An Evidence Map of Research Linking Dietary Sugars to Potentially Related Health Outcomes

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Abstract

Background: Evidence mapping is an emerging tool used to systematically identify, organize, and summarize the quantity, distribution, and characteristics of published studies with the goal of identifying knowledge gaps and future research needs.

Objective: The aim of the study was to present an evidence-map database of all published studies that investigated dietary sugars and to select health outcomes for explicating research trends and gaps.

Methods: To update an evidence-map database previously published in 2013, we performed a literature search in MEDLINE to identify English-language, peer-reviewed human intervention and prospective cohort studies published from January 2013 to December 2016. Abstracts and full-text articles were dual screened on the basis of predefined eligibility criteria. We classified outcomes into 7 health outcome categories that are potentially affected by dietary sugar. Data from the updated evidence-map database were merged with those from the previous database for analysis and charting.

Results: There were 918 sugar and control intervention arms from a total of 298 intervention studies from 1966 to December 2016. A variety of sugar interventions were investigated across the included intervention studies, and it appears that the research interest across all outcome categories (cardiovascular disease risks, diabetes risks, body weight, body composition, appetite, dietary intake, and liver health–related outcomes) sharply increased from 2006. Bubble plots showed research gaps in long-term intervention studies and in intervention studies in patients with diabetes. In contrast, all 25 included cohort studies had long-term follow-up durations and much larger sample sizes than did intervention studies. None of the cohort studies evaluated dietary intake outcomes, and only one cohort study each examined appetite- and liver health–related outcomes.

Conclusions: The research trends and research gaps have not changed since 2013 when the original evidence-map database was updated. With continuous updating, evidence mapping can facilitate the process of knowledge translation and possibly reduce research waste. *Curr Dev Nutr* 2018;2:nzy059.

Introduction

The term *sugars,* or simple carbohydrates, chemically refers to a group of compounds comprising carbon, hydrogen, and oxygen atoms that are classified as either monosaccharides or disaccharides (1). Three common monosaccharides are glucose, fructose, and galactose. Common disaccharides include maltose (2 linked glucose molecules), lactose (glucose linked to galactose), and sucrose (glucose linked to fructose). Sugars occur naturally in some foods, including fruits and dairy products, and are frequently added to foods during processing. The latter are called *added sugars,* a term often used in the scientific literature but lacking a universal definition (2). Recently, the US FDA defined added sugars as "sugars that are either added during the processing

Keywords: dietary sugars, fructose, sucrose, added sugars, evidence map, scoping review, research gaps

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Abbreviations used: CVD, cardiovascular disease; HFCS, high-fructose corn syrup; PC, prospective cohort.

of foods, or are packaged as such, and include sugars (free, mono- and disaccharides), sugars from syrups and honey, and sugars from concentrated fruit or vegetable juices that are in excess of what would be expected from the same volume of 100% fruit or vegetable juice of the same type" (3). The WHO defined *free sugars* as "all monosaccharaides and disaccharides added to foods by the manufacturer, cook, or consumer, plus sugars naturally present in honey, syrups, and fruit juices" (4). Two major sources of added sugars include sucrose and high-fructose corn syrup (HFCS), which are used for sweetening foods and beverages. Dietary sucrose is hydrolyzed by sucrase in the small intestine to equimolar amounts of glucose and fructose. HFCS contains varying amounts of unbound glucose and fructose (5).

Evidence mapping is an emerging rapid review method that involves a systematic search and characterization of extant research on a topic of interest, aiming to identify gaps in knowledge and future research needs (6). Although there are currently no methodologic standards, evidence mapping typically includes a systematic process to create a searchable evidence-map database; this permits descriptive analyses or visuals of the database, such as bubble plots, to identify research gaps (7). Study characteristics can be summarized using the data to inform future study designs or to identify gaps in research. Conversely, evidence mapping can also help identify areas rich in studies, for which systematic reviews and meta-analyses can be conducted. Unlike systematic reviews, evidence mapping does not assess the quality (or risk-of-bias) of the included studies nor does it synthesize the study results.

Several organizations have relied on evidence maps to make evidence-informed decisions and to prioritize strategic research (8–10). Keeping databases up to date is crucial to best leverage this method and to facilitate translation of scientific knowledge into policy or practice (6). In 2013, an open evidence-map database of all published studies on dietary sugars and select health outcomes was created (herein referred to as "the 2013 evidence-map database"; available from http://srdr.ahrq.gov/projects/136) as an integral part of a research prioritization project by a multidisciplinary stakeholder panel (11). Given the recent proliferation of research on dietary sugars, the increasing interest in their potential health effects, and the importance of this public health topic, the World Sugars Research Organization commissioned an update of the 2013 evidence-map database (11), with a goal of explicating research trends and gaps.

Methods

Literature search and selection

We conducted an electronic search strategy in MEDLINE (gateway.ovid.com) using both medical subject headings and text words for specific dietary sugar terms. No restrictions were set with regard to outcome terms. Search results were limited to English-language, peer-reviewed human intervention studies and prospective cohort (PC) studies published from January 2013 to December 2016 (**Supplemental Table 1**). This was the same search strategy and study eligibility criteria utilized in creating the 2013 evidence-map database (11). We did not search for or include any unpublished studies, clinical trial registries, or gray literature such as government or organization reports.

To assess study eligibility, we used inclusion and exclusion criteria that included specific sugar exposures, study designs, and human subjects (**Table 1**). Two independent reviewers screened all titles and abstracts using a low threshold to exclude irrelevant abstracts, such as animal studies, in vitro studies, or studies with no interventions or exposures of interest. We then retrieved full-text articles of potentially relevant abstracts and double-screened them. Any discrepancies during either screening phase were resolved via group consensus. Included studies must have examined $\geq$1 quantifiable dietary sugar; we excluded studies examining sugar-sweetened beverages without adequate quantification of sugar amount (e.g., information only on serving sizes or frequency of intake). We also excluded studies with intravenous sugar administration or studies that exclusively examined dental caries, pain, cancer, athletic performance, or cognition outcomes.

Data extraction

Data were recorded in a customized extraction form shared via Google Drive to facilitate collaboration among research team members and to allow for simultaneous data entry of relevant study details: publication date, study design, intervention duration and follow-up time, population characteristics (e.g., baseline health status, age, and anthropometric measures), reported outcomes (i.e., all study endpoints listed in the full text), and funding source. For intervention studies, we also extracted the characteristics of the dietary sugar intervention and control groups, including type of sugar, dose, and form of administration. For PC studies, we extracted relevant dietary assessment methods and definitions of total or added sugars. All data were extracted by one reviewer and randomly checked by a second reviewer. All extracted data, including the database codebook, are included in the supplemental data files (**Supplemental Datasets 1** and **2**).

Data analysis and charting

For this study, we merged data from the updated evidence-map database with those from the previous database (studies published before 2013) for analysis. We treated multiple studies reported in one publication as separate studies in the analysis. Moreover, we did not check whether multiple publications reported results from the same study population. We extracted the names of all health outcomes reported in each individual study. To allow meaningful descriptive analyses and identification of research gaps, outcomes were classified into the following outcome categories that are potentially affected by dietary sugar: *diabetes risks, cardiovascular disease risks, body weight, body composition, appetite, dietary intake,* and *liver health.* It is important to note that the specific outcomes that comprise each outcome category were heterogeneous. For example, the *dietary intake* outcome category includes various dietary pattern scores and intakes of macronutrients, micronutrients, or food groups, and the *liver health* outcome category includes various liver health indexes (e.g., liver enzymes, bilirubin, and liver fat) and diagnosis of nonalcoholic fatty liver disease. We classified any outcome that did not fit into 1 of these 7 categories as *other* outcome category.

We conducted descriptive analyses to summarize characteristics of the included studies, including study sample size, study duration,

TABLE 1 Study eligibility criteria

Inclusion criteria	Exclusion criteria
• Population: human • Intervention or exposures: monosaccharides, disaccharides, sugar-sweetened beverages, corn syrup, honey, and other unspecified dietary sugars • Study designs: intervention studies of any design and prospective cohort studies (including nested case-control studies or case-cohort studies)	• Population: infants (i.e., <1 y old) and animal studies • Intervention or exposures: intravenous sugar administration or sugar-sweetened beverages without quantification of sugar amount (i.e., serving sizes or intake frequencies were not considered as adequate quantification of sugar amount) • Outcomes: dental caries, pain, cancer, athletic performance, and cognition outcomes • Language: non-English–language publications • Study designs: cross-sectional studies, retrospective case-control studies, case series, and case reports

funding source, the demographic characteristics of the population studied (including age and sex), and the baseline health status of the subjects (including BMI). For studies in the 2013 evidence-map database, we imputed the arm-specific study size by dividing the extracted total sample size by the number of arms, because only total sample size had been extracted into the database. For study duration, we created categories on the basis of the length of follow-up (i.e., for intervention studies: <1 d, 1–14 d, 15 d to 1 mo, >1 to 6 mo, >6 mo to 1 y, >1 to 2 y, and >2 y; for PC studies: 1–2, >2 to 5, >5 to 10, >10 to 20, and >20 y). We also tabulated the aforementioned health outcome categories and the sugar interventions under study. For the sugar interventions, we classified each intervention arm as *fructose, glucose, high-fructose corn syrup, honey, lactose, sucrose, mixed sugars* (>1 type of sugar), *unspecified sugar,* or *controls* (nonsugar intervention arms). These sugar intervention classifications were based on which specific type of sugar was quantified in the original studies. For example, *fructose* interventions included both pure fructose interventions and whole-diet interventions that quantified the amount of fructose consumed.

For bivariate data exploration, we examined how funding sources were related to study characteristics (e.g., sample size, study duration, and exposures) with the use of chi-square and Fisher's exact test when appropriate. To visualize gaps in research, we created bubble plots (one type of weighted scatterplots) grouping studies by outcome categories, study duration, baseline health status, and types of sugar interventions. We conducted all analyses and created all bubble plots using Stata version 14 (StataCorp) with a 2-sided α level of 0.05.

Results

Our MEDLINE literature search identified 3126 citations from 2013 through 2016. Of these, we deemed 238 abstracts to be potentially relevant and included them in full-text screening. A total of 111 studies (97 intervention studies and 14 PC studies) were included in the update evidence-map database. **Figure 1** shows a summary of the literature search and study selection flow used in the update. We merged the updated database with the 2013 evidence-map database, which contained a total of 212 studies (201 intervention studies and 11 PC studies), for analyses. Intervention studies were analyzed separately from the PC studies.

Intervention studies

There were 918 sugar and control intervention arms from a total of 298 studies (**Table 2**). Of the 298 studies, 50% were crossover design trials, 28% were parallel-arm trials, 11% were nonrandomized trials, 7% were single-arm trials, and the remaining 4% were another type of intervention design. Most of the recent studies were acute, studying effects of <24 h. Only a small number of studies (5%) were >1 y in duration. The majority of studies were conducted in adults aged ≥18 y. Most interventions were tested in healthy subjects; 12% of studies were in subjects with obesity and 15% in subjects with diabetes (type 1 or type 2). Most studies (81%) did not provide details on study power calculations.

A variety of sugar interventions were investigated in the included studies: sucrose, fructose, and glucose in 18%, 15%, and 8% of interventions, respectively, and HFCS, honey, and lactose interventions in <2% of interventions. Thirty percent of sugar interventions did not specify the type of sugar used (**Table 3**).

Many intervention studies investigated the effects of dietary sugars on multiple outcome categories (Table 2). **Figure 2** shows the commutative frequency of studies, published from 1966 to 2016, or the cumulative publication growth over time (excluding the *other* outcome category). The plot showed that there was a steady increasing trend in the number of publications reporting cardiovascular disease (CVD) risk and diabetes risk outcomes from 1966 to 2016. The research published in all outcome categories sharply increased from 2006.

Using bubble plots to identify research gaps

The first bubble plot shows that none of the studies that investigated liver health had intervention durations >6 mo (**Figure 3**). None of the studies that investigated dietary intake and body-composition outcomes had intervention durations >1 y. Only a few studies examined effects of long-term (>1 y) sugar interventions on appetite, body weight, CVD risks, and diabetes risks. The second bubble plot shows that very few studies among patients with diabetes investigated the effects of sugar interventions on body composition, dietary intake, and liver health outcomes; and none investigated appetite outcomes (**Figure 4**).

PC studies

A total of 14 PC studies were identified from 2013 through 2016 and were merged with the 11 studies from the previous evidence-map database for the analyses (**Table 4**). Of the 25 included studies, all had follow-up durations >1 y and 14 (56%) had a follow-up duration >5 y. One study (4%) did not report the follow-up duration. The sample size of the PC studies ranged from 630 to 353,751 participants, with a mean of 44,124 participants. Most of the PC studies were conducted in generally healthy populations (68%) and the majority (76%) were conducted in adults.

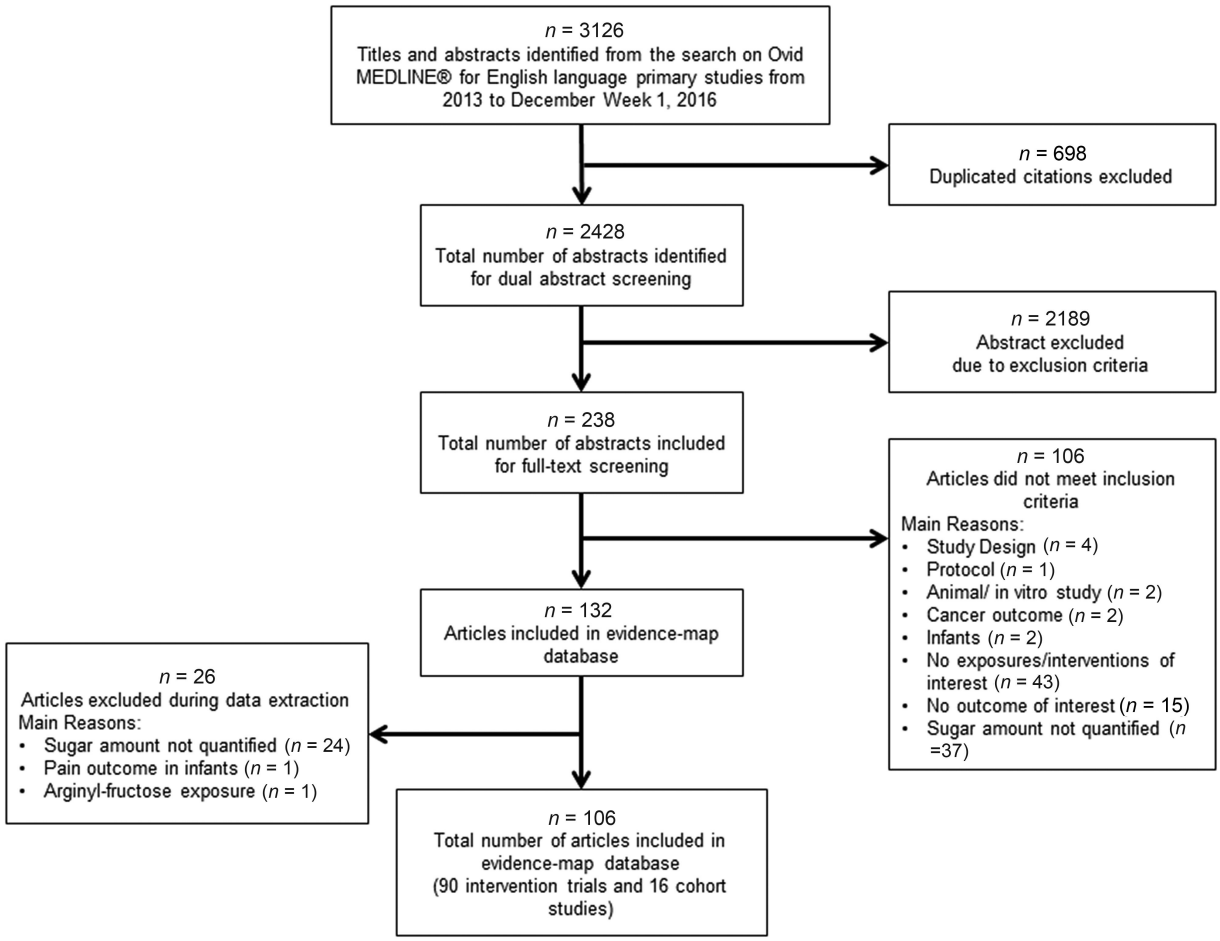

FIGURE 1 Literature search and selection flow.

Unlike the intervention studies, most of the PC studies (76%) investigated a single outcome category, and only 1 study each examined appetite and liver health outcomes. Diabetes risks, CVD risks, body weight, and body-composition outcomes were examined in 24%, 20%, 24%, and 16% of the studies, respectively. Other outcomes were examined in 40% of the PC studies, including serum HDL concentration, psychological outcomes, urinary system diseases, and age at menarche.

Sugar intake was measured by an FFQ or its combination with other dietary assessment methods in 64% of the PC studies, whereas 12% and 20% of the studies used diet records and 24-h recall, respectively. Approximately half of the PC studies quantified total sugar intake. *Added sugar* intake was investigated in 8 of the PC studies (32%), with slight differences in their definitions (**Table 5**).

Funding sources and their association with study characteristics

Approximately 80% of intervention studies reported their funding sources. Government funding was the most common (44% of studies), and 22% of studies exclusively received government funding. Approximately 17% of studies were funded only by nonprofit sources and 16% of the included studies were exclusively funded by industry sources.

Intervention studies with industry-only funding had significantly larger sample sizes compared with studies funded by government only, nonprofit only, mixed sources, or those studies that did not report funding source ($P = 0.0001$). The funding sources were associated with whether the study was randomized ($P = 0.02$). There were no significant associations across the studies between different funding sources and categories of study durations, study design, or whether studies reported power calculations (**Table 6**).

Last, there was a significant relation between funding sources and whether an intervention study investigated the effects of HFCS or fructose. Twenty-five percent of studies with government-only funding included a study arm of fructose or HFCS, compared with 19% of studies with mixed funding, 18% of studies with exclusive nonprofit funding, 11% of studies funded by industry, and 10% of studies that did not report funding source ($P < 0.0001$, Fisher's exact test).

Among the 25 PC studies, only 1 study was exclusively funded by industry. Other studies ($n = 24$) were funded by government (52%), nonprofit research foundations (11%), or a mix of both (33%) (Table 4). Funding sources were not significantly associated with sample sizes or categories of study duration among PC studies (**Table 7**).

TABLE 2 Summary of study design and population characteristics of included intervention studies in updated, original, and combined data sets[1]

	Studies published from 2013 to 2016 (*n* = 97)	Original evidence map (*n* = 201)	Combined (*n* = 298)
Design, *n* (%)			
Randomized (parallel)	27 (28)	45 (22)	72 (24)
Randomized (crossover)	58 (60)	91 (45)	149 (50)
Nonrandomized (with control)	3 (3)	29 (14)	32 (11)
Single-arm	7 (7)	25 (12)	32 (11)
Other[2]	2 (2)	11 (5)	13 (4)
Study duration, *n* (%)			
<1 d	41 (43)	84 (42)	125 (42)
1–14 d	24 (25)	45 (23)	69 (23)
15 d to 1 mo	14 (14)	26 (13)	40 (13)
>1 to 6 mo	16 (16)	41 (20)	57 (19)
>6 mo to 1 y	1 (1)	2 (1)	3 (1)
>1 to 2 y	1 (1)	10 (5)	14 (5)
>2 y	0 (0)	1 (1)	1 (0.3)
Sample size, *n*	22 (6–465)	18 (5–2026)	19 (5–2026)
Published power calculation, *n* (%)	32 (33)	24 (12)	56 (19)
Age,[3] y	29.8 (1.5–77.7)	35.4 (5–72)	33.7 (1.5–77.7)
Study population, *n* (%)			
Adults	75 (77)	180 (90)	255 (86)
Children	12 (12)	11 (5)	23 (8)
Adolescents	8 (8)	3 (1)	11 (4)
Mixed	0 (0)	7 (3)	7 (2)
Baseline health status, *n* (%)			
Healthy	47 (48)	108 (54)	155 (52)
Overweight/obese	19 (20)	18 (9)	37 (12)
Diabetes	4 (4)	42 (21)	46 (15)
Mixed healthy and nonhealthy	1 (1)	16 (8)	17 (6)
Other	12 (12)	16 (8)	28 (9)
Not specified	14 (14)	1 (1)	15 (5)
Funding source, *n* (%)			
Government	26 (27)	39 (19)	65 (22)
Industry	23 (24)	24 (12)	47 (16)
Nonprofit	21 (22)	31 (15)	52 (17)
Government and industry	5 (5)	23 (11%)	28 (9)
Government and nonprofit	7 (7)	24 (12)	31 (10)
Nonprofit and industry	1 (1)	6 (3)	7 (2)
Government, industry, and nonprofit	0 (0)	8 (4)	8 (3)
No data given	14 (14)	46 (23)	60 (20)
Outcome categories,[4] *n* (%)			
Diabetes risks	54 (56)	147 (73)	201 (67)
Cardiovascular disease risks	38 (39)	109 (54)	147 (49)
Body weight	22 (23)	52 (26)	74 (25)
Body composition	19 (20)	18 (9)	37 (12)
Appetite	28 (29)	31 (15)	59 (20)
Dietary intake	13 (13)	32 (16)	45 (15)
Liver health	9 (9)	15 (7)	24 (8)
Other outcomes	45 (46)	111 (55)	156 (52)

[1]Values are *n* (%) or means (minimum–maximum). The unit of analysis is 1 study, with the exception of *Sample size* and *Age*.
[2]*Other* designs include quasi-experimental design or unclear intervention designs.
[3]Fifteen studies did not report mean or median age so were not included in the calculation. Minimum and maximum mean ages are shown in parentheses.
[4]Because some studies examined multiple outcomes across multiple categories, percentages sum to >100%.

TABLE 3 Summary of sugar intervention arms in the updated, original, and combined data sets, by study intervention arm[1]

	Intervention arms of studies published from 2013–2016 (n = 225)	Intervention arms of studies in original evidence map (n = 470)	Combined (n = 695)
Fructose	48 (15)	81 (14)	129 (15)
Glucose	34 (11)	39 (7)	73 (8)
Sucrose	62 (20)	97 (17)	159 (18)
High-fructose corn syrup	16 (5)	6 (1)	22 (2)
Honey	6 (2)	12 (2)	18 (2)
Mixed sugars	26 (8)	0 (0)	26 (8)
Lactose	2 (1)	0 (0)	2 (1)
Unspecified sugar (type of sugar not specified)	31 (10)	235 (41)	266 (30)

[1]Values are n (%). The unit of analysis is one intervention arm.

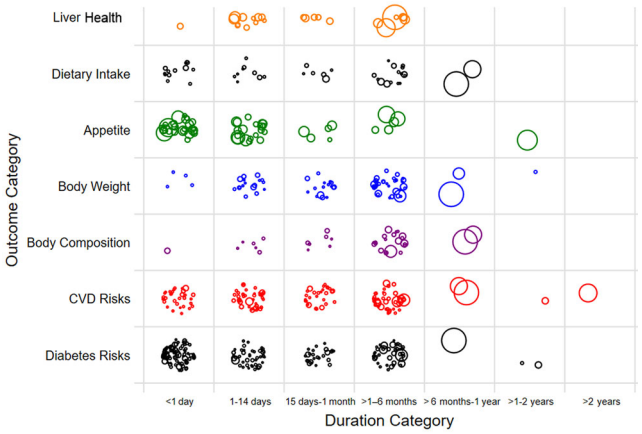

FIGURE 3 Bubble plot of intervention studies by outcome categories and by study duration. Each bubble in the figure represents 1 study, and the size of the bubble is proportional to the study sample size. CVD, cardiovascular disease.

Discussion

In this article, we updated and analyzed a literature database of published intervention studies and PC studies that examined the relations between dietary sugar intakes and select health outcomes. A variety of sugar interventions were investigated across the included intervention studies, and it appears that the research interest across all outcome categories (CVD risks, diabetes risks, body weight, body composition, appetite, dietary intake, and liver health–related outcomes) sharply increased from 2006. Bubble plots showed research gaps in long-term intervention studies and in intervention studies in patients with diabetes. In contrast, all included PC studies had long-term follow-up durations and much larger sample sizes than did intervention studies. None of the PC studies evaluated dietary intake outcomes and only one PC study each examined appetite- and liver health–related outcomes. On the basis of these results, we concluded that the research trends and research gaps have not changed since 2013, when the evidence-map database was updated. Therefore, the 14 prioritized research questions (research needs) in the broad field of dietary sugars and health outcomes remain valid (**Supplemental Table 2**) (11). These 14 high-priority research questions were identified by a multidisciplinary stakeholder panel following a structured approach that integrated evidence mapping with expertise or viewpoints from the panel.

Our exploratory analyses showed some interesting findings. We found that industry funding sources were associated with some, but not all, good study design features for intervention studies, such as randomization and larger sample sizes. Government funding sources were associated with whether an intervention study investigated the effects of HFCS or fructose. However, these exploratory analysis results should be interpreted with caution because the classification of funding

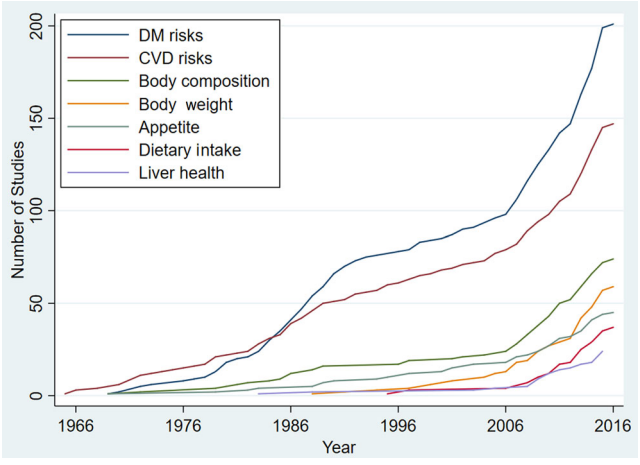

FIGURE 2 Cumulative frequency of published studies, by outcome categories. CVD, cardiovascular disease; DM, diabetes mellitus.

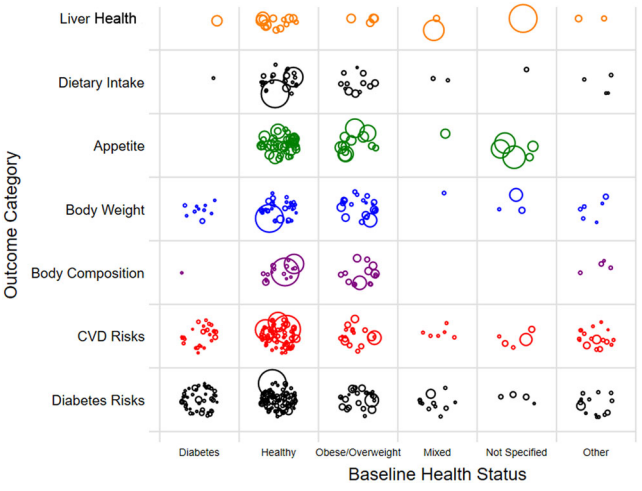

FIGURE 4 Bubble plot of intervention studies by outcome categories and by baseline population health status. Each bubble in the figure represents 1 study, and the size of the bubble is proportional to the study sample size. CVD, cardiovascular disease; Mixed, mixed healthy and nonhealthy conditions; Other, other disease conditions.

TABLE 4 Summary of study design and population characteristics of included prospective cohort studies in updated, original, and combined databases[1]

	Updated (n = 14)	Original (n = 11)	Combined (n = 25)
Study duration, *n* (%)			
1–2 y	4 (29)	0 (0)	4 (16)
>2–5 y	3 (21)	3 (27)	6 (24)
>5–10 y	3 (21)	6 (55)	9 (36)
>10–20 y	2 (14)	2 (18)	4 (16)
>20 y	1 (7)	0 (0)	1 (4)
Not reported	1 (7)	0 (0)	1 (4)
Sample size, *n*	37,609 (630–353,751)	35,738 (1064–223,230)	44,124 (630–353,751)
Age,[2] y	23 (6.1–50.6)	53 (48–57.4)	36 (6.1–57.4)
Study population, *n* (%)			
Adults	8 (57)	11 (100)	19 (76)
Children	6 (43)	0 (0)	6 (24)
Baseline health status, *n* (%)			
Healthy	9 (64)	8 (73)	17 (68)
Pregnant	2 (14)	1 (9)	3 (12)
Other	2 (14)	2 (18)	4 (16)
Not specified	1 (7)	0 (0)	1 (4)
Funding source, *n* (%)			
Government	6 (43)	7 (64)	13 (52)
Industry	1 (7)	0 (0)	1 (4)
Nonprofit	1 (7)	1 (9)	2 (8)
Government and industry	0 (0)	0 (0)	0 (0)
Government and nonprofit	6 (43)	3 (27)	9 (36)
Nonprofit and industry	0 (0)	0 (0)	0 (0)
Government, industry, and nonprofit	0 (0)	0 (0)	0 (0)
No data given	0 (0)	0 (0)	0 (0)
Outcome categories,[3] *n* (%)			
Diabetes risks	3 (21)	3 (27)	6 (24)
Cardiovascular disease risks	1 (7)	4 (36)	5 (20)
Body weight	5 (36)	1 (9)	6 (24)
Body composition	3 (21)	1 (9)	4 (16)
Appetite	1 (7)	0 (0)	1 (4)
Dietary intake	0 (0)	0 (0)	0 (0)
Liver health	1 (7)	0 (0)	1 (4)
Other outcomes	7 (50)	3 (27)	10 (40)
Dietary assessment methods, *n* (%)			
FFQ	6 (43)	8 (73)	14 (56)
Diet record	3 (21)	0 (0)	3 (12)
24-h recall	3 (21)	2 (18)	5 (20)
FFQ + others	2 (14)	0 (0)	2 (8)
Unclear	0 (0)	1 (9)	1 (4)

[1]Values are *n* (%) or means (minimum–maximum). The unit of analysis is 1 study, with the exception of *Sample size* and *Age*.
[2]Fourteen studies did not report mean or median age so were not included in the calculation. Number represents the mean of mean ages of studies. Minimum and maximum mean ages are shown in parentheses.
[3]Because some studies examined multiple outcomes across multiple categories, percentages sum to >100%.

source categories may be inaccurate and the *mixed* funding category is ambiguously defined. Moreover, we did not assess the quality or risk-of-bias of the included studies in the evidence-map database. Study design alone is insufficient for judging the quality of the studies. There have been several systematic reviews investigating the effects of fructose-containing sugars on cardiometabolic risk factors (20–26), body weight (26–28), and nonalcoholic fatty liver disease or liver fat (29–31). These systematic reviews reported that a large portion of research had small sample sizes, were short-term trials, and were rated as high risk-of-bias. Our descriptive analyses of the evidence-map database support these findings, although we did not assess the risk-of-bias of the included studies. In addition, most of the studies in the evidence-map database focused on healthy adults, with a dearth of studies in children, adolescents, or adults with other health conditions. A large proportion (42%) of the intervention studies in the evidence-map database were acute (<1 d) mechanistic studies of a single dose of sugar ingestion. The results from mechanistic studies have little applicability to longer-term health outcomes because individual sugars are rarely ingested alone in the real world. On the other hand, well-controlled mechanistic studies can build a foundation for causal inference because they can elucidate the biological mechanisms of the postulated effects.

TABLE 5 Definitions of *added sugar* used in prospective cohort studies[1]

First author, year (reference)	Definition
Borgen et al., 2012 (12)	The Norwegian Food Composition Table (available online at http://www.matportalen.no/Matvaretabellen; 2006) lists the concentrations of added sugar: "Added sugar comprises refined and industrial processed sugars such as glucose, sucrose, fructose and glucose syrup."
Chortatos et al., 2013 (13)	Not reported
Gangwisch et al., 2015 (14)	"Added sugars were assessed according to the MyPyramid Equivalents 2.0 and included all sugars used as ingredients in processed and prepared foods such as breads, cakes, sodas, jellies, chocolates, and ice cream and sugars consumed separately or added to foods at the table."
Lee et al., 2014 (15)	"Sugars added during the processing or preparation of foods and beverages"
Suadicani et al., 1996 (16)	"Sugar used in hot beverages"
Tasevska et al., 2014 (17)	"Sugars added at the table or used as ingredients in processed or prepared foods and drinks"
Vorster et al., 2014 (18)	"Added sugars were defined as all monosaccharides and disaccharides added to foods and beverages during processing, cooking, and at the table; these sugars included honey and jams as well as sugar added to beverages."
Wang et al., 2014 (19)	"The USDA Database for the Added Sugars Content of Selected Foods was used for estimating added sugars."

[1] $n = 8$ studies.

TABLE 6 Associations between funding sources and study characteristics for intervention studies

	Study funding source[1]					
	Mixed ($n = 74$)	Government only ($n = 65$)	Industry only ($n = 47$)	Nonprofit only ($n = 52$)	Not reported ($n = 60$)	P[2]
Median sample size,[3] *n*	18	18	33	17.5	17	0.0001*
Duration, *n* (%)						0.14
<1 d	24 (32)	25 (38)	21 (45)	24 (46)	31 (52)	
1–14 d	23 (31)	20 (31)	9 (19)	12 (23)	5 (8)	
15–31 d	12 (16)	7 (11)	2 (4)	9 (17)	10 (17)	
>1 to 6 mo	13 (18)	12 (18)	13 (28)	7 (13)	12 (20)	
>6 to 1 y	1 (1)	1 (2)	1 (2)	0 (0)	0 (0)	
>1 to 2 y	0 (0)	0 (0)	1 (2)	0 (0)	2 (3)	
>2 y	1 (1)	0 (0)	0 (0)	0 (0)	0 (0)	
Study design, *n* (%)						0.06
Randomized (parallel)	16 (22)	13 (20)	15 (32)	18 (35)	10 (17)	
Randomized (crossover)	29 (39)	39 (60)	25 (53)	22 (42)	34 (57)	
Nonrandomized	14 (19)	5 (8)	2 (4)	3 (6)	8 (13)	
Single-arm	11 (15)	4 (6)	3 (6)	6 (12)	8 (13)	
Other	4 (5)	4 (6)	2 (4)	3 (6)	0 (0)	
Included power calculation, *n* (%)						0.40
Yes	2 (15)	11 (42)	8 (36)	8 (38)	3 (21)	
No	11 (85)	15 (58)	14 (64)	13 (62)	11 (79)	
Study is randomized, *n* (%)						0.02*
Yes	45 (61)	52 (80)	40 (85)	40 (77)	44 (73)	
No	29 (39)	13 (20)	7 (15)	12 (23)	16 (27)	
Outcome categories, *n* (%)						
Diabetes risks	53 (72)	40 (62)	27 (57)	35 (67)	46 (77)	0.20
Cardiovascular disease risks	45 (61)	33 (51)	20 (43)	26 (50)	23 (38)	0.10
Body weight	23 (31)	14 (22)	12 (26)	15 (29)	10 (17)	0.34
Body composition	14 (19)	8 (12)	5 (11)	7 (13)	3 (5)	0.20
Appetite	19 (26)	13 (20)	11 (23)	8 (15)	8 (13)	0.38
Dietary intake	19 (26)	7 (11)	7 (15)	8 (15)	4 (7)	0.03*
Liver health	8 (11)	3 (5)	4 (9)	7 (13)	2 (3)	0.23
Other	44 (59)	41 (63)	22 (47)	26 (50)	23 (38)	0.04*

[1] *Mixed* indicates studies funded by >1 funding source category; *Government only* indicates studies exclusively funded by a government source.
[2] *P* values were derived by chi-square test, with the exception of *Sample size* (Kruskal-Wallis test). *Significant, $\alpha = 0.05$.
[3] The median sample size in each category.

TABLE 7 Associations between funding sources and study characteristics for prospective cohort studies

	Study funding source[1]				
	Mixed ($n = 9$)	Government only ($n = 13$)	Industry only ($n = 1$)	Nonprofit only ($n = 2$)	P^2
Median sample size,[3] *n*	2899	35,060.5	2379	51,675	0.15
Study duration, *n* (%)					0.88
1–2 y	3 (33)	1 (8)	0 (0)	0 (0)	
>2–5 y	2 (22)	3 (25)	0 (0)	1 (50)	
>5–10 y	3 (33)	4 (33)	1 (100)	1 (50)	
>10–20 y	1 (11)	3 (25)	0 (0)	0 (0)	
>20 y	0 (0)	1 (8)	0 (0)	0 (0)	

[1] *Government only* indicates studies exclusively funded by a government source; *Mixed* indicates studies funded by >1 funding source category.
[2] *P* values were derived by using chi-square test, with the exception of *Sample size* (Kruskal-Wallis test). $\alpha = 0.05$.
[3] The median sample size in each category.

Our evidence-map database included only 25 PC studies, primarily because many cohort studies investigating the relation between *sugar-sweetened beverage* intake (without quantifying sugar amount) and health outcomes were excluded. All 25 included PC studies measured dietary sugar intake with the use of self-report dietary assessment methods. Limitations of self-report dietary assessment methods have been widely discussed and recognized. Both random errors and systematic bias in self-report intake estimates can invalidate nutritional observational study findings. Currently, there are no established sugar intake biomarkers. Furthermore, the lack of a universal definition of *added sugars* hampers the ability to easily compare study findings. Of note, added sugars cannot be analytically determined. They must be calculated with the use of a nutrient database, which uses different equations to calculate the amount of added sugars, thus resulting in a range of values (2).

Evidence mapping requires less time and effort than a systematic review to achieve an understanding of the distribution of evidence and often includes a much broader research landscape than a systematic review. However, it has several limitations. Only the MEDLINE database was searched, so many studies may have been missed. Because evidence mapping does not access the quality (or risk-of-bias) of the included studies, it also cannot identify research gaps in which high volumes of poor-quality studies exist (therefore, there is still a research need) or in which high volumes of high-quality studies show consistent results (therefore, there is no need for further research). Moreover, it should be noted that research gaps identified by the bubble plots do not necessarily equate to research needs. The determination of research needs requires consideration of the importance, desirability, feasibility, and potential impact of research gaps, highlighting the importance of stakeholder engagement in this process.

We systematically collected and organized a literature database of research linking dietary sugars to potentially related health outcomes. Research funders, researchers (including systematic reviewers), and practitioners can query and analyze this database to acquire information necessary for decision making, such as directions for future research, and to formulate systematic review research plans to anticipate potential challenges (e.g., heterogeneity). By continuously updating the evidence-map database, evidence mapping can facilitate the process of knowledge translation from scientific findings into health practice or policy recommendations, and possibly reduce research waste.

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