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Original Research Article

The Sweet Tooth Trial: A Parallel Randomized Controlled Trial Investigating the Effects of A 6-Month Low, Regular, or High Dietary Sweet Taste Exposure on Sweet Taste Liking, and Various Outcomes Related to Food Intake and Weight Status

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A B S T R A C T

Background: Public health organizations currently recommend lowering the consumption of sweet-tasting foods, on the assumption that a lower exposure to sweet-tasting foods lowers preferences for sweet taste, decreasing sugar and energy intake, and aiding obesity prevention. However, empirical data supporting this narrative are lacking.

Objectives: The objective of this study was to assess the effects of a 6-mo low, regular, and high dietary sweet taste exposure on liking for sweet taste.

Methods: In a parallel-groups randomized controlled intervention study, 180 healthy adults (female/male: 123/57; aged: 35 ± 15 y; body mass index (in kg/m^2): 23 ± 3) were provided with dietary advice and ~50% daily energy needs for 6 mo, where 7% (low sweet taste exposure, $n = 61$), 35% (regular sweet taste exposure, $n = 60$), or 80% (high sweet taste exposure, $n = 59$) provided foods and beverages were sweet tasting from sugars, low-calorie sweeteners, fruits and dairy. Before, at 6 mo, and at a 4-mo follow-up, sweet taste liking, sweet taste intensity perception, food choice, energy intake, body weight, markers for diabetes and cardiovascular disease, and adverse events were assessed.

Results: Sweet food consumption varied between groups over the intervention period (self-reported dietary measures (percentage energy, percentage weight): smallest $\chi^2(16) = 59.4$, $P < 0.001$; urinary markers for sucrose, sucralose, and saccharin: smallest $\chi^2(10) = 21.0$, $P = 0.02$). However, from baseline to month 6, no differences between groups were found in sweet taste liking ($\chi^2(40) = 37.9$, $P = 0.56$), sweet taste intensity perception ($\chi^2(40) = 20.7$, $P = 0.99$), sweet food choice ($\chi^2(10) = 10.1$, $P = 0.43$), energy intake ($\chi^2(10) = 12.7$, $P = 0.24$), body weight ($\chi^2(10) = 14.3$, $P = 0.16$), markers for diabetes and cardiovascular disease (largest $\chi^2(10) = 15.9$, $P = 0.10$) or adverse events. After the intervention, participants also spontaneously returned to baseline levels of sweet food intake.

Conclusions: In the current trial, altering exposure to sweet-tasting foods did not change sweet taste liking, nor other outcomes. These results do not support public health advice to reduce exposure to sweet-tasting foods, independent of other relevant factors such as energy density and food form. This trial was registered at clinicaltrials.gov as NCT04497974.

Keywords: humans, diet intervention, sweet taste, preference, energy intake, body weight

Introduction

Humans love sweet taste [1]. However, this innate liking may result in excessive sugar consumption, high energy intake, and related noncommunicable disease risk [2]. Many public health agencies, including the WHO, accordingly advise reducing dietary exposure to sweet taste [3–7]: WHO (2023): "*People should reduce the sweetness of the diet altogether*" [7]. The rationale for this advice is that frequent exposure to sweet taste, regardless of whether the sweet taste stems from sugar, low-calorie sweeteners (LCS), or natural sources, increases liking, leading to greater sugar and calorie intake and, eventually, a higher body weight. Some public health agencies offer this

Abbreviations: CVD, cardiovascular disease; HSE, high sweet taste exposure; LCS, low-calorie sweeteners; LSE, low sweet taste exposure; PABA, para-aminobenzoic acid; RCT, randomized controlled trial; RSE, regular sweet taste exposure; TGL, triglycerides.

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rationale explicitly: Health Canada (2025): "*regularly eating foods that taste sweet can lead to a preference for sweet foods*" [4], Pan American Health Organization (2016): "*the habitual use of sweet flavors (sugar-based or not) promotes the intake of sweet foods and drinks*" [6, p. 13], and National Health Service (United Kingdom) (2022): "*Even low-calorie drinks and no-added-sugar drinks can encourage children to develop a sweet tooth*" [5]. Note, the reference here to *sweet taste*, rather than sugar consumption, and throughout this work, we focus on *sweet taste*.

At first sight, this reasoning appears compelling. It is well documented that repeated exposure to a specific flavor or food can lead to an increased preference [8]. Indeed, many food preferences are thought to be learned from past exposure and experience [8]. Further, fundamental research on salt taste preferences shows that salt preferences covary with the level of dietary exposure [9,10]. However, recent systematic reviews on the effects of repeated exposure to different levels of dietary sweet taste do not confirm a similar mechanism for sweetness [11,12].

The second part of the above reasoning is also appealing. The sweet tooth hypothesis of obesity – that individuals with a high preference for sweet foods are more likely to consume high-calorie, sweet-tasting foods, leading to increased energy intake and body weight, stems from the notion that sweet taste is conceived to signal the energy content of foods, and as people with overweight/obesity have higher energy needs, they "must" have a higher liking for sweet taste [13,14]. However, although early work suggests some misappropriation of effects due to the fat content of many sweet foods [14], recent studies show that sweet taste intensity and energy content are independent from each other in a range of foods [15]. There is broad agreement on the link between excessive added sugar intake and weight gain [16,17]; however, studies on the relationship between sweet taste liking and sugar intake often fail to find a relationship [18], and evidence connecting overall dietary sweet taste exposure to energy intake and body weight remains weak [19,20].

Causal understanding is limited by a lack of well-controlled randomized controlled trials (RCTs) with varying levels of dietary sweet taste to better understand the long-term effects of sweet taste exposure on sweet taste preferences [11,12] and body weight [19,20]. Here, we report the results of a long-term RCT in Dutch adults (www.clinicaltrials.gov, NCT04497974). Using 3 parallel groups, we investigated the effects of low, regular, and high dietary sweet taste exposure for 6 mo on liking for sweet taste, sweet taste perceptions, food choice, energy intake, anthropometry, several biomarkers for diabetic and cardiometabolic health, and adverse events. Our null hypothesis was that, regardless of sweet taste exposure level, liking for sweet foods and beverages would not change from baseline (month 0) to month 6. This paper reports on the primary and the majority of the secondary outcomes of the trial. Additional papers will report on additional taste-related and biochemical outcomes.

Methods

Study design

The Sweet Tooth Trial was a RCT with partial food provision investigating the effects of low, regular, and high dietary sweet taste exposure for 6 mo on sweet taste liking, sweet taste perception, various measures of food intake, anthropometry, several biomarkers for diabetic and cardiometabolic health, and adverse events, with a 4-mo follow-up (see Figure 1). The study was conducted in a public health context, so it was intended to remain as realistic as possible while addressing our research question. The rationale and methodology have been described in detail previously [21]. As our primary outcome, we paid special attention to the measurement of a generalized preference or liking for sweet taste, through the measurement of liking for a broad range of sweet taste concentrations in familiar and unfamiliar foods and beverages [22].

All procedures were approved by the Medical Ethical Committee of Wageningen University & Research (METC-WU; ABR number NL72134), and the study was registered at clinicaltrials.gov (identification number NCT04497974). All procedures with participants met the guidelines of the Declaration of Helsinki; all participants gave written informed consent and received financial compensation for their participation. We adhered to our registration and published protocol in all respects, with exceptions only due to the COVID-19 pandemic, as detailed below.

The study was conducted from September 2020 to June 2024 at the Human Research Unit at Wageningen University & Research, the Netherlands, with all baseline assessments conducted between September 2020 and September 2023. During this time, restrictions on daily life were in place due to the COVID-19 pandemic from December 2020 to January 2021, and from December 2021 to January 2022. These restrictions resulted in the failure to collect in-person test session data from 9 participants at the month 1 time point. Individuals

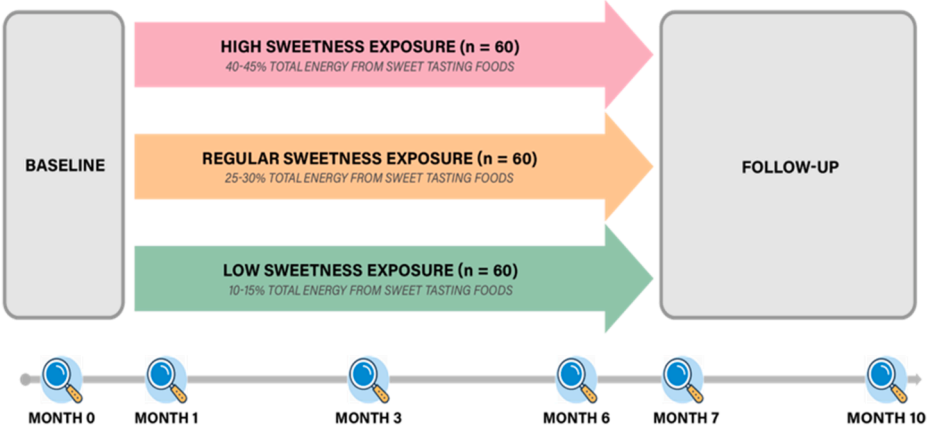

FIGURE 1. Overview of the Sweet Tooth Trial design - a randomized controlled trial on the effect of 6-mo low, regular, and high dietary sweet taste exposure on liking for sweet foods. Magnifying glass icons represent assessment visits conducted at baseline (month 0), and months 1, 3, 6, 7, and 10.

who declared experiencing COVID-19–related taste or smell impairments were also retested for good taste perception prior to undertaking all subsequent taste assessments. All other aspects of the study went ahead as planned.

The study was monitored by BioFortis (Biofortis Clinical Research, https://www.merieuxnutrisciences.com). This involved 2 onsite visits (April 2022, March 2024), and several online meetings between September 2020 and September 2024. The scope of the monitoring included reviewing training logs, verifying source data, protocol adherence, reviewing adverse events, blinding assessments, site facilities and equipment, the investigator site file, informed consent forms, subject logs, investigational product accountability, and biological sample collection and storage.

Study participants

One hundred eighty healthy Dutch-speaking participants took part. Participants were considered eligible if they were aged 18–65 y, had a BMI of 18.5–30, and were in good general health. Exclusion criteria were abnormal blood glucose concentrations (fasting glucose concentration: ≥6.1 mmol/L; nonfasting glucose concentration ≥7.8 mmol/L), self-reported diabetes and other metabolic disorders, >3 kg unintended weight change in the past 3 mo, eating or sensory disorders, medication affecting taste or glucose metabolism, known food allergies or intolerances for the foods provided, pregnancy, lactation, excessive use of alcohol (>14 glasses of alcohol per week), any recreational drug use, affiliation with the Division of Human Nutrition and Health at Wageningen University & Research and participating or planning to participate in another study. Systematic weight change of 4 kg or more over any 3-mo period during the intervention also resulted in exclusion for ethical reasons.

Participants were recruited from Wageningen and its surroundings via a pre-existing participant database, internet-based advertisements, printed media, and flyer distribution. The study was promoted to participants as "*The i-sense study - a study on the effects of food color, taste and texture on eating habits and diabetic indicators*" to blind participants to the true purpose of the study and reduce effects due to demand characteristics.

Inclusion and exclusion criteria were assessed during a screening visit aided by a medical investigator. Demographic, dietary, and lifestyle characteristics were collected by questionnaire, body weight and height were measured, and BMI was calculated by dividing the weight in kilograms by the square of height in meters. Blood glucose concentrations were measured using a finger prick (FreeStyle Freedom Lite; Abbott), and the ability to taste (total score: ≥12 out of 20) was assessed using a validated standardized taste strip test [23]. Additionally, sweet liker phenotype was assessed using 100-unit visual analog scale (VAS) liking ratings for a single 1 mol sucrose solution, as recommended by Iatridi et al. [24], with participants categorized as published, where those scoring 0–34 of 100 were classed as "sweet dislikers," those scoring 35–65 of 100 were classed as "moderate sweet likers" and those scoring 66–100 of 100 were classed as "sweet likers" [24].

Randomization

Eligible participants were randomly assigned to low sweet taste exposure (LSE), regular sweet taste exposure (RSE), or high sweet taste exposure (HSE) groups, at a ratio of 1:1:1, using a stratified process based on sex (male, female), age (18–34 y, 35–49 y, and 50–65 y), BMI (18.5–24.9, 25–30), and sweet liker phenotype (sweet liker, moderate sweet liker, and sweet disliker), as assessed at the screening visit. Randomization was performed according to a computer-generated schedule by an independent researcher. Participants, researchers, and analysts remained blind to treatment allocation during all data collection and analyses.

Dietary intervention

Sweet taste exposure was defined by the percentage of total daily energy intake consumed from sweet-tasting foods and beverages. The LSE diet group had a target consumption of 10%–15% of energy from sweet foods and beverages, the RSE had a target consumption of 25%–30% of energy from sweet foods and beverages, and the HSE had a target consumption of 40%–45% of energy from sweet foods and beverages. These targets were based on data from the Dutch food consumption survey 2007–2010 [25], where the usual Dutch diet contains ~28% of energy from sweet foods and beverages [26], and all 3 group ranges fell within the natural range of sweet-tasting food and beverage consumption.

The intervention was semi-controlled; participants were provided with daily menus and ~50% of the food and beverage items from their allocated diet. The differences between groups in sweet taste exposure were created by varying the proportion of sweet-tasting foods and beverages provided: LSE: 7% of provided foods and beverages were sweet-tasting, RSE: 35%, and HSE: 80% of the foods and beverages provided were sweet-tasting. Classification of foods and beverages as sweet or nonsweet was based on the Dutch taste database [27] and the work by van Langeveld et al. [28], which provides detailed information on the sweet taste intensity of various foods and beverages, and classifies foods into 6 taste clusters: "neutral," "salt, umami, and fat," "sweet and fat," "sweet and sour," "fat," and "bitter." We considered sweet foods for our intervention to be any food or beverage prespecified in this publication to lie in the "sweet and fat" or "sweet and sour" clusters. Foods in the "sweet and fat" cluster include biscuits, chocolate, dessert, and cake; foods in the "sweet and sour" cluster include predominantly fruits, yogurts, and related beverages. Provided foods were sugar-sweetened, no- and low-calorie-sweetened, and nonsweet items to reflect the diversity in a real-world food environment, and were primarily breakfast, lunch, beverage, and snack items, such as bread toppings, dairy products, nuts, chocolates, and crackers. Example foods include savory biscuits, unsalted nuts and vegetable spread for the LSE group; low-sugar fruit jam, unsalted nuts with cranberries, and rice crackers with chocolate flavor for the RSE group, and fruit and yogurt biscuits, chocolate spread and yogurt drink for the HSE group; a full list of foods, by taste classification and sweet taste source is provided in the Supplementary Materials, Supplemental Table 1. Previous research conducted in the Netherlands has shown that dietary taste patterns typically vary most during breakfast and snacking occasions [26], making these the best opportunities to create differences in dietary sweet taste exposure. All provided foods were commercially available in the Netherlands at the time of the study, were not tampered with in any way, and were provided as sourced from a local supermarket. The use of commercially available foods was important to avoid concerns over consumption by our participants, e.g., in terms of allergens, and to retain the public health relevance of our work.

Foods and beverages were provided ad libitum, without specific instructions on the quantity to be consumed, allowing participants to consume their diet as they wished. Additional consumption was also possible through voluntary purchasing, as above. Intervention diets were designed to be comparable in energy, energy density, macronutrient (carbohydrate (CHO), fat, protein, and fiber) composition, and

composition of liquid, semisolid, and solid foods, considering the lower taste exposure gained from liquids. An overview of the intended diet per group is given in the Supplementary Materials, Supplemental Table 2, with further details also given in our protocol paper [21]. Participants were provided with daily diet menu plans that included the provided intervention foods and beverages, and attended monthly counseling sessions with a research dietitian. The primary purpose of these sessions was to monitor diet adherence, provide support allowing enhanced adherence to the intended intervention (research dietitians were aware of participant group allocation), while ensuring diets and dietary behavior remained healthy, report adverse events, and track body weight. Participants were provided with advice specific to their intervention allocation (without revealing this to them), alongside general dietary advice, including practical suggestions to aid adherence. Additional support was also available via email, telephone, or video call, as requested. The intervention phase lasted for 6 mo.

Compliance

Compliance with the intervention was monitored using self-administered web-based dietary 24-h recalls via the tool Compl-eat (www.compleat.nl; Wageningen University). Participants were asked to report all foods and beverages consumed in 1 24-h period (to include both foods provided as part of the study and foods that they provided themselves), with 24-h recalls undertaken for 1 d/mo across the intervention (months 0–6), and at months 7 and 10 (months 1 and 4 of the follow-up). Multiple dietary recalls are an established, validated method for assessing free-living food intakes [29], recommended for both describing and investigating the effects of diet on subsequent outcomes [29]. These self-reported intake data were analyzed to provide the percentage of energy and the percentage of weight consumed from sweet foods.

Outcome measures

Our primary outcome was the change in sweet taste liking from baseline (month 0) to month 6 (end of intervention). Secondary outcomes were change in sweet taste perceptions, various measures of food intake, anthropometry, several biomarkers for diabetic and cardiometabolic health, adverse events, from baseline to month 6, and all outcomes at other time points (months 1, 3, 7, and 10).

Sweet taste liking and sweet taste perceptions

Sweet taste liking was assessed in 6 sweet stimuli that varied in familiarity (familiar, unfamiliar), sweet taste intensity (5 concentrations), and food form (liquid, semisolid, and solid). Three familiar (strawberry-flavored lemonade, chocolate-flavored custard, and plain cake) and 3 unfamiliar (watermelon-flavored lemonade, elderflower-flavored custard, and tamarind-flavored cake) products were created at 5 different concentration levels of sweet taste (L-2, L-1, L-0, L+1, L+2), by varying the amount of sucrose and LCS, with the middle concentration (L-0) based on the amount present in commercial products or recipes, representing the optimal concentration of sweet taste for the general population. Liking for 2 familiar salty foods, at 5 concentration levels of salt (NaCl), and salt taste were also assessed, to ensure that any potential effects of dietary sweet taste exposure were specific to sweet taste. An overview of all test foods is given in Table 1. All foods were developed specifically for the study, with full details of the development processes previously published [22].

To assess liking, all foods were rated during sensory testing using Ranking on a Scale methodology [22]. Participants were simultaneously presented with all 5 samples of the same product, tasted and swallowed a mouthful of each sample, and rated their liking using a 100-unit VAS (anchored at 0: "dislike extremely"; 50: "neither dislike nor like"; 100: "like extremely"). This approach allowed participants to directly compare the different samples, with ties permitted if 2 or more samples were equally liked.

Sweet taste intensity was also assessed in the same 6 sweet and 2 salty products, again at all 5 concentrations of sweet taste and salty taste (6 × 5 sweet samples, 2 × 5 salty samples). These assessments were made in a separate tasting session, where participants were presented with all 5 concentrations of each sample 1-at-a-time and asked to taste and rate sweet or salt taste intensity on a 100-unit VAS, end-anchored "not sweet/salty at all" and "extremely sweet/salty."

Participants evaluated all 5 concentrations of all 8 stimuli, twice during every study assessment visit, first for liking and second, after a 1-h break, for taste intensity. All 5 concentrations of each stimulus were presented together in a random order, with stimulus order also randomized. All samples were provided in standardized amounts, either cold (5°C) or at room temperature (22°C), in translucent 30 mL

TABLE 1
Sweet and salty (control) test foods at each concentration level of sweet or salty taste. Amounts of sucrose and low-calorie sweeteners (cyclamate and saccharin) reflect the amount added to a base vehicle product.

	Test food	Food form	Serving size	Serving temperature, °C	Sweetener concentration (sucrose[1] + LCS[2]) (% by weight)				
					L-2	L-1	L-0	L+1	L+2
Familiar	Strawberry-flavored lemonade	Liquid	20 mL	22	0.0 + 0.0	1.3 + 0.0	3.1 + 0.0	8.6 + 0.0	15.1 + 0.0
	Chocolate-flavored custard	Semisolid	15 g	5	3.4 + 0.0	6.6 + 0.0	12.4 + 0.0	17.6 + 0.0	26.3 + 0.0
	Plain cake	Solid	20 g	22	9.1 + 0.0	16.7 + 0.0	18.2 + 0.9	17.6 + 4.2	16.9 + 8.2
Unfamiliar	Watermelon-flavored lemonade	Liquid	20 mL	22	0.0 + 0.0	1.3 + 0.0	3.1 + 0.0	8.6 + 0.0	15.1 + 0.0
	Elderflower-flavored custard	Semisolid	15 g	5	3.6 + 0.0	7.1 + 0.0	13.2 + 0.0	18.4 + 0.6	21.9 + 5.9
	Tamarind-flavored cake	Solid	20 g	22	9.1 + 0.0	16.6 + 0.0	18.1 + 0.9	17.5 + 4.2	16.8 + 8.1
					Salt concentration (NaCl) (% by weight)				
					L-2	L-1	L-0	L+1	L+2
Familiar	Gazpacho	Liquid	20 mL	22	0.1	0.2	0.3	0.7	1.5
	Butter cracker	Solid	3.5 g	22	0.0	0.7	1.4	3.5	7.1

Abbreviations: LCS, low-calorie sweeteners; NaCl, sodium chloride.
[1] Sucrose (Kristal suiker, Van Gilse).
[2] Liquid sweetener based on cyclamate and saccharin, in a water vehicle (Rio Zoetstof; Sweet Life AG).

cups or on small aluminum trays, labeled using 3-digit random codes. All samples were evaluated in sensory booths under normal lighting and odor-free conditions, with tap water provided as a palate-cleanser, and breaks of 30 s between each tasting, to control for possible carry-over effects. Ratings were digitally recorded using EyeQuestion (version 6.0.5, EyeQuestion Software).

Sweet food choice and energy intake at an ad libitum breakfast meal

Food choice and energy intake were measured at a breakfast meal, where participants were offered a wide variety of foods to consume *ad libitum* until pleasantly satisfied. These assessments were undertaken to examine whether exposure to sweet taste influences the choice and intake of other sweet foods. The available foods and beverages varied in taste (sweet, savory, neutral, fatty, and bitter). Sweet foods were bread rolls with raisins and nuts, sweet bread toppings (sprinkles and fruit jam), and orange juice. Savory foods were cheese bread rolls, savory bread toppings (cheese, ham, and vegetarian paté), and tomato juice. Neutral foods were plain brown bread rolls, water, milk, and unsweetened tea. Coffee was the only bitter food offered at breakfast. All food consumption was measured. The proportion of sweet compared with nonsweet foods consumed was calculated, and energy and macronutrient intake were calculated using the Dutch food composition database [30].

Daily energy intake

Self-reported daily energy intake, energy consumed from macronutrients, and from mono- and disaccharides were assessed from the self-administered web-based dietary 24-h recalls, used to measure compliance, using the Dutch food composition database [30]. Participants reported all foods consumed (both foods provided as part of the study and foods that they provided themselves).

Urinary markers for sugar and LCS consumption

Urinary markers for sugar and LCS consumption were also undertaken to confirm our dietary recall measures, and further understand free-living sugar, LCS, and sweet food consumption. Excretion of sucrose and fructose [31], and 5 commonly consumed LCS: acesulfame-K, saccharin, sucralose, cyclamate, and steviol glucuronide [32], were measured in 24 h urine samples using a validated liquid chromatography coupled to tandem mass spectrometry method [33]. Urine samples were collected in containers prepared with boric acid (1 g; Sigma Aldrich), 6 times in total (baseline, months 1, 3, 6, 7, and 10). Urine collection started after the first voiding in the morning, the day before the test session, with the last collection immediately before participants came to the Human Research Unit. Participants received written and verbal instructions on urine collection and all necessary equipment. Possible deviations from the protocol (e.g., missing urine) were reported. To check for completeness of the 24 h urine, participants ingested 3 tablets of 120 mg para-aminobenzoic acid (PABA) (KAL) during their 3 main meals, e.g., 08:00, 13:00, and 18:00. A PABA recovery of 78% was considered acceptable [34]. A homogenous sample of urine was stored at −80°C and analyzed only after the last sample was collected. If analyses resulted in values under detection limits, values were imputed with the lowest detection limit, that is, 1 mg/L for PABA, 540 ng/mL for fructose, and 28 ng/L for all the other sweeteners. The average intra-assay variation coefficient for PABA was 9.95%, for fructose was 30.4%, for sucrose was 6.7%, for cyclamate was 12.0%, for sucralose was 8.9%, for acesulfame-K was 4.7%, for saccharin was 6.9% and for steviol glucuronide was 10.1%.

Anthropometry and body composition measures

Weight and height were measured with participants wearing light clothing and no footwear after voiding. Height was measured to the nearest 0.1 cm using a stadiometer (SECA). Weight was measured twice with a calibrated digital weighing scale (SECA) to the nearest 0.1 kg, and the average of the 2 measurements was recorded in the dataset. BMI was calculated by dividing weight in kilograms by the square of height in meters. Waist and hip circumference were measured twice using a flexible tape (SECA 201) and recorded to the nearest 0.5 cm. The average of the 2 measures was recorded in the dataset. Body composition (lean body mass, body fat percentage) was measured by a dual-energy x-ray absorptiometry scan (Lunar Prodigy; GE Healthcare) at baseline, month 6, and month 10.

Biomarkers for diabetic and cardiometabolic health

Various biomarkers were assessed from fasting venous blood. Samples were obtained by a trained phlebotomist. HbA1c was analyzed in full blood within 4 h. The other blood samples were centrifuged within 2 h of collection, stored at −80°C, and subsequently analyzed. Glucose, HbA1c, total cholesterol, HDL, LDL, and triglycerides (TGLs) were analyzed in a clinical laboratory (ISO 15189 accredited; Hospital Gelderse Vallei), using enzymatic methods (AtellicaR CH analyzer; Siemens) and/or HPLC. Insulin was measured with ELISA (catalog no. 10.1132-01; Mercodia Ultrasensitive Insulin ELISA) in the laboratory at Wageningen University & Research (Division of Human Nutrition and Health), the Netherlands. Three samples were diluted to allow detection by the commercial kits used. The interassay variation of insulin was 7.5%.

Adverse events

Adverse events were recorded in a case report form, monitored by a medical investigator and the Medical Ethical Committee. Adverse events were categorized into 5 categories, dependent on their likely relation with the dietary intervention: definite (A) (e.g., an allergic reaction to 1 of the provided products), probable (B) (e.g., digestive complaints which started with the start of the diet), possible (C) (e.g., gut complaints related to food intake, toothache), unlikely (D) (e.g., gut/abdominal complaints unlikely to be related to food intake), and unrelated (E) (e.g., common cold, influenza).

Outcome assessment

Study assessments were conducted at baseline, at months 1, 3, and 6 of the intervention, and at months 7 and 10 of the follow-up, at the Human Research Unit, located on Wageningen Campus, the Netherlands. An overview of the assessment schedule is given in Table 2. Each assessment visit lasted ~6 h and included assessment of all outcomes (with the exception of body composition and glucose homeostasis) in a prespecified order following a strict standardized operating procedure, completed by a researcher blinded to participant group allocation. The order of assessments in each visit was as follows: *1*) fasting blood draw for biomarkers related to cardiovascular disease (CVD) and diabetes; *2*) body weight, waist, hip circumference, body composition (depending on the test session); *3*) ad libitum breakfast meal for measured energy intake and food choice; *4*) dietary taste questionnaires (not reported here); *5*) sweet liker status (not reported here); *6*) sensory evaluations for our primary outcome – sweet taste liking; *7*) additional dietary taste and lifestyle questionnaires (not reported here); *8*) sensory evaluation for secondary outcomes; and *9*) take-away snack choice (not reported here). Participants were asked to avoid vigorous physical activity the day before the test and to refrain

TABLE 2
Schedule of assessments, including detail of the measurements taken for each. Includes only the outcomes reported in this paper. Assessments for additional secondary outcomes are given in our protocol paper. These will be reported elsewhere.

Domain	Outcome to be measured	Data collection method	Baseline	Intervention			Follow-up	
				1 mo	3 mo	6 mo	7 mo	10 mo
Taste liking	Sweet taste liking	Rank-rating scale	✓	✓	✓	✓	✓	✓
	Salt taste liking		✓	✓	✓	✓	✓	✓
Taste intensity perception	Sweet taste perception	100-unit VAS	✓	✓	✓	✓	✓	✓
	Salt taste perception		✓	✓	✓	✓	✓	✓
Compliance	Daily dietary intake – sweet food consumption	Online 24-h recall	✓	✓	✓	✓	✓	✓
Behavioral outcomes	Daily dietary intake – energy intake, macronutrients	Online 24-h recall	✓	✓	✓	✓	✓	✓
	Food intake – energy intake, macronutrients	Breakfast buffet meal	✓	✓	✓	✓	✓	✓
	Food choice – sweet food consumption, other taste consumption	Breakfast buffet meal	✓	✓	✓	✓	✓	✓
Anthropometric outcomes	Weight	Digital scale	✓	✓	✓	✓	✓	✓
	Waist-hip circumference	Measuring tape	✓	✓	✓	✓	✓	✓
	Body composition	DEXA	✓			✓		✓
Biochemical outcomes	Biomarkers related to CVD and diabetes	Fasting blood sample	✓	✓	✓	✓	✓	✓
	Biomarkers of sugars / LCS intakes	Urine sample (24-h sample)	✓	✓	✓	✓	✓	✓
Adverse events	Adverse events, medication use	Questionnaires, diary	✓	✓	✓	✓	✓	✓

Abbreviations: CVD, cardiovascular disease; DEXA, dual-energy x-ray absorptiometry; LCS, low-calorie sweeteners; VAS, visual analog scale.

from eating or drinking anything except water after 22:00 on the evening prior to the test day. In the final study visit, participants also completed a debrief questionnaire to assess satisfaction with the diet and the success of the cover story for blinding the study aims.

Calculations and statistical analysis

Power and sample size

Our sample size calculation was based on our primary outcome: change in sweet taste liking ratings from 0–6 mo [21]. Following demonstrations of changes in taste preference tests in other studies of around 10% [21], we estimated that 147 participants would be needed to detect an effect size of 0.1, assuming a parallel-groups study design with 3 groups, and 2 repeated measures (baseline compared with 6-mo), and assuming a correlation between measures of 0.7, at a power of 80% for a significance level of 0.05. Assuming a dropout rate of 20%, we aimed to recruit 180 participants (60 per group) [21].

Data processing

The study employed a 2-step de-blinding process to ensure unbiased analysis. During the data cleaning and preprocessing phase, participant numbers (P001–P180) were paired with random letters corresponding to their assigned diet groups, without revealing the specific diet group identity. All data were analyzed under these blinded conditions. In the second step, diet group identity was revealed, fully unblinding the data, and analyses were repeated to interpret the results.

Statistical analyses

Data were analyzed using R, following a predefined statistical analysis plan as attached to our trial registration (clinicaltrials.gov, identification number NCT04497974). Two-tailed $P < 0.05$ was considered statistically significant. Baseline characteristics were compared between the diet groups using analyses of variance for normally distributed data or Kruskal-Wallis for non-normally distributed continuous data (mean ± SD) and using Fisher's exact test for categorical data (*n*, percentage).

An intention-to-treat analysis was used, which assumes that data are missing at random. A mixed model analysis of variance with repeated measures (package: nlme, function: lme) was used to test intervention effects on primary and secondary outcomes by comparing diet groups LSE, RSE, and HSE. The model included group (LSE, RSE, and HSE) as a fixed factor, time (baseline, 1 mo, 3 mo, 6 mo, 7 mo, and 10 mo) as a fixed factor (covariance structure), and participant number as a random factor. The model for the primary outcome variable - change in sweet taste liking score, and secondary outcome variable - sweet taste intensity perception, also included concentration level (L-2, L-1, L-0, L+1, L+2) as a fixed factor. Additional factors of potential impact on taste perception or food choice, e.g., stimulus form (liquid, semisolid, and solid), participant sex, or BMI group, were not added as factors to retain power. For the covariance structure of the mixed models, we assessed different structures to determine the most appropriate fit for our data. The models for the primary outcome variable were compared using the Akaike information criterion. The autoregressive covariance structure of order 1 was ultimately selected, as it demonstrated a lower Akaike information criterion value (260885.8) compared with the standard linear mixed model (261992.2), indicating a better fit for our primary outcome data. Subsequently, the autoregressive covariance structure of order 1 was applied to all models for every outcome measure.

For our primary outcome - sweet taste liking and secondary outcome - sweet taste intensity perception, our primary interest was in the interaction between group × time × concentration, demonstrating a change in the most liked/most sweet concentration of sweet taste between intervention groups over time. For all other outcomes, our primary interest was in the interaction effect between group and time, which would indicate a change in an outcome between the intervention groups over time. Post hoc analyses were performed only where significant interactions were found, using predefined contrasts of relevance to our research questions, to compare baseline with month 6, differences between the 3 treatment groups (LSE, RSE, and HSE) and between the 6 time points (0 mo, 1 mo, 3 mo, 6 mo, 7 mo, and 10 mo). Bonferroni adjustments, allowing for the number of predefined contrasts, were applied to control for multiple comparisons. Estimated marginal means with unadjusted 95% confidence intervals (CIs) are reported. Statistics for all interactions are reported; statistics for main effects and post hoc tests are only reported where these were

statistically significant. Change over time was calculated from baseline (baseline – subsequent time point); thus, an increase is reported with a negative value, and a decrease with a positive value.

Model assumptions were tested by plotting values and visually inspecting residual histograms and Q-Q plots, to check for homogeneity of variances and normality of residuals, respectively. Skewed variables (all LCS in urine, fasting insulin, cholesterol, TGL, and LDL) were log-transformed to improve normality, and back-transformed means and CI are reported. If normality was not improved, a generalized linear mixed model (glmm) was analyzed (this was only the case for waist-hip ratio, using family γ).

Results

Participant characteristics

In total, 180 healthy adult participants (123 (69%) female, mean ± SD age = 35 ± 15 y, mean ± SD BMI = 23 ± 3) were randomly assigned over the 3 dietary sweet taste exposure groups: low (LSE) (n = 61), regular (RSE) (n = 60) and high (HSE) (n = 59) (see Figure 2 for the Flow chart diagram). The 3 groups were balanced on baseline characteristics (Table 3). Of these randomly assigned participants, 163 (91%) completed the 6-mo dietary intervention, with 159 (88%) also completing the 4-mo follow-up. There was no significant difference between the groups in dropout rate or loss to follow-up [$\chi^2(4) = 0.7$, P = 0.95] (see Figure 2).

Compliance measures

Self-reported dietary measures revealed differences over the intervention between all 3 groups in sweet food consumption (percentage of energy consumed: group × time $\chi^2(16) = 59.4$, $P < 0.001$; percentage of weight consumed: $\chi^2(16) = 129.2$, $P < 0.001$) (Figure 3, Supplemental Table 3). From month 1–6, LSE consumed 14.3% (95% CI: 11.7%, 17.0%) energy and 9.7% (95% CI: 7.3%, 12.2%) weight from sweet foods, a decrease from baseline of 6.1% and 5.6%, respectively; RSE consumed 20.7% (95% CI: 18.0%, 23.3%) energy and 13.3% (95% CI: 10.8%, 15.8%) weight from sweet foods, a maintenance of 0.2% and 0.4%, respectively; and HSE consumed 27.0% (95% CI: 24.4%, 29.7%) energy and 24.0% (95% CI: 21.5%, 26.5%) weight from sweet foods, an increase from baseline of 3.9% and 10.2%, respectively. After the intervention period, especially at month 10, the 3 diet groups no longer differed in intake of sweet foods.

Blinding

Blinding was considered successful; no participant revealed their dietary consumption to the researchers collecting outcome data. Only 17 (9%) participants correctly identified the purpose of the study (4 (7%) in LSE, 6 (10%) in RSE, and 7 (13%) in HSE).

Liking for sweet foods

Likings for sweet foods (3 familiar, 3 nonfamiliar, 5 concentrations of each, rated from 0–100) did not change for individual concentrations of sweet taste in any diet group (group × time × concentration level, $\chi^2(40) = 37.9$, $P = 0.56$), although liking scores differed between concentration levels, in all diet groups ($\chi^2(4) = 2471$, $P <$ 0.001), as would be expected (see Figure 4, Supplemental Table 4). Likewise, there was no overall change over the intervention period in any group (group × time: $\chi^2(10) = 7.6$, $P = 0.66$). The RSE group reported a higher mean liking for the L+1 concentration level at all time points compared with HSE (group × concentration level, $\chi^2(8) =$ 41.6, $P < 0.001$, $\text{mean}_{\text{diff}} = 4.8$, $P = 0.04$). Liking score for the least

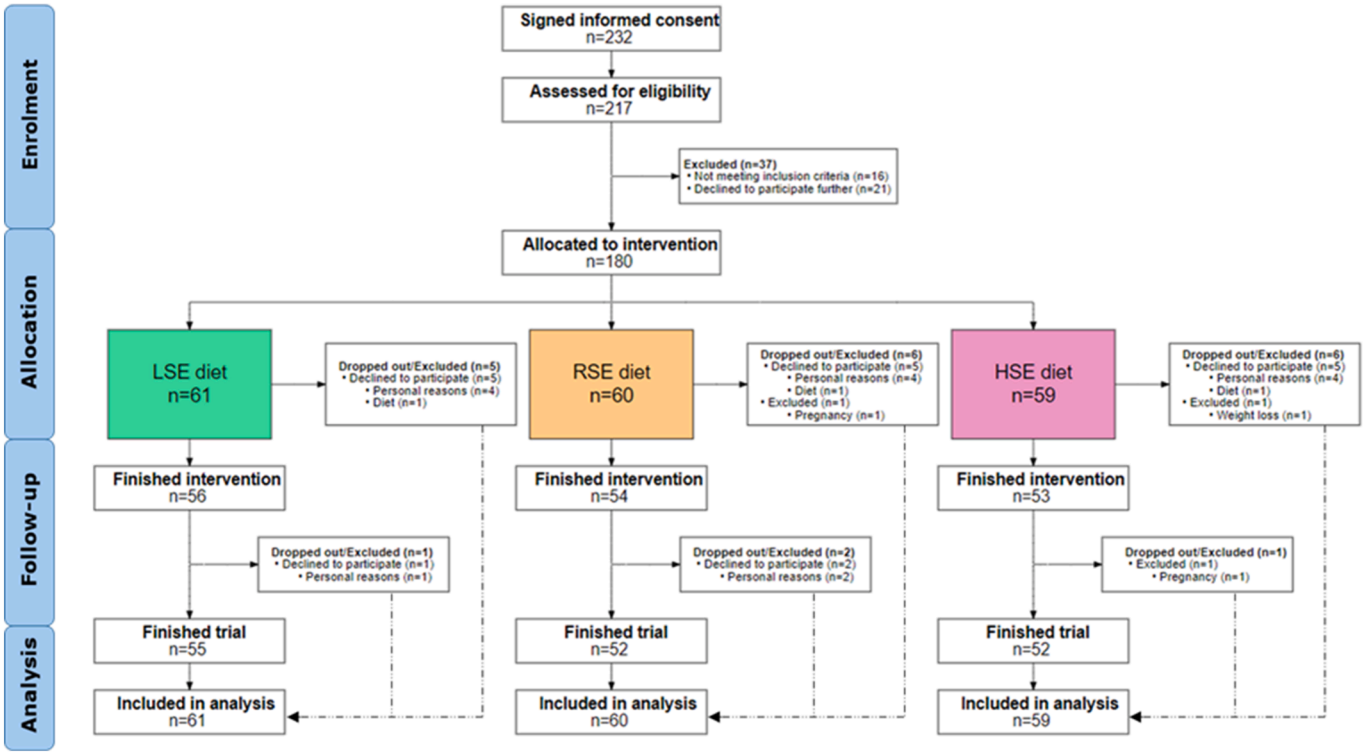

FIGURE 2. CONSORT flow chart of participant enrolment, eligibility, and flow through the Sweet Tooth Trial. Analyses were conducted on an intention-to-treat basis. CONSORT, consolidated standards of reporting trials; HSE, high sweet taste exposure group; LSE, low sweet taste exposure group; RSE, regular sweet taste exposure group.

TABLE 3
Characteristics of the participants of the Sweet Tooth Trial ($n = 180$).

	Total	Diet groups			P value[1]
	($n = 180$)	LSE ($n = 61$)	RSE ($n = 60$)	HSE ($n = 59$)	
Gender, *n* (%)					
Females	123 (69)	40 (66)	42 (70)	41 (69)	0.85
Males	57 (31)	21 (34)	18 (30)	18 (31)	
Age (y)					
Mean ± SD	35 ± 15	37 ± 16	34 ± 15	35 ± 14	0.45
(range)	(18 – 65)	(18 – 64)	(18 – 65)	(18 – 64)	
Weight (kg)					
Mean ± SD	71 ± 12	71 ± 12	71 ± 10	72 ± 12	0.86
(range)	(45 – 106)	(45 - 95)	(47 - 105)	(52 – 106)	
BMI (kg/m^2)					
Mean ± SD	23 ± 3	24 ± 3	23 ± 3	23 ± 3	0.85
(range)	(18.5 – 30)	(18.5 - 29.9)	(18.5 - 29.9)	(18.5 - 29.1)	
Weight status, *n* (%)					
Normal weight	130 (73)	42 (69)	47 (78)	43 (73)	0.50
Overweight	48 (27)	19 (31)	13 (22)	16 (27)	
Sweet liker phenotype, *n* (%)					
Sweet disliker	62 (35)	20 (33)	15 (25)	18 (31)	0.78
Moderate sweet liker	58 (33)	13 (21)	17 (28)	17 (28)	
Sweet liker	58 (33)	28 (46)	28 (46)	24 (41)	
Diet, *n* (%)					
No	149 (84)	50 (82)	54 (90)	46 (78)	0.20
Yes	29 (17)	11 (18)	6 (10)	13 (22)	
Employment status, *n* (%)					
Student	76 (43)	23 (38)	30 (50)	27 (46)	
Working	83 (47)	30 (49)	27 (45)	28 (47)	
No job, not looking for a job	5 (3)	1 (2)	1 (2)	3 (5)	0.11
No job, looking for a job	5 (3)	5 (8)	0 (0)	0 (0)	
Retired	5 (3)	2 (3)	2 (3)	1 (2)	
Education level, *n* (%)					
lower/primary	5 (3)	3 (5)	1 (2)	1 (2)	
intermediate	69 (39)	18 (30)	26 (43)	25 (42)	0.39
higher	104 (58)	40 (66)	33 (55)	33 (56)	
Smoking, *n* (%)					
Yes	42 (24)	10 (16)	17 (28)	16 (27)	0.24
No	136 (76)	51 (84)	43 (72)	43 (73)	

Abbreviations: ANOVA, analyses of variance; BMI, body mass index; HSE, high sweet taste exposure group; LSE, low sweet taste exposure group; RSE, regular sweet taste exposure group; SD, standard deviation.
[1] Differences are tested between groups with ANOVA, Tukey correction, or χ^2 for categorical variables.

sweet (L-2) concentration also increased over the study period in all diet groups (time × concentration level, $\chi^2(20) = 32.9$, $P = 0.03$).

Familiar test foods were more liked than unfamiliar foods (mean$_{familiar}$ = 48.1; 95% CI: (46.6, 49.6), mean$_{unfamiliar}$ = 40.6; 95% CI: (39.1, 42.0), $\chi^2(1) = 851$, $P < 0.001$) (Supplemental Figure 1), as would also be expected, but again no differences were found between diet groups, based on sweet taste concentration level, or over time (group × time × concentration level × familiarity, $\chi^2(40) = 14.7$, $P = 0.99$) (Supplemental Figure 2).

Likings for 2 familiar salty (control) foods also did not differ between diet groups nor change over time (group × time: $\chi^2(10) = 15.1$, $P = 0.12$; group × time × concentration level, $\chi^2(40) = 23.5$, $P = 0.98$), but the same main effect of concentration level was found ($\chi^2(4) = 756$, $P < 0.001$), (Supplemental Figure 3).

Taste perceptions

Perceptions of sweet taste intensity for all sweet foods (rated from 0–100) also did not change over the intervention period in any dietary exposure group (group × time × concentration level, $\chi^2(40) = 20.7$, $P = 0.99$) (Figure 5)), although perceived intensity increased linearly with increasing sweetness concentration ($\chi^2(4) = 60583$, $P < 0.001$), as would be expected. Significant interactions were also observed between the sweet taste exposure group and time (group × time, $\chi^2(10) = 26.3$, $P = 0.003$) and between the diet group and concentration level (group × concentration level, $\chi^2(20) = 30.7$, $P < 0.001$); however, after further investigation, no specific effects were found.

The same pattern was also found for perceived salt taste intensity for the salty foods: no effects of sweet taste exposure on salt taste perception (group × time × concentration level, $\chi^2(40) = 18.9$, $P = 0.99$), but higher concentrations of salt consistently led to greater perceptions of intensity ($\chi^2(4) = 9295$, $P < 0.001$) (Supplemental Figure 4). An interaction between diet group and concentration level was again found (diet × concentration level, $\chi^2(8) = 16.2$, $P = 0.04$), but again, after further investigation, no specific effects were detected.

Measured sweet food choice and energy intake at the ad libitum breakfast meal

For energy intake measured during the ad libitum breakfast meal, no differences between diet groups over time were found (group × time, $\chi^2(10) = 12.7$, $P = 0.24$). Over time, in all diet groups, measured energy intake at this 1 meal was highest at baseline (mean: 716 kcal; 95% CI: 677, 755 kcal) and lowest at month 1 (mean: 659 kcal; 95% CI: 620, 698 kcal) (mean$_{diff}$ = 56.8 kcal, $P = 0.004$), to increase again by month 10 (mean$_{diff}$ = −52.3, $P = 0.03$) ($\chi^2(5) = 19.1$, $P = 0.001$),

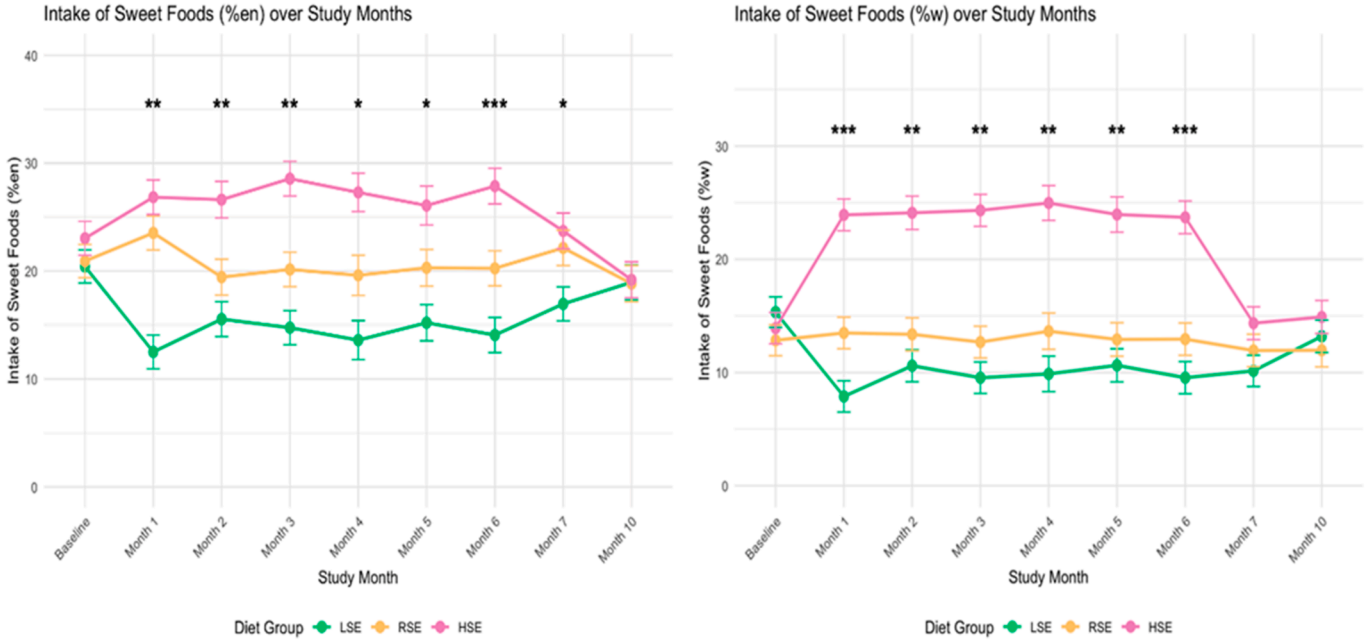

FIGURE 3. Self-reported intake of sweet foods between intervention groups (high sweet taste exposure group (HSE), regular sweet taste exposure group (RSE), low sweet taste exposure group (LSE)) in % energy (left) and % weight (right). Values are means ± SEMs. LSE $n = 61$ (month 1: $n = 58$, month 2: $n = 54$, month 3: $n = 57$, month 4: $n = 42$, month 5: $n = 50$, month 6: $n = 54$, month 7: $n = 58$, month 10: $n = 53$); RSE $n = 60$ (month 1: $n = 57$, month 2: $n = 51$, month 3: $n = 56$, month 4: $n = 40$, month 5: $n = 49$, month 6: $n = 54$, month 7: $n = 53$, month 10: $n = 50$), HSE n = 59 (month 1: $n = 56$, month 2: $n = 49$, month 3: $n = 55$, month 4: $n = 44$, month 5: $n = 43$, month 6, 7: $n = 52$, month 10: $n = 51$). Sample sizes are smaller for some months because of missing data. Data were analyzed using mixed model analysis: group (LSE, RSE, HSE) × time. The interaction effect involving time and diet group was significant. Number of stars reflects the number of diet groups that were significantly different from 1 another: *** indicates that all 3 groups were different, ** indicates that 2 of the groups were different from 1 group but not from each other. * indicates that only 2 groups were different. SEM, standard error of the mean.

(Supplemental Figure 5, Supplemental Table 5). Measured energy intake from macronutrients (fat, protein, and CHOs) differed over time across diet groups (group × time: fat ($\chi^2(10) = 24.3$, $P = 0.007$), protein ($\chi^2(10) = 20.4$, $P = 0.025$), and CHOs ($\chi^2(10) = 25.9$, $P = 0.004$). However, post hoc comparisons with Bonferroni correction identified only 2 significant differences: fat intake in the LSE group increased from baseline to month 6 by 4% ($P = 0.016$), and CHO intake in the RSE group decreased between baseline and month 1 by 4.8% ($P = 0.031$). No significant pairwise differences were found for protein intake or for other comparisons (Supplemental Table 5).

Measured intake of sweet foods (%en) at this 1 meal also did not differ between sweet taste exposure groups over time (group × time interaction: $\chi^2(10) = 10.1$, $P = 0.43$). In all groups over time ($\chi^2(5) = 22.8$, $P < 0.001$), measured intake of sweet-tasting foods at this meal decreased from baseline (mean: 36.7%; 95% CI: 33.8%, 39.6%) to month 1 (mean: 31.6%, 95% CI: 28.6%, 34.5%), month 3 (mean: 31.9%; 95% CI: 29.0%, 34.9%) and month 6 (mean: 30.6%; 95% CI: 27.1%, 33.2%) (Supplemental Figure 6).

Measured intake (%en) based on the other taste modalities (savory, neutral, fatty, and bitter) at this meal also did not differ between sweet taste exposure groups over time (largest group × time interaction: $\chi^2(10) = 12.3$, $P = 0.27$) (Supplemental Figure 6).

Differences over time regardless of group were found in neutral food consumption ($\chi^2(5) = 25.1$, $P > 0.001$): with an increase from baseline (mean: 26.3%; 95% CI: 23.6%, 28.9%) to month 1 ($\text{mean}_{\text{diff}} = -5.8\%$, $P < 0.001$), month 3 ($\text{mean}_{\text{diff}} = -5.2\%$, $P = 0.002$), and month 7 ($\text{mean}_{\text{diff}} = -4.3\%$, $P = 0.049$); and in fatty food consumption ($\chi^2(5) = 19.9$, $P = 0.001$), with an increase from baseline (mean: 3.1%; 95% CI: 2.4%, 3.8%) to month 1 ($\text{mean}_{\text{diff}} = -1.0\%$, $P = 0.03$) and month 10 ($\text{mean}_{\text{diff}} = -1.5\%$, $P < 0.001$).

Differences were found between groups regardless of time in savory food consumption ($\chi^2(2) = 9.3$, $P = 0.009$: LSE (mean: 28.2%; 95% CI: 24.3%, 32.2%) < both RSE (mean: 35.8%; 95% CI: 31.8%, 39.8%) and HSE (mean: 35.8%; 95% CI: 31.7%, 39.8%)), and neutral food consumption ($\chi^2(2) = 8.8$, $P = 0.01$: LSE (mean: 34.4%, 95% CI: 30.9%, 38.0%) > HSE (mean: 27.5%; 95% CI: 23.9%, 31.1%), but not different than RSE (mean: 28.4%; 95% CI: 24.8%, 32.1%).

Self-reported daily energy intake

For daily energy intake as self-reported in the 24 h recalls, LSE self-reported a lower daily energy intake compared to RSE during the first month of the intervention (group × time: $\chi^2(16) = 26.8$, $P = 0.04$; $\text{mean}_{\text{diff}} = 311$ kcal), but no differences were found between RSE and HSE ($\text{mean}_{\text{diff}} = 116$ kcal, $P = 1.0$) and LSE and HSE ($\text{mean}_{\text{diff}} = 195$ kcal, $P = 0.35$), nor between any of the groups during other time points. All groups self-reported an increase in daily energy intake from baseline over the intervention (time: $\chi^2(8) = 75.7$, $P < 0.001$; $\text{mean}_{\text{diff}}$ from baseline = −189 kcal), but following the intervention period, this returned to baseline levels (month 7 $\text{mean}_{\text{diff}}$ from baseline = 67 kcal, $P = 0.99$; month 10 $\text{mean}_{\text{diff}}$ from baseline = 160 kcal, $P = 0.31$). Daily self-reported energy density and macronutrient consumption did not differ between diet groups or change over time (group × time: energy density (LSE: 0.72–0.76 kcal/g; RSE: 0.77–0.82 kcal/g; HSE: 0.66–0.79 kcal/g): $\chi^2(16) = 0.14$, $P = 0.14$; %en from CHO (LSE: 43–46 %en; RSE: 42–48 %en; HSE: 44–47 %en): $\chi^2(16) = 12.2$, $P = 0.73$; %en from protein (LSE: 16–18 %en; RSE: 15–17 %en; HSE: 15–16 %en): $\chi^2(16) = 16.6$, $P = 0.41$; %en from fat (LSE: 33–37 %en;

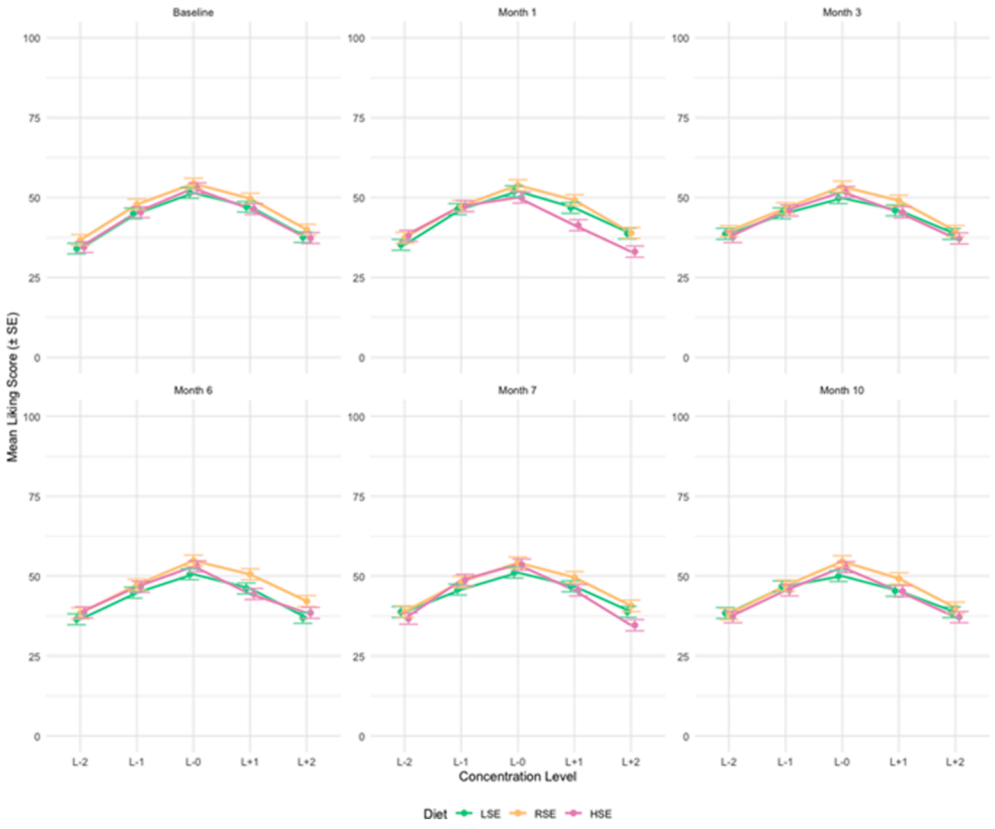

FIGURE 4. Mean liking scores for diet groups (high sweet taste exposure group (HSE), regular sweet taste exposure group (RSE), low sweet taste exposure group (LSE)) across concentration levels (L-2, L-1, L-0, L+1, L+2) averaged over sweet test foods. Values are means ± SEMs. LSE group, $n = 61$ (month 1: $n = 55$, month 3: $n = 55$, month 6: $n = 55$, month 7: $n = 53$, month 10: $n = 55$); RSE, control group, $n = 60$ (month 1: $n = 56$, month 3: $n = 57$, month 6: $n = 52$, month 7: $n = 46$, month 10: $n = 50$), HSE group, $n = 59$ (month 1: $n = 54$, month 3: $n = 54$, month 6: $n = 53$, month 7: $n = 50$, month 10: $n = 51$). Sample sizes are smaller for some months because of missing data. Data were analyzed using mixed model analysis: group (LSE, RSE, HSE) × concentration (L-2, L-1, L-0, L+1, L+2) × time. The interaction effect involving time, diet group, and concentration was nonsignificant. L-2, L-1, L-0, L+1, L+2, 5 different concentration levels of sweet taste; SE, standard error; SEM, standard error of the mean.

RSE: 33–40 %en; HSE: 34–37 %en): $\chi^2(16) = 17.7$, $P = 0.34$), (Supplemental Table 6, Supplemental Figure 7). Differences were found between diet groups over the intervention period in self-reported intakes of mono- and disaccharides (group × time: $\chi^2(16) = 51.1$, $P < 0.001$). These reflect the findings in sweet food consumption, and returned to baseline levels at the end of the intervention. Full details of the dietary consumption in each group are given in Supplemental Table 6.

Urinary biomarkers

Differences in intake were supported by recovery of urinary markers of sugars and LCS (Supplemental Table 7). Differences between groups were found in urinary markers for sucrose intake (group × time: $\chi^2(10) = 25.8$, $P < 0.01$) and for the 2 LCS most frequently contained in the sweetened products provided (sucralose: group × time: $\chi^2(10) = 40.4$, $P < 0.001$, saccharin: group × time: $\chi^2(10) = 21.0$, $P = 0.02$). LSE showed a reduction in sucrose excretion from baseline (mean: 0.19 mg; 95% CI: 0.13, 0.27 mg) to month 6 (mean: 0.09 mg; 95% CI: 0.06, 0.13 mg), and then an increase in sucrose excretion from month 6 to months 7 (mean: 0.22 mg; 95% CI: 0.15, 0.32 mg) and 10 (mean: 0.22 mg; 95% CI: 0.15, 0.31 mg). HSE showed an increase in sucralose excretion from baseline (mean: 7.69 mg; 95% CI: 4.87, 12.1 mg) to month 3 (mean: 20.7 mg; 95% CI: 12.9, 33.1 mg), and then a decrease from months 1 (mean: 14.98 mg; 95% CI: 9.70, 22.2 mg) and 3 to months 7 (mean: 4.01 mg; 95% CI: 2.29, 7.03 mg) and 10 (mean: 4.85 mg; 95% CI: 2.98, 7.89 mg). For saccharin, HSE showed an increase in excretion from baseline (mean: 10.8 μg; 95% CI: 6.13, 19.2 μg) to month 3 (mean: 36.5 μg; 95% CI: 20.1, 65.9 μg), and then a decrease from month 1 (mean: 18.6 μg; 95% CI: 11.1, 31.3 μg) to month 7 (mean: 5.21 μg; 95% CI: 2.59, 10.5 μg), from month 3 to month 10 (mean: 12.04 μg; 95% CI: 6.53, 22.2 μg), and from month 6 (mean: 19.6 μg; 95% CI: 9.93, 38.8 μg) to month 7. No effects were found in fructose excretion (group × time: $\chi^2(10) = 5.27$, $P = 0.87$), or in the other LCS consumed elsewhere in the diet (cyclamate: group × time: $\chi^2(10) = 10.7$, $P = 0.38$; acesulfame-K: group × time: $\chi^2(10) = 7.96$, $P = 0.63$; steviol glucuronide: group × time: $\chi^2(10) = 9.68$, p = 0.47). Overall, PABA recovery was lower than expected (median = 68%); 28% ($n = 277$) of urine collections were considered complete and were included in the statistical analyses.

Anthropometry (body weight, BMI, waist:hip ratio, body composition)

We also found no changes over time based on sweet taste exposure in body weight (Figure 6), BMI, body composition: percentage fat

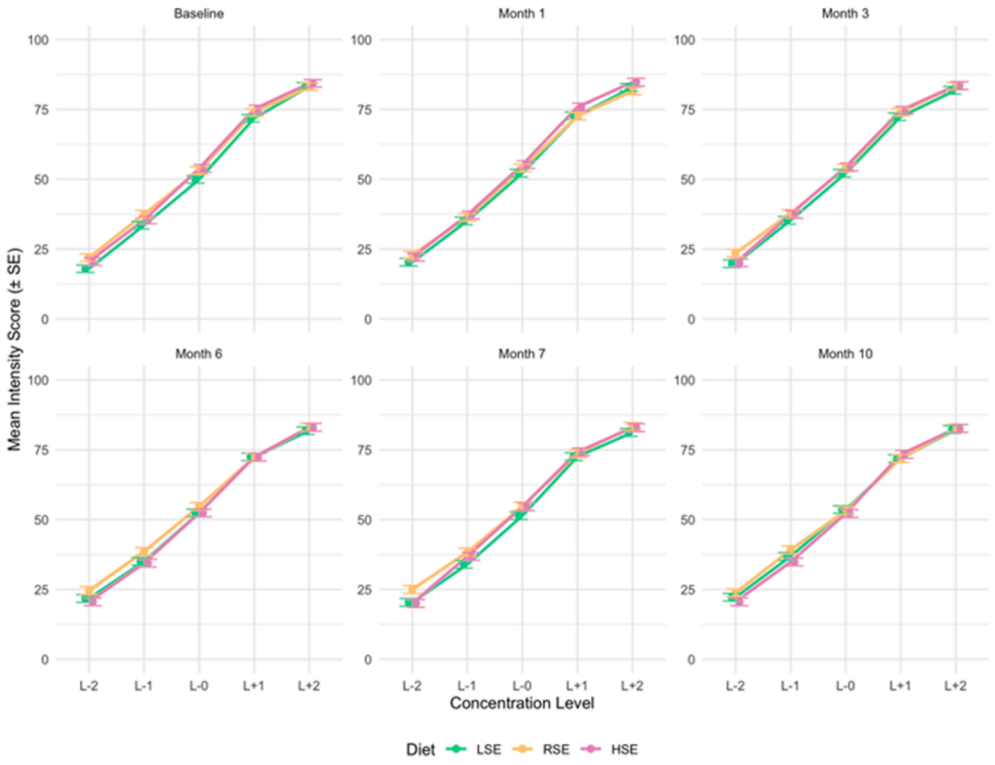

FIGURE 5. Perceived intensity ratings for diet groups (high sweet taste exposure group (HSE), regular sweet taste exposure group (RSE), low sweet taste exposure group (LSE)) across concentration levels (L-2, L-1, L-0, L+1, L+2) averaged over all sweet test foods. Values are means ± SEMs. LSE group, n = 61 (month 1: n = 55, month 3: n = 54, month 6: n = 55, month 7: n = 52, month 10: n = 55); RSE, control group, n = 60 (month 1: n = 56, month 3: n = 57, month 6: n = 52, month 7: n = 46, month 10: n = 49), HSE group, n = 59 (month 1: n = 54, month 3: n = 53, month 6: n = 53, month 7: n = 50, month 10: n = 51). Sample sizes are smaller for some months because of missing data. Data for each model stimulus were analyzed using mixed models: group (LSE, RSE, HSE) × concentration (L-2, L-1, L-0, L+1, L+2) × month. The interaction effect involving month, diet group, and concentration was nonsignificant. L-2, L-1, L-0, L+1, L+2, 5 different concentration levels of sweet taste; SE, standard error; SEM, standard error of the mean.

mass and percentage lean mass (group × time: weight: $\chi^2(10) = 14.3$, $P = 0.16$; BMI: $\chi^2(10) = 15.9$, $P = 0.99$; percentage fat mass: $\chi^2(4) = 2.3$, $P = 0.68$; percentage lean mass: $\chi^2(4) = 3.8$, $P = 0.44$), or, on investigation, in waist:hip ratio (Supplemental Figure 8). An interaction between diet group and time was significant for waist:hip ratio (group × time, $\chi^2(10) = 27.6$, $P = 0.002$), but on further investigation, no specific effects were found.

However, regardless of diet group (body weight: $\chi^2(5) = 20.5$, $P = 0.001$; BMI: $\chi^2(5) = 19.7$, $P = 0.001$; percentage fat mass: $\chi^2(2) = 7.0$, $P = 0.03$), body weight increased from month 0 (mean: 71 kg; 95% CI: 47, 95 kg), to month 7 by 0.5 kg ($P = 0.01$) and decreased by 0.4 kg between months 7 and 10 ($P = 0.005$). Similarly, BMI increased from month 0 (mean: 23; 95% CI: 17, 29) to month 7 by 0.2 ($P = 0.008$), and decreased by 0.1 between months 7 and 10 ($P = 0.009$) (Supplemental Figure 8). Percentage fat mass increased from baseline (mean: 27.7%; 95% CI: 26.4%, 29.0%) to month 6 by 0.5% ($P = 0.03$).

Biomarkers of diabetic and cardiometabolic health

We also found no changes over time based on sweet taste exposure in measures of fasting glucose, insulin, or HbA1c (group × time, fasting glucose: $\chi^2(10) = 10.2$, $P = 0.42$; insulin: $\chi^2(10) = 6.3$, $P = 0.79$; HbA1c: $\chi^2(10) = 14.0$, $P = 0.17$) (Supplemental Figure 9) or lipid markers for TGL, HDL, or LDL (group × time, TGL: $\chi^2(10) = 15.9$, $P = 0.10$; HDL: $\chi^2(10) = 7.6$, $P = 0.67$; LDL: $\chi^2(10) = 12.2$, $P = 0.27$) (Supplemental Figure 10). An interaction between diet group and time was significant for the lipid marker for cholesterol (group × time, $\chi^2(10) = 18.5$, $P = 0.047$). Cholesterol decreased for the LSE group from baseline (mean: 4.6 mmol/L; 95% CI: 4.4, 4.8 mmol/L), to month 1 by 0.31 mmol/L ($P < 0.001$) and to month 3 by 0.27 mmol/L ($P = 0.003$) (Supplemental Figure 10).

Furthermore, regardless of diet group (HbA1c ($\chi^2(5) = 15.7$, $P = 0.008$; cholesterol: $\chi^2(5) = 30.8$, $P < 0.001$; LDL: $\chi^2(5) = 32.1$, $P < 0.001$), HbA1c decreased from month 0 (mean: 34.6 mmol/mol; 95% CI: 34.2, 35.1 mmol/mol), to month 1 by 0.3 mmol/mol ($P = 0.03$), cholesterol decreased from month 0 (mean: 4.5 mmol/L; 95% CI: 4.2, 4.7 mmol/L), to months 1 and 3 by 0.16 mmol/L ($P < 0.001$) and to month 7 by 0.09 mmol/L ($P = 0.004$), and LDL decreased from month 0 (M: 2.6 mmol/L; 95% CI: 2.4, 2.7 mmol/L) to month 1 by 0.11 mmol/L ($P < 0.001$) and to month 3 by 0.13 mmol/L ($P < 0.001$), and increased by 0.11 mmol/L between months 3 and 10 ($P = 0.012$) (Supplemental Figure 10).

Adverse events

Over the course of the study, 158 individuals reported 412 adverse events: 49 individuals (142 events) in the LSE group, 54 individuals (125 events) in RSE, and 55 individuals (145 events) in HSE (Supplemental Table 8). Most adverse events (86%) were considered to be

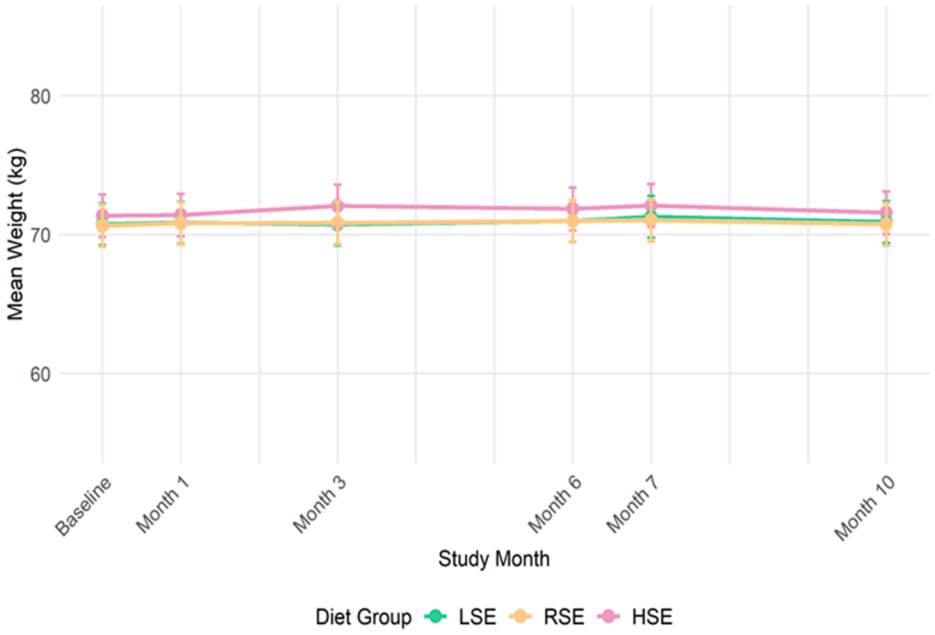

FIGURE 6. Mean body weight for diet groups (high sweet taste exposure group (HSE), regular sweet taste exposure group (RSE), low sweet taste exposure group (LSE)). Values are means ± SEMs. LSE group, $n = 61$ (month 1: $n = 56$, month 3: $n = 56$, month 6: $n = 55$, month 7: $n = 54$, month 10: $n = 55$); RSE, control group, $n = 60$ (month 1: $n = 56$, month 3: $n = 57$, month 6: $n = 52$, month 7: $n = 48$, month 10: $n = 51$), HSE group, $n = 59$ (month 1, 3: $n = 54$, month 6: $n = 53$, month 7, 10: $n = 52$). Sample sizes are smaller for some months because of missing data. Data were analyzed using mixed model analysis: group (LSE, RSE, HSE) × time. Interaction effect involving time, diet group and concentration was not significant. SEM, standard error of the mean.

unrelated to the study, with only 1 adverse event definitely related to the study – an allergic reaction to a provided food, reported by an individual in the HSE group, and only 1 adverse event was probably related to the study – bowel complaints reported by a second individual in the HSE group.

Discussion

Our results demonstrate clearly that neither low nor high whole-diet exposure to sweet taste for 6 mo has effects on liking for sweet taste; sweet taste liking was stable across the full 10 mo of the study and remained independent of dietary exposure. Low or high sweet taste exposure also had no effect on perceived sweet taste intensity, sweet food choice, energy intake, body weight, or biomarkers for diabetes and CVD.

Our results concur with the results of 2 other long-term RCTs on the stability of sweet taste liking. Wise et al. [35] observed no effect of a 3-mo reduction in sugar intake on liking for sweet taste in a semi-solid food and a beverage. Mah et al. [36] also recently demonstrated no change in liking for the most preferred sweet taste concentration in soft drinks throughout a 6-mo intervention, although a *generalized* liking for sweet taste (i.e., a liking expressed in nonexposed foods) was not tested in this study. Only 2 studies of which we are aware suggest that the long-term exposure to sweet taste may affect subsequent preferences for sweet taste, in sweet solutions [37] or in highly sweet solutions [38]. In both studies, however, effects were found in limited test stimuli that were very similar to the exposure stimuli; thus, a change in liking for *generalized* sweet taste is difficult to argue. Our results concur with the general conclusions of systematic reviews on generalized sweet taste by Appleton et al. [11] and Mela and Risso [12].

Two remarkable results of our study further indicate a stability to sweet taste preferences in adulthood, i.e., that on average humans seek a particular balance in their dietary exposure to sweet taste: not too much and not too little. First, the high dietary sweet taste exposure group reached, on average, a level of 28% energy from sweet-tasting foods compared with a planned level of 40%–45% energy. Secondly, as soon as the intervention was complete, both our LSE and HSE groups returned to baseline levels of dietary sweet taste, at around 20% energy, even though all foods consumed throughout the intervention remained available for participants as a result of our use of commercially available foods from local supermarkets. This return to baseline levels of sweet food consumption was also found in the study by Wise et al. [35], and speaks not only to the stability of sweet taste preferences but also to the difficulty that may be endured in following recommendations to change dietary sweet taste, and the potential futility of these recommendations. Bielat et al. [39] also demonstrate clear self-reported difficulty from participants asked to change their sweet food consumption, in this case, only for 1 wk.

In relation to our secondary aims, we also found no effects of dietary sweet taste exposure on sweet or salt taste intensity perception, measured food choice, and/or self-reported food, energy, or macronutrient intakes. Our findings on sweet taste perception differ from those of Wise et al. [35], who reported an increase in sweet taste intensity perception following a 3-month sugar reduction diet, and from recent findings of Bielat et al. [39], where increased sweet taste intensity perception was found after a 1-wk whole-diet sweet taste

reduction. These effects were explained as a result of the contrast in taste between the original diet and the new diet [35,39], and were possibly not found in our study, as a result of the lesser contrast between the original diet and the new diet. These findings do not negate our findings on liking for sweet taste. Changes in liking have been suggested regardless of contrast; in fact, gradual changes are recommended, and are generally preferred for product reformulation, to allow adjustment to new taste concentrations [40–42].

Importantly, the absence of effects on self-reported energy intake or macronutrient choice as assessed in the diet diaries also demonstrate no overconsumption of sweet foods in response to sweet taste exposure, and alongside the absence of effects on self-reported food, energy or macronutrient intakes, we also find no effects of sweet taste exposure on body weight, body composition, or select markers for cardiometabolic disease risk. Weight gain and disease risk have been linked to the consumption of added sugars, most frequently in sugar-sweetened beverages; however, changes in weight have been shown to be mediated by changes in energy intake, rather than sugar intake *per se* [18]. Our results do not demonstrate increased risk of overconsumption or excess energy intake in response to sweet taste exposure, in line with previous findings from recent literature reviews reporting limited evidence on the association between dietary sweet taste and body weight [19,20], and challenge the assumption that reducing or increasing sweet-tasting food intake substantially influences body weight. Our findings directly contradict the assumptions made by many public health agencies and suggest that, although overweight remains a global public health concern, excess energy intake is unlikely to be affected by advice to reduce our exposure to, or intakes of, sweet taste. We reject the sweet tooth hypothesis of overweight and obesity.

The strengths of our study include the following: our target sample size, based on a-priori power calculations, was achieved; our randomization processes resulted in 3 equivalent trial arms; and these differed significantly in sweet taste exposure throughout the intervention period; dropout was low; and blinding was maintained. Linear increases in perceived intensity with increasing taste concentration, and the appearance of well-established effects of familiarity and of sweetness concentration on sweet taste liking [43,44], further demonstrate sensitivity and validity to our measures. Comparable findings in measured sweet food choice during the breakfast meal also confirm the absence of effects in our liking measures.

Our study also has some limitations. First, sweet taste exposure was not as high in our study population at baseline as originally expected, and did not differ between groups over the intervention period as greatly as originally planned. Sweet taste exposure, however, was statistically significant between groups over the whole intervention period, and was significantly lower than baseline in LSE and higher than baseline in HSE. A greater degree of difference both between groups and from baseline may have increased our chances of finding effects, and this may suggest that a stricter or more controlled dietary intervention may have been preferable. Our study design, however, was intended to reflect the public health context, and our findings provide important information on what is likely to be achievable in this context. We also chose to investigate all outcomes at select time points rather than monthly. It is possible that this assessment schedule may have missed transitory effects, but these were not our primary interest, we have no reason to believe that effects would reverse between time points, and we sought to mitigate participant burden. Related to participant burden, recovery of PABA from urine was low. We are unclear why this was the case, but suggest that this may have been related to the high burden of collecting urine, particularly alongside the semi-controlled nature of the intervention, and the burden of all other measures. Although this low recovery has resulted in fewer samples for the analyses of urinary markers, we have no reason to believe, based on the dietary records, that these samples differ from those that may be missing.

Second, our study was conducted only in adults, and our sample was predominantly female, relatively healthy, based on BMI and smoking rates, and highly educated. These characteristics may have impacted willingness to undertake the dietary interventions as provided, and may explain both the lower sweet food consumption at baseline and the modest increase in sweet food consumption in HSE. We have no reason to believe that our findings are limited to the specific population investigated, but the generalizability of the results is compromised. A study of children, in particular, would be of interest. Indeed, a recent study linking sugar rationing early in life with protection from diabetes and CVD almost 6 decades later [45] postulates that sugar rationing during the first 1000 d led to "lifelong (lower) preferences for sweetness." Although our findings suggest stability in liking for sweet taste in adulthood and underscore a role for familiarity in this liking, further exploration in infants and children is warranted. Early exposure to sweet taste, both in utero and during early childhood, may not only increase the risk for conditions like diabetes [45] but may also establish a liking for sweet taste that becomes difficult to adjust later in life. So far, limited causal data on this issue exist. One recent study failed to find an association between sweet taste exposure and sweet taste liking in infants $\leq$12 mo of age [46]; a lack of association that is also reported in reviews of observational studies in children [11,12].

Our study population was also composed of individuals with differing levels of liking for sweet taste at baseline. "Sweet likers," "moderate sweet likers," and "sweet dislikers" were evenly distributed across intervention groups to avoid confounding as a result of these phenotypes [24], but a recent study on the effects of replacing sugar-sweetened beverage consumption with unsweetened beverages on perceptions of those beverages finds differing effects in sweet likers and moderate sweet likers [47]. Exploratory analyses to investigate differential effects in different sweet liker phenotypes will be reported elsewhere. Indeed, various individual differences, e.g., in sweet taste detection and perception [15], or in baseline levels of sweet food intake, may also have impacted responses to the intervention at an individual level. Some investigation of these differences between individuals is planned and will be reported elsewhere. Some aspects of our intervention may also warrant unpicking, e.g., taste exposure via foods compared with beverages, or via meals compared with snacks.

The implications of our results for public health nutrition are that recommendations to avoid energy overconsumption that focus on the reduction of exposure to sweet taste are unlikely to achieve success on a population-wide basis. Individuals may be differently affected, both as a result of their abilities to change their diet and the effects of those diets on energy intake and body weight, but at the population level, other food-based strategies have extensive empirical support, such as reducing the energy density of foods and drinks [48], limiting portion sizes [49], and avoiding foods with a high energy intake rate and often poor compensation, such as sugar-sweetened beverages [50]. These evidence-based strategies to improve a healthy food environment need support from both the public health nutrition sector and the private sector.

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Author contributions

The authors' responsibilities were as follows – EMC, MM, KMA, KdG: designed the research; EMC, MM, LP, MvdK, CST, MB: conducted the research; EMC, MM, LP, MvdK: analyzed the data; EMC: wrote the first version of the manuscript; MM, LP, MvdK, CST, HBTdJ, MB, KMA, KdG: added to the writing process and gave feedback on the manuscript in several rounds; EMC, MM, KMA, KdG: have a shared responsibility for the final content of the manuscript; and all authors: read and approved the final manuscript.

Conflict of interest

EMC, CST, LP, HBTdJ, MvdK declare that they do not have any competing interests. MM has previously received research funding from Royal Cosun (sugar beet refinery) and Sensus (inulin producer) and has received expenses from ILSI Europe. MB has received research funding from Horizon 2020 SWEET (grant agreement ID 774293). KMA has previously received research funding from the International Sweeteners Association, BE, and has current funding from The Coca Cola Company, US, and Ajinomoto Health and Nutrition North America Inc. US; KMA has received speaker's expenses from EatWell Global and PepsiCo. KdG is a member of the Global Nutrition Advisory Board of Mars company. KdG has received travel, hotel, and speaker renumeration from the International Sweeteners Association, and received speaker expenses from ILSI North America.

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Data availability

Data sharing is described in our trial registration. Data described in the manuscript, code book, and analytical code will be made available upon reasonable request to MM, Wageningen University and Research, the Netherlands.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ajcnut.2025.09.041.

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