Appendix E.2.45: Evidence Portfolio

Part D. Chapter 6: Cross-Cutting Topics of Public Health Importance

What is the relationship between the intake of added sugars and the risk of type 2 diabetes?

Conclusion Statement: Strong evidence shows that higher consumption of added sugars, especially sugar-sweetened beverages, increases the risk of type 2 diabetes among adults and this relationship is not fully explained by body weight.

DGAC Grade: Strong

Review of Evidence

Evidence for this question and conclusion came from five SRs and MA published between January 2010 and August 2014.\textsuperscript{1-5} Four of the reviews focused on sugar-sweetened beverages\textsuperscript{1-3,5} and one review examined sugar intake.\textsuperscript{4} Combined, a total of 17 articles were considered in these reviews, of which nine were included in two or more reviews. Increased consumption of sugar-sweetened beverages was consistently associated with increased risk of type 2 diabetes. Pooled estimated relative risks ranged from 1.20 to 1.28, and included 1.20 (95\% CI = 1.12 to 1.29)/330 ml/day of sugar-sweetened soft drinks;\textsuperscript{1} 1.26 (95\% CI = 1.12 to 1.41) for sugar-sweetened beverages,\textsuperscript{3} and 1.28 (95\% CI = 1.04 to 1.59) for sugar-sweetened fruit juices.\textsuperscript{5} Comparably, a hazard ratio of 1.29 (1.02, 1.63) was identified for sugar-sweetened beverages.\textsuperscript{2} These consistently positive associations between sugar-sweetened beverages and type 2 diabetes were attenuated, but still existed, after adjustment for BMI, suggesting that body weight only partly explains the deleterious effects of sugar-sweetened beverages on type 2 diabetes. Although the studies were highly heterogeneous, findings from the MA by Malik et al. tentatively showed that consumption of more than one 12-ounce serving per day of sugar-sweetened beverage increased the risk of developing type 2 diabetes by 26 percent, compared to consuming less than one serving per month. Insufficient high-quality data are available to determine a dose-response line or curve between sugar-sweetened beverage consumption and type 2 diabetes risk.

The issue of generalizability, whether the participants included in this body of evidence are representative of the general U.S. population, was not specifically addressed in the literature reviewed, but the large sample sizes of the pooled data (several hundred thousand subjects from different populations) are noteworthy.
Table 1. Summary of existing reports, systematic reviews, and meta-analyses examining the relationship between the intake of added sugars and risk of type 2 diabetes?

| Author, Year Publication Type | Added Sugars Definition | Date Range Searched | Included Studies** (Number and Design) | Recommendations, Evidence/Conclusion Statements, and/or Main Results from Existing Report/ SR/ MA |
|-------------------------------|-------------------------|---------------------|----------------------------------------|-------------------------------------------------------------------------------------------------
| Greenwood, 2014               | Sugar-sweetened beverages (carbonated, sugar-sweetened colas and soft drinks, total fruit punch, non-diet soda, full-energy sweetened soft drinks) | 1990 to Nov 2009, with an update in June 2013 PCSs; English language; original research article; at least 3 yr duration; differentiated between sugar and artificially sweetened beverages; participants from a generally healthy population | 11 publications from 9 cohorts (5 publications from 6 cohorts used in meta-analysis of SSBs) | Conclusion: The included studies were observational, so their results should be interpreted cautiously, but findings indicate a positive association between sugar-sweetened soft drink intake and T2D risk, attenuated by adjustment for BMI. **Main Results:** The summary relative risk for sugar-sweetened soft drinks was 1.20/330 ml per d. The association with sugar-sweetened soft drinks was slightly lower in studies adjusting for BMI, consistent with BMI being involved in the causal pathway. |
| Romaguera, 2013 (Note: Included in Greenwood, 2014) | Sweet beverages (juices [either from 100% fruit and vegetables or concentrates], nectars [juices with up to 20% added sugar], and total soft drinks [sugar-sweetened and artificially sweetened]) | N/A | Eight cohorts of the EPIC study | Conclusion: This study corroborates the association between increased incidence of T2D and high consumption of sugar-sweetened soft drinks in European adults. **Main Results:** In adjusted models, one 336 g (12 oz) daily increment in sugar-sweetened soft drink consumption was associated with HR for T2D of 1.22 (95% CI: 1.09 to 1.38). After further adjustment for energy intake and BMI, the association of sugar-sweetened soft drinks with T2D persisted (HR 1.18, 95% CI: 1.06 to 1.32). Juice and nectar consumption was not associated with T2D incidence. |
| Malik, 2010                  | Sugar-sweetened beverages (soft drinks, carbonated soft drinks, fruitades, fruit drinks, sports drinks, energy and vitamin water drinks, sweetened iced tea, punch, cordials, | 1966 to May 2010 PCSs; English language; presentation of relative risk and associated measure of variance; definition and metric for SSB intake; adults | 8 PCSs | Conclusion: Higher consumption of SSBs is associated with development of T2D. **Main Results:** Individuals in the highest quantile of SSB intake (most often 1–2, 12-oz servings/day) had a 26% greater risk of developing T2D than those in the lowest quantile (none or <1 serving/month) (RR=1.26). |
### Sonestedt, 2012

**Systematic Review**

**AMSTAR:** 9/11

<table>
<thead>
<tr>
<th>Sugar intake (intrinsic, added, and total sugar intake from sugar-sweetened beverages, sugars, sucrose, and fructose)</th>
<th>2000 to 2010, with update through Dec 2011</th>
<th>9 PCSs (4 on total sugars, sucrose, or fructose and 6 reported on SSBs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incidence of T2D (also searched for impaired glucose tolerance and insulin sensitivity)</td>
<td>PCSs with 4 or more yrs of follow-up; RCTs with at least 4 wks duration, drop-out rate &lt;50%, and replacement of sugars with corresponding amount of CHO; English or Nordic language; generally healthy populations</td>
<td>Conclusion: Data from PCSs suggest that SSBs probably increase the risk of T2D. The results were limited or inconsistent on the adverse effect of intake of total sugars, glucose, or fructose on the incidence of T2D.</td>
</tr>
</tbody>
</table>

**Main Results:**
The results from the 4 studies on the association between intake of total sugars, sucrose, or fructose and T2D were inconclusive, with studies showing positive, negative, and no association. The 6 studies reporting on SSBs were more conclusive, with 4 reporting a positive association, and a fifth reporting a positive association in the model not adjusting for BMI.

### Xi, 2014

**Systematic Review and Meta-Analysis**

**AMSTAR:** 10/11

<table>
<thead>
<tr>
<th>Sugar-sweetened fruit juice and 100% fruit juice</th>
<th>Up to Dec 2013 PCSs; English language; reported covariate adjusted RRs or HRs with 95% CIs for highest vs. lowest category of fruit juice intake; for multiple articles from same cohort, selected only the study with the largest sample size</th>
<th>Conclusion: The findings support dietary recommendations to limit SSBs, such as fruit juice with added sugar, to prevent the development of T2D.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incidence of T2D</td>
<td>4 PCSs examined sugar-sweetened fruit juice and 4 PCSs examined 100% fruit juice</td>
<td>Main Results: A higher intake of sugar-sweetened fruit juice was significantly associated with risk of T2D (RR = 1.28), while intake of 100% fruit juice was not associated with risk of developing T2D (RR = 1.03).</td>
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</tbody>
</table>

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* A measurement tool for the ‘assessment of multiple systematic reviews’ (AMSTAR)

**Reference overlap: Of the 17 articles included in total across the reviews, 9 were included in two or more reviews.**

### References Included in Review


Supplementary Information:

Analytical Framework

Target Population
Children and adults (2y+), healthy and at risk for chronic disease

Intervention/exposure
Added sugars (Including studies on sugar-sweetened beverages)
Comparator
Different levels of intake of added sugars

Cardiovascular Disease
Approach for answering question: Existing Reports/Reviews

Body Weight/Obesity
Approach for answering question: Existing Reports/Reviews

Type 2 Diabetes
Approach for answering question: Existing Reports/Reviews

Dental Caries
Approach for answering question: Existing Reports/Reviews

Question:
What is the relationship between the intake of added sugars and cardiovascular disease, body weight/obesity, type 2 diabetes, and dental caries?

Methodology

The Committee relied on existing SRs/MA published since January 2010 to address the intake of added sugars and risk of type 2 diabetes.

Search Strategy for Existing Systematic Reviews/Meta-Analyses

PubMed:

AND

Embase:

(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 '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*)):ti,ab OR concentrate OR sweets:ti,ab OR caramel:ti,ab OR (malt* NEAR/1 barley) OR ('syrup'/exp OR syrup*:ti,ab) OR sugar: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

('food'/exp OR 'beverage'/exp OR diet/exp OR 'dietetics'/exp OR nutrition/exp OR cane OR rice OR sorghum OR malt OR golden OR 'food additive'/exp)
AND
("insulin":ti OR inflammtation:ti,ab OR (glucose NEXT/1 intoleran*):ti,ab OR diabetes:ti,ab OR "hemoglobin A1c":ti,ab OR (“impaired fasting” AND (glucose OR glycemi*)) OR “onset diabetes” OR “impaired glucose” OR ‘insulin resistance’/exp OR (insulin NEXT/1 resistan*):ti,ab OR 'glucose intolerance'/exp OR ‘non insulin dependent diabetes mellitus'/exp OR 'glycosylated hemoglobin'/exp OR 'impaired glucose tolerance'/exp OR ‘maturity onset diabetes mellitus'/exp) 'systematic review'/exp OR ‘meta analysis'/exp

Cochrane:

“insulin resistance”:ti,ab OR “insulin":ti OR inflammation:ti OR (glucose NEXT/1 intoleran*):ti,ab OR diabetes:ti,ab OR "Hemoglobin A":ti AND Glycosylated:ti OR "hemoglobin A1c ":ti OR (“impaired fasting”:ti AND (glucose:ti OR glycemi*:ti)) OR “onset diabetes”:ti OR “impaired glucose”:ti

(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
Appendix E-2.45: Added Sugars and Type 2 Diabetes Evidence Portfolio

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*:ti,ab 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,ab OR (dietary NEXT sugar*):ti,ab OR sugar:ti OR (sugar NEAR/3 sweet*):ti,ab OR sugar:ti OR (sugar NEAR/3 coat*):ti,ab OR (dietary NEAR/1 sugar*):ti,ab OR confectioner*:ti,ab OR (fizzy NEXT/1 drink*):ti,ab OR chewing gum*:ti,ab ("body weight" OR obesity:ti,kw,ab OR overweight:ti,kw,ab OR "body fat":ti,kw,ab OR adipose*:ti,kw,ab OR weight:ti,kw,ab OR waist:ti,kw,ab OR "body mass":ti,kw,ab OR bmi:ti,kw,ab OR "Metabolic syndrome":ti,kw,ab)

Navigator:

((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:pastry OR (ice NEAR/1 cream*) 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*)

Inclusion Criteria

Date Range:
• Published between December 2011 and August 2014 (in English in a peer-reviewed journal)

Study Design:
• Systematic review and/or meta-analysis that included randomized controlled trials and/or prospective cohort studies

Study Subjects:
• Reviews that included studies from high or very high human development (2012 Human Development Index)
• Healthy or at elevated chronic disease risk

Intervention/Exposure:
• Added sugars, including sugar-sweetened beverages
• Added sugars are sugars that are either added during the processing of foods, or are packaged as such, and include sugars (free, mono- 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.28

Outcome:
• Glucose intolerance, insulin resistance, or incidence of type 2 diabetes

Quality:
• Reviews rated 8-11 on AMSTAR (A measurement tool for the ‘assessment of multiple systematic reviews’)

Search Results

Excluded Articles with Reason for Exclusion


