

REVIEW

From biology to behavior: a cross-disciplinary seminar series surrounding added sugar and low-calorie sweetener consumption

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Summary

Introduction

This report presents a synopsis of a three-part, cross-sector, seminar series held at the George Washington University (GWU) in Washington, DC from February–April, 2018. The overarching goal of the seminar series was to provide a neutral forum for diverse stakeholders to discuss and critically evaluate approaches to address added sugar intake, with a key focus on the role of low-calorie sweeteners (LCS).

Methods

During three seminars, twelve speakers from academic institutions, federal agencies, non-profit organizations, and the food and beverage industries participated in six interactive panel discussions to address: 1) Do Farm Bill Policies Impact Population Sugar Intake? 2) What is the Impact of Sugar-sweetened Beverage (SSB) Taxes on Health and Business? 3) Is Sugar Addictive? 4) Product Reformulation Efforts: Progress, Challenges, and Concerns? 5) Low-calorie Sweeteners: Helpful or Harmful, and 6) Are Novel Sweeteners a Plausible Solution? Discussion of each topic involved brief 15-minute presentations from the speakers, which were followed by a 25-minute panel discussion moderated by GWU faculty members and addressed questions generated by the audience. Sessions were designed to represent opposing views and stimulate meaningful debate. Given the provocative nature of the seminar series, attendee questions were gathered anonymously using Pigeonhole™, an interactive, online, question and answer platform.

Results

This report summarizes each presentation and recapitulates key perspectives offered by the speakers and moderators.

Conclusions

The seminar series set the foundation for robust cross-sector dialogue necessary to inform meaningful future research, and ultimately, effective policies for lowering added sugar intakes.

Keywords: Dietary sugar, low-calorie sweeteners, obesity, sugar-sweetened beverages.

Background

Added sugars comprise approximately 13% of daily calories in the American diet (1). Higher consumption of added sugars is associated with obesity (2), type 2

diabetes (3), cardiovascular disease (4), non-alcoholic fatty liver disease (5), and cancer (6). Given the well-established adverse health effects of excess added sugar intake (4), minimizing added sugar intake is central to the prevention and management of obesity and related

chronic diseases (7). The 2015 Dietary Guidelines for Americans (8) and the World Health Organization (9) recommend limiting added sugar to less than 10% of total energy intake (10).

Unlike naturally occurring sugars in foods such as fruit and milk, the majority of manufactured foods and beverages sold in the United States contain added sugars (11), defined as sugars and syrups added during processing or preparation, and/or low-calorie sweeteners (LCS), which provide sweetness with no or few calories. It is paramount to develop a framework that meaningfully addresses factors that influence added sugar intake to devise reasonable strategies for lowering added sugar consumption. This approach requires consideration of the positions of various stakeholders to better understand factors that influence dietary choices and to assess impacts of proposed programs and policies across sectors.

Seminar overview

The consumption of added sugars and low-calorie sweeteners (LCS) is a cross-cutting issue relevant to numerous disciplines. On February 22nd, March 22nd, and April 26th, 2018, faculty members at the George Washington University (GWU) in Washington, DC convened a total of approximately 500 individuals from academia, government, non-profit organizations, private industry, and healthcare, along with independent consultants, dietitians and university students, to participate in a cross-disciplinary discussion surrounding added sugar and LCS intake. The symposium was funded internally by several entities within GWU (see Acknowledgements). No industry

funding was obtained. However, travel expenses for each speaker from private industry were covered by their respective companies. In some cases, presentations from industry speakers were reviewed and approved by their respective companies and in some cases, employees of the respective company provided input regarding edits to earlier drafts of this conference report. Travel expenses for non-industry speakers were paid for by GWU through the University Seminars mechanism.

The overarching purpose of the seminar series was to provide a neutral forum for discussing and critically evaluating approaches to lowering added sugar intake, in a manner that facilitated representation of a range of diverse stakeholder perspectives. The series focused on unanswered questions pertinent to lowering added sugar intake on a population level, and was designed to elicit diverse, and sometimes opposing, views among experts in the field. Thus, not all views expressed in this paper represent the perspective of all authors and not all statements are necessarily substantiated by scientific evidence.

Each of the six debates (two per seminar, shown in Table 1) followed an identical format. A GWU faculty member gave a brief introductory presentation, after which two speakers (typically with different perspectives) delivered 15-minute presentations, in a point-counterpoint format. A 10-minute break followed the presentations to gather questions anonymously from remote and in-person attendees using an online platform (Pigeonhole™). These questions were posed to both speakers during a 25-minute panel discussion, moderated by a GWU faculty member.

Table 1 Topics covered during the GW Sugar and Low-calorie Sweetener Seminar Series

Seminar Date	Debates	Speakers
February 22 nd	Do Farm Bill Policies Impact Population Sugar Intake?	Kathleen Merrigan, PhD (GWU)
'Are Proposed Policies for Reducing Sugar Intake on a Population Level Viable?'	What is the Impact of SSB Taxes on Health and Business?	Vincent Smith, PhD (Montana State University)
Moderator: Bill Dietz, MD PhD		Michael Long, PhD (GWU)
March 22 nd	Is Sugar Addictive?	Richard Black, PhD (Quadrant D Consulting)
'Why is Reducing Sugar Intake so Difficult?'	Product Reformulation Efforts: Progress, Challenges, and Concerns?	Nicole Avena, PhD (Princeton Univ.)
Moderator: Kim Robien, PhD		Courtney Gaine, PhD (The Sugar Association)
April 26 th	Low-calorie Sweeteners: Helpful or Harmful?	Danielle Greenberg, PhD (PepsiCo)
'Are Sugar Alternatives or Other Novel Ingredients Viable Options for Reducing Sugar Intake at the Population Level?'	Are Novel Sweeteners a Plausible Solution?	Margo G. Wootan, DSc (Center for Science in the Public Interest)
Moderators: Sameera Talegawkar, PhD		Allison Sylvetsky Meni, PhD (GWU)
Uriyoan Colon-Ramos, PhD		Marge Leahy, PhD (Food, Nutrition & Policy Solutions LLC)
		Andrew Ohmes, MBA (Cargill Inc.)
		Julie A. Mennella, PhD (Monell Chemical Senses Center)

Seminar 1: Are proposed policies for reducing added sugar intake on a population level viable?

Question #1: 'How Does the Farm Bill Affect Population Sugar Intake?'

Dr. Kathleen Merrigan, Director of the Food Institute at GWU, provided a backdrop on US sugar production to set the stage for policy discussion. The US is one of the largest sugar producers in the world (12). About 4,500 farmers grow sugar crops, 45% of which consist of sugarcane grown primarily in three southern states (13) and 55% of which are sugar beets (14). Almost all US sugar beets, but not sugarcane, are genetically modified. Year after year, the price of US sugar is significantly higher than the world market price (12); which means higher ingredient costs for US manufacturers.

Congress passes the farm bills that set sugar policy, which include several different elements: price supports, production limits, non-recourse loans, and import restrictions. Unlike some farmers, sugar growers do not receive direct subsidies from the government, but these policy mechanisms provide sugar producers with a significant price safety net.

The US Farm Bill, which is renegotiated every 5 years, encompasses 70% of United States Department of Agriculture (USDA) operating budget, and governs agriculture and food programs spanning food safety, trade, nutrition support, and subsidies for farmers (15). Congress is currently negotiating the 2018 Farm Bill, and there are many groups seeking to use the Farm Bill mechanism to modernize sugar policy. Free market think tanks, many of which are opposed to farm programs generally, support sugar policy reform. The lobbyists from food and beverage manufacturers argue that the high cost of sugar upheld by current policy increases costs for US consumers.

Dr. Vincent Smith, Professor of Agricultural Economics at Montana State University, focused on the economics of sugar crops. Sugar beets have a greater production output and are responsible for 45% of sugar (vs. 33% from sugar cane), with the remaining 22% of US sugar being imported. The majority of US added sugar consumption is from sugar beets and sugar cane (approximately 56% combined, 57% and 43% of which is from beets and cane, respectively), and high fructose corn syrup (approximately 31%), with very little overall consumption attributable to other forms, such as honey, rice syrup, wheat syrup or other sources (<15% combined) (16). Despite widespread consumption, the price of sugar in the US is approximately 50% higher than the world price. The increased price is attributable to the US Sugar

Program, a federal commodity support program, which maintains sugar prices for US producers (17). While global sugar prices increased from 2007 to 2012 due to natural disasters, the price of high-fructose corn syrup has also risen due to higher production costs.

According to Dr. Smith, the US Sugar Program results in a net increase of \$1–1.2 billion in net revenues, shared by 4,500 growers, but the distribution of the revenue is heavily skewed to a limited number of individuals (18). Thus, in his opinion the US Sugar Program adversely affects the processing industry and benefits big farms. A major contributor to the high price of sugar is supply controls, including import quotas (high tariffs on imports after a quota is reached), marketing allotments (limits on domestic sugar production based on land space), and loan rates that guarantee a minimum price for refined sugar and, effectively, sugar cane and sugar beets (17), all of which result in a 'hidden tax' to the consumer. However, the Sugar Modernization Act (19) would have modestly reformed these supply controls, increasing competition and lowering the price for the consumer. Dr. Smith concluded that the US Sugar Program should be eliminated. Nevertheless, the new 2018 farm bill, signed by President Trump in December, 2018, maintained the program as established in the previous (2014) farm bill legislation and included a modest, approximately 5 percent increase in the support price for cane sugar, raising the cost of the program for consumers.

During the panel discussion, questions were raised related to production costs of different sweeteners, environmental impacts related to sugar pricing, and hypothetical consequences of dismantling the US Sugar Program. Dr. Smith explained that sugar pricing relates directly to the price of corn, and that the US Farm Bill would not have much of an impact, other than through subsidies that incentivize crop insurance. Overall, Dr. Merrigan concurred with Dr. Smith regarding sugar pricing and the impact of environmental factors.

The speakers offered slightly different perspectives regarding the implications of dismantling the US Sugar Program. While Dr. Merrigan commented that there would not be a large impact on consumption of added sugars given the relatively low price of added sugar, Dr. Smith felt that removing the program would indeed shift consumption, but that the magnitude was unclear.

Question #2. 'What is the Impact of SSB Taxes on Health and Business?'

Dr. Michael Long, Assistant Professor in the Department of Prevention and Community Health at GWU, began by highlighting the fundamental economic concept that when prices go up, people buy less. According to a

systematic review of the literature on the price elasticity of demand for SSBs by Powell et al. (20), on average a 10% price increase is expected to result in a 12% reduction in purchases. Dr. Long presented a logic model for how an SSB excise tax would impact health (Figure 1) based on simulation models of the impact of an SSB tax in the United States (21,22). He discussed evidence supporting the position that SSB taxes will improve population health, but that uncertainty remains as to how much people will benefit (21).

One source of uncertainty is the degree to which taxes will be passed on to consumers. The national tax in Mexico was passed through fully to consumers (23). Estimates of how much of the tax was incorporated into shelf prices from Berkeley, California, ranged from 21.7 to 174% (24). If consumers reduce purchases and consumption of SSBs, including sodas, sports drinks, fruit drinks, and sweetened tea, the tax would only improve health if declines in SSB consumption are not offset by increases in other energy-dense and nutrient-poor foods. Compared to solid foods for which caloric compensation is quite precise, ingestion of SSBs induces only a weak compensatory response (25). Reductions in SSB consumption are therefore expected to lower total calorie intake, leading to weight loss (26,27). Dr. Long shared his work with colleagues on the Childhood Obesity Intervention Cost Effectiveness Study (www.choicesproject.org) in which they estimated that SSB taxation could prevent over half a million cases of childhood obesity and save \$14.2 billion over ten years (22).

Dr. Richard Black, Founder and CEO of Quadrant D Consulting, Adjunct Professor of the Practice at Tufts University's Friedman School of Nutrition Science & Policy, presented challenges to SSB taxation. While SSB consumption is declining, obesity continues to rise, suggesting that taxation alone may not address the problem. Data from the National Health and Nutrition Examination Survey (NHANES) demonstrate that while approximately half of the United States population reports SSB consumption, only a small segment overconsumes them (28,29). Therefore, SSB taxation would likely reduce total calorie intakes only among a subset of the US population.

The food and beverage industry has taken action to reduce added sugar consumption, including front of

package calorie labeling and product reformulation. However, reformulation is costly and is often not well accepted by consumers. It is difficult to match consumer expectations when a product is changed. Releasing new products with lower added sugar content (e.g. Mountain Dew Kickstart™) can be more effective, most likely because there is not a pre-existing expectation as to how a product will taste based on prior experience with a full-sugar formulation.

With regard to SSB taxation, Dr. Black proposed focusing on the added sugar content of beverages, rather than drink volume. If a tax is based on volume, there is not an incentive for manufacturers to reduce the amount of added sugar, because selling less volume is not an incentive for manufacturers. In contrast, taxation based on added sugar quantity creates an incentive for lowering product added sugar content, and ultimately reducing the amount available in the market. Dr. Black proposed that a tax could be modelled after the cap and trade system often proposed for carbon dioxide reduction (30), with the analogy that manufacturers "emit" added sugars into the food supply. Continuing the analogy, an added sugar cap would be set, and manufacturers using less than their permitted cap could sell their extra "emissions" to other manufacturers. Conversely, manufacturers emitting more than their permitted cap could purchase their needed emissions until the pool is exhausted, after which point, products would have to be reformulated to meet the cap. The cap could then be gradually lowered over a period of 20 years, resulting in a substantial reduction of added sugar available in the food supply (30).

In the panel discussion, attendee questions largely challenged the rationale for SSB taxation and highlighted additional key concerns related to SSB taxes. The first question was whether added sugar consumption on a population level is truly excessive. Dr. Black explained that calories are over-consumed, not added sugar specifically, yet added sugar, particularly in beverages, is an easier target for intervention. Dr. Long agreed that other foods contribute to overconsumption, but posited that beverage consumption may result in lower satiety (31,32) which may lead to overconsumption, further justifying targeting SSBs. Dr. Black added that removal of added sugar [and salt] adversely impacts product quality,



Courtesy of Dr. Michael Long

Figure 1 This logic model demonstrates how a sequence of logical steps can be used to synthesize evidence from a range of sources in a simulation model to estimate the health impact of sugar-sweetened beverage (SSB) tax policies.

posing a hurdle for manufacturers (33). Practical challenges in removing added sugar were then discussed (Table 3).

A question was raised as to whether a SSB tax would disproportionately impact low-income communities and small convenience or corner stores (34). The speakers approached the question quite differently. Dr. Long noted that low-income consumers would spend less money on SSBs after the tax. According to a review by Powell et al. (20), a 10% tax will result in a 12% reduction in consumption. Dr. Black suggested that a tiered tax, where beverages are taxed proportionately to their added sugar content, would address this concern, as there would be a minimal change in price and thus, the tax would not be regressive. Dr. Black explained that a tax could be structured such that beverages with lower added sugar content (below a certain threshold, say 80 kcal per 500 ml) have no additional tax burden, whereas beverages above that threshold are taxed on an added sugar content basis, increasing the burden for each additional gram of added sugar. The ability of low-income communities to purchase low sugar beverages, if they chose to continue to purchase SSBs, would be unchanged. This outcome presumes that lower sugar content SSBs are at a minimum equally preferred to full sugar products.

Incentivizing healthy products using differential pricing structures was also discussed, as well as PepsiCo's pledge to lower calories in the market by 20% (35). Dr. Long stated that ideally the Supplemental Nutrition Assistance Program (SNAP) would combine healthy incentive and SSB restriction, but acknowledged that this would not be cost neutral. With regard to PepsiCo's pledge, Dr. Black explained that the emphasis is on LCS (**Seminar 3**), as well as reduced advertising and promotion of full-calorie versions. Advertising practices were then discussed, comparing campaigns to lower tobacco intakes with those to lower added sugar. Dr. Black believed that the health impact was much greater for tobacco, yet Dr. Long felt that using tobacco as an example, the SSB tax should be greater than currently proposed. Dr. Dietz added that efforts for lowering tobacco were not implemented at the federal level (36), but rather, shifts in the medical community's views on tobacco pushed industry to change.

Seminar 2: Why is reducing added sugar intake so difficult?

Question #1. 'Is Sugar Addictive?'

Dr. Nicole Avena, Assistant Professor in the Department of Neuroscience at Mount Sinai University and Visiting

Professor in the Department of Psychology at Princeton University, first addressed the question of 'why sugar is addictive.' According to the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) (37), addiction is defined as 'a cluster of cognitive behavioral, and physiological symptoms indicating that the individual continues using the substance despite significant substance-related problems.' Excessive sugar intake can result in a state that meets several criteria for substance use disorders, including impaired control (bingeing, desire to limit, cravings), risky use (continued substance use despite knowledge of hazard), and pharmacological (tolerance and withdrawal). Excessive sugar intake does not meet a fourth criterion, pertaining to social impairments (e.g. interpersonal problems, giving up activities) related to its use (38). However, Dr. Avena pointed out that not all criteria need to be met to constitute an addictive disorder.

The concept of sugar addiction is supported by studies in rodents, where restricted access results in overconsumption when available (38–41). Consumption of large amounts of sugar by rats results in a rise in dopamine levels, mimicking responses to drugs of abuse (38). Rodents also develop symptoms suggesting anxiety, stress, and withdrawal symptoms when sugar is removed and exhibit potentially harmful behaviours, such as crossing a shock grid, to regain access (40). An altered brain response to drinking glucose and fructose has also been reported in children with obesity (42). Despite convincing evidence presented, Dr. Avena addressed several common critiques challenging the concept of sugar addiction (Table 2).

Dr. P. Courtney Gaine, President and CEO of The Sugar Association, explained that sugar serves multiple purposes in foods beyond sweetness (Table 3) and may need to be replaced with several ingredients when removed from foods and beverages. Importantly, while added sugar intakes have declined over the past 15 years (43), obesity rates have continued to rise (44) (Figure 2). She pointed to data showing that on average, added sugars currently comprise approximately 13% of total calorie intake in the US population, thus only exceeding federal guidance by 3%, which would not explain current obesity rates (45). Increases in obesity are due to overconsumption of calories from all sources, and sugar is not by itself driving this trend (46).

Dr. Gaine stated that individuals consume foods rather than nutrients alone, and thus, addiction to food or the behavior of eating is more plausible than addiction to a specific nutrient (47). She reiterated that heavy reliance on rodent models lowers enthusiasm for the existence of sugar addiction in humans, since rodent findings are not necessarily translatable to human consumption.

Table 2 Common critiques to the concept of sugar addiction

Critique Identified by Dr. Avena	Response (also by Dr. Avena)
Too much of anything is bad for you (e.g., too much water could technically harm you)	People consume excess sugar because it tastes good and is difficult to regulate intake, which limits self-control. This argument would be analogous to recommending that individuals consume 'only a little bit of heroin.'
We need food to survive	There are a variety of foods available to consume. We need food for calories and nutrition, but we do not need the foods that contain excessive amounts of added sugar to survive.
The act of eating is addictive, not the food Rodents are not humans	Why do not people overconsume broccoli and carrots? Humans share 99% of our genome with rodents. Rodent models provide important functional information, which then can be validated and confirmed in humans.
Sugar addiction is less severe than real addictions	The most common addiction in modern society is smoking. Smokers are typically fully functioning individuals with little noticeable intoxication. Meanwhile, smoking is the largest contributor to preventable death in the United States. The severity and impairment does not have to be particularly extreme (as one sees with heroin or other drug overdoses) to constitute an addiction.

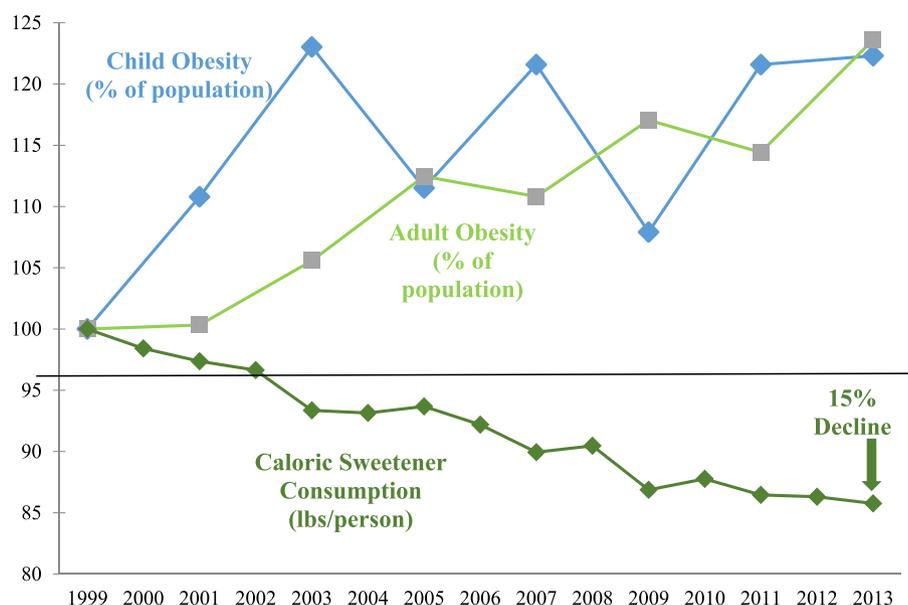
Table 3 Functional roles of added sugars in food and beverage products

Functional Role	Description	Examples
Product Colour	Required for Maillard browning reaction, caramelization	Baked goods, soft drinks
Product Texture	Provides lightness, bulk, mouthfeel	Baked goods, candies, cereals, ice creams
Preservation	Reduces water activity in foods thereby dehydrating microorganisms	Jams, preserves, frozen fruit
Fermentation	Food source for microorganisms	Yogurt, wine, beer, cheese, bread
Bitter Masking, Increasing Palatability	Adds sweetness. Diminishes or eliminates the unpleasant tastes (e.g. bitter) of ingredients or byproducts of processing/manufacturing	Many foods, beverages, medications

During the discussion, Drs. Avena and Gaine both reiterated the importance of research surrounding added sugar, while simultaneously addressing other contributors to obesity. Both agreed that added sugar was not the only nutrient that could be associated with addiction or over-eating and that research focused on other dietary constituents is warranted. Dr. Avena pointed out that the whereas the dopamine response typically habituates with repeated exposure to a given food, rodents elicit comparable dopamine responses following each exposure to sweet tasting stimuli, consistent with patterns observed with drugs of abuse (40). Both further agreed that the 'dose is the poison,' necessitating improved nutrition education to reduce intakes.

Question #2. 'Product Reformulation Efforts: Progress, Challenges, and Concerns?'

Dr. Danielle Greenberg, Senior Director and Senior Fellow in Nutrition at PepsiCo Inc., started by explaining that 'sugar' encompasses a range of compounds, including monosaccharides, disaccharides, sugar derivatives, fruit sugars, and syrups, and reiterated the functional properties of added sugars in foods and beverages (Table 3). She described how the food industry has worked to lower added sugar using various strategies, including offering smaller portion sizes, reformulating products, using flavours to enhance sweetness, and using LCS. For example, PepsiCo has removed approximately 434,000



Source: Sugar Data -- Economic Research Service/USDA:
<http://www.ers.usda.gov/Briefing/sugar/data/table51.xls>.
 Obesity Data -- Centers for Disease Control and Prevention/HHS.
 Note: Official obesity data available only for years shown.

Figure 2 Despite increases in obesity among children and adults from 1999 to 2013, caloric sweetener consumption decreased over the same period.

metric tons of added sugars from their beverage portfolio in the US and Canada since 2006 (35). Similarly, Coca-Cola has removed 96,000 tons from their portfolio in Western Europe, the equivalent of 384 billion calories (48). And Nestle removed 39,000 tons globally between 2014 and 2016 (49).

The remainder of Dr. Greenberg's presentation focused on the use of LCS, which was a key topic of the third seminar and is discussed below (see Seminar 3).

Dr. Margo G. Wootan, Vice President for Nutrition at the Center for Science in the Public Interest (CSPI), focused on the extent to which the food environment makes it difficult for individuals to make healthy choices (50). This is in large part due to the ubiquity of food, food formulations, product packaging and pricing, portion size (51,52), and powerful marketing and advertising by the food industry (53). Unhealthy defaults are external influences which facilitate poor dietary choices, often without one being aware of this influence (54,55). For example, the checkout aisle at most retail outlets is replete with added sugar-rich candies, and the widespread availability of such products has become a societal norm (56). Given that consumption of food outside of the home has increased markedly since 1970 (57,58), Dr. Wootan suggested that excess calorie intakes promoted by large portion sizes at restaurants (59,60) likely play a significant role in the rise in obesity over time (61). Furthermore, in-store marketing and product placements play an

important role in encouraging purchases of energy-dense and high-sugar foods and beverages.

Dr. Wootan argued that although the food industry has taken steps to reformulate products, companies must do more to offer lower-calorie products and promote them to the same or greater extent as full calorie offerings. Approaches should include more aggressive efforts to improve nutritional quality and reduce portion sizes at restaurants, implement food service guidelines in schools, hospitals, public property, and other organizations, remove candy and other nutritionally poor items at checkout, and to use policy, including SSB taxation to encourage healthier choices.

In the panel discussion, both speakers agreed that large portion sizes are problematic. Dr. Greenberg reiterated the extent to which there has been tremendous progress in this area, citing the release of 7.5 ounce soda cans and the growth of sparkling water in the past five years. Dr. Greenberg also explained that while excess added sugar intake is indeed a concern, there is a need to address the whole diet. Dr. Wootan agreed that other aspects of the diet are problematic, but cautioned that there may be danger in addressing too many components simultaneously. Rather, she stated that careful targeting of key contributors to excess calorie intake, such as SSBs, is paramount.

The speakers debated the extent to which SSBs are key contributors to total calorie intakes. Dr. Greenberg felt

that while SSBs are the greatest contributors to sugar calories, SSBs comprise only 7% of total calorie intake (45) and stated that other foods, such as pizza are greater contributors to total calorie intakes in the US compared to SSBs (62). In response, Dr. Wootan cautioned that it depends on how SSBs are represented. When fruit drinks, sweetened teas, and other sugar-containing beverages are included in addition to soda, SSBs comprise a greater proportion of sugar calories (63) and therefore, Dr. Wootan believed that it would be a mistake to overlook these beverages. She pointed out that SSBs have been linked to type 2 diabetes, cardiovascular disease, among other health conditions (64). In addition, if SSBs comprise 7% of total calorie intake on average, this means that a large subset of the population is consuming more than this amount.

Although Dr. Greenberg agreed that it is important to address added sugar, she argued that the food industry, as a whole, has been committed to lowering sugar intake, yet industry efforts to lower added sugar have been largely ignored by the public health community. Despite marked reductions in added sugar intake, obesity rates have not declined (46), which in Dr. Greenberg's opinion, suggests that while further reductions in sugar intake are possible, this may not result in a reduction in obesity. However, Dr. Greenberg pointed out that additional efforts could absolutely be put forth to lower sugar intake, such as reducing portion sizes and changing offerings in restaurants, actions which are not limited to only targeting SSBs.

Dr. Wootan agreed, and further suggested that beverage companies, such as PepsiCo, work with restaurants with whom they have exclusive contracts to make changes to restaurant offerings, such as removing SSBs from the kids menu. Dr. Greenberg felt that this was a good idea and described actions that companies have already taken with respect to children, for example, removing full-sugar SSBs from schools (65). She also mentioned that the American Beverage Association has a commitment to reduce calories in its portfolio by 20% by 2025 (65), while individual companies have additional goals.

Dr. Wootan commended the industry for introducing smaller product sizes, but urged a change in marketing practices to support consumption of reformulated and/or re-packaged products. Dr. Greenberg responded that the industry is indeed shifting marketing efforts, as evidenced by recent 2018 Super Bowl advertisements for zero-calorie beverages, including PepsiMax™ and new a line of Diet Coke products. Dr. Wootan felt that similar efforts to promote lower-calorie products must especially target in-store advertising and not just 'one-time' advertisements, such as a television commercial. Both

agreed that there is great value in forging cooperative partnerships between industry and non-profits and advocacy groups. Such collaborations (66) have already been successful in related areas, including removal of SSBs from schools (67) and menu labeling (68).

Seminar 3: Are added sugar alternatives or other novel ingredients viable options for reducing added sugar intake at the population level?

Question #3. 'Non-nutritive Sweeteners: Helpful or Harmful?'

Dr. Allison Sylvetsky, Assistant Professor in the Department of Exercise and Nutrition Sciences at GWU discussed discrepant findings between observational and interventional studies evaluating the role of LCS in weight and health (69). Whereas prospective cohort studies have generally reported positive associations between LCS consumption, weight gain, and diabetes (70), the majority of RCTs demonstrate that LCS are helpful in achieving weight loss (71).

Potential explanations for discrepancies were then described. While reverse causality and residual confounding are inherent to observational studies, and, in part, explain associations between LCS consumption and unfavourable health outcomes, several biologically plausible mechanisms have been proposed, and are likely not mutually exclusive. These include LCS-induced changes in the gut microbiota resulting in metabolic perturbations (72), promotion of adipogenesis leading to fat accumulation (73), and a disturbance of the body's expected response to sweetness (74). Despite data to support these mechanisms in cellular and rodent models, few studies have tested these mechanisms in humans.

While RCTs examining effects of LCS on body weight demonstrate that LCS are indeed helpful for weight management, the context of LCS administration in RCTs is often not generalizable to free-living individuals (69). For example, many studies test LCS as 1:1 replacements for added sugars, yet LCS are not only used as replacements. Studies lacking a control group (e.g. water or another unsweetened beverage or no intervention) cannot address effects of incorporating LCS in addition to one's usual diet (75). Recent studies comparing effects of LCS with water have reported benefits of LCS on body weight. However, these studies often occur within a weight loss intervention, enrol participants who already habitually consume LCS, and are of a relatively short duration (typically <1 year) in comparison to prospective cohort studies. Participants receiving concomitant behavioural

support or who are instructed to continue their usual LCS consumption rather than switching to plain water, have favourable outcomes (76). While LCS may serve as a useful tool for increasing adherence to calorie-restricted diets, study context and factors such as life stage, type of LCS, source of LCS, weight status, and motivation for use, must be considered. In addition, few RCTs have tested LCS effects on glycemia, inflammation, and cardiometabolic biomarkers.

Dr. Marge Leahy, independent consultant in food science, nutrition, and policy and formerly the Director of Health and Nutrition Science at the Coca-Cola Company, highlighted several key benefits of LCS. These include provision of sweetness with no or few calories, offering a sweet option for those with diabetes, their non-cariogenic nature (77), and the ability of LCS to assist with weight management (71) and improve diet quality (78). The extent to which LCS are helpful for weight management was primarily based on results of recent systematic reviews and meta-analyses investigating the role of LCS in weight loss and maintenance (70,71,79).

The majority of RCTs show that replacement of SSBs with LCS reduces body weight (71). Although only a few studies have compared administration of LCS containing beverages with water, LCS use is equivalent, if not superior, for weight loss (76,80). Evidence from systematic reviews (81) indicates that replacement of added sugar with LCS produces weight loss. This may also be the case when LCS are used in place of water (71), particularly when administered in beverages (71). While reductions in body weight observed with LCS use are modest, it is unlikely that a single dietary change or relatively short intervention would elicit significant weight loss. The extent to which study findings depend on the comparator (e.g. SSB, water, nothing) was also reiterated.

Dr. Leahy then focused on associations between LCS consumption and diet quality. Two RCTs demonstrated beneficial effects of diet beverages on diet quality, one reporting lower dessert consumption (82) and the other reporting higher whole grain and lower trans-fat intakes (83), in those randomized to LCS whereas cross-sectional data are inconsistent. In Dr. Leahy's opinion, LCS have generally positive effects based on the totality of the available evidence. However, their potential to aid in weight management depends on how LCS are used.

In the panel discussion, both presenters agreed that the context of LCS use differs when comparing study designs. Dr. Sylvetsky reiterated that cohort studies have the advantages of long follow-up periods compared to RCTs, which is important because chronic diseases develop over the course of several years. Dr. Leahy cautioned that findings in observational studies often do not predict findings in RCTs, which may be due to

difficulties in dietary assessment and residual confounding inherent to observational analyses (81).

Elaborating on contextual factors surrounding LCS use, Dr. Sylvetsky stated that LCS are predominantly consumed in beverages (84). LCS are also widely present in condiments, tabletop packets, and foods, further complicating accurate measurement of LCS intake using traditional dietary assessment methods (85). Dr. Leahy echoed the difficulty of assessing LCS intake, globally and in the United States. In addition, efforts to better understand motivations for LCS use are also important for elucidating health outcomes related to LCS use. While biomarkers offer a potential solution for addressing the limitations of self-report methods, the development of reliable biomarkers by LCS intake is in its infancy and practical challenges exist, particularly for aspartame which is degraded rapidly after ingestion (86).

Another important area of discussion pertained to the role of LCS in diet quality. Both presenters emphasized the importance of looking at the totality of the evidence, and that specific emphasis be placed on the comparators in a given study (75). The two speakers expressed different viewpoints with regard to the hypothesis that LCS use may encourage a stronger preference for sweetness. Dr. Leahy cited two RCTs reporting no increases in added sugar intake with LCS consumption (82,83), while Dr. Sylvetsky stated that this question may be difficult to assess in adults, and may be most important for children who are known to consume more of a given substance when it is sweeter (87). The remainder of the discussion covered priorities and challenges for translating findings in rodent models into the context of human consumption. The speakers agreed that additional well-designed studies in humans, particularly assessing outcomes other than body weight, are urgently needed (88).

Question 2. 'Are Novel Sweeteners a Plausible Solution?'

Mr. Andrew Ohmes, Global Product Line Leader for High Intensity Sweeteners at Cargill, provided an introduction to Cargill as a company and presented how novel sweeteners offer a solution for reducing added sugar intake. Mr. Ohmes also clarified that the term 'new' sweeteners is preferred, as the sweeteners discussed in his presentation have existed for as many as ten years. As for whether the new sweeteners are a plausible solution for reducing sugar intake at the population level, Mr. Ohmes felt strongly that the answer was 'yes,' citing that two new sweeteners, stevia and polyols, have replaced more than two billion pounds of sugar in the market in the last five years (Cargill internal sales data), which translates to over three trillion calories.

Mr. Ohmes then addressed why new sweeteners are necessary, given that there are already numerous caloric and non-caloric sweeteners available on the market. He reiterated the extent to which added sugar intake in the United States exceed the World Health Organization recommendation (9) and further explained that the majority of Americans are trying to avoid or limit sugars and 'artificial sweeteners (89), which underscores the need for novel LCS from natural sources. Artificial sweeteners were the sixth most avoided ingredient reported by consumers (90), following added sugar, salt, high fructose corn syrup, fats/oils, and other artificial ingredients (89), highlighting the need for something new. The food industry is responding to consumer desire to lower added sugar, while maintaining product palatability, (91–93) but from the standpoint of a consumer packaged goods company, there are numerous issues to consider. These include guidance to reduce added sugar from public health organizations (9), proposed changes to the nutrition facts panel, proposed policies to reduce added sugar intake such as SSB taxes (94), and consumer desire to reduce added sugar intake (95), all reiterating the need to lower product sugar content. However, while there is significant pressure to reduce sugar and while consumers express a desire to avoid artificial sweeteners, the International Food Information Council (IFIC) 2017 Food and Health survey revealed that 'taste' remains a key driver of food selection and consumer purchasing decisions (89). And thus, despite consumers concerns surrounding their added sugar intake, Ohmes commented that if something is healthy but does not taste good, no one will buy it. Someone might buy it once, but if they do not like the taste, they are not going to purchase it again (90).

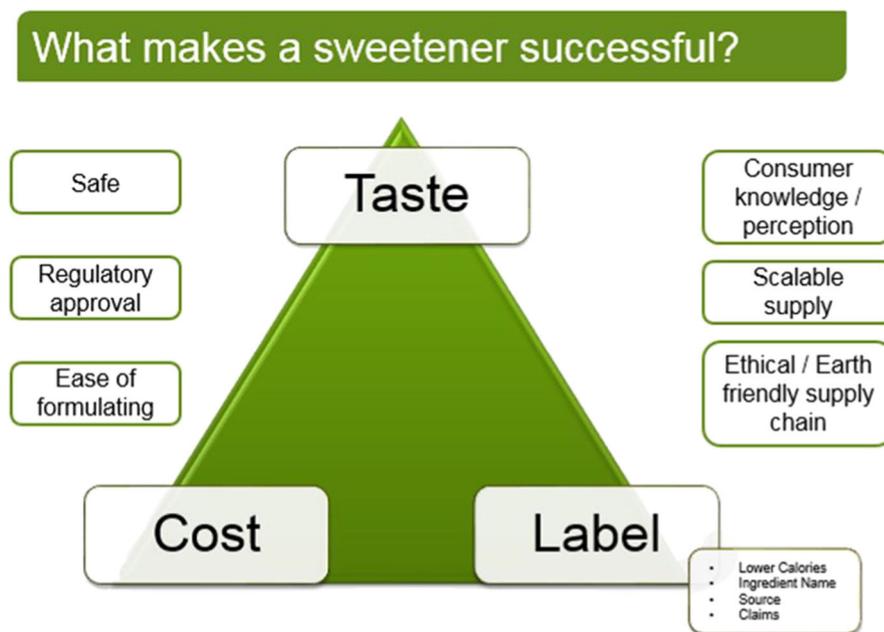
Given mixed consumer acceptance of artificial sweeteners such as aspartame, saccharin, and sucralose (89), several new sweeteners provide alternatives to these artificial LCS. Stevia leaf extract is a zero-calorie high potency sweetener, is approximately 250X sweeter by weight compared to sucrose, is non-glycemic, and is heat, light, and pH stable, making it well-suited for use in a variety of applications. It is extracted from the stevia plant, originally grown in South America, and the sweet parts of the plant are called steviol glycosides (96). Monk fruit extract, also known as Luo Han Guo, is similarly high-intensity (200–250 times sweeter than sucrose by weight) and zero-calorie, and is extracted from a small round fruit grown in Southeast Asia. The sweet parts of the plant are called mogrosides. It is relatively new to the US market and does not have wide global regulatory approval at present (97). Another alternative LCS is erythritol, which is 70% as sweet as sucrose by weight and is naturally occurring in many fruits (e.g. grapes, pears, melons) and fermented foods (98) and can be made commercially

through fermentation. Erythritol can replace added sugar because has a similar density and serves as a bulking agent, a limitation of higher-potency ingredients which cannot provide that mouthfeel alone (99). Importantly, erythritol not only enhances sweetness, but also decreases bitterness and licorice tastes which consumers often find unpleasant (Cargill internal sensory analysis report #1220). According to Mr. Ohmes, the success of a sweetener is based on taste, cost, and labeling, in addition to being established as safe, gaining necessary regulatory approval, being environmentally friendly, and being relatively easy to formulate (Figure 3). Novel sweeteners that satisfy these criteria have great potential to support adherence to sugar-reduction targets and consumers need to be educated on their safety (100) and multitude of potential uses (101).

Mr. Ohmes then provided an example of what needs to happen for a sweetener to be successful, using stevia as an example. From a regulatory perspective, he explained that prior to 2007, stevia was not available in the United States as a food additive, but could be purchased as a dietary supplement. As of 2008, stevia, specifically high purity rebaudioside A received a designation of generally recognized as safe (GRAS) (100). However, the problem was that stevia had taste challenges when used at high levels for sugar reduction, and thus, Cargill further experimented with a variety of glycosides to find a combination that was more palatable to consumers (Cargill internal sensory analysis data).

In their commitment to help reduce added sugar intake in the food supply, Cargill offers US manufacturers alternative sweetener options such as stevia leaf extracts, fermentation-derived steviol glycosides, chicory root fibre, and erythritol (102). There is large growth in products placed into the marketplace containing stevia-based sweeteners (103). These formulations span product portfolios including beverages, dairy, snacks, cereal, bakery, ice cream, and confectionary, as well as dietary supplements and sports nutrition products (103).

Dr. Julie Mennella, a member of the Monell Chemical Senses Center, discussed the biology of for sweet taste and its impact on food preferences among children. In an environment with limited nutrients and abundant poisonous plants, our sensory systems evolved to detect and prefer perceptions that specify crucial nutrients such as the once rare energy (carbohydrate)-rich plants that taste sweet and the saltiness of a needed mineral, while rejecting potential toxins that taste bitter (104,105). While this "sweet" attraction may have served children well in a feast-or-famine setting, attracting them to mothers' milk and then to energy-rich foods during periods of growth, (106,107) today it makes them vulnerable to our current food environment, which is replete with nutrient-poor



Courtesy of Mr. Andrew Ohmes

Figure 3 The success of a sweetener is based on several factors, primarily taste, cost, and labeling, in addition to being established as safe, gaining necessary regulatory approval, and being relatively easy to formulate. Novel sweeteners that satisfy these criteria have great potential to support adherence to added sugar reduction targets.

foods and beverages rich in sweetness from added sugars, sweet enhancers and LCS (108).

From age of two years, an American is more likely to consume a manufactured sweet than a fruit or vegetable on a given day (109). Children's intakes of added sugar, typically from SSB and manufactured foods (110), far exceed the recommended levels of less than 25 grams daily (111), a troubling statistic given that food preferences are established early in life.

Dr. Mennella then provided an overview of the biology of sweet taste perception, which is mediated by the binding of sweet-tasting chemicals to peripheral taste receptors, which then relay signals to various regions of the brain, many of which are involved in reward (112). Although once thought to be restricted to the oral cavity, taste receptors are ubiquitous throughout the body and play a role in a variety of functions including immune defense (113,114) and metabolism (115). Both added sugars and LCS also play a functional role in food science, not only by adding a preferred taste but masking the bitterness and other bad or off tastes (116) (Table 3).

She then reviewed the convergence of scientific evidence that humans can detect and prefer sweetness from an early age. Within hours of birth, infants will ingest (117,118) and suck more (119) of a sweetened solution than water and will make more hand-to-mouth movements (120) display facial expressions of relaxation and pleasure (121) when a sweet-tasting substance is in the

oral cavity, a behavioural response that is phylogenetically well-conserved (121,122). During infancy (123) and childhood (124,125), tasting a sweet liquid blunts expression of pain from minor painful procedures (e.g., heelprick) or during a cold pressor test, respectively. To determine whether the effect on pain was due to the sweet taste *per se* (e.g., activating brain reward network (126)) or post-ingestive consequences, investigators determined whether the effects of LCS were similar to sucrose in crying infants. The infants' behavioural responses when tasting an aspartame solution was similar to that when tasting sucrose (120), most likely due to activation of the brain-reward network underlying pain (126).

Preferences for sweetness remain elevated during childhood, coinciding with periods of maximal growth (106,107). Using a forced-choice psychophysical method validated for the NIH Toolbox, research has shown that children most prefer a higher level of sweetness from nutritive sugars (e.g., sucrose (127), fructose (128)) than do adults. The concentration of sucrose most preferred by children is equivalent to approximately 14 teaspoons of sugar in 237 ml of water (i.e., an eight-ounce glass), nearly twice the sugar concentration of a typical cola which represents the most preferred level of adults (108). Recent evidence suggests that children also prefer higher levels of some (e.g., sucralose, aspartame) but not all (e.g., Acesulfame K [Ace-K], Stevia) LCS (108). Some LCS, like Ace-K elicit an objectionable bitter off-taste in addition to

sweetness that varies in intensity across individuals. Like adults, variation in the liking of AceK is explained by variation in one of the bitter taste receptor genes (129), highlighting how some children may have an inborn vulnerability (e.g., blind to the bitterness of the LCS) which may lead to overconsumption of Ace-K-containing foods and beverages.

Adult patterns of lower preferred sweetness emerge during mid-adolescence (108,127,130). Such developmental changes may result from central, rather than peripheral changes, as evidenced by the finding that age-related declines in the level of sweetness most preferred parallel the age-related declines in dopamine receptor binding in the striatum (131), a subcortical region of the brain involved in reward circuitry and sweetness (132).

Research has shown that through familiarization and repeated exposure, children develop a sense of what should, or should not, taste sweet early. Early exposure to sweetened liquids is associated with greater preferences for sweetness during childhood (133). As such, while replacement of added sugars with LCS may lower the caloric content, it teaches the child about the context of sweetness, that is how sweet a food or beverage should taste and may promote overconsumption.

The panel discussion began with a question about the safety of novel LCS. Both speakers agreed that safety is paramount, and Mr. Ohmes explained that safety and regulatory considerations are a key aspect of evaluating the potential success of new LCS. Dr. Mennella further commented that there are few human studies on the metabolic effects of stevia. She also pointed out that many parents are not aware of the presence of LCS in packaged foods and beverages (134). Parents often purchase products containing LCS, despite not wanting to feed them to their children, which highlights the consumers' confusion surrounding food labeling (135).

The conversation then shifted to discuss the sweetness of the food supply and the extent to which exposure to sweet tasting foods and beverages early in life may affect future dietary choices. Dr. Mennella explained that the research on sweet taste in children is international and repeatedly shows that preference for sweetness is elevated during childhood and that children learn to like what they eat. Thus, the widespread use of LCS in the food supply may be teaching children that many otherwise not sweetened or lightly sweetened foods, should have a high level of sweetness. More research is needed to understand how children learn to like the taste of a family diet that is nutrient rich in healthy foods such as fruit and vegetables to set them on a healthy start.

Mr. Ohmes agreed that it is difficult to gauge the sweetness of a product from its label, and used the

example of stevia, which reaches a maximum sweetness threshold and therefore, like many high-potency LCS, cannot reach extremely high sweetness levels and rather, has an unpleasant and bitter aftertaste at high concentrations. Furthermore, there are numerous extracts of the Stevia plant, which vary in taste (101). Through using stevia and other newer LCS, Mr. Ohmes explained that the meaning of 'full-calorie' could be re-defined, with potential to markedly impact calorie intake and obesity.

As Dr. Mennella pointed out, reductions in added sugar in foods and beverages is often achieved by the use of LCS alone or blends of added sugar, LCS and/or other ingredients that enhance sweetness. Meanwhile, the long-term impact that LCS ingestion has on the developing child, specifically with regard to metabolism and contextual learning about sweetness, remains an important area for future research (87,105,136).

Overall conclusions

The GWU Sugar and Low-calorie Sweetener Seminar Series provided a neutral forum for discussing and critically evaluating approaches to lowering added sugar intake and facilitated representation of a range of stakeholder perspectives. The series was not intended to produce consensus or actionable conclusions, but rather, was designed to set the foundation for robust cross-sector dialogue necessary to inform meaningful future research, and ultimately, effective policies for lowering added sugar intakes.

The organizers plan to continue to engage key representatives across disciplines with the long-term goal of achieving consensus regarding the acceptability and feasibility of the strategies discussed. The immediate next step is to convene experts across sectors who will present their viewpoints regarding various proposed strategies for lowering added sugar intake. This process will elucidate approaches that are most likely to be successfully implemented and will allow for more informed prioritization. Recordings of the presentations will again be made publicly accessible and information will be posted at <http://publichealth.gwu.edu/redstone-center> once available.

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final version. In most cases, the views expressed by the speakers in this report do not necessarily reflect the views of their organizations. However, in the cases of some industry speakers, the views expressed by the speakers in this report were reviewed by their respective companies.

Conflict of Interest Statement

The following authors have no conflicts relevant to this topic to report: Allison C. Sylvestsky, Audrey Hiedacavage, Niyeti Shah, Paige Pokorney, Kim Robien, Jennifer Sacke, Bill Dietz, Uriyoan Colon-Ramos, Sameera Talegawkar, Michael W. Long, Kathleen Merrigan, Nicole Avena, Margo G. Wootan, Julie A. Mennella.

The following authors acknowledged the conflicts of interest listed below:

Richard Black currently consults for The Bill & Melinda Gates Foundation, The American Egg Board, Weight Watchers and has previously worked in the food and beverage industry with the following companies: Kellogg, Nestlé, Novartis, Kraft Foods/Mondelēz, PepsiCo.

P. Courtney Gaine is President and CEO of The Sugar Association, Inc.

Danielle Greenberg was at the time of the conference a full-time employee of PepsiCo Inc.

Marge Leahy is currently an independent consultant. She worked in the food and beverage industry, at Ocean Spray Cranberries Inc. and the Coca-Cola Company. She recently served as senior nutrition advisor at the North American Branch of the International Life Sciences Institute, a public, non-profit scientific foundation that advances the understanding and application of science related to the nutritional quality and safety of the food supply, which provided funding for her travel for this meeting.

Andrew Ohmes is a full-time employee of Cargill, Incorporated.

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