Applied Physiology, Nutrition, and Metabolism

OPEN ACCESS | Perspective

Low- and no-calorie sweeteners and health: unravelling the evidence and controversy

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Abstract

Low- and no-calorie sweeteners (LNCS) (also referred to as non-nutritive sweeteners) have been the subject of controversy, especially considering recent conditional recommendations by the World Health Organization (WHO) not to use LNCS as a means of controlling weight and disease risk reduction. We summarize the data presented and discussions held between a panel of international nutrition research experts at a high-level Canadian Nutrition Society Thematic conference on "Non-nutritive sweeteners and health: unravelling the evidence and controversy", which took place in Toronto, Canada on 27 January 2024. This paper summarizes the proceedings, including discussions on global sugar reduction policies, the toxicological safety and public perceptions of LNCS, divergence between public health and clinical practice guidance, and potential biological mechanisms underlying their effects. Randomized controlled trials show benefits of LNCS when substituting for sugars, while long-term cohort data have methodological limitations such as reverse causation and residual confounding. Mechanistic evidence does not support major adverse effects on energy intake regulation, glycemia, or gut microbiota. Together, these findings highlight the need for harmonized global policies, rigorous study designs that model real-world substitutions, and improved communication strategies to address misinformation.

Key words: nutrition epidemiology, nutrition, obesity, metabolic syndrome

Introduction

High intakes of free and added sugars have been associated with poor dietary quality, obesity, and risk of noncommunicable diseases (NCDs) such as cardiovascular disease and type 2 diabetes (Malik and Hu 2019, 2022). In 2015, the World Health Organization (WHO) issued guidance on limiting free sugars intake to reduce the risk of unhealthy weight gain and dental caries (World Health Organization 2015). Following the release of this guideline and as dietary guidance and public health measures continue to call for reductions in intake of free sugars to prevent weight gain and cardiometabolic risk, there is growing interest in low- and no-calorie sweeteners (LNCS), compounds that sweeten without providing significant food energy. Several LNCS have been approved for use by Health Canada, including aspartame, acesulfame-potassium, sucralose, and steviol glycosides (stevia) (Magnuson et al. 2016; Health Canada 2024), and all are widely used in the food supply to replace sugars and to lower calories in several packaged products (Popkin and Nielsen 2003; Sylvetsky and Rother 2016; Dunford et al. 2018; Russell et al. 2023). However, inconsistent findings across and between both observational studies and clinical trials (Rios-Leyvraz and Montez 2022) have obscured dietary guidance regarding LNCS, giving rise to confusion among the scien-

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tific community (Diabetes UK 2018 Nutrition Working Group 2018; Johnson et al. 2018; Sievenpiper et al. 2018; Health Canada 2019; Dietary Guidelines Advisory Committee 2020; American Diabetes Association 2022; Rios-Leyvraz and Montez 2022; World Health Organization 2023) and the public (Garza et al. 2019). This is reflected in the recent 2023 WHO guidelines (World Health Organization 2023) that caution against use of LNCS for weight control or NCD risk reduction based on a commissioned systematic review and meta-analysis of the scientific evidence (Rios-Leyvraz and Montez 2022). Findings suggest shorter-term benefits or neutral effects of LNCS use on body weight in trials lasting from 4 weeks to 3 years, and a mix or neutral and harmful results from longer-term prospective cohort studies (Rios-Leyvraz and Montez 2022). However, cohort studies are prone to residual confounding that can result in spurious positive associations, and reverse causation since individuals may consume LNCS to control their body weight or metabolic risk, especially if only baseline measures are utilized (Sievenpiper et al. 2017; Malik 2019; Mela et al. 2020). Further adding to the complexity of the evidence is a limited understanding of potential biological mechanisms supporting a link between LNCS and adverse health, and that different LNCS may elicit different metabolic effects (Magnuson et al. 2016).

Sugars reduction—Where are we and what do we need to do?

In 2021, a virtual pre-conference workshop entitled, "The Scoop on Sugar: New Research Findings on Sugar and Health" (Canadian Nutrition Society 2021), was delivered by the Canadian Nutrition Society (CNS) in partnership with the Canadian Institute for Health Research–Institute of Nutrition, Metabolism and Diabetes (CIHR-INMD) to provide an overview and update of research findings and emphasizing knowledge translation. Given the public health priority to reduce intake of free sugars and the potential role LNCS can play in this process, a comprehensive understanding of the evidence on LNCS and health was needed to guide practitioners and policymakers in helping Canadians achieve free sugars targets. Consequently, a meeting of international nutritional scientists and dietitians was held in January 2024 to share novel research and insights on the state of science on LNCS. This paper summarizes the discussions held at the meeting.

The reduction of free (i.e., sugars extracted from their original food matrix) and added sugars (i.e., sugars added during food processing or preparation) continues to be a central objective of nutrition policy globally, driven by evidence linking high intakes of free and added sugars to dental caries, obesity, and NCDs (World Health Organization 2015; Health Canada 2019; USDA 2025; U.S. Department of Health and Human Services and U.S. Department of Agriculture 2025).

Both Health Canada and WHO strongly recommended *free* sugars be reduced to less than 10% of energy (World Health Organization 2015; Health Canada 2019), whereas the United States Department of Agriculture (USDA) recommends *added* sugars consumption to be less than 10% of energy (U.S. Department of Health and Human Services and U.S. Department of Agriculture 2025; USDA 2025). These recommendations have translated into policies to promote sugar reduction, including taxation, front-of-pack (FOP) labeling, and marketing restrictions to children (Malik and Hu 2022). In 2023, the WHO released guidelines to protect children from the impact of food marketing, as foods marketed to children are higher in sugars and sweeteners (Cruz-Casarrubias et al. 2021). Canada has not yet implemented policies to restrict food marketing to children.

Over 50 countries, including Canada, now have some form of sweet beverage tax, of which one third also include LNCSs as a taxed beverages (Global Food Research Program 2026). These beverage taxes are diverse in designs ranging from flat rates to tiered levies based on sugar content and operate at the national, provincial or municipal level (Andreyeva et al. 2022). The "golden rule" observed across jurisdictions is that a 10% tax typically results in a 10% reduction in SSB purchases (Teng et al. 2019).

Canada will be implementing two labeling policies by 2026. Firstly, the amount of LNCS will no longer be required in the ingredients list, which will align labeling requirements of LNCS and other food additives. Secondly, as part of Canada's healthy eating strategy, all packaged products will display a "high in" FOP nutrition symbol, highlighting three nutrients-of-concern: saturated fats, total sugars and sodium. It is estimated that 25% of the packaged food supply will be required to display a "high in total sugars" claim on their FOP (Lee et al. 2023). Globally, there is heterogeneity in FOP policies, including whether they are mandatory or voluntary and if they include LNCS in their scoring e.g., Warning labels (Reyes et al. 2019), Health Star rating (Shahid et al. 2020), Nutri-Score (Vandevijvere 2020). Evidence from Chile demonstrates that FOP warning labels are particularly effective in changing consumer behavior, leading to substantial reductions in purchases of SSBs and increased purchases of LNCS-products (Taillie et al. 2020; Rebolledo et al. 2023). Mexico, like Chile, implemented combined taxation and FOP policies, but unlike Chile, they have also implemented a FOP label cautioning against LNCS use, particularly in children. These FOP warning labels in Mexico have reduced the perceived healthfulness of low- and no-calorie sweetened beverages (LNCSB) (Arellano-Gómez et al. 2023). When FOP labels do not include LNCS in their algorithms e.g., Health Star Rating (Shahid et al. 2020), products with LNCS are given a healthier rating, whereas the opposite is true for FOP labels that deem LNCS-products as unhealthy e.g., Nutri-Score (Vandevijvere 2020) leading to inconsistencies in policy messaging, public perception, and different incentives for product reformulation across jurisdictions.

While sugar reduction is a public health priority, jurisdictions and authorities implement LNCS policies differently (e.g., encouragement to reformulate, avoid or promote LNCS-products) leading to the potential for dissimilar consequences across the world. Policy and guideline makers should continue to consider the role of energy control and food source when it comes to consumption of sugars for the prevention and management of NCDs. Targeting free and added sugars, particularly from SSBs, as a source of excess calories

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remains a prudent strategy, because sugary foods and beverages can be a proximate pathway to overconsumption. However, the replacement of sugars in foods with other ingredients, such as LNCS and refined starches to replace sweetness and bulk, can contribute energy and result in unintended consequences e.g., replacing sugars with refined starches increases the glycemic index. Thus, blanket reductions of all sugars may overlook the complexity of food sources. Future work must be conducted to encourage policy and recommendation harmonization globally, and to identify effective SSB replacement strategies. Additionally, future studies should identify whether effects are modified by sex, gender and social determinants of health to ensure guidelines are inclusive and equitable.

Role of LNCS—Are they safe? What are the perceptions?

All LNCS approved by The Food and Agriculture Organization of the United Nations–WHO (FAO-WHO) Joint Expert Committee on Food Additives (JECFA) have been determined to be safe for use if they are consumed below their respective acceptable daily intake (ADIs), but national guidance have the final say in which sweeteners are approved in the respective country, leading to differences in LNCS availability across jurisdictions. Each LNCS has different absorption, distribution, metabolism and excretion profile and, consequently, different ADIs (Magnuson et al. 2016), despite LNCS often being lumped together as one group.

JECFA is a World Health Organization (WHO) committee responsible for evaluating risks i.e., hazards and exposure. Recently, the WHO International Agency for Research on Cancer (IARC) evaluated aspartame as a possible carcinogen (International Agency for Research on Cancer 2023). However, IARC is responsible for evaluating hazards only without consideration for the possible exposure, not risk. Aspartame is completely metabolized upon ingestion into amino acids and methanol. Even the highest human consumers of aspartame, the contribution of amino acids from aspartame is trivial in comparison to dietary proteins from foods, and results in no change in human blood levels nor any change in brain amino acid uptake (Magnuson et al. 2007). Regarding methanol, higher levels of intake of aspartame only contributes about 1%–10% of total dietary methanol intake (EFSA Panel on Food Additives and Nutrient Sources added to Food 2013). The systemic circulation never contains intact aspartame, meaning there is no biologically plausible mechanism for aspartame causing cancer. IARC evaluated aspartame as a possible carcinogen using its scale that assumes any substance is a hazard until adequate evidence confirms this is not the case. Thus, the IARC rating was based on the paucity of human data on this question, and of important limitations present in the available literature (Stepien et al. 2016; Debras et al. 2022; Jones et al. 2022; McCullough et al. 2022).

At doses below the ADI, there are multiple potential benefits of LNCS use include enhanced quality of life in patient populations (described below), associations with improved diet quality (through reduced sugars intake and behaviour clustering), reduced risk of dental caries and weight management. With respect to sugars reduction, consumers recognize the value of reducing free and/or added sugars intake to less than 10% of energy (Health Canada 2019; International Food Information Council 2021; USDA 2025; U.S. Department of Health and Human Services and U.S. Department of Agriculture 2025). However, intake remains above the recommended levels in the USA (DiFrancesco et al. 2022) and Canada (Wang et al. 2023), due, in part, to consumer desire for sweetness in their diet (International Food Information Council 2021). Thus, LNCS present a relevant strategy to meet dietary goals. Intake data support this approach; the consumption of LNCS has been increasing globally (Popkin and Nielsen 2003; Sylvetsky and Rother 2016; Dunford et al. 2018; Russell et al. 2023), especially in people with obesity (Czoli et al. 2019), and moderate intake of LNCS is associated with lower intakes of sugars in several studies, including the WHO systematic review and meta-analysis (Bassett et al. 2020; Dan et al. 2023, Sun et al. 2024). Although LNCSB are the top food source of LNCS (Popkin and Nielsen 2003; Sylvetsky and Rother 2016), LNCS are increasingly being added to other foods, including those advertised as “keto”, “diet”, or “sugar free”. A survey revealed that 52% of young Canadian adults consider aspartame less healthy than real sugar, and that “natural sweeteners” e.g., stevia, raw sugar, and agave, were healthier (Goodman et al. 2020). On social media, messaging about LNCS is often fear mongering and by the nature of social media algorithms, interacting with negative content often amplifies more negative content being shown.

Another concern of LNCS use is their use in vulnerable populations, including children. High intakes can be reached more easily due to differences in size compared to adults, which can displace vital energy and displace vital nutrients from foods with long-term consequences for growth and development (World Health Organization 2023). The American Academy of Pediatrics released a statement in 2019 discouraging LNCS use before two years of age for this reason, while also acknowledging that there are limited data in this age group. Of the limited data, they note that LNCS use is associated with reduced dental carries and not associated with hyperactivity, appetite change or taste preferences (Baker-Smith et al. 2019). They also advise that, in children living with excess adiposity, LNCS should not be used to achieve weight loss, but parents should instead habituate their children to a less sweet diet (Baker-Smith et al. 2019). In clinical practice, parents view offering young children “sweet tasting” foods and beverages often as negative or concerning feeding patterns.

Another vulnerable population to consider are females in reproductive ages. Health Canada considers the majority of LNCS safe for use in pregnancy (except saccharin) (Fitch and Keim 2012). There have not been any studies on the effect of LNCS on breast milk production in humans, but some LNCS, e.g., acesulfame-potassium and sucralose, appear in breast milk after consumption, however the evidence in human is preliminary and requires further investigation (Fitch and Keim 2012; Sylvetsky et al. 2015; Magnuson et al. 2016). Concentrations of sucralose in breast-feeding newborns with

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mothers consuming this sweetener are highly variable and present in very low in concentration (Sylvetsky et al. 2017, 2024; Roberts et al. 2000).

Finally, the speakers acknowledged that LNCS-products may play diverse roles in people living with mental health challenges or experiencing taste changes during active chemotherapy, including but not limited to joy, reward, self-regulation, taste change, digestion, perceived energy and to offset side-effects from drug therapies. Understanding the value LNCS-products bring to any patient is important in clinical practice to educate them and dispel misinformation (Consroe et al. 1980; Doty et al. 2008; Moriconi et al. 2020; Tompkins et al. 2025). When patients are curious about LNCS, it is important to verify their consumption habits, understand the value LNCS brings to their life quality. This will enable the assessment of intake habits and whether modification can be implemented to change, improve or align LNCS intake with ADI levels, or specific goals of the patient, ensuring LNCS are not replacing essential nutrients or hydration.

While all commercially available LNCS are safe, patients are often faced with misinformation on social media and among their peers that leads to confusion. While it is important that LNCS-products do not displace essential nutrients, especially in growing children, LNCS may still be helpful and valuable to patients for purposes beyond weight or blood sugar management. Future work communicating recommendations and introducing more nuanced views on social media should be prioritized to address LNCS misinformation. Additionally, future work is needed to address the lack of human studies related to LNCS and cancer, along with specific LNCS types (e.g., acesulfame-potassium, saccharin, sucralose etc.).

What is guidance saying: public health versus clinical practice?

From the public health perspective, the WHO 2023 guideline issued a conditional recommendation against using LNCS as a strategy for preventing obesity and NCDs (World Health Organization 2023). This recommendation was driven by concerns about limited evidence of long-term benefit, potential for reverse causation and residual confounding in observational studies, and low certainty of evidence in long-term trials (World Health Organization 2023). The WHO's recommendation is not based on a high level of confidence. meaning the desirable effects of following it probably outweighs the harms of not following it, and policy decisions may require substantive discussion related to the findings from specific studies. The WHO left it up to individual countries to interpret the evidence based on their population characteristics e.g., extent of sugars consumption in different age groups. Similarly, some country's public health guidelines, e.g., Canada's Food Guide, explicitly discourage substitution of sugars with LNCS, preferring approaches to reduce the overall sweetness of the diet (Health Canada 2019), while others, e.g., Dietary guidelines for Americans 2020–2025 note that replacing added sugars with low- and no-calorie sweeteners may reduce energy intake in the short-term and aid in weight management, while acknowledging that questions remain about their effectiveness as a long-term weight management strategy (Department of Health, Services and Department 2021). Increasing evidence that, unlike the case for salt and fat, preferred sweetness levels of foods and beverages may not reflect and be modified by dietary exposure levels, raises questions about the efficacy of an approach based on retraining sweet taste preferences (Cad et al. 2025). Low- and no-calorie sweeteners, which can also be called high-intensity sweeteners, are not recommended for children younger than age two (Department of Health, Services and Department 2021).

There are several reasons why the WHO's recommendation was deemed low/very low certainty: some of the evidence from adults was extrapolated to children, adolescents and pregnant women; the evidence was largely indirect, i.e., the direct replacement of LNCS for sugars was often inferred and not explicit' and the minor weight loss and other improvements in NCD risk factors observed in RCTs were not reflected in long-term observational studies, and were not considered a health benefit by the WHO guideline committee (Rios-Leyvraz and Montez 2022; World Health Organization 2023). However, according to the speakers at this meeting, the evidence on LNCS consumption and adiposity is more consistent than inconsistent when viewed critically. Several meta-analyses of prospective cohort studies indicate LNCS use is associated with a slight positive association with BMI or, more commonly, no effect (Miller and Perez 2014; Rogers et al. 2016; Lee et al. 2020). The discrepancy between different meta-analyses may be related to different questions asked (Higgins et al. 2024). For example, naïve prevalent models which assess baseline or prevalent LNCS exposure only, do show adverse associations of LNCS on adiposity and NCD outcomes (Lee et al. 2020; Higgins et al. 2024; Ayoub-Charette et al. 2025). However, analyses of the WHO meta-analysis cohort data when the substitution of LNCS for sugars was modelled, and of systematic reviews and meta-analyses of LNCS substitution and change models, reveals replacing LNCS for sugars is associated with benefits on those same outcomes (Khan et al. 2023; Khan et al. 2024; Ayoub-Charette et al. 2025). The discrepancy in findings between these two approaches may be attributable to the susceptibility of cohort studies to reverse causality, where being at high risk of obesity and other NCDs leads an individual to increase LNCS intake as a risk reduction strategy, and residual confounding (Sievenpiper et al. 2017; Malik 2019; Mela et al. 2020).

In RCTs, the effect of substitution of energetic sugars with LNCS can be directly assessed by selecting appropriate comparators. The WHO systematic review and meta-analysis conducted subgroup analyses by comparator, and highlighted that the benefits of LNCS observed in the shorter-term were driven specifically by their comparison against sugars (Rios-Leyvraz and Montez 2022; World Health Organization 2023) (the most relevant comparison), resulting in a lowering of sugars intake, with no differences between LNCS and water (Rios-Leyvraz and Montez 2022; World Health Organization 2023), a finding that has been replicated in other systematic

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reviews and meta-analyses (McGlynn et al. 2022; Higgins et al. 2024; Ayoub-Charette et al. 2025), and RCTs ((Harrold et al. 2024; Pang et al. 2025). While RCTs themselves have several limitations, including their shorter timelines relative to cohort studies, and consequently, their inability to investigate disease or mortality outcomes (except in rare RCTs), they still offer the strongest level of evidence and the lowest risk of bias.

The WHO guidelines committee also considered mitigating factors in the development of their recommendation: there were no undesirable effects or other mitigating factors that would argue against not using LNCS, but LNCS are not essential, they have no nutritional value and there are other methods to reduce sugars intake (Rios-Leyvraz and Montez 2022; World Health Organization 2023).

In contrast to the WHO recommendation, clinical practice guidelines for obesity, diabetes and cardiovascular disease generally support the use of LNCS for reducing carbohydrate and energy intake in individuals living with obesity or diabetes (Goldstein 2001; Sievenpiper et al. 2018; Brown et al. 2022; International Food Information Council 2023). This divergence between clinical and public health guidance reflects a tension between population-level precaution and individual-level pragmatism. Public health bodies tend to issue guidance for the general population, applying precautionary principles where evidence is uncertain (Goldstein 2001). Clinical guidelines, however, focus on patient management, emphasizing that even modest calorie reductions achieved through LNCS substitution can support weight and glycemic control. Thus, framing LNCS as one option among many, rather than as a panacea or a threat, may help align public health messaging with clinical practice realities.

To summarize, clinical and public health guidance, prioritizing different levels of evidence (RCTs, substitution and change models vs. naïve observational studies) and balancing pros and cons of LNCS use dependent on the guideline committee's perspectives and goals has led to divergent LNCS recommendations, leading to scientific and public confusion about their roles in everyday life. Future observational research should employ rigorous methods of analysis for assessing the association of LNCS with NCDs. To facilitate knowledge translation and applicability of scientific knowledge to guideline committees, a combination of careful but idealistic RCTs, of which there are several (Blackburn et al. 1997; Madjd et al. 2018; Ebbeling et al. 2020; Harrold et al. 2024), and pragmatic study designs that address the nature of the comparator, and pragmatic LNCS exposures should be considered. Additionally, guideline contradictions may be resolved by addressing the discrepant findings between observational studies (e.g., prospective cohorts) and RCTs.

Mechanisms: Is there biological plausibility?

The final theme focused on biological plausibility, addressing whether there are mechanistic pathways through which LNCS might influence health beyond simple calorie displacement. There are several proposed mechanisms LNCS could affect body weight management and glycemic response, including energy dilution/compensation, sweetness/energy uncoupling, and through gut microbiota alterations.

Neuronal pathways, energy dilution, and compensation hypothesis

This mechanism originates from animal data and proposes that LNCS partially activates the food reward pathway, which has been suggested to lead to increased appetite and lower satisfaction after consuming LNCS compared to sugars, resulting in energy compensation partially because of these neuronal changes. Energetic sweeteners, like sugars, activate the dopaminergic reward circuit. While human neuroimaging studies do show differential neuronal responses to LNCS compared with sugars (Dalenberg et al. 2020; Khan and Sievenpiper 2021), the consequences of these differences are unclear (Yunker et al. 2020) and require further investigation. Additionally, because LNCS are sensorily sweet, their intake may encourage sugars cravings, dependencies and habituate individuals to a highly sweet diet i.e., increase preference (f)or sweet foods, resulting in overconsumption of less nutrient-dense foods or compensatory eating to make up for the lower satisfaction after consuming LNCS-products. The habituation hypothesis assumes that (1) increased sweetness exposure will lead to increased sweetness preference, and that (2) increased sweetness preference will lead to increased energy intake from sweet foods, resulting in increased adiposity and risk for NCDs. However, there is no evidence for either assumption (Higgins et al. 2022; Cad et al. 2025).

Uncoupling hypothesis and the cephalic phase insulin response

This theory suggests that repeated exposure to sweetness without energy may disrupt conditioned associations between sweetness and energy, impairing the body's ability to regulate energy balance (Davidson and Swithers 2004). When the tongue tastes sweetness, it primes digestive processes including the preabsorptive secretion of insulin in anticipation of incoming calories (i.e., the cephalic phase insulin response). The evidence for this hypothesis originates from the concept of Pavlovian conditioning, however, a systematic review and meta-analysis of animal studies does not support this hypothesis (Rogers et al. 2016) and questions about the mechanism have been raised with additional consideration of human studies (Langhans et al. 2023). Similarly, in a systematic review and meta-analysis of human acute RCTs where LNCS were either uncoupled, coupled with calories or delayed coupling with calories, did not show effects on post-prandial glucose, insulin, GLP-1, GIP, PYY, ghrelin or glucagon, indicating there is little human evidence supporting this theory (Dalenberg et al. 2020; Greyling et al. 2020; Khan and Sievenpiper 2021; Zhang et al. 2023). Further, euglycemic clamp studies that independently manipulate plasma glucose and insulin concentrations, reveal that LNCS are not causally related to appetitive sensations (Chapman et

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al. 1998). In the methodologically strongest controlled studies, no effects of LNCS were observed on acute or longer-term appetite (Fantino et al. 2018). Still, an influence of LNCS on intake may be posited, independent of effects on appetite. However, again, a recent meta-analysis of intervention trials documents LN)CS use is associated with lower energy intake (Rogers and Appleton 2021).

Gut microbiota alterations

Preclinical research suggested saccharin at very high doses alters microbiota and glucose tolerance (Suez et al. 2014), despite the fact that only 5%–15% of the ingested saccharin reaches the colon (Magnuson et al. 2016). The top LNCS types globally (i.e., aspartame and acesulfame potassium) (Tran et al. 2021) do not reach the colon in meaningful amounts (Magnuson et al. 2016). Subsequent human trials, including trials designed to be pragmatic and use real-world LNCS and doses have failed to replicate these findings (Thomson et al. 2019; Ahmad et al. 2020; Serrano et al. 2021; Mohan et al. 2023, 2024; Singh et al. 2024; Stamataki et al. 2020; Sylvetsky et al. 2023; Kwok et al. 2024). Of the literature on LNCS and gut microbiota changes (Thomson et al. 2019; Ahmad et al. 2020; Serrano et al. 2021; Mohan et al. 2023, 2024; Singh et al. 2024; Stamataki et al. 2020; Sylvetsky et al. 2023; Kwok et al. 2024), only three intervention studies (two by the Weismann Institute (Suez et al. 2014, 2022) and one not exploring the whole microbiota community but only a few specific bacteria species (Méndez-García et al. 2022)) support harmful effects of LNCS on the gut microbiota (Suez et al. 2014, 2022; Méndez-García et al. 2022), and speakers at this meeting agreed that all three of these studies have major methodological limitations that prohibit causal inferences to be drawn. Moreover, the validity of simply measuring shifts of selected bacterial species provides little to no evidence of a functional impact (Heintz-Buschart and Wilmes 2018; Luca et al. 2018; Miyoshi et al. 2020; Schneider 2024; Yang et al. 2025). Therefore, overall, there is little evidence that LNCS may adversely disrupt the gut microbiota.

One important nuance in the interpretation of this literature is recognition that while the class of LNCS compounds share a property of imparting sweetness while providing little or no energy, they are distinct chemicals that bind to sweet receptors differently, evoke different intracellular signaling, have different sensory side-notes, and are digested, absorbed, and excreted differently (Magnuson et al. 2016). Thus, they differ in the physiological responses (Higgins and Mattes 2019; Steffen et al. 2023). Failure to account for their distinctive properties may also mask their role in weight management. Taken together, the evidence documents that LNCS use does not lead to disordered glycemia, altered appetite or increased energy intake or a dysfunctional microbiome, and their use is associated with lower adiposity, especially when used to displace energy-yielding sugars. Further, some LNCS may be more effective than others, but this requires additional study. Novel methodological advancements at every level are required to bridge the gap between mechanistic studies, animal models, controlled trials, and observational research in LNCS research.

Conclusions

Reducing free and added sugars remains a central nutrition policy goal, and LNCS can play a pragmatic role in supporting this objective when used as substitutes for sugar-containing products. Current toxicological evidence confirms their safety within risk-based ADIs, and clinical data show benefits in energy reduction and weight management, particularly when compared directly to sugars. Nonetheless, divergent interpretations of the evidence across public health and clinical practice guidelines, combined with widespread misinformation, have created uncertainty for policymakers, practitioners, and the public. Additionally, LNCS are a diverse group of compounds, and clinical and epidemiological results are not necessarily generalizable across all LNCS. Moving forward, long-term pragmatic trials, nuanced cohort analyses, and mechanistic studies are needed to clarify differential effects among different types of LNCS and across population subgroups. Harmonizing policy approaches and strengthening communication will be essential to ensure evidence-based, consistent, and equitable dietary guidance that enables populations to reduce free sugars while safeguarding against unintended consequences of LNCS.

Acknowledgements

During the preparation of this work, the authors used ChatGPT 4o from OpenAI and Claude.ai from Anthropic to harmonize the text. After using the tool, the authors diligently reviewed, edited and re-inserted relevant references as needed. The authors take full responsibility for the content of this publication.

Article information

History dates

Received: 21 October 2025
Accepted: 8 January 2026
Version of record online: 20 April 2026

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Data availability

This manuscript is based on data presented and discussions held between a panel of international nutrition research experts at a high-level Canadian Nutrition Society Thematic conference on the topic of “Non-nutritive sweeteners and health: unravelling the evidence and controversy” (https://thematic2024.cns-scn.ca/presentations) which took place in Toronto, Canada on 27 January 2024.

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Data curation: SA-C, MN, LC, RDM, RJdS, TAK, KAH, NS, DM, SP, JLS, VSM
Formal analysis: SA-C, MN, LC, RDM, RJdS, TAK, KAH, NS, DM, SP, JLS, VSM
Funding acquisition: SP
Project administration: SA-C, JLS, VSM
Resources: JLS, VSM
Supervision: JLS, VSM
Writing – original draft: SA-C, MN
Writing – review & editing: SA-C, MN, LC, RDM, RJdS, TAK, KAH, NS, DM, SP, JLS, VSM

Competing interests

SA-C avoids consuming sugars sweetened beverages (SSBs) and non-nutritively sweetened beverages (NSBs) and has received an honorarium from the International Food Information Council (IFIC) for a talk on artificial sweeteners, the gut microbiome, and the risk for diabetes, and from the Arkansas Children's Hospital for participation in a "lumping versus splitting" event. LC has received research funding from the Canadian Institutes of Health Research (CIHR), Protein Industries Canada (a Government of Canada Global Innovation Cluster), the United Soybean Board (The United States Department of Agriculture Soybean "Check-off" Program), and the Alberta Pulse Growers. She has received honoraria from the Arkansas Children's Hospital and Plant-Based Health Professionals UK and travel funding from the World Sugars Research Organization for an internal presentation in 2022. RDM: Serves on scientific advisory boards for the Grain Food Foundation, Mars Foods, and Bell Institute of Health and Nutrition. He is currently receiving or has recently received research funding from Eli Lilly, the Grain Food Foundation, and The Clinical and Translational Science Institute funded by the NIH. He has consulted for and received travel funds and/or honoraria from multiple private and public entities. RJdS has served as an external resource person to the World Health Organization's Nutrition Guidelines Advisory Group on trans fats, saturated fats, and polyunsaturated fats. The WHO paid for his travel and accommodation to attend meetings from 2012–2017 to present and discuss this work. He has presented updates of this work to the WHO in 2022. He has also done contract research for the Canadian Institutes of Health Research's Institute of Nutrition, Metabolism, and Diabetes, Health Canada, and the World Health Organization for which he received remuneration. He has received speaker's fees from the University of Toronto, and McMaster Children's Hospital. He has served as an independent director of the Helderleigh Foundation (Canada) and as a member of the Nutrition Science Advisory Committee to Health Canada (Government of Canada). He serves as co-chair of the Methods working group of the ADA/EASD Precision Medicine in Diabetes group and is a co-opted member of the Scientific Advisory Committee on Nutrition (SACN) Subgroup on the Framework for the Evaluation of Evidence (Public Health England). He has held grants from the Canadian Institutes of Health Research, Canadian Foundation for Dietetic Research, Population Health Research Institute, and Hamilton Health Sciences Corporation as a principal investigator, and is a co-investigator on several funded team grants from the Canadian Institutes of Health Research. TAK was funded by a Toronto3D Foundation Postdoctoral Fellowship Award. He reports receiving grants from Canadian Institutes of Health Research (CIHR), Institute for the Advancement of Food and Nutrition Sciences (IAFNS, formerly ILSI North America), and National Honey Board (USDA Checkoff program) and Toronto 3D Knowledge Synthesis and Clinical Trials foundation. He has received honorariums from Advancement of Food and Nutrition Sciences (IAFNS), the International Food Information Council (IFIC), and the Calorie Control Council (CCC), the International Sweeteners Association (ISA), AmCham Dubai, and Ontario Maple Syrup Producers' Association (OMSPA). KAH is an employee at Exponent, Inc., which provides scientific consulting to the food and beverage industry; was previously employed at the USDA-ARS; received honorarium from the National Pork Board; served as President to the Institute of Food Technologists (IFT) Washington, DC section. DM: reports receiving research funds from Canadian Institutes of Health Research (CIHR), Social Sciences and Humanities Research Council (SSHRC), the Kidney Foundation of Canada, Diabetes Canada, the Weston Family Foundation, Research Manitoba, Mitacs Canada, Pepsico and Prairie Oat Growers Association. He has also received an honorarium from Abbott Nutrition to present on the use of continuous glucose monitors and glycemic management targets, as well as an honorarium from Pepsico to attend a panel discussion on non-nutritive sweeteners. He has also had travel and accommodations covered by Diabetes Canada to present on updates to the Diabetes Canada Clinical Practice Guidelines, on which he is a steering committee member and chapter author. Dr. John L Sievenpiper has received research support from the Canadian Foundation for Innovation, Ontario Research Fund, Province of Ontario Ministry of Research and Innovation and Science, Canadian Institutes of Health Research (CIHR), Diabetes Canada, American Society for Nutrition (ASN), The United Soybean Board (USDA soy "Checkoff" program), Protein Industries Canada (a Government of Canada Global Innovation Cluster), Almond Board of California, European Fruit Juice Association, The Glycemic Control and Cardiovascular Disease in Type 2 Diabetes Fund at the University of Toronto (a fund established by the Alberta Pulse Growers), The Plant Protein Fund at the University of Toronto (a fund which has received contributions from IFF among other donors), The

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Plant Milk Fund at the University of Toronto (a fund established by the Karuna Foundation through Vegan Grants), and The Nutrition Trialists Network Fund at the University of Toronto (a fund established by donations from the Calorie Control Council, Physicians Committee for Responsible Medicine, and Login5 Foundation). He has received food donations to support randomized controlled trials from the Almond Board of California, California Walnut Commission, Danone, Mantra Pharma, Terra Delyssa, House Foods, General Mills, WK Kellogg Company, Quaker, Procter & Gamble (P&G), Abbott, and Dairy Farmers of Canada. He has received travel support, speaker fees and/or honoraria from Nestlé, Abbott, General Mills, International Food Information Council (IFIC), International Sweeteners Association, Calorie Control Council, International Stevia Council, Mantra Pharma Inc., Chinese Institute of Food Science and Technology (CIFST), and Collaborative CME and Research Network (CCRN). He has or has had ad hoc consulting arrangements with Almond Board of California, Perkins Coie LLP, Ingredion, and Brightseed. He is on the Clinical Practice Guidelines Expert Committees of Diabetes Canada, European Association for the study of Diabetes (EASD), Canadian Cardiovascular Society (CCS), and Obesity Canada/Canadian Association of Bariatric Physicians and Surgeons. He serves as an unpaid member of the Board of Trustees of IAFNS. He is Vice President – Clinical of the Canadian Nutrition Society (CNS), founding member of the International Carbohydrate Quality Consortium (ICQC), Secretary and Executive Board Member of the Diabetes and Nutrition Study Group (DNSG) of the EASD, and Director of the Toronto 3D Knowledge Synthesis and Clinical Trials foundation. His spouse is an employee of AB InBev. VSM has received funding from the Canada Research Chairs Program; Connaught New Researcher Award, University of Toronto; The Joannah & Brian Lawson Centre for Child Nutrition, University of Toronto; Temerty Faculty of Medicine Pathway Grant, University of Toronto; Canada Foundation for Innovation; Ontario Research Fund; Canadian Institutes of Health Research; Novo Nordisk Network for Healthy Populations, University of Toronto; Data Science Institute, University of Toronto; National Institutes of Health and has served as a consultant for the City and County of San Francisco for litigation related to health warning labels on sugar-sweetened beverages and on the Robert Wood Johnson Healthy Eating Research Advisory Committee for child beverage guidance. She has also received honoraria for peer review from the Peanut Institute and California Almond Board and travel support from the Canadian Nutrition Society, Diabetes Nutrition and Study Group, International Nut & Dried Fruit Council, and the University of Ottawa. MN, NS, and SP report no conflicts of interests.

Funding information

This work was supported by a CIHR Planning and Dissemination grant (505733) awarded to the Canadian Nutrition Society. S.A.-C. was funded by a CIHR Canadian Graduate Scholarship Doctoral Award (funding reference number 476251). The funders had no role in the study design, collection, analysis, interpretation of data, or writing of the report, and they had no involvement or restrictions regarding publication.

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