustig RH,Hsu CY. Sugar-sweetened beverages, serum uric acid, and blood pressure in adolescents. J Pediatr. 2009;154(6):807-13. PMID:19375714. http://www.ncbi.nlm.nih.gov/pubmed/19375714 | Study Design |
| 149. | Nguyen S,Lustig RH. Just a spoonful of sugar helps the blood pressure go up. Expert Rev Cardiovasc Ther. 2010;8(11):1497-9. PMID:21090921. http://www.ncbi.nlm.nih.gov/pubmed/21090921 | Study Design |
| 150. | Nikkila EA,Kekki M. Effects of dietary fructose and sucrose on plasma triglyceride metabolism in patients with endogenous hypertriglyceridemia. Acta Medica Scandinavica Supplement. 1972;542(#number#):221-7. PMID:CN-00663715. http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/715/CN-00663715/frame.html | Publication Date |
| 151. | Niknam M,Saadatnia M,Shakeri F,Keshteli AH,Esmaillzadeh A. Consumption of sugar-sweetened beverages in relation to stroke: a case-control study. Int J Food Sci Nutr. 2013;64(1):1-6. PMID:22694119. http://www.ncbi.nlm.nih.gov/pubmed/22694119 | Study Design |
| 152. | Njike VY,Faridi Z,Shuval K,Dutta S,Kay CD,West SG,Kris-Etherton PM,Katz DL. Effects of sugar-sweetened and sugar-free cocoa on endothelial function in overweight adults. Int J Cardiol. 2011;149(1):83-8. PMID:20036019. http://www.ncbi.nlm.nih.gov/pubmed/20036019 | Independent Variable |
| 153. | Nseir W,Nassar F,Assy N. Soft drinks consumption and nonalcoholic fatty liver disease. World J Gastroenterol. 2010;16(21):2579-88. PMID:20518077. http://www.ncbi.nlm.nih.gov/pubmed/20518077 | Study Design |
| 154. | Ogbac F,Quimpo R,Hilado JE,Sy RA,Luz V,Tankeh-Torres S. A meta-analysis on sugar cane policosanol as treatment for hypercholesterolemia. Phillippine Journal of Internal Medicine. 2010;48(2):26-32. PMID:#accession number#. http://www.embase.com/search/results?subaction=viewrecord&from=export&id=L363007134 | Study Design |
| 155. | O'Neil CE, 3rd Fulgoni VL,Nicklas TA. Association of candy consumption with body weight measures, other health risk factors for cardiovascular disease, and diet quality in US children and adolescents: NHANES 1999-2004. Food Nutr Res. 2011;55(#number#):#pages#. PMID:21691462. http://www.ncbi.nlm.nih.gov/pubmed/21691462 | Study Design |
| 156. | O'Neil CE, 3rd Fulgoni VL,Nicklas TA. Candy consumption was not associated with body weight measures, risk factors for cardiovascular disease, or metabolic syndrome in US adults: NHANES 1999-2004. Nutr Res. | Study Design |

## Excluded Articles: Added Sugars & Risk of Cardiovascular Disease

The table below lists the excluded articles with at least one reason for exclusion, but may not reflect all possible reasons.

| | Excluded Citations | Reason for Exclusion |
|---|---|---|
| | 2011;31(2):122-30. PMID:21419316. http://www.ncbi.nlm.nih.gov/pubmed/21419316 | |
| 157. | Onyesom I. Honey-induced stimulation of blood ethanol elimination and its influence on serum triacylglycerol and blood pressure in man. Ann Nutr Metab. 2005;49(5):319-24. PMID:16088097. http://www.ncbi.nlm.nih.gov/pubmed/16088097 | Independent Variable |
| 158. | Ouyang X,Cirillo P,Sautin Y,McCall S,Bruchette JL,Diehl AM,Johnson RJ,Abdelmalek MF. Fructose consumption as a risk factor for non-alcoholic fatty liver disease. J Hepatol. 2008;48(6):993-9. PMID:18395287. http://www.ncbi.nlm.nih.gov/pubmed/18395287 | Study Design, Outcomes, Unhealthy Subjects |
| 159. | Overby NC,Margeirsdottir HD,Brunborg C,Dahl-Jorgensen K,Andersen LF. Sweets, snacking habits, and skipping meals in children and adolescents on intensive insulin treatment. Pediatr Diabetes. 2008;9(4 Pt 2):393-400. PMID:18774998. http://www.ncbi.nlm.nih.gov/pubmed/18774998 | Study Design, Unhealthy Subjects |
| 160. | Parks EJ,Skokan LE,Timlin MT,Dingfelder CS. Dietary sugars stimulate fatty acid synthesis in adults. J Nutr. 2008;138(6):1039-46. PMID:18492831. http://www.ncbi.nlm.nih.gov/pubmed/18492831 | Independent Variable |
| 161. | Preiser JC. NICE-SUGAR: the end of a sweet dream?. Crit Care. 2009;13(3):143. PMID:19490594. http://www.ncbi.nlm.nih.gov/pubmed/19490594 | Study Design |
| 162. | Quiles i Izquierdo J. [Consumption pattern and recommended intakes of sugar]. Nutr Hosp. 2013;28 Suppl 4(#number#):32-9. PMID:23834090. http://www.ncbi.nlm.nih.gov/pubmed/23834090 | Study Design |
| 163. | Quinn TJ,Dawson J,Walters MR. Sugar and stroke: cerebrovascular disease and blood glucose control. Cardiovasc Ther. 2011;29(6):e31-42. PMID:20491782. http://www.ncbi.nlm.nih.gov/pubmed/20491782 | Study Design |
| 164. | Qureshi S,Mink R. Aspiration of fruit gel snacks. Pediatrics. 2003;111(3):687-9. PMID:12612261. http://www.ncbi.nlm.nih.gov/pubmed/12612261 | Independent Variable |
| 165. | Raben A,Moller AC,Vasilaras TH,Astrup A. A randomized 10 week trial of sucrose vs artificial sweeteners on body weight and blood pressure after 10 weeks [abstract]. Obesity Research. 2001;9(#number#):86s. PMID:CN-00986187. http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/187/CN-00986187/frame.html | Study Design |
| 166. | Ragsdale FR,Gronli TD,Batool N,Haight N,Mehaffey A,McMahon EC,Nalli TW,Mannello CM,Sell CJ,McCann PJ,Kastello GM,Hooks T,Wilson T. Effect of Red Bull energy drink on cardiovascular and renal function. Amino Acids. 2010;38(4):1193-200. PMID:19653067. http://www.ncbi.nlm.nih.gov/pubmed/19653067 | Independent Variable |
| 167. | Rankin JW,Andreae MC,Oliver Chen CY,O'Keefe SF. Effect of raisin consumption on oxidative stress and inflammation in obesity. Diabetes Obes Metab. 2008;10(11):1086-96. PMID:18355330. http://www.ncbi.nlm.nih.gov/pubmed/18355330 | Independent Variable |
| 168. | Renwick AG,Molinary SV. Sweet-taste receptors, low-energy sweeteners, glucose absorption and insulin release. Br J Nutr. 2010;104(10):1415-20. PMID:20619074. http://www.ncbi.nlm.nih.gov/pubmed/20619074 | Study Design |
| 169. | Reyna NY,Cano C,Bermudez VJ,Medina MT,Souki AJ,Ambard M,Nunez M,Ferrer MA,Inglett GE. Sweeteners and beta-glucans improve metabolic and anthropometrics variables in well controlled type 2 diabetic patients. Am J Ther. 2003;10(6):438-43. PMID:14624282. http://www.ncbi.nlm.nih.gov/pubmed/14624282 | Independent Variable, Unhealthy Subjects |

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The table below lists the excluded articles with at least one reason for exclusion, but may not reflect all possible reasons.

| | Excluded Citations | Reason for Exclusion |
|---|---|---|
| 170. | Rezvani R,Cianflone K,McGahan JP,Berglund L,Bremer AA,Keim NL,Griffen SC,Havel PJ,Stanhope KL. Effects of sugar-sweetened beverages on plasma acylation stimulating protein, leptin and adiponectin: relationships with metabolic outcomes. Obesity (Silver Spring). 2013;21(12):2471-80. PMID:23512943. http://www.ncbi.nlm.nih.gov/pubmed/23512943 | Independent Variable |
| 171. | Richelsen B. Sugar-sweetened beverages and cardio-metabolic disease risks. Curr Opin Clin Nutr Metab Care. 2013;16(4):478-84. PMID:23624652. http://www.ncbi.nlm.nih.gov/pubmed/23624652 | Study Design |
| 172. | Ritze Y,Bardos G,D'Haese JG,Ernst B,Thurnheer M,Schultes B,Bischoff SC. Effect of high sugar intake on glucose transporter and weight regulating hormones in mice and humans. PLoS One. 2014;9(7):e101702. PMID:25010715. http://www.ncbi.nlm.nih.gov/pubmed/25010715 | Unhealthy Subjects |
| 173. | Ruff RR,Akhund A,Adjoian T,Kansagra SM. Calorie Intake, Sugar-Sweetened Beverage Consumption, and Obesity Among New York City Adults: Findings from a 2013 Population Study Using Dietary Recalls. J Community Health. 2014;#volume#(#number#):#pages#. PMID:24671367. http://www.ncbi.nlm.nih.gov/pubmed/24671367 | Study Design, Outcomes |
| 174. | Ruxton CH,Gardner EJ,McNulty HM. Is sugar consumption detrimental to health? A review of the evidence 1995-2006. Crit Rev Food Sci Nutr. 2010;50(1):1-19. PMID:20047137. http://www.ncbi.nlm.nih.gov/pubmed/20047137 | Study Design |
| 175. | Saab KR,Kendrick J,Yracheta JM,Lanaspa MA,Pollard M,Johnson RJ. New Insights on the Risk for Cardiovascular Disease in African Americans: The Role of Added Sugars. J Am Soc Nephrol. 2014;#volume#(#number#):#pages#. PMID:25090991. http://www.ncbi.nlm.nih.gov/pubmed/25090991 | Study Design |
| 176. | Saldana TM,Basso O,Darden R,Sandler DP. Carbonated beverages and chronic kidney disease. Epidemiology. 2007;18(4):501-6. PMID:17525693. http://www.ncbi.nlm.nih.gov/pubmed/17525693 | Study Design, Outcomes |
| 177. | Samman S,Sivarajah G,Man JC,Ahmad ZI,Petocz P,Caterson ID. A mixed fruit and vegetable concentrate increases plasma antioxidant vitamins and folate and lowers plasma homocysteine in men. J Nutr. 2003;133(7):2188-93. PMID:12840177. http://www.ncbi.nlm.nih.gov/pubmed/12840177 | Independent Variable |
| 178. | Seneff S,Wainwright G,Mascitelli L. Is the metabolic syndrome caused by a high fructose, and relatively low fat, low cholesterol diet?. Arch Med Sci. 2011;7(1):8-20. PMID:22291727. http://www.ncbi.nlm.nih.gov/pubmed/22291727 | Study Design |
| 179. | Shang XW,Liu AL,Zhang Q,Hu XQ,Du SM,Ma J,Xu GF,Li Y,Guo HW,Du L,Li TY,Ma GS. Report on childhood obesity in China (9): sugar-sweetened beverages consumption and obesity. Biomed Environ Sci. 2012;25(2):125-32. PMID:22998817. http://www.ncbi.nlm.nih.gov/pubmed/22998817 | Country |
| 180. | Shankar P,Ahuja S,Sriram K. Non-nutritive sweeteners: review and update. Nutrition. 2013;29(11-12):1293-9. PMID:23845273. http://www.ncbi.nlm.nih.gov/pubmed/23845273 | Study Design |
| 181. | Sharma S,Roberts LS,Lustig RH,Fleming SE. Carbohydrate intake and cardiometabolic risk factors in high BMI African American children. Nutr Metab (Lond). 2010;7(1):10. PMID:20181134. | Study Design |

## Excluded Articles: Added Sugars & Risk of Cardiovascular Disease

The table below lists the excluded articles with at least one reason for exclusion, but may not reflect all possible reasons.

| | Excluded Citations | Reason for Exclusion |
|---|---|---|
| | http://www.ncbi.nlm.nih.gov/pubmed/20181134 | |
| 182. | Shay CM,Stamler J,Dyer AR,Brown IJ,Chan Q,Elliott P,Zhao L,Okuda N,Miura K,Daviglus ML,Van Horn L. Nutrient and food intakes of middle-aged adults at low risk of cardiovascular disease: the international study of macro-/micronutrients and blood pressure (INTERMAP). Eur J Nutr. 2012;51(8):917-26. PMID:22057680. http://www.ncbi.nlm.nih.gov/pubmed/22057680 | Study Design, Independent Variable |
| 183. | Shin A,Lim SY,Sung J,Shin HR,Kim J. Dietary intake, eating habits, and metabolic syndrome in Korean men. J Am Diet Assoc. 2009;109(4):633-40. PMID:19328258. http://www.ncbi.nlm.nih.gov/pubmed/19328258 | Study Design |
| 184. | Shoham DA,Durazo-Arvizu R,Kramer H,Luke A,Vupputuri S,Kshirsagar A,Cooper RS. Sugary soda consumption and albuminuria: results from the National Health and Nutrition Examination Survey, 1999-2004. PLoS One. 2008;3(10):e3431. PMID:18927611. http://www.ncbi.nlm.nih.gov/pubmed/18927611 | Study Design |
| 185. | Siervo M,Montagnese C,Mathers JC,Soroka KR,Stephan BC,Wells JC. Sugar consumption and global prevalence of obesity and hypertension: an ecological analysis. Public Health Nutr. 2014;17(3):587-96. PMID:23414749. http://www.ncbi.nlm.nih.gov/pubmed/23414749 | Study Design |
| 186. | Sievenpiper JL,de Souza RJ,Cozma AI,Chiavaroli L,Ha V,Mirrahimi A. Fructose vs. glucose and metabolism: do the metabolic differences matter?. Curr Opin Lipidol. 2014;25(1):8-19. PMID:24370846. http://www.ncbi.nlm.nih.gov/pubmed/24370846 | Study Design |
| 187. | Sievenpiper JL,de Souza RJ. Are sugar-sweetened beverages the whole story?. Am J Clin Nutr. 2013;98(2):261-3. PMID:23803892. http://www.ncbi.nlm.nih.gov/pubmed/23803892 | Study Design |
| 188. | Sievenpiper JL. Fructose: where does the truth lie?. J Am Coll Nutr. 2012;31(3):149-51. PMID:23204150. http://www.ncbi.nlm.nih.gov/pubmed/23204150 | Study Design |
| 189. | Skoczynska A,Jedrychowska I,Poreba R,Affelska-Jercha A,Turczyn B,Wojakowska A,Andrzejak R. Influence of chokeberry juice on arterial blood pressure and lipid parameters in men with mild hypercholesterolemia. Pharmacological Reports. 2007;59(SUPPL. 1):177-182. PMID:#accession number#. http://www.embase.com/search/results?subaction=viewrecord&from=export&id=L351067961 | Independent Variable |
| 190. | Soleimani M. Dietary fructose, salt absorption and hypertension in metabolic syndrome: towards a new paradigm. Acta Physiol (Oxf). 2011;201(1):55-62. PMID:21143427. http://www.ncbi.nlm.nih.gov/pubmed/21143427 | Study Design |
| 191. | Sonestedt E,Overby NC,Laaksonen DE,Birgisdottir BE. Does high sugar consumption exacerbate cardiometabolic risk factors and increase the risk of type 2 diabetes and cardiovascular disease?. Food Nutr Res. 2012;56(#number#):#pages#. PMID:22855643. http://www.ncbi.nlm.nih.gov/pubmed/22855643 | Study Design |
| 192. | Sonestedt E,Wirfalt E,Wallstrom P,Gullberg B,Drake I,Hlebowicz J,Nordin Fredrikson G,Hedblad B,Nilsson J,Krauss RM,Orho-Melander M. High disaccharide intake associates with atherogenic lipoprotein profile. Br J Nutr. 2012;107(7):1062-9. PMID:22011476. http://www.ncbi.nlm.nih.gov/pubmed/22011476 | Study Design |
| 193. | Sonestedt E. Artificial and sugar-sweetened beverages are associated with increased incidence of | Study Design |

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The table below lists the excluded articles with at least one reason for exclusion, but may not reflect all possible reasons.

| | Excluded Citations | Reason for Exclusion |
|---|---|---|
| | hypertension. Evid Based Med. 2013;18(4):e38. PMID:23213115. http://www.ncbi.nlm.nih.gov/pubmed/23213115 | |
| 194. | Song S,Lee JE,Song WO,Paik HY,Song Y. Carbohydrate intake and refined-grain consumption are associated with metabolic syndrome in the Korean adult population. J Acad Nutr Diet. 2014;114(1):54-62. PMID:24200655. http://www.ncbi.nlm.nih.gov/pubmed/24200655 | Study Design |
| 195. | Sorensen LB,Raben A,Stender S,Astrup A. Effect of sucrose on inflammatory markers in overweight humans. Am J Clin Nutr. 2005;82(2):421-7. PMID:16087988. http://www.ncbi.nlm.nih.gov/pubmed/16087988 | Outcomes |
| 196. | Stanhope KL,Bremer AA,Medici V,Nakajima K,Ito Y,Nakano T,Chen G,Fong TH,Lee V,Menorca RI,Keim NL,Havel PJ. Consumption of fructose and high fructose corn syrup increase postprandial triglycerides, LDL-cholesterol, and apolipoprotein-B in young men and women. J Clin Endocrinol Metab. 2011;96(10):E1596-605. PMID:21849529. http://www.ncbi.nlm.nih.gov/pubmed/21849529 | Independent Variable |
| 197. | Stanhope KL,Griffen SC,Bair BR,Swarbrick MM,Keim NL,Havel PJ. Twenty-four-hour endocrine and metabolic profiles following consumption of high-fructose corn syrup-, sucrose-, fructose-, and glucose-sweetened beverages with meals. Am J Clin Nutr. 2008;87(5):1194-203. PMID:18469239. http://www.ncbi.nlm.nih.gov/pubmed/18469239 | Independent Variable |
| 198. | Stanhope KL,Havel PJ. Fructose consumption: considerations for future research on its effects on adipose distribution, lipid metabolism, and insulin sensitivity in humans. J Nutr. 2009;139(6):1236s-1241s. PMID:19403712. http://www.ncbi.nlm.nih.gov/pubmed/19403712 | Study Design |
| 199. | Stanhope KL,Havel PJ. Fructose consumption: potential mechanisms for its effects to increase visceral adiposity and induce dyslipidemia and insulin resistance. Curr Opin Lipidol. 2008;19(1):16-24. PMID:18196982. http://www.ncbi.nlm.nih.gov/pubmed/18196982 | Study Design |
| 200. | Stanhope KL,Havel PJ. Fructose consumption: recent results and their potential implications. Ann N Y Acad Sci. 2010;1190(#number#):15-24. PMID:20388133. http://www.ncbi.nlm.nih.gov/pubmed/20388133 | Study Design |
| 201. | Stanhope KL,Schwarz JM,Havel PJ. Adverse metabolic effects of dietary fructose: results from the recent epidemiological, clinical, and mechanistic studies. Curr Opin Lipidol. 2013;24(3):198-206. PMID:23594708. http://www.ncbi.nlm.nih.gov/pubmed/23594708 | Study Design |
| 202. | Stanhope KL,Schwarz JM,Keim NL,Griffen SC,Bremer AA,Graham JL,Hatcher B,Cox CL,Dyachenko A,Zhang W,McGahan JP,Seibert A,Krauss RM,Chiu S,Schaefer EJ,Ai M,Otokozawa S,Nakajima K,Nakano T,Beysen C,Hellerstein MK,Berglund L,Havel PJ. Consuming fructose-sweetened, not glucose-sweetened, beverages increases visceral adiposity and lipids and decreases insulin sensitivity in overweight/obese humans. J Clin Invest. 2009;119(5):1322-34. PMID:19381015. http://www.ncbi.nlm.nih.gov/pubmed/19381015 | Independent Variable |
| 203. | Stolarz-Skrzypek K. Sugar and salt in the pathogenesis of elevated blood pressure. Hypertension. 2011;57(4):676-8. PMID:21357281. http://www.ncbi.nlm.nih.gov/pubmed/21357281 | Study Design |
| 204. | Subasini U,Thenmozhi S,Sathyamurthy D,Rajamanickam GV. Attenuation of fructose induced hyperlipidemia of | Study Design, |

## Excluded Articles: Added Sugars & Risk of Cardiovascular Disease

The table below lists the excluded articles with at least one reason for exclusion, but may not reflect all possible reasons.

| | Excluded Citations | Reason for Exclusion |
|---|---|---|
| | enicostemma axillare. International Journal of Pharmaceutical and Phytopharmacological Research. 2012;1(5):306-312. PMID:#accession number#. http://www.embase.com/search/results?subaction=viewrecord&from=export&id=L368610070 | Independent Variable |
| 205. | Sun SZ,Anderson GH,Flickinger BD,Williamson-Hughes PS,Empie MW. Fructose and non-fructose sugar intakes in the US population and their associations with indicators of metabolic syndrome. Food Chem Toxicol. 2011;49(11):2875-82. PMID:21889564. http://www.ncbi.nlm.nih.gov/pubmed/21889564 | Study Design |
| 206. | Sundborn G,Thornley S,Te Morenga L,Merriman T. FIZZ Sugary Drink Free Pacific by 2030--Symposium Declaration. N Z Med J. 2014;127(1392):98-101. PMID:24806253. http://www.ncbi.nlm.nih.gov/pubmed/24806253 | Study Design |
| 207. | Sunehag AL,Toffolo G,Campioni M,Bier DM,Haymond MW. Short-term high dietary fructose intake had no effects on insulin sensitivity and secretion or glucose and lipid metabolism in healthy, obese adolescents. J Pediatr Endocrinol Metab. 2008;21(3):225-35. PMID:18540249. http://www.ncbi.nlm.nih.gov/pubmed/18540249 | Unhealthy Subjects |
| 208. | Swarbrick MM,Stanhope KL,Elliott SS,Graham JL,Krauss RM,Christiansen MP,Griffen SC,Keim NL,Havel PJ. Consumption of fructose-sweetened beverages for 10 weeks increases postprandial triacylglycerol and apolipoprotein-B concentrations in overweight and obese women. Br J Nutr. 2008;100(5):947-52. PMID:18384705. http://www.ncbi.nlm.nih.gov/pubmed/18384705 | Independent Variable |
| 209. | Swithers SE,Martin AA,Davidson TL. High-intensity sweeteners and energy balance. Physiol Behav. 2010;100(1):55-62. PMID:20060008. http://www.ncbi.nlm.nih.gov/pubmed/20060008 | Study Design |
| 210. | Tappy L,Le KA,Tran C,Paquot N. Fructose and metabolic diseases: new findings, new questions. Nutrition. 2010;26(11-12):1044-9. PMID:20471804. http://www.ncbi.nlm.nih.gov/pubmed/20471804 | Study Design |
| 211. | Tappy L,Le KA. Does fructose consumption contribute to non-alcoholic fatty liver disease?. Clin Res Hepatol Gastroenterol. 2012;36(6):554-60. PMID:22795319. http://www.ncbi.nlm.nih.gov/pubmed/22795319 | Study Design |
| 212. | Tappy L,Le KA. Metabolic effects of fructose and the worldwide increase in obesity. Physiol Rev. 2010;90(1):23-46. PMID:20086073. http://www.ncbi.nlm.nih.gov/pubmed/20086073 | Study Design |
| 213. | Tate DF,Turner-McGrievy G,Lyons E,Stevens J,Erickson K,Polzien K,Diamond M,Wang X,Popkin B. Replacing caloric beverages with water or diet beverages for weight loss in adults: main results of the Choose Healthy Options Consciously Everyday (CHOICE) randomized clinical trial. Am J Clin Nutr. 2012;95(3):555-63. PMID:22301929. http://www.ncbi.nlm.nih.gov/pubmed/22301929 | Independent Variable, Outcomes |
| 214. | Tavani A,Bosetti C,Negri E,Augustin LS,Jenkins DJ,La Vecchia C. Carbohydrates, dietary glycaemic load and glycaemic index, and risk of acute myocardial infarction. Heart. 2003;89(7):722-6. PMID:12807839. http://www.ncbi.nlm.nih.gov/pubmed/12807839 | Study Design |
| 215. | Te Morenga LA,Howatson AJ,Jones RM,Mann J. Dietary sugars and cardiometabolic risk: systematic review and meta-analyses of randomized controlled trials of the effects on blood pressure and lipids. Am J Clin Nutr. 2014;100(1):65-79. PMID:24808490. http://www.ncbi.nlm.nih.gov/pubmed/24808490 | Study Design |

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The table below lists the excluded articles with at least one reason for exclusion, but may not reflect all possible reasons.

| | Excluded Citations | Reason for Exclusion |
|---|---|---|
| 216. | Teff KL,Elliott SS,Tschop M,Kieffer TJ,Rader D,Heiman M,Townsend RR,Keim NL,D'Alessio D,Havel PJ. Dietary fructose reduces circulating insulin and leptin, attenuates postprandial suppression of ghrelin, and increases triglycerides in women. J Clin Endocrinol Metab. 2004;89(6):2963-72. PMID:15181085. http://www.ncbi.nlm.nih.gov/pubmed/15181085 | Independent Variable |
| 217. | Trout DL,Hallfrisch J,Behall KM. Atypically high insulin responses to some foods relate to sugars and satiety. Int J Food Sci Nutr. 2004;55(7):577-88. PMID:16019302. http://www.ncbi.nlm.nih.gov/pubmed/16019302 | Study Design |
| 218. | Van Rompay MI,McKeown NM,Castaneda-Sceppa C,Ordovas JM,Tucker KL. Carbohydrate nutrition differs by diabetes status and is associated with dyslipidemia in Boston Puerto Rican adults without diabetes. J Nutr. 2013;143(2):182-8. PMID:23269655. http://www.ncbi.nlm.nih.gov/pubmed/23269655 | Study Design |
| 219. | Vanis L,Hausken T,Gentilcore D,Rigda RS,Rayner CK,Feinle-Bisset C,Horowitz M,Jones KL. Comparative effects of glucose and xylose on blood pressure, gastric emptying and incretin hormones in healthy older subjects. Br J Nutr. 2011;105(11):1644-51. PMID:21294929. http://www.ncbi.nlm.nih.gov/pubmed/21294929 | Outcomes |
| 220. | Visvanathan R,Chen R,Garcia M,Horowitz M,Chapman I. The effects of drinks made from simple sugars on blood pressure in healthy older people. Br J Nutr. 2005;93(5):575-9. PMID:15975155. http://www.ncbi.nlm.nih.gov/pubmed/15975155 | Independent Variable |
| 221. | Visvanathan R,Chen R,Horowitz M,Chapman I. Blood pressure responses in healthy older people to 50 g carbohydrate drinks with differing glycaemic effects. Br J Nutr. 2004;92(2):335-40. PMID:15333165. http://www.ncbi.nlm.nih.gov/pubmed/15333165 | Independent Variable |
| 222. | 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. Am J Clin Nutr. 2014;99(6):1479-1486. PMID:24740206. http://www.ncbi.nlm.nih.gov/pubmed/24740206 | Country |
| 223. | Vos MB,Kimmons JE,Gillespie C,Welsh J,Blanck HM. Dietary fructose consumption among US children and adults: the Third National Health and Nutrition Examination Survey. Medscape J Med. 2008;10(7):160. PMID:18769702. http://www.ncbi.nlm.nih.gov/pubmed/18769702 | Study Design, Outcomes |
| 224. | Wang J. Consumption of added sugars and development of metabolic syndrome components among a sample of youth at risk of obesity. Appl Physiol Nutr Metab. 2014;39(4):512. PMID:24669994. http://www.ncbi.nlm.nih.gov/pubmed/24669994 | Study Design |
| 225. | Weed DL,Althuis MD,Mink PJ. Quality of reviews on sugar-sweetened beverages and health outcomes: a systematic review. Am J Clin Nutr. 2011;94(5):1340-7. PMID:21918218. http://www.ncbi.nlm.nih.gov/pubmed/21918218 | Study Design |
| 226. | Weeratunga P,Jayasinghe S,Perera Y,Jayasena G,Jayasinghe S. Per capita sugar consumption and prevalence of diabetes mellitus--global and regional associations. BMC Public Health. 2014;14(#number#):186. PMID:24555673. http://www.ncbi.nlm.nih.gov/pubmed/24555673 | Study Design |
| 227. | Welsh JA,Lundeen EA,Stein AD. The sugar-sweetened beverage wars: public health and the role of the | Study Design |

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The table below lists the excluded articles with at least one reason for exclusion, but may not reflect all possible reasons.

| Excluded Citations | | Reason for Exclusion |
|---|---|---|
| | beverage industry. Curr Opin Endocrinol Diabetes Obes. 2013;20(5):401-6. PMID:23974767. http://www.ncbi.nlm.nih.gov/pubmed/23974767 | |
| 228. | Welsh JA,Sharma A,Abramson JL,Vaccarino V,Gillespie C,Vos MB. Caloric sweetener consumption and dyslipidemia among US adults. Jama. 2010;303(15):1490-7. PMID:20407058. http://www.ncbi.nlm.nih.gov/pubmed/20407058 | Study Design |
| 229. | Welsh JA,Sharma A,Cunningham SA,Vos MB. Consumption of added sugars and indicators of cardiovascular disease risk among US adolescents. Circulation. 2011;123(3):249-57. PMID:21220734. http://www.ncbi.nlm.nih.gov/pubmed/21220734 | Study Design |
| 230. | White JS. No unique role for fructose sweeteners in obesity or cardiorenal disease. Am J Clin Nutr. 2008;87(4):1062-3; author reply 1063-6. PMID:18400732. http://www.ncbi.nlm.nih.gov/pubmed/18400732 | Study Design |
| 231. | White JS. Sugar-sweetened beverage effect on cardiovascular risk factors lacks significance. J Pediatr. 2010;156(5):860-1; author reply 861-2. PMID:20227715. http://www.ncbi.nlm.nih.gov/pubmed/20227715 | Study Design |
| 232. | White JS. Challenging the fructose hypothesis: new perspectives on fructose consumption and metabolism. Adv Nutr. 2013;4(2):246-56. PMID:23493541. http://www.ncbi.nlm.nih.gov/pubmed/23493541 | Study Design |
| 233. | Wiebe N,Padwal R,Field C,Marks S,Jacobs R,Tonelli M. A systematic review on the effect of sweeteners on glycemic response and clinically relevant outcomes. BMC Med. 2011;9(#number#):123. PMID:22093544. http://www.ncbi.nlm.nih.gov/pubmed/22093544 | Study Design |
| 234. | Wiernsperger N,Geloen A,Rapin JR. Fructose and cardiometabolic disorders: the controversy will, and must, continue. Clinics (Sao Paulo). 2010;65(7):729-38. PMID:20668632. http://www.ncbi.nlm.nih.gov/pubmed/20668632 | Study Design |
| 235. | Xi B,Li S,Liu Z,Tian H,Yin X,Huai P,Tang W,Zhou D,Steffen LM. Intake of fruit juice and incidence of type 2 diabetes: a systematic review and meta-analysis. PLoS One. 2014;9(3):e93471. PMID:24682091. http://www.ncbi.nlm.nih.gov/pubmed/24682091 | Study Design |
| 236. | Xu P. Fructose 1,6-diphosphate for stroke and brainn injury. Clinical Medical Journal of China. Zhongguo Linchuang Yixue.. 2001;3(#number#):282. PMID:CN-00783316. http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/316/CN-00783316/frame.html | Study Design, Unhealthy Subjects |
| 237. | Yaghoobi N,Al-Waili N,Ghayour-Mobarhan M,Parizadeh SM,Abasalti Z,Yaghoobi Z,Yaghoobi F,Esmaeili H,Kazemi-Bajestani SM,Aghasizadeh R,Saloom KY,Ferns GA. Natural honey and cardiovascular risk factors; effects on blood glucose, cholesterol, triacylglycerole, CRP, and body weight compared with sucrose. ScientificWorldJournal. 2008;8(#number#):463-9. PMID:18454257. http://www.ncbi.nlm.nih.gov/pubmed/18454257 | Independent Variable |
| 238. | Yamada M,Murakami K,Sasaki S,Takahashi Y,Okubo H. Soft drink intake is associated with diet quality even among young Japanese women with low soft drink intake. J Am Diet Assoc. 2008;108(12):1997-2004. PMID:19027402. http://www.ncbi.nlm.nih.gov/pubmed/19027402 | Study Design |

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The table below lists the excluded articles with at least one reason for exclusion, but may not reflect all possible reasons.

| | Excluded Citations | Reason for Exclusion |
|---|---|---|
| 239. | Yang ZH,Miyahara H,Takeo J,Katayama M. Diet high in fat and sucrose induces rapid onset of obesity-related metabolic syndrome partly through rapid response of genes involved in lipogenesis, insulin signalling and inflammation in mice. Diabetol Metab Syndr. 2012;4(1):32. PMID:22762794. http://www.ncbi.nlm.nih.gov/pubmed/22762794 | Unhealthy Subjects |
| 240. | Zhang YH,An T,Zhang RC,Zhou Q,Huang Y,Zhang J. Very high fructose intake increases serum LDL-cholesterol and total cholesterol: a meta-analysis of controlled feeding trials. J Nutr. 2013;143(9):1391-8. PMID:23825185. http://www.ncbi.nlm.nih.gov/pubmed/23825185 | Study Design |