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Title: Scoping review and evidence map on the relationship between exposure to

dietary sweetness and body weight-related outcomes in adults

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Abbreviations List: BMI, body mass index; BW, body weight; EI, energy intake; h, hour(s); IAFNS, Institute for the Advancement of Food and Nutrition Sciences; JBI, Joanna Briggs Institute; LCS, low calorie sweeteners; n, study count; NS, not significant; OSF, Open Science Framework; PI(E)COS, Populations,

Interventions/Exposures, Comparators, Outcomes, and Study Designs or Settings; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analysis; PRISMA-ScR, Preferred Reporting Items for Systematic Reviews and Meta-Analysis Extension for Scoping Review; RCT, randomized controlled trial; SRDR, Systematic Review Data Repository; SRMA, systematic review/meta-analysis; SSB, sugarsweetened beverage(s); TOP, Transparency and Openness Promotion; VAS, visual analog scale; W:H, waist to hip; WC, waist circumference; wk, week(s); y, year(s) REAMAN

Abstract

Background: Numerous governmental and health organizations recommend reduced intake of added sugars due to the health risks associated with excess intake, including the risk of obesity. Some organizations further recommend avoiding dietary sweetness, regardless of the source.

Objective: A scoping review and evidence map were completed to characterize the research investigating dietary sweetness and body weight. The aim was to identify and map studies that investigate total dietary sweetness, sweet food/beverage, sugar, or sweetener intake and body weight-related outcomes and/or energy intake. Design: Using pre-registered search terms (osf.io/my7pb), 36,779 publications (duplicates removed) from PubMed, Cochrane Library, and Scopus were identified and screened for inclusion. Eligible studies were clinical trials, longitudinal cohorts, case-control studies, cross-sectional studies, and systematic reviews conducted among adults (≥18 years) which investigated associations between dietary sweetness, sweet food/beverage, sugar, or sweetener (energetic or non-energetic) intake and body weight, body mass index, adiposity, and/or energy intake.

Results: A total of 833 eligible publications were identified, detailing 804 studies. Only 7 studies (0.9% of included studies) (2 clinical trials, 4 cross-sectional studies, 1 other design type) investigated associations between total dietary sweetness and a body weight-related outcome and/or energy intake. An additional 608 (75.6%) studies investigated sweet food/beverage, sugar, or sweetener intake and body weight-related outcomes and/or energy intake, including 225 clinical trials, 81 longitudinal cohorts, 4 case-control studies, and 280 cross-sectional studies. Most studies (90.6%) did not

measure the sweetness of the diet or individual foods consumed. Ninety-two (11.4%) publications reported on dietary patterns that included sweet foods/beverages alongside other dietary components and 97 (12.1%) systematic reviews addressed different but related research questions.

Conclusions: While there is a breadth of evidence from studies that investigate sweet food/beverage, sugar, and sweetener intake and body weight, there is limited evidence on the association between total dietary sweetness and body weight.

Keywords: Body composition, ingestive behavior, sweetness, sweeteners, sugars,

sensory, evidence map, scoping review

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Statement of Significance: Despite popular belief, there is limited evidence published to date to determine if there is an association between dietary sweetness and body weight. The available evidence is compiled for open access use for future investigations (osf.io/ckh9v/).

Dietary recommendations from numerous governmental and public health organizations recommend reduced intake of added sugars [defined as "sugars that are either added during the processing of foods, or are packaged as such (e.g., a bag of sugar)"(1)] due to many associated health risks (2-6), including an increased risk of overweight and obesity. Some public health organizations (including Health Canada and the Pan American Health Organization) also recommend avoiding dietary sweetness (7, 8), regardless of the source of the sweet taste [e.g., sugars, low calorie sweeteners (LCS)] to facilitate reductions in sugar intake. The latter recommendation is based on the hypothesis that chronic and frequent exposure to dietary sweetness will increase the preference and desire for sweet foods/beverages, referred to colloquially as the development of a "sweet tooth" (8). A developed preference for sweetness may have negative implications for body weight, due to the ease with which excess energy from sources of sugar can be consumed in an ad libitum diet (9).

Despite the belief that heightened exposure to sweetness may lead to an increased preference or desire for sweet foods and beverages, there is no consensus as to whether the sweetness of the diet drives excess energy intake (10, 11). Changes to salt and fat preference in response to dietary manipulations have been observed in clinical trials (12, 13). However, while heightened sweetness *perception* was observed with reduced dietary sugar intake compared to a habitual diet in a three-month randomized controlled trial (RCT), no changes in sweet *preference* were observed (14). A systematic review designed to determine the association between sweet taste exposure and food acceptance, preference, and choice found that the available

evidence from 21 studies (7 cohorts and 14 controlled trials) was "very heterogeneous and does not provide clear, consistent support for a relation between sweet taste exposures and the outcomes considered" (10).

Whether or not dietary sweetness influences dietary preferences and energy intake has important implications for body weight management. If exposure to sweetness has no effect on dietary preferences, then diets that enhance compliance to energy requirements, independent of level of sweetness, can be encouraged to facilitate weight maintenance. If reductions in dietary sweetness (regardless of the source) leads to reduced sweetness preference and results in reduced sweet food/beverage intake, then reduced dietary sweetness exposure may help facilitate body weight management.

The uncertainty of the relationship between dietary sweetness and body weight is due in part to the many challenges associated with determining the sweetness of the entire diet. The human diet is complex and includes many foods and beverages with varying sensory properties consumed alone or in combination with other food components. While the level of sugar and sweeteners within foods and perceived sweetness are correlated (15, 16), this relationship is weakened by the presence of other components in the food matrix that can sequester sweeteners, physically preventing them from binding to the sweet taste receptor, or can centrally inhibit sweetness perception, such as the suppression of sweetness when a sweetener is consumed with a bitter compound (12). Quantifying intake of sweet foods/beverages, sugars, and sweeteners provides insufficient information for determining the sweetness of the entire diet, because intake of sweet foods/beverages at a given meal may result in compensation for other sources of sweetness in the diet. It is unclear to what degree compensation for sweetness at subsequent eating events occurs, though some research suggests at least partial compensation (17). Therefore, the type of sweetness exposure evaluated in a study (i.e., total dietary sweetness, sweet food/beverage, sugar, or sweetener intake) has important implications for interpreting the results from these studies.

Before a conclusion on the association between dietary sweetness and body weight can be determined, it is necessary to determine the availability of the evidence in the published literature. This scoping review and evidence map was conducted to characterize the evidence on the association between dietary sweetness and body weight-related outcomes and/or energy intake to help identify future research priorities. The primary aim was to identify and map studies that investigate the association between total dietary sweetness and body weight-related outcomes and/or energy intake among healthy adults. As a secondary aim, this review aimed to identify and map the availability of studies that investigate sweet food/beverage, sugar, or sweetener intakes and body weight-related outcomes and/or energy intake.

Methods

A scoping review is a systematic search of the literature to determine the number and characteristics of the studies on a particular topic (18). The resulting eligible evidence can be synthesized as an evidence map to identify patterns or future research needs (19, 20). This review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) extension for scoping reviews (PRISMA-ScR) (21) (**Supplemental Checklist**) and followed the Joanna Briggs Institute (JBI) scoping review framework (18). The methodology used in this scoping review and evidence map was registered in the Open Science Framework (OSF) Registries (osf.io/my7pb) (22) and adopted The Center for Open Science's Transparency and Openness Promotion (TOP) Guidelines (23). Scoping reviews and evidence maps were not eligible for registration on the international prospective register of systematic reviews at the initiation of this work (i.e., PROSPERO). A systematic review and quantitative meta-analysis were not included as part of this review.

Systematic Search

Literature searches were conducted in PubMed, Cochrane Library, and Scopus on August 24, 2021. There were no restrictions on the publication period. Research presented in languages other than English was excluded. Search strings were developed and tested to ensure the collection of relevant studies. The search strings used to conduct the search are provided in **Supplemental Methods**. Results from the database searches were managed using EndNote X9.

Eligibility Criteria

The Population, Intervention/Exposure, Comparator, Outcome, and Study Design or Setting [PI(E)COS] criteria for inclusion in this review are included in **Table 1**.

<u>Population:</u> Studies conducted among adults (\geq 18 y) were considered suitable for inclusion. Studies conducted among child/adolescent populations (< 18 y) that track measures of body weight into adulthood (\geq 18 y) were included, but studies that focus solely on body weight outcomes in childhood were not considered. The primary population of interest was generally healthy populations; however, studies conducted among populations with diseases prevalent in Western populations (i.e., obesity, hypertension, hyperlipidemia, type II diabetes) were considered. Populations with chronic diseases (i.e., cancer, chronic kidney disease, chronic lung disease, heart disease, HIV/AIDS), metabolic disorders (i.e., irritable bowel syndrome, phenylketonuria, maple syrup urine disease), or clinical nutrient deficiencies were excluded. Studies among populations with sensory disorders, eating disorders, following bariatric surgery, or taking appetite suppressants or other anti-obesity medications or supplements (24-27) were also not considered. Studies among pregnant and lactating populations were excluded.

Interventions: The primary interventions/exposures of interest in this review were studies that investigate total dietary sweetness. However, due to the challenges associated with defining the sweetness of the diet, studies that investigated the frequency and/or quantity of foods/beverages that were described as sweet or sweetened or were conventionally considered to be sweet (i.e., food/beverages with high sweetness ratings in taste databases (28-30)) were also considered as supportive evidence. Examples of food/beverages that were conventionally considered sweet include, but are not limited to, sugar sweetened beverages (SSB), LCS beverages, cakes, pies, cookies, ice cream, pastries, candy, sweetened dairy products, chewing gums, fruit, and fruit juices. Studies on diets high in total sugars, added sugars, or LCS were also considered for inclusion, but studies on food sources that may be high in mono- or di-saccharides or LCS that are not designated as sweet were excluded (e.g., sandwich bread, condiments). In addition, studies that provide sweeteners without oral exposure (e.g., in encapsulated form) were not considered. Studies that investigated the effect of dietary patterns high or low in sugar and/or sweet foods/beverages that did not provide sufficient information to differentiate the level of sweetness between treatment

and control intervention/exposures and included other components of the dietary pattern that may influence body weight-related outcomes were excluded (e.g., Western versus Mediterranean dietary pattern, Western versus Dietary Approaches to Stop Hypertension (DASH) dietary pattern, high versus low glycemic dietary pattern). <u>Comparison</u>: To be included in the evidence map, all studies were required to include a low sweet comparator. Studies that compared results between treatments with

the same level of sweetness were excluded. Studies that did not have a comparator group and provided comparisons to baseline only were excluded due to the inability to control for confounding factors that may have occurred throughout the study.

<u>Outcomes:</u> Primary outcomes of interest were body weight (BW) and body mass index (BMI). Secondary outcomes were measures of energy intake and adiposity. Potential measures of adiposity included but were not limited to fat mass, body fat percentage, waist circumference (WC), and waist-to-hip ratio (W:H ratio). Studies that only included measurement of energy intake or a body weight-related outcome as part of safety monitoring, compliance, or measures of hydration status were excluded. Studies that reported food/beverage intake in weight or volume that could not be converted to energy intake were excluded.

<u>Study Design:</u> This evidence map included clinical trials, longitudinal cohorts, case-control studies, and cross-sectional studies published in peer-reviewed journals. Results from studies published as conference abstracts were excluded.

Screening and Selection

Screening of the search results was managed using Microsoft Access. Screening templates were developed and piloted prior to the literature search. Additional

duplicates beyond those identified in EndNote were identified based on title, author, and journal information and removed. Automated tools (summarized in **Supplemental Methods**) were developed to screen out studies based on the specified inclusion/exclusion criteria. Among the remaining publications, two reviewers (KAH, RR) independently determined if a publication met the inclusion/exclusion criteria based on the title and abstract. Publications that both reviewers determined to be ineligible were excluded. During the second round of screening, two reviewers (KAH, RR) determined if the screened publications meet the inclusion/exclusion criteria based on the entire research article with discrepancies resolved by a third reviewer if necessary (DJB or KMA). A PRISMA flow diagram was completed to outline the identification of relevant studies included in this review.

Data Extraction

Publications that reported results from multiple studies were disaggregated and classified as separate studies, and multiple publications from the same study were aggregated in order to determine the number of relevant studies (as opposed to the number of publications). These included studies that provided two different types of analyses [e.g., data from a RCT reported in two publications, data from a baseline and follow-up from the same longitudinal cohort]; the study was classified under the study design type of strongest quality of evidence (31) or relevance of the intervention/exposure and outcomes. Key study characteristics were extracted from eligible studies that investigated the effect of total dietary sweetness, sweet foods/beverages, sugars, or sweeteners on body weight-related outcomes by two reviewers (KAH, RR, DJB, LEO, or KMA). Relevant characteristics included study

design, description of sweetness intervention/exposure, description of comparator intervention/exposure, methods to evaluate sweetness, population characteristics (age, gender, body weight status, health status), sample size, study duration, and outcomes measured. Within the descriptions of the sweetness intervention/exposure and comparator, information on delivery vehicle (e.g., solid, liquid, total diet) and relative differences in energy content between the intervention/exposure and comparator were extracted. Information on how specific characteristics were extracted from the studies is provided in **Supplemental Methods**.

A list of relevant systematic reviews and meta-analyses identified in the literature search was tabulated. These publications were not analyzed further in the current evidence map, because each of these systematic reviews addressed relevant but different research questions, including different population, intervention/exposure, and comparator.

Hierarchy of Evidence

A hierarchy of evidence was created to classify relevant studies that investigated the association between sweetness interventions/exposures and body weight-related outcomes based on the sweetness interventions/exposures depicted in **Figure 1**: total dietary sweetness, sweet food/beverage, sugar, sweetener, or other sweet intake. Within each of these levels, a further distinction was made between the studies that measured the sweet taste of the diets, foods, and beverages using a sensory method (i.e., sweetness measured) and those where the sweet taste was assumed based on the contents of the intervention/exposure (i.e., sweetness assumed).

Of primary importance were the studies that evaluated the sweetness of the entire diet (i.e., total dietary sweetness), because no/minimal assumptions were needed to classify the level of sweetness of the intervention/exposure and comparator diets. Secondary importance was given to studies that investigated diets high in specific sweet foods/beverages [(i.e., foods/beverages described as sweet or conventionally considered sweet (28-30)], sugars [i.e., added and/or total sugars (1, 32)], or sweeteners (i.e., LCS or other energetic or non-energetic sweeteners used as substitutes or alternatives for sugar), because only one or limited elements of the diet that contribute sweetness were evaluated in these studies (i.e., individual sweet) foods/beverages, sugars, or sweeteners) opposed to sweetness from all dietary sources (i.e., total dietary sweetness). Interventions/exposures that were sweet but high in dietary bioactives (e.g., fruits, 100% fruit juices, sweetened dairy products), sweet oral exposures that were not swallowed (e.g., chewing gum, oral rinses), or additives that alter sweet taste perception (e.g., sweetness enhancers, sweetness antagonists) that could influence the outcomes of interest were classified as "other" sweet interventions/exposures.

In addition to the sweet interventions/exposures classified above, additional studies that investigated the association between sweet dietary patterns and body weight were identified in the search. A dietary pattern study incorporated multiple components of the diet to describe an individual's eating behavior. A sweet dietary pattern was either described as sweet by the authors or included sweet food/beverage components within the dietary pattern. These studies were included in the evidence map but considered separately and not further analyzed, because a low sweet

comparator of direct comparability to the intervention could not be confirmed in these studies.

Data Synthesis

Summary data on study counts were compiled in a tabular and graphical form and accompanied by a descriptive summary. The number of studies and population characteristics were summarized by sweetness intervention/exposure type (total dietary sweetness, sweet food/beverage, sugar, sweetener, or other sweet intake) for all included studies. Studies that evaluated multiple sweet dietary interventions/exposures (e.g., sugar and LCS intake, SSB, and fruit juice intake) were included in multiple levels within the hierarchy of evidence. Population characteristics of the study included age, sex, health status, and body weight status. Studies were further categorized as a clinical trial, longitudinal cohort, case-control study, cross-sectional study, or other study design (e.g., study design not specified, secondary or post-hoc analyses of a RCT in which the randomized intervention was not an eligible sweetness intervention/exposure). Information on sample size, study duration, and outcomes measured was tabulated for each sweetness intervention/exposure and study design. Heat maps were developed to graphically depict the number of studies by sweetness intervention/exposure, study design, and outcomes reported. All tables and heat maps were completed using Microsoft Excel and SAS software, Version 9.4.

Results

The study flow of this evidence map is outlined in **Figure 2**. A total of 36,779 publications (duplicates removed with EndNote) were recovered in the literature searches. Of these, 33,569 publications were excluded during the title and abstract

screening. An additional 2,377 publications were excluded during the full text review. Therefore, 833 publications summarizing results from 804 studies were determined to meet the inclusion criteria. These studies included 227 clinical trials (28.2% of all included studies), 81 longitudinal cohorts (10.1%), 4 case-control studies (0.5%), 284 cross-sectional studies (35.3%), and 19 studies of other design (2.4%) that investigated the association between total dietary sweetness, sweet food/beverage, sugar, sweetener, or other sweet exposure intake and a body weight-related outcome and/or energy intake (references included in **Supplemental References**). Ninety-two studies (11.4%) that investigated the association between a sweet dietary pattern and a body weight-related outcome and/or energy intake were identified in the literature search. In addition, 97 systematic reviews (12.1%) that addressed relevant but different research questions related to sweetness interventions/exposures and BW and/or energy intake were identified. A list of these studies is provided in Supplemental References.

Summary characteristics by sweetness intervention/exposure type are described below and presented in both the graphical and tabular format. Each category of sweetness intervention/exposure is described by study design, duration, the method used to evaluate sweetness, and outcomes reported. Summary population characteristics are provided in **Table 2**. Study duration and sample size by type of sweetness intervention/exposure are summarized in **Table 3** and **Table 4**, respectively. Heat maps of the number of studies identified by sweetness intervention/exposure and study design type for each outcome (BW/BMI, energy intake, fat mass/body fat percentage, and WC/W:H ratio) are displayed in **Figure 3**. Characteristics of each of the individual studies are included in the accompanying Microsoft Access database (osf.io/ckh9v/) (33).

Studies on total dietary sweetness intake

<u>Study Design:</u> A total of 7 studies (0.9% of all included studies) investigated associations between total dietary sweetness and a body weight-related outcome and/or energy intake. These studies were two clinical trials (34, 35), four cross-sectional studies (36-39), and one other study design (40).

Duration: One of the clinical trials controlled the sweetness of the diet for 24 hours (h) (34) and one controlled sweetness for 24 weeks (wk) with an additional 24 wk follow up after the sweetness intervention was completed (35). The cross-sectional studies were based on either 2, 24 h dietary recalls (36, 37, 39) or 4 weighed dietary records (38). One study of other design type used crowd-sourced MyFitnessPal data from an unspecified duration to evaluate the correlation between taste exposures and BMI (40).

Methods to evaluate sweetness: While the two clinical trials compared diets that were designed to be of different levels of sweetness, neither trial directly quantified the sweetness of the whole diet. Three of the four cross-sectional studies used taste databases to estimate the sensory profile of foods consumed within the diet. These databases were developed using modified versions of the Spectrum [™] method (41) of quantitative descriptive analysis to measure the sensory profile of 476 (36, 37) or >720 (39) foods commonly consumed foods/beverages. The other cross-sectional study had participants assign a predominant taste to each food consumed in a series of 4 food records to estimate total dietary sweetness exposure (38). The crowd-sourced study

used a machine learning algorithm to classify foods by taste from crowd sourced data, but did not measure the sweetness of the foods consumed (40).

Outcomes: BW, BMI, energy intake, and WC were measured in the clinical trial that exposed individuals to isoenergetic high and low sweetness diets for 24 wk (35). No difference in BW or BMI were observed after 24 wk of sweetness intervention and both diets achieved a similar reduction in energy intake, yet a larger decrease in WC was observed among participants consuming the low sweetness diet compared to the high sweetness diet. Energy intake was measured in the clinical trial ≤ 24 h in duration (34); no difference in ad libitum energy intake was observed between a predominantly sweet versus predominantly savory or mixed diet. BW and energy intake were measured in 3 of the 4 cross-sectional studies, while one study only measured energy intake (38). The only relevant outcome reported in the crowd-sourced study was BMI (40). Among these studies, individuals with obesity consumed less energy from sweet tasting foods compared to normal weight individuals [men (37); (40)] or consumed levels of sweet tasting foods/beverages that were not significantly different than normal weight individuals [women (37); (38, 39)]; no difference in percent of energy from sweet tasting foods was identified between individuals with normal weight were compared to individuals with overweight or obesity (36).

Studies on sweet food/beverage intake

Study Design: A total of 433 studies (53.9% of all included studies) investigated the associations between intake of sweet foods/beverages and a body weight-related outcome and/or energy intake. These studies included 135 clinical trials, 67 longitudinal cohorts, 3 case-control studies, 212 cross-sectional studies, and 16 studies of other study design. Within the clinical trials, 46 clinical trials (5.7% of all included studies) measured the sweetness of the foods/beverage exposures; no longitudinal cohorts, case-control studies, cross-sectional studies, or studies of other study design measured the sweetness of the exposures.

The studies within this level of evidence assessed exposure to one or more sweet foods/beverages. Among the studies that measured the sweetness of the exposure (n=46), the exposures included intakes of SSB (n=22 studies), sugar sweetened solid/semi-solid foods (n=19), LCS beverages (n=17), and LCS solid/semi-solid foods (n=8). Note that the sum of these exposures does not add to 46 studies, because some studies provided multiple exposures (e.g., a SSB arm and a LCS beverage arm). In studies that did not measure sweetness (n=387), sweetness exposures included intakes of SSB (n=279), sugar sweetened solid/semi-solid foods (n=149), LCS beverages (n=115), and LCS solid/semi-solid foods (n=5).

<u>Duration</u>: The clinical trials that measured the sweetness of the exposure were generally short in duration, with 40 of the 46 studies lasting ≤24 h in duration. The remaining 6 studies were >24 h to <4 wk in duration. Of the studies in which the sweetness of the exposure was assumed based on the foods/beverages consumed (n=89 studies), the clinical trials ranged from ≤24 h to <5 years (y) in duration, with most of the studies (n=53) lasting ≤24 h. The longitudinal cohort studies (n=67) ranged from 4 wk to ≥10 y in duration, with the majority of cohorts (n=39) lasting ≥5 y.

<u>Methods to evaluate sweetness:</u> Among the studies that measured sweetness of the foods/beverage exposures (n=46), the most common method used to measure sweetness was a visual analog scale (VAS) (n=27, 58.7% of studies that measured

sweetness). Other methods included categorical scales (n=3, 6.5%), sweet taste recognition (n=2, 4.3%), labeled magnitude scale (n=1, 2.2%), magnitude estimation (n=1, 2.2%), discrimination (n=1, 2.2%), or did not specify the method used (n=12, 26.1%). Note, one study used two measurement methods (42), thus numbers of studies do not total 46.

Outcomes: Due to the short duration of the clinical trials that measured sweetness, energy intake was the predominant outcome of interest measured in all 46 studies. BW and/or BMI was measured in 2 of the 46 studies (4.3%). This observation is consistent with the studies that assumed sweetness of the exposure. Energy intake was the most common outcome measured in the clinical trials both \leq and >24 h in duration. There were 27 that measured BW in the 36 clinical trials >24 h in duration. Other outcomes measured in clinical trials >24 h in duration included fat mass and/or body fat percentage (n=8, 22.2%) and WC and/or W:H ratio (n=13, 36.1%). Among the 67 longitudinal cohorts, 63 studies (94.0%) measured BW and/or BMI, 20 studies (29.9%) measured energy intake, 5 studies (7.5%) measured fat mass and/or body fat percentage, and 20 studies (29.9%) measured WC and/or W:H ratio. Among the 3 case-control studies, BW and/or BMI was reported in 3 studies, energy intake was reported in 1 study, and WC and/or W:H ratio was reported in 1 study. Among the 212 cross-sectional studies, 194 studies (91.5%) reported BW and/or BMI, 62 studies (29.2%) reported energy intake, 13 (6.1%) studies reported fat mass and/or body fat percentage, and 48 (22.6%) studies reported WC and/or W:H ratio. Among the 16 studies of other design type, all 16 studies (100%) reported BW and/or BMI, 5 studies

(31.3%) reported energy intake, 2 studies (12.5%) reported fat mass and/or body fat percentage, and 4 studies (25.0%) reported WC and/or W:H ratio.

For some of the studies (n=30, 6.9% of the 433 studies) that investigated intake of sweet foods/beverages (both measured and assumed sweetness), the sweetness exposure was also the outcome measurement (e.g., amount of sweet food consumed from a choice of sweet and non-sweet foods, ad libitum intake of sweet food). This measure of energy intake (measurement of ad libitum energy from sweet foods/beverages) is different from studies that investigate energy intake of subsequent meals after sweet food/beverage intake. These studies were included because they met the inclusion/exclusion criteria of this evidence map. However, the search terms were not designed to capture all studies that measured sweet food intake as an outcome; therefore, this may not be a comprehensive list of studies.

Studies on sugar intake

<u>Study Design:</u> A total of 129 studies (16.0% of all studies included) investigated the associations between sugar intake and a body weight-related outcome and/or energy intake. These studies were 44 clinical trials, 15 longitudinal cohorts, 68 crosssectional studies, and 2 of other study design.

<u>Duration:</u> The 44 clinical trials investigating the association between sugar intake and body weight-related outcomes and/or energy intake were all >24 h in duration, with most studies (n=28) investigating sugar intake for 4 wk to <0.5 y. The 15 cohort studies were all at least a year in duration: either 1 to <5 y (n=5), 5 to <10 y (n=5), or \geq 10 y (n=5) in duration. One study of other design type [a secondary analysis of a weight loss RCT with follow-up (43)], lasted 1 to <5 y; another study of other design type was a prepost intervention, but the only relevant analyses for this scoping review and evidence map were cross-sectional in nature (44). The remaining studies were all cross-sectional analyses.

<u>Methods to evaluate sweetness</u>: None of these studies measured the sweetness of the intervention/exposure.

<u>Outcomes:</u> BW and/or BMI were the most common outcomes measured across all study design types [measured in n=41 (93.2%) clinical trials, n=15 (100%) longitudinal cohorts, n=62 (91.2%) cross-sectional, n=2 (100%) other study designs], followed by energy intake [n=28 (63.6%), n=7 (46.7%), n=32 (47.1%), n=0 (0%), respectively], WC and/or W:H ratio [n=11 (25.0%), n=6 (40.0%), n=26 (38.2%), n=0 (0%), respectively], and fat mass and/or body fat percentage [n=15 (34.1%), n=2 (13.3%), n=4 (5.9%), n=0 (0%), respectively].

Studies on sweetener intake

<u>Study Design:</u> A total of 32 studies (4.0% of all included studies) investigated the associations between sweetener intake and a body weight-related outcome and/or energy intake. These studies were 9 clinical trials, 4 longitudinal cohorts, 1 case-control study, and 18 cross-sectional studies.

<u>Duration</u>: The clinical studies were either ≤ 24 h (n=4 studies), 4 wk to <0.5 y (n=4), or 0.5 to <1y (n=1) in duration. The longitudinal cohorts were either 1 to <5 y (n=3) or ≥ 10 y (n=1) in duration.

<u>Methods to evaluate sweetness:</u> One RCT measured the sweetness of sucralose, sucralose and maltodextrin, and water solutions using a VAS (45).The remaining 31 studies did not measure the sweetness of the intervention/exposure.

<u>Outcomes:</u> BW and/or BMI were measured in all clinical trials >24 h in duration; clinical trials \leq 24 h in duration measured energy intake only. Among the clinical trials >24 h in duration, energy intake was measured in 1 study (11.1%), fat mass and/or body fat percentage was measured in 3 studies (33.3%), and WC and/or W:H ratio was measured in 2 studies (22.2%). BW and/or BMI was measured in all longitudinal cohorts; energy intake (n=2, 50.0%) and WC and/or W:H ratio (n=1, 25.0%) was also measured in select cohorts. Only BW and/or BMI was reported in the case-control study. Among the cross-sectional studies, BW and/or BMI, energy intake, and WC and/or W:H ratio, were reported in 18 (100%), 6 (33.3%), and 3 studies (16.7%), respectively.

Studies on other sweet intake

(n=2)

<u>Study Design:</u> A total of 127 studies (15.8% of all included studies) investigated the association between other sweet dietary exposures and a body weight-related outcome and/or energy intake. These studies included 49 clinical trials, 22 longitudinal cohorts, 50 cross-sectional studies, and 6 other study designs. The other sweet exposures included, but were not limited to, flavored/sweetened dairy products, fruit, fruit juices, chewing gum, and sweetness enhancers (e.g., miraculin).

<u>Duration:</u> All clinical trials investigating other sweetness exposures were <0.5 y in duration, with the bulk of studies (n=36) lasting \leq 24 h. The longitudinal cohort studies ranged from 0.5 y to \geq 10 y in duration, most frequently ranging from 1 to <5 y (n=8). The other studies of other design were either 1 to <10 y in duration (n=4) or cross-sectional

<u>Methods to evaluate sweetness:</u> The sweetness of the exposure was measured in 10 clinical trials (20.4% of the clinical trials): 4 studies used VAS, 2 used categorical scales, 1 used a labeled magnitude scale, and 3 did not specify the method used to evaluate sweetness.

<u>Outcomes:</u> Energy intake was the most common outcome measured in clinical trials. It was the only outcome reported in clinical trials \leq 24 h in duration and reported in 10 of the 13 clinical trials \geq 24 h in duration. BW and/or BMI, fat mass and/or body fat percentage, and WC and/or W:H ratio was reported in 12 (92.3%), 9 (69.2%), and 6 (46.2%) clinical trials \geq 24 h in duration. BW and/or BMI was most commonly reported in longitudinal cohorts (n=20, 90.9%), cross-sectional studies (n=46, 92.0%), and other study designs (n=6, 100%). Fat mass and/or body fat percentage (n=1, 4.5%; n=7, 14.0%; n=0, 0%; respectively) and WC and/or W:H ratio were also measured in select longitudinal cohorts, cross-sectional studies, and other study designs (n=5, 22.7%; n=13, 26%; n=2, 33.3%; respectively).

Evidence Gaps

The heat maps of the number of studies identified by sweetness intervention/exposure and study design type for each body weight-related outcome displayed in Figure 3 provide a graphical representation of the available evidence on dietary sweetness and body weightrelated outcomes. These heat maps were used to determine where evidence gaps exist.

Few studies (n=7) investigated associations between total dietary sweetness and a body weight-related outcome and/or energy intake, the primary interest of this scoping review. The bulk of the available evidence on sweetness exposures focuses on the intake of individual foods/beverages assumed to be sweet or the level of sugars or sweeteners. In addition, these studies were predominantly cross-sectional or short in duration (\leq 24 h) (34, 36-40) except for

one clinical trial that studied sweetness exposures for 24 wk (35). More research investigating the association between total dietary sweetness and body weight, particularly in the form of clinical trials and/or cohort trials of long duration, are needed in order to draw conclusions regarding the effect of dietary sweetness on body weight.

Not only are there a limited number of studies that evaluated the sweetness of the total diet or individual foods/beverages, but there are many and variable methods used in the studies that do measure sweetness. Taste databases developed using a modified Spectrum[™] approach to determine the sensory attributes of different commonly consumed foods (36, 37, 39) allow for systematic evaluations of total dietary sweetness exposure. The taste databases developed to date are based on the foods consumed within a specific country, and thus are country specific. Current databases are developed in Australia, France, Netherlands, and Malaysia; consideration of cuisines consumed in additional countries would be of value. Utilizing the currently available taste databases to determine associations between sweet taste exposure and body weight status are important research priorities. Such taste databases may also be adapted for use in clinical trials to evaluate dietary sweetness, but direct measures of sweetness of the foods/beverages consumed within a diet by the specific study sample may be more applicable for clinical trials that have been specifically designed to measure the effect of differences in dietary sweetness on body weight.

Discussion

The goal of this scoping review and evidence map was to summarize the published evidence on dietary sweetness exposure and body weight-related outcomes and/or energy intake. While 225 clinical trials and 383 observational studies have

investigated intake of various dietary sources of sweetness on body weight-related outcomes and/or energy intake, only seven studies evaluated the sweetness of the entire diet (34-40). Among these seven studies designed to compare high versus low total dietary sweetness intake, there is little evidence to suggest that dietary sweetness is associated with body weight and/or energy intake. In the one long-term clinical trial that exposed individuals to an isoenergetic high and low sweetness diet (35), no effect on body weight or BMI were observed while beneficial changes to WC were observed among participants consuming the low sweetness diet compared to the high sweetness diet. In the 24 h clinical trial, no difference in ad libitum energy intake was observed between a predominantly sweet versus predominantly savory or mixed diet (34). Among the cross-sectional studies and study using crowd-sourced data, individuals with overweight or obesity consumed less energy or similar amounts of energy from sweet tasting foods compared to normal weight individuals (36-40). Collectively, these results do not suggest that high dietary sweetness adversely affects body weight, but further systematic evaluation of study quality and risk of bias of these studies is required.

The limited availability of evidence on total dietary sweetness may be due to the many challenges associated with determining the sweetness of the entire diet. Sweetness is a basic taste quality that can be measured in individual foods and beverages using a variety of methods (12). The sweetness of the diet, however, is determined by the source (e.g., sugars, LCS), intensity (e.g., concentration), food matrix (e.g., solid, semi-solid, liquid), amount (e.g., weight, volume), frequency (e.g., times per day), and duration (e.g., time per consumption event) of each individual dietary exposure. Therefore, the complex nature of the diet makes it difficult to characterize the taste of an entire diet. While there is not a standardized method to determine total dietary sweetness (12), development of taste databases has made progress towards evaluating total dietary taste exposures. Taste databases have been developed based on food consumed in Australia (28), France (29), Netherlands (46), and Malaysia (46). The Australian and Dutch taste databases have been used to evaluate an association between total dietary sweetness exposure and body weight at the time of the literature search (36, 37, 39). Since the search was conducted for the current review, a similar analysis (47) of the association between taste exposures, dietary intake, and body weight was published utilizing the food consumption data from the follow-up Singapore Multi-Ethnic Cohort Phase 2 (MEC2) study in combination with the Dutch and Malaysian taste databases (46). Further utilization of currently available taste databases could address gaps in evidence regarding the association between total dietary sweetness and body weight, but development of population-specific taste databases may be necessary to evaluate sweetness exposures in other population-level analyses.

The provision of sweetness with little to no energy, as can be achieved with LCS, further complicates the relationship between sweetness exposure and body weight. The focus of this review was total dietary sweetness, not specific sources of sweetness. However, LCS are unique from most sugars in that they contribute little to no energy, an important characteristic when body weight and energy intake are the outcomes of interest. In addition, LCS are not just inert sweetness vehicles; they bind to taste 1 receptor member 2 / taste 1 receptor member 3 (T1R2/T1R3) G-protein coupled sweet taste receptor heterodimer located throughout the gastrointestinal track, pancreas, and hypothalamus (48-50). Each LCS has a unique chemical structure, which influences

how it binds to the T1R2/T1R3 heterodimer (51-53) and its metabolic fate (54); both of which may influence the post-ingestive effects of LCS intake. Recent systematic reviews of RCTs suggest that the substitution of sugar with LCS may be beneficial for body weight (55-57), yet evidence from observational studies suggest LCS may have either no effect (58, 59) or adverse effects on body weight indices (55, 58, 60). While LCS may be a valuable tool to help reduce total sugar intake while maintaining dietary palatability, their post-ingestive effects may influence their efficacy for facilitating body weight maintenance and should not be ignored.

Most of the studies identified that measured the sweetness of individual foods/beverages consumed within the diet were not designed to measure body weight. These studies were predominantly laboratory-based interventions, acute in duration, and measured energy intake only. Laboratory-based interventions are tightly controlled and have a high degree of internal validity, but lack external validity due to other external factors that influence energy intake while free-living (61). While long-term changes in energy balance may influence body weight, intraindividual variation in daily energy intake deviates widely (62, 63), thus energy intake at a single meal or a single day is a poor predictor of body weight. Longer term studies of usual energy intake, capturing day-to-day variations, are needed to provide additional insight regarding the chronic association between sweetness exposure and body weight changes.

A product of this review was a database of published literature which is publicly available for use by the scientific community to further investigate this body of evidence and to highlight gaps in knowledge regarding dietary sweetness and body weight (osf.io/my7pb). The search terms used to identify relevant publications were piloted to

ensure relevant studies would be captured, a strength of this review. Yet, the search was restricted to publications in English, and some studies may have been missed because of different key terms used (e.g., studies where the sweetness exposure was also the outcome measurement; studies that assessed foods/beverages that were not conventionally considered sweet and provided insufficient information on the level of sweetness). Additionally, some excluded studies measured total dietary sweetness but did not meet at least one other component of the PI(E)COS criteria; in particular, studies that looked at dietary sweetness but did not report a body weight- related outcome and studies that looked at sweet preference or sensitivity but not sweet taste exposure. For example, one cross-sectional study determined total dietary sweetness exposure based on 7-days of food records, and reported a correlation between the percent of calories from sweet foods with macronutrient composition of the diet, but did not report energy intake (64). Another study analyzed sweet preference (not sweet food/beverage intake) but otherwise met the inclusion criteria (65). Only published evidence was included in this evidence map and the authors were not contacted to obtain additional information. It is possible that some excluded studies may have relevant data that is either unpublished or published in papers that were not identified in the search.

This scoping review and evidence map identified evidence gaps in the published literature based primarily on study count and is not a critical appraisal of the available evidence. It is outside the scope of the scoping review/evidence map methodology to critically appraise study quality or risk of bias. The included evidence was ordered based on type of sweetness exposure and study design type, but no further judgments of study quality were made. This would be required before conclusions based on the

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evidence available can be drawn. In addition, quantitative analyses (e.g., metaanalyses) were not undertaken. There is no agreed upon minimum number of studies that are needed to conduct a quantitative meta-analysis (66); Cochrane states that a minimum of two studies are needed, with the caveat that those studies should have similar methods and results that can be meaningfully pooled (67). While 7 studies (2) clinical trials, 4 cross-sectional studies, and 1 of other study design) assessed the association between total dietary sweetness and a body weight-related outcome, further critical evaluation of this literature is necessary to determine if these studies can be systematically combined to quantify this association. The sweet exposures detailed in the studies included in the database were systematically categorized as either total dietary sweetness, sweet foods/beverages, sugar, sweetener, or other sweet exposure. However, some exposures could be categorized in multiple categories [e.g., high sucrose diets (sugar intake) achieved by adding SSB to the diet (sweet food/beverage intake)]. While the hierarchy based on sweetness exposures used to classify the identified studies was appropriate for the current review, it may need to be adapted for subsequent analyses, depending on the research question. Further evaluation of the systematic reviews identified in this literature search was outside of the scope of the current review. A systematic review of the identified systematic reviews could help further understand the relationship between sweetness interventions/exposures and body weight-related outcomes.

The focus of this scoping review and evidence map was the effect of sweetness on body weight. However, sweetness is only one dimension of taste and one component that determines the palatability of foods and the diet. Sweetness is rarely

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consumed in isolation from other sensory properties; it tends to cluster with sour (e.g., fruit, sweetened yogurt) or fat (e.g., pastry, cake, biscuits, ice cream) (36, 37). These other sensory properties also influence palatability (68). Thus, a high sweetness diet alone may not be prone to excess consumption, but instead a highly palatable diet, which may include sweetness, may influence food choice and body weight (69). Other sensory properties and the palatability of the diet were not investigated in this evidence map but should be considered when exploring whether sensory properties of the diet influence dietary habits and body weight.

Conclusion

While there is a breadth of evidence from studies that investigate sweet food/beverage, sugar, and sweetener intake and body weight, there is limited evidence on the association between total dietary sweetness and body weight. Utilization of the open access database of studies that investigate associations between sweetness exposures and body weight-related outcomes and/or energy intake developed as part of this evidence map can provide additional insights into this relationship.

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Data Sharing

Data described in the manuscript will be made publicly and freely available without restriction at https://osf.io/ckh9v/.

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Table 1. PI(E)COS criteria to identify studies that investigated the association

between dietary sweetness and body weight related-outcomes and/or energy

Criteria	Inclusion Criteria	Exclusion Criteria
Population	-Adults (≥ 18 y) -Generally healthy or with disease prevalent among Western populations ¹	-Children/adolescent populations that do not track body weight into adulthood -Populations with eating disorders or
	- Children/adolescent populations that track body weight into adulthood	sensory disorders -Bariatric surgery patients -Populations taking medications known to affect sensory perception, appetite, or body weight ² -Populations with chronic diseases ³ , metabolic disorders ⁴ , or clinical putrient deficiencies
		-Pregnant or breast-feeding populations
Intervention/	-Primary: high total dietary	-Sweeteners delivered without oral
Exposures	sweetness	exposure
	-Secondary: more frequent or	-Foods high in sugars, LCS, or SSB
	nigner intake of sweet	that are not considered sweet"
	Tood/beverage consumption	
	- Terliary: higher intake of	
Comparison	Drimany: Jow total diotary	Comparisons to control with the
Companson	-Filling y. low total dietally	same level of sweetness ⁷
	-Secondary: less frequent or lower	-Comparison to baseline only (i.e.
	intake of sweet food/beverage	no control group)
	consumption	-Dietary patterns low in sugars LCS
	-Secondary: lower intake of	or SSB that are not considered low
	total/added sugars or sweeteners	sweet ⁸
Outcomes	-Primary: body weight, BMI	-Body weight related outcome for
	-Secondary: energy intake, fat	safety monitoring, compliance, or
	mass, body fat %, WC, W:H ratio	hydration.
		-Food/beverage intake reported in
	>	weight or volume that cannot be
		converted to energy intake
Study	-Observational studies (i.e., cross-	-Case studies, animal trials, <i>in vitro</i>
Design/	sectional, longitudinal cohort, case-	trials, narrative reviews, opinion
Setting	control), clinical trials, systematic	articles, position papers, protocols
)	reviews, meta-analyses	(i.e., no results reported), ecological

intake among adults

Criteria Inclusion Criteria

Exclusion Criteria

analysis, descriptive analysis, conference abstracts

BMI, body mass index; LCS, low calorie sweeteners; PI(E)COS, Populations,

Interventions/Exposures, Comparators, Outcomes, and Study Designs or Settings;

SSB, sugar-sweetened beverages; WC, waist circumference; W:H, waist:hip

¹ i.e., obesity, hypertension, hyperlipidemia, type II diabetes

² e.g., Acetazolamide, Amiodarone, Benzphetamine, Captopril, Cisplatin, Diethylpropion

Ephedrine, Eszopiclone, Liraglutide, Lithium, Lorcaserin, Maribavir, Naltrexone-

Bupropion, Orlistat, Phendimetrazine, Phentermine, Phenylpropanolamine,

Procainamide, Terbenafine, Topiramate (24-27)

³ i.e., cancer, chronic kidney disease, chronic lung disease, heart disease, HIV/AIDS

⁴ i.e., irritable bowel syndrome, phenylketonuria, maple syrup urine disease

⁵ i.e., intravenous, encapsulated

⁶ e.g., savory sauces or dishes

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⁷ Interventions/exposures with the same level of sweetness. If a study compared two sugars (i.e., glucose versus fructose, sucrose versus high fructose corn syrup) but did not provide information on the sweetness intensity, the comparisons were considered to be the same sweetness and excluded.

⁸ i.e., Mediterranean dietary pattern, Dietary Approaches to Stop Hypertension (DASH) dietary pattern, low glycemic dietary pattern

	Sweetness Intervention/Exposure ¹					
	Total dietary sweetness	Sweet food/bev, measured ²	Sweet food/bev, assumed ³	Sugars ⁴	Sweeteners ⁴	Other⁵
	(n= 7)	(n= 46)	(n= 387)	(n= 129)	(n= 32)	(n= 127)
			n (%)	6	Y	
Population Characteristic ⁷				QY		
Age (years)						
<18	0 (0)	0 (0)	11 (1.8)	3 (0.5)	0 (0)	1 (0.2)
18-64	2 (0.3)	41 (6.7)	200 (32.5)	56 (9.1)	16 (2.6)	71 (11.5)
≥65	0 (0)	0 (0)	0 (0)	3 (0.5)	0 (0)	0 (0)
<18-64	0 (0)	0 (0)	8 (1.3)	4 (0.7)	0 (0)	2 (0.3)
18- ≥ 65 +	5 (0.8)	1 (0.2)	145 (23.6)	55 (8.9)	13 (2.1)	45 (7.3)
<18 - ≥ 65 +	0 (0)	0 (0)	14 (2.3)	6 (1.0)	2 (0.3)	4 (0.7)
Age not specified	0 (0)	4 (0.7)	9 (1.5)	2 (0.3)	1 (0.2)	4 (0.7)
Body Weight Status ⁸						
All BMIs	2 (0.3)	0 (0)	165 (26.8)	45 (7.3)	15 (2.4)	50 (8.1)
Normal weight - Obese	2 (0.3)	1 (0.2)	46 (7.5)	11 (1.8)	5 (0.8)	19 (3.1)
Normal weight - Overweight	0 (0)	14 (2.3)	27 (4.4)	17 (2.8)	2 (0.3)	5 (0.8)
Normal weight	1 (0.2)	20 (3.3)	39 (6.3)	8 (1.3)	5 (0.8)	23 (3.7)
Overweight	0 (0)	2 (0.3)	21 (3.4)	10 (1.6)	0 (0)	3 (0.5)
Overweight - Obese	1 (0.2)	> 0 (0)	29 (4.7)	10 (1.6)	0 (0)	5 (0.8)
Obese	0 (0)	0 (0)	14 (2.3)	4 (0.7)	3 (0.5)	6 (1.0)
Other ⁹	1 (0.2)	5 (0.8)	16 (2.6)	7 (1.1)	1 (0.2)	9 (1.5)
Not specified	0 (0)	4 (0.7)	30 (4.9)	17 (2.8)	1 (0.2)	7 (1.1)
Gender	N'					
Females	0 (0)	10 (1.6)	56 (9.1)	15 (2.4)	2 (0.3)	23 (3.7)
Males	0 (0)	12 (2.0)	32 (5.2)	14 (2.3)	1 (0.2)	15 (2.4)
Males/Females	7 (1.1)	24 (3.9)	294 (47.8)	97 (15.8)	29 (4.7)	88 (14.3)
\bigcirc						

Table 2. Summary population characteristics of studies that investigated the association between dietary sweetness and a body weight related outcomes among adults by sweetness exposure (615 studies)

Not specified	0 (0)	0 (0)	5 (0.8)	3 (0.5)	0 (0)	1 (0.2)
Health Status ^{10, 11} Generally Healthy ¹² Prediabetes/Diabetes Prehypertensive/ Hypertensive	7 (1.1) 0 (0) 0 (0)	46 (7.5) 0 (0) 0 (0)	376 (61.1) 7 (1.1) 1 (0.2)	106 (17.2) 18 (2.9) 0 (0)	27 (4.4) 4 (0.7) 0 (0)	125 (20.3) 1 (0.2) 0 (0)
Hyperlipidemia Other ¹³	0 (0) 0 (0)	0 (0) 0 (0)	0 (0) 3 (0.5)	2 (0.3) 4 (0.7)	0 (0) 1 (0.2)	1 (0.2) 0 (0)
			AMA	SCRIF		

BMI, body mass index; n, study count

¹ See Figure 1 and "Hierarchy of Evidence" for definitions of each sweetness exposure type. The sum of all of the sweetness intervention/exposure categories does not sum to the total number of studies identified (n=804), because some studies analyzed multiple sweetness interventions/exposures.

² Sweet foods/beverages, sweetness of foods/beverages measured

³ Sweet foods/beverages, sweetness of foods/beverages assumed

⁴ None of the studies that investigated these exposures measured the sweetness of the intervention/exposure; therefore, sweetness was assumed.

⁵ Includes studies where the sweetness of the intervention/exposure was measured or assumed.

⁶ Number of studies and percentage of 615 included studies. Percentages within a characteristic may not sum to 100%, because some studies investigated multiple sweetness exposures (e.g., one study that investigated both sugars and sweeteners).

⁷ Information on how this population characteristic data was extracted from the included studies is summarized in Supplementary Data IV.

⁸ Body weight status of population included in relevant analyses. This information was based on the inclusion criteria, if provided, or the summary population characteristics; population characteristics at baseline were used for longitudinal studies. If the inclusion criteria were not provided, then the BMI was based on range, prevalence of BMI categories,

mean/median BMI of the population, or body weight status as described by the study's authors. If prevalence of BMI categories (e.g., 25% of sample was overweight or obese) did not add up to 100%, then it was assumed that all BMI categories were represented in the sample.

⁹ Other body weight statuses including normal weight and obese, underweight – overweight, underweight – normal weight.

¹⁰ Population or subgroup of the population reported to have a disease prevalent among Western populations (i.e., hypertension, hyperlipidemia, type II diabetes) as defined by the study author. This diagnosis was not based on biomarkers that may be reported in the manuscript.

¹¹ Not all study counts add to the sum of the number of studies per sweetness intervention/exposure for this characteristic. This is because some studies include multiple categories (e.g., one study that investigated sugar intake included individuals with both diabetes and hyperlipidemia).

¹² Generally healthy as stated by study authors or the health status of the population was not explicitly stated to be diseased.

¹³ Population or subgroup of the population reported to have another disease state that was not considered to be an excluded population (e.g., NAFLD, morbid obesity, kidney transplant patients, arthritis).

Table 3. Study duration of clinical trials and longitudinal cohorts that investigated the association between dietary sweetness and a body weight related outcomes among adults by sweetness exposure (227 clinical trials and 81 longitudinal cohorts)

	Sweetness Exposure ¹					
	Total dietary Sweetness	Sweet food/bev, measured ²	Sweet food/bev, assumed ³	Sugars ⁴	Sweeteners ⁴	Other ⁵
			n (%) ⁶	4	$\boldsymbol{\wedge}$	
Clinical trials	n= 2	n= 46	n= 89	n= 44	n= 9	n= 49
≤24 h	1 (0.4)	40 (17.6)	53 (23.3)	0 (0)	4 (1.8)	36 (15.9)
>24 h - <4 wk	0 (0)	6 (2.6)	11 (4.8)	12 (5.3)	0 (0)	3 (1.3)
4 wk - <0.5 y	1 (0.4)	0 (0)	11 (4.8)	28 (12.3)	4 (1.8)	10 (4.4)
0.5 y - <1 y	0 (0)	0 (0)	9 (4.0)	4 (1.8)	1 (0.4)	0 (0)
1 y - <5 y	0 (0)	0 (0)	5 (2.2)	0 (0)	0 (0)	0 (0)
Longitudinal cohort	n=0	n=0	n=67	n=15	n=4	n=22
4 wk - <0.5 y			3 (3.7)	0 (0)	0 (0)	0 (0)
0.5 y - <1 y			4 (4.9)	0 (0)	0 (0)	3 (3.7)
1 y - <5 y			21 (25.9)	5 (6.2)	3 (3.7)	8 (9.9)
5 y - <10 y			19 (23.5)	5 (6.2)	0 (0)	5 (6.2)
10 y			20 (24.7)	5 (6.2)	1 (1.2)	6 (7.4)

h, hour(s); n, study count; wk, week(s); y, year(s)

¹ See Figure 1 and "Hierarchy of Evidence" for definitions of each sweetness exposure type. The sum of all of the sweetness intervention/exposure categories does not sum to the total number of studies identified (n=804), because some studies analyzed multiple sweetness interventions/exposures.

² Sweet foods/beverages, sweetness of foods/beverages measured

³ Sweet foods/beverages, sweetness of foods/beverages assumed

⁴ None of the studies that investigated these exposures measured the sweetness of the intervention/exposure; therefore, sweetness was assumed.

⁵ Includes studies where the sweetness of the intervention/exposure was measured or assumed.

⁶ Number of studies and percentage of 227 clinical trials and 81 longitudinal cohorts, respectively. Percentages within a study design type may not sum to 100%, because some studies investigated multiple sweetness exposures (e.g., one MAN study that investigated both sugars and sweeteners).

	Sweetness Intervention/Exposure ¹					
	Total dietary Sweetness	Sweet food/bev, measured ²	Sweet food/bev, assumed ³	Sugars ⁴	Sweeteners ⁴	Other ⁵
			n (%) ⁶			
Clinical trials	n= 2	n= 46	n= 89	n= 44	n= 9	n= 49
≤10	0 (0)	4 (1.8)	7 (3.1)	6 (2.6)	1 (0.4)	6 (2.6)
11-20	0 (0)	16 (7.0)	17 (7.5)	13 (5.7)	3 (1.3)	9 (4.0)
21-50	1 (0.4)	21 (9.3)	30 (13.2)	12 (5.3)	1 (0.4)	16 (7.0)
51-100	0 (0)	5 (2.2)	17 (7.5)	10 (4.4)	2 (0.9)	12 (5.3)
101-500	1 (0.4)	0 (0)	17 (7.5)	3 (1.3)	2 (0.9)	6 (2.6)
501-1,000	0 (0)	0 (0)	1 (0.4)	0 (0)	0 (0)	0 (0)
Longitudinal Cohort	n=0	n=0	n=67	→ n=15	n=4	n=22
51-100			2 (2.5)	0 (0)	0 (0)	1 (1.2)
101-500			13 (16)	1 (1.2)	2 (2.5)	3 (3.7)
501-1,000			5 (6.2)	0 (0)	0 (0)	0 (0)
1,001-5,000			18 (22.2)	12 (14.8)	1 (1.2)	4 (4.9)
5,001-10,000			10 (12.3)	0 (0)	0 (0)	3 (3.7)
10,001-20,000			5 (6.2)	1 (1.2)	0 (0)	3 (3.7)
≥20,001			14 (17.3)	1 (1.2)	1 (1.2)	8 (9.9)
Case Control	n=0	n=0	n=3	n=0	n=1	n=0
51-100			0 (0)		1 (25.0)	
101-500			2 (50.0)		0 (0)	
501-1,000		\mathbf{N}	0 (0)		0 (0)	
1,001-5,000		$\langle \rangle$	0 (0)		0 (0)	
5,001-10,000			0 (0)		0 (0)	
10,001-20,000		71	0 (0)		0 (0)	
≥20,001		Y	1 (25.0)		0 (0)	
Cross-sectional	n=4	n=0	n=212	n=68	n=18	n=50
21-50	0 (0)		4 (1.4)	1 (0.4)	0 (0)	1 (0.4)
	OF					

Table 4. Sample size of studies that investigated the association between dietary sweetness and a body weight related outcomes among adults by sweetness exposure and study design type (615 studies)

51-100	1 (0.4)		6 (2.1)	3 (1.1)	1 (0.4)	1 (0.4)
101-500	0 (0)		57 (20.1)	20 (7.0)	6 (2.1)	15 (5.3)
501-1,000	1 (0.4)		25 (8.8)	5 (1.8)	1 (0.4)	4 (1.4)
1,001-5,000	1 (0.4)		55 (19.4)	24 (8.5)	5 (1.8)	15 (5.3)
5,001-10,000	1 (0.4)		22 (7.7)	5 (1.8)	0 (0)	3 (1.1)
10,001-20,000	0 (0)		11 (3.9)	6 (2.1)	3 (1.1)	4 (1.4)
≥20,001	0 (0)		31 (10.9)	4 (1.4)	2 (0.7)	7 (2.5)
Not specified	0 (0)		1 (0.4)	0 (0)	0 (0)	0 (0)
Other Study Design ⁷	n=1	n=0	n=16	n=2	n=0	n=6
21-50	0 (0)		0 (0)	2 (10.5)		1 (5.3)
51-100	0 (0)		3 (15.8)	0 (0)		1 (5.3)
101-500	0 (0)		7 (36.8)	0 (0)		1 (5.3)
501-1,000	0 (0)		1 (5.3)	0 (0)		0 (0)
1,001-5,000	0 (0)		3 (15.8)	0 (0)		2 (10.5)
5,001-10,000	0 (0)		0 (0)	0 (0)		0 (0)
10,001-20,000	0 (0)		1 (5.3)	0 (0)		1 (5.3)
≥20,001	1 (5.3)		1 (5.3)	0 (0)		0 (0)
n study count						

n, study count

¹ See Figure 1 and "Hierarchy of Evidence" for definitions of each sweetness exposure type. The sum of all of the

sweetness exposure categories does not add to the total number of studies identified, because some studies analyzed

multiple sweetness interventions/exposures. RICHAL ² Sweet foods/beverages, sweetness of foods/beverages measured

³ Sweet foods/beverages, sweetness of foods/beverages assumed

⁴ None of the studies that investigated these exposures measured the sweetness of the intervention/exposure; therefore, sweetness was assumed.

⁵ Includes studies where the sweetness of the intervention/exposure was measured or assumed

⁶ Number of studies and percentage of 227 clinical trials, 81 longitudinal cohorts, 4 case control studies, 284 crosssectional studies, and 19 studies of other study design types, respectively. Percentages within a study design type may not sum to 100%, because some studies investigated multiple sweetness exposures (e.g., one study that investigated both sugars and sweeteners).

⁷ e.g., study design not specified, secondary analyses of RCT in which the primary intervention was not an included sweetness exposure

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Figure 1. Categories and definitions of dietary sweetness exposures included in the

scoping review and evidence map

No legend

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Figure 2. PRISMA Flow Diagram of studies that investigated the association between dietary sweetness and a body weight related outcomes among adults included in the scoping review and evidence map

Legend:

¹Duplicates removed not captured by EndNote.

² Automation tools described in Supplemental Methods.

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Figure 3. Heat Maps of specific outcomes reported in studies that investigated the association between dietary sweetness and a body weight-related outcomes among adults by study design type and sweetness exposure

Legend: A, number of studies that measured BW and/or BMI; B, number of studies that measured energy intake; C, number of studies that measured fat mass and/or body fat percentage; D, number of studies that measured WC and/or W:H ratio.

The different colors represent the different number of studies that report each outcome by study design type and sweetness exposure.

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