Supplemental Material 2 - Evidence Mapping Methods

This evidence mapping describes the quantity, design and characteristics of the published research linking dietary sugars and potentially related health outcomes. A 2-step process was used to build an evidence-map database for our evidence-mapping analyses. In step 1, a broad literature search (further described below) was conducted to capture all randomized trials and prospective cohort studies relating to sugars of interest, including dietary fructose and sucrose, honey, and high fructose corn syrup, without specifying outcome terms. Next, titles and abstracts were screened to select relevant articles capturing broad research topics. In step 2, more detailed full-text article screening criteria were developed with input from the stakeholder panel. Finally, data from the full-text articles that met our eligibility criteria were extracted on SRDR™ (Systematic Review Data Repository; http://srdr.ahrq.gov) to form a database of primary studies for our evidence-mapping analyses. Detailed methods are described below.

a. Data sources and search strategies

A broad literature search was conducted on Ovid Medline® (1946 to March 2013). The search strategy employed the National Library of Medicine’s (NIH) Medical Subject Headings (MeSH) keyword nomenclature developed for Medline®. The goal was to cover the broad topics of dietary sugars and health; thus, the search strategy was comprehensive overview of published human randomized trials and prospective cohort studies on dietary sugars without restricting to any health outcomes. For example, following terms for specific dietary sugars of interest were used in our search strategy: “fructose”, “sucrose”, “juice”, “sugar”, “high fructose corn syrup,” and other sugars (including refined sugar, total sugar, added sugar, and unspecified sugars). Unpublished studies, clinical trial registries or grey literature (such as government or organization reports) were not searched. The complete search strategy is described in section d.

Full search strategies.

b. Study selection process

The research team downloaded citations identified from the Ovid Medline search to Abstrackr™, a web-based citation-screening tool (http://abstrackr.cebmbrown.edu/) for title and abstract screening. A training round of 300 abstracts was used to calibrate screening accuracy.
Discrepant screening results or disagreements were resolved after discussions among the entire research team to ensure the same interpretations of screening criteria among reviewers. The remaining abstracts were single-screened by investigators in the research team.

The Step 1 Evidence Mapping included a large number of articles (708 articles) after abstract and title screening using operationalized inclusion criteria for health outcomes of interest. The operationalized definitions for health outcomes of interest were any clinical diagnosis, patient-centered outcome, and well-established intermediate endpoints indicative of disease risk. Animal, case-control, cross-sectional and in-vitro studies were excluded. During the abstract screening period, it was brought up by the sponsor that there was an ongoing systematic review by the World Health Organization (WHO), which included key questions on the effects of sugar intake on dental caries in pediatric populations. Thus, dental caries and pain outcomes (studies mostly conducted in infant population) were initially deemed to be outside of the scope of this project, and were excluded during Step 1 so that the project can be completed in the timeline and budget. The decision to exclude these two outcomes was later confirmed by a majority of our stakeholder panel. With input from our stakeholder panel, the study eligibility criteria for full-text screening were refined in Step 2. During these refinement periods, the majority of the stakeholder panel members decided to include satiety, “addiction,” and appetite outcomes. Because these outcomes were not considered as potential health outcomes of interest in Step 1, a supplemental literature search was conducted specifically for identifying studies reporting these outcomes. The complete search strategy is described in section d. Full search strategies. Additional exclusion criteria as determined by the majority of the stakeholder panel members were to exclude studies using intravenous sugar administration, studies of sugar-sweetened beverages without quantification of sugar amount (serving size comparisons were not considered as sufficient quantification of sugar amount), studies in infants, and studies with cancer, athletic performance, or cognition as outcomes. Table 1 summarizes the final study eligibility criteria.

c. Data Collection and Analysis

Step 1 Evidence Mapping
Information on PI(E)COD (Population, Intervention/Exposure, Control/Comparator, Outcomes, and Study Design) from the abstracts were extracted to help better assess the literature base and to refine study eligibility criteria. The PI(E)COD information, abstracts, citations, and reviewers’ comments for relevant abstracts were stored in an Excel database (i.e., Step 1 Evidence Map). Full-text articles of the abstracts that were either deemed “relevant” or “unable to be determined” were retrieved for Step 2 Evidence Mapping screening.

**Step 2 Evidence Mapping**

As described earlier, with input from stakeholder panel, the study eligibility criteria were refined for full-text screening (Table 1). The bibliography of relevant systematic reviews was searched to add studies that were not captured in Step 1 Evidence Mapping. A standardized data extraction form was used to collect data on study design, funding source, and duration; population characteristics such as health status, weight, age, and sex; and information on sugar intake such as doses, sources, and forms of administration. A list of complete study outcome endpoints reported at the title, abstract, and full-text level was also extracted. All data were stored on SRDR™ (available on http://srdr.ahrq.gov/projects/136).

**Evidence-map Analysis**

Using data stored in the evidence-map database, descriptive analyses were performed to describe study design and population characteristics. All analyses were performed using Stata 2013 (Stata Statistical Software: Release 13. College Station, TX: StataCorp LP). A “bubble plot” of the outcome counts in each outcome categories was produced in Microsoft Visio 2013.

d. Full search strategies

d1. Medline Search Strategy

1 ("saccharose" or "sucrose" or "table sugar" or "dietary sucrose" or "dietary sugars" or "sugars dietary" or "sucrose dietary").mp.
2 exp Fructose/ or fructose.mp.
3 ("levulosa grifols" or "levulosa braun" or "apir levulosa" or "ern brand of fructose" or "levulosa fleboplast" or "levulosado vitulia" or "braun brand of fructose" or "levulosa ibys" or "fructose" or "levulose" or "plast apyr levulosa mein" or "grifols brand of fructose" or "levulosa apir" or "levulosa mein" or "fleboplast levulosa" or "baxter brand of fructose" or "levulosa" or "levulosado bieffe medit" or "levulosa ife" or
"institutofarmacologico brand of fructose" or "levulosado braun" or "fresenius kabi brand of fructose" or "levulosabaxter" or "bieve brand of fructose").mp. (31948)
4 ("high fructose corn syrup" or "HFCS" or "glucose fructose syrup" or "high fructose maize syrup" or "corn syrup" or "maize syrup" or "corn sugar" or "corn sweetener" or "sugar" or "brown sugar" or "honey" or "invert sugar" or "molasses" or "syrup" or "cane sugar" or "fruit juice concentrate$" or "agave").mp.
5 exp Sucrose/ or sucrose.mp. or sugar.mp.
6 (added adj2 sugar).mp.
7 exp Dietary Sucrose/
8 or/1-7
9 randomized controlled trial.pt.
10 controlled clinical trial.pt.
11 randomized controlled trials/
12 Random Allocation/
13 Double-blind Method/
14 Single-Blind Method/
15 clinical trial.pt.
16 Clinical Trials.mp. or exp Clinical Trials/
17 (clinic$ adj25 trial$).tw.
18 ((singl$ or doubl$ or trebl$ or tripl$) adj (mask$ or blind$)).tw.
19 Placebos/
20 placebo$.tw.
21 random$.tw.
22 trial$.tw. (529658)
23 (randomized control trial or clinical control trial).sd.
24 (latin adj square).tw.
25 Comparative Study.tw. or Comparative Study.pt.
26 exp Evaluation studies/
27 Follow-Up Studies/
28 Prospective Studies/
29 (control$ or prospectiv$ or volunteer$).tw.
30 Cross-Over Studies/
31 or/9-30
32 8 and 31
33 limit 32 to (english language and humans)
34 limit 33 to (addresses or bibliography or biography or case reports or comment or dictionary or editorial or guideline or in vitro or interview or lectures or legal cases or letter or "review")
35 33 not 34

d2. Supplemental Search Strategy
exp Satiation/
exp Satiety Response/
(appetite adj2 alteration$).mp.
exp Appetite Regulation/
("intake regulation$" adj2 food$).mp.
Online Supporting Material

(satiety-related adj2 hormone$).mp.
((satiety adj2 hormone$) or (hunger adj2 hormone$)).mp.
addictive behavior$.mp. or exp addictive behavior/
uncontrollable eating$.mp. or exp Obesity, Morbid/ or exp Eating Disorders/ or exp Bulimia/
abusive eating$.mp. or exp Eating Disorders/
excessive craving$.mp. or exp Behavior, Addictive/
binge eating$.mp. or exp Bulimia/

d3. Systematic Reviews Search Strategy

Published systematic reviews were searched separately using systematic review search filter and combined with our Medline search strategy described in section d1. However systematic reviews were not included in our evidence-map database. They are used to generate the initial list of future research recommendations, which were later refined and developed by the stakeholder panel.


References:

