The Use of Low-Calorie Sweeteners by Adults: Impact on Weight Management1–3

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Abstract

The application of low-calorie sweeteners (LCS) in foods and beverages has increased over the past 35 y. At the same time, many characteristics of the American diet have changed, including variations in fat and carbohydrate content and composition, increased nutrient additions, and new dietary patterns due to changing lifestyles and attitudes toward food and the changing cost of food. During this same time period, the prevalence of overweight and obesity has increased from ~30 to 70% of adults in the United States. Clearly, these trends lead to a variety of hypotheses and efforts to explain the role of LCS in this association. The aim of this review is to gain clarity on the role of LCS in weight management and their impact on diet quality. In addition, because the majority of studies aimed at identifying associations between LCS and these outcomes are based on observational data, the pitfalls in designing and evaluating data from observational studies are also discussed. We conclude that there is no evidence that LCS can be claimed to be a cause of higher body weights in adults. Similarly, evidence supporting a role for LCS in weight management is lacking. Due to the confounders in most observational studies, randomized controlled trials are needed to advance understanding. J. Nutr. 142: 1163S–1169S, 2012.

Introduction

The impact of low-calorie sweeteners (LCS)8 in foods and beverages on energy intake, diet quality, and body weight of adults remains unclear in spite of their obvious characteristic of being lower in energy compared with sugar. Many explanations can be offered for this, including complexity and lack of understanding of the environmental and behavioral determinants of obesity, the failure of short-term experimental studies to predict long-term outcomes, and limitations of observational studies on the populations. These factors were addressed in a session of the International Life Sciences Institute North America Workshop, “Low-Calorie Sweeteners, Appetite and Weight Control: What the Science Tells Us,” held April 7–8, 2011, in Washington, DC, and will be discussed in this review.

Weight Loss and Weight Management

Two-thirds of adults in the United States are overweight or obese (1). Americans are gaining an average of 1–2 lb (0.45–0.9 kg)/y. If the present trend is not halted, it is projected that by the year 2030, 86.3% of adults in the United States will be overweight or obese (2).

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There is no single cause for overweight or obesity. Both are influenced by genetic and environmental factors, including one’s race or ethnicity, age, diet, physical activity level, and psychosocial factors. Weight management, however, is a function of energy balance. According to the Dietary Guidelines for Americans, 2010 (3), there is no substitute for the simple formula of “calories consumed must equal calories expended” in order to manage weight. Achieving and maintaining a healthy body weight depends on the wise management of energy from all food and drink sources and a habit of regular physical activity.

Intuitively, LCS have the potential to play an important role in helping motivated adults control weight. It has been estimated that adults can prevent weight gain by reducing intake by 100 kcal/d (4). Replacing a regular soda with a diet soda will save ~150 kcal and using a LCS rather than 2 tsp (18 g) of sugar in a cup of coffee 3 times/d will save ~100 kcal (5). However, a hypothesis emerged in the mid-1980s suggesting that LCS cause people to compensate for the energy they are saving in foods and beverages by increasing appetite, hunger, or food intake or inducing cravings for sweets, thereby having no benefit or actually causing weight gain (6). In contrast, the overall results of more current observational, intervention, and short-term experimental studies do not support this hypothesis.

Some nonrandomized, longitudinal, and cross-sectional studies have reported an association between LCS and weight over time (7) and some have not (8). However, these results are difficult to interpret, because they do not meet the Bradford-Hill criteria (strength, consistency, specificity, temporality, biological gradient, plausibility, coherence, experiment, analogy) (9) for causal inference. Correlational studies cannot determine whether adults become overweight because of LCS use or whether overweight adults are including them in dietary strategies to help lose weight or stop gaining weight (which seems more plausible). Researchers generally conclude that there is no significant evidence from observational studies that LCS associate with weight gain (10,11), although some are cautious that the evidence for long-term efficacy for weight management is lacking (3,12,13) and needs to be examined in randomized controlled trials (RCT) (12).

Controlled intervention trials with LCS use in normal-weight adults for 3–4 wk (14,15), in overweight adults for 10 wk (16), and for over 2 y as part of a comprehensive weight loss intervention (17) showed lower energy intake among the LCS users. Among overweight and obese adults, there were significant decreases in intake of sucrose and carbohydrates after 10 wk (16) and in sucrose and carbohydrates after 2 y (17). In addition, weight maintainers used a number of dietary strategies, including increased consumption of LCS, to accomplish their goals (18).

Short-term experimental studies have examined food intake after preloads of LCS in a beverage (11–17), food (18–21), or capsule (19). Many studies suggest that LCS do not significantly affect appetite or hunger or the desire for sweetness in adults (15,17,19–27). Three short-term studies showed that LCS increased appetite or hunger (14,28,29), whereas 2 studies reported that hunger or appetite decreased (30,31). Recent reviews have concluded that there can be reductions in energy intake arising from LCS use, particularly as a replacement for sugars in food and beverages (10,32–38). For example, in their review of intense sweeteners and the impact on hunger, food intake, and body weight, Rolls et al. (21) concluded that: “It needs to be stressed that there are no data suggesting that consumption of food and drinks with intense sweeteners promotes food intake and weight gain.” Similarly, Mattes and Popkin (12) concluded that: “Substitution of NNS [i.e., nonnutritive sweeteners] for a nutritive sweetener generally elicits incomplete energy compensation, but evidence of long-term efficacy for weight management is not available.” Rolls et al. (21) also concluded that: “It is clear that low energy sweeteners can be as satisfying as sugars during a meal, particularly when subjects are unaware of the caloric manipulation.” The results from RCT are consistent in showing that LCS use does not cause weight gain in adults (14,16,17,39).

The lack of evidence in support of the hypothesis that LCS may cause weight gain is easily explained by the fact that weight management is a function of energy balance. According to the Dietary Guidelines for Americans, 2010 (3), “The total number of calories consumed is the essential dietary factor relevant to body weight.” As noted by Bellisle and Drewnowski (13), “Intense sweeteners are not appetite suppressants. Their ultimate effects will depend on their integration within a reduced calorie diet.” All energy counts. Ignoring this fact diverts attention from developing realistic solutions to the problem of obesity and related diseases.

**LCS Consumption and Impact on Diet Quality**

Diet quality is affected by food patterns. Thus, it has been hypothesized that low-energy macronutrient substitutes will lead to inadvertent shifts in food patterns and selection that may lead not only to increased energy intake but also to a decrease in diet quality (6).

Guidelines for the assessment of diet quality have been developed. The adequacy of nutrient intakes in the United States is assessed using the Dietary Reference Intake tables (40) and the Healthy Eating Index (HEI) (41). The HEI, which also assesses food patterns, includes the following components: total fruit, whole fruit, total vegetables, dark green and orange vegetables, total grains, whole grains, milk, meat and beans, oils, saturated fat, sodium, and solid fats and added sugars.

Assessment of dietary quality is dependent on self-reported intake data. Thus, the accuracy of diet quality and its relationship to specific foods and dietary components is contingent upon the precision of self-reported data (42). Researchers have used diet records, diet recalls, and FFQ to ascertain relationships between LCS and diet quality in observational cross-sectional and prospective studies. All of these methods have major limitations, including, but not restricted to, inaccuracy due to faulty memory, social desirability, purposeless untruthfulness, respondent bias, and inaccurate portion-size estimations (over or under).

Two analyses have been conducted specifically to determine the diet quality of users of low-calorie–sweetened foods and beverages (LCSFB) in the U.S. population. An analysis published in 2005 was the first to compare LCSFB users to those reporting use of the full-sugar versions of similar products (non-LCSFB). The study was based on the 1994–1996 Continuing Survey of Food Intakes by Individuals (CSFII) (43). LCSFB users were significantly more likely to be females, white, older, educated, and of higher socioeconomic status and they reported higher dietary supplementation (P < 0.01). Although self-reported heights and weights resulted in mean BMI >25 (overweight) that were higher for both male and female LCSFB users, their reported energy intakes did not differ. However, the food records of the LCSFB users provide some indication that they may have made dietary changes consistent with achieving weight loss or weight maintenance. LCSFB users reported higher intakes of fruits, dark green and yellow vegetables, calcium, and magnesium as well as lower intakes of discretionary fat, added sugars, and...
saturated fats ($P < 0.01$ for all comparisons). In addition, LCS users were more likely to report reading labels to determine the sugar, fat, and energy levels of purchased foods ($P < 0.01$).

An unpublished analysis of data from the 2001–2002 NHANES (44) for individuals also suggests that there are differences in the dietary patterns of LCSFB users and non-LCSFB consumers. LCSFB consumers reported higher intakes of total fat ($P < 0.001$), saturated fat ($P < 0.01$), protein ($P < 0.001$), calcium ($P < 0.001$), sodium ($P < 0.001$), magnesium ($P < 0.01$), and vitamin E ($P < 0.01$) along with lower intakes of energy ($P < 0.01$), carbohydrates ($P < 0.001$), and added sugars ($P < 0.001$). Analysis of total HEI found that LCSFB users had an overall higher score ($P < 0.001$) (54.7) than non-LCSFB users (51.1) despite several individual HEI scores in which the non-LCSFB users scored better (specifically, sodium and saturated fats).

Several studies have examined associations between the use of LCS beverages and metabolic syndrome (45,46), type 2 diabetes (47,48), and obesity (49) and also contain diet quality information. This article includes a summary comparison of the study designs and populations of these studies (Table 1), differences in macronutrient intakes (Table 2), and selected micronutrient comparisons (Table 3) for those studies that provided such information. The overall dietary pattern for the 3 studies performing such analysis is also compared (Table 4). All users of LCS products were overweight or obese. In general, users of LCS foods and beverages reported diets of overall higher quality than those who did not use these products. Meat intakes could explain the higher intakes of fats and saturated fats. Indeed, those studies investigating relationships between LCS and chronic disease states that were published after the 1994–1996 CSFII study seem to reflect the general population trend from low-fat diets to low-carbohydrate (and high-protein) diets.

No single pattern of diet quality associated with the use of LCSFB emerges from these studies, even when adjusted for variables known to be associated with obesity or metabolic syndrome. Unfortunately, other known variables (such as psychosocial measures, stress, depression, sleep, and economic conditions) were not included. The authors recognized these limitations, emphasizing that observational studies do not demonstrate causality and that residual confounding maintains limitations, emphasizing that observational studies do not demonstrate causality and that residual confounding lifestyle factors need to be considered.

Clearly, there is a multifactorial relationship between individuals and their environment regarding food choices and health behaviors (Fig. 1) (30). This schema shows the complexity of this relationship and demonstrates the psychobiological core, surrounded by cultural and social factors that interface with the immediate and distal environments. It is at the interface of the individual and the environment where lifestyle choices are made. Exploring the interface between biological and psychosocial factors may enable a better understanding of how LCS affect diet quality.

A clearer picture of the role of LCS in the diet may emerge if we had a better understanding of consumer motivation for choosing LCS. Questions that need to be answered include the following: Why do individuals choose to use LCS? Do they expect to lose or maintain weight? Do they believe LCS are appetite suppressants? Are they currently dieting and, if so, are they enrolled in an intervention? How intense is the intervention? Do they believe they can impact their weight status (based on theoretical constructs including self-efficacy, sense of coherence, locus of control, health belief model, transtheoretical model of change, etc.) (51)? These questions might best be answered through the integration of qualitative and quantitative studies. Mixed-method approaches can capture nuances that remain hidden when only quantitative measures are used.

Data presented from the NPD Group’s ongoing national food and beverage survey provided some clues specific to consumer attitudes about sugars and sweeteners and use of reduced-calorie/low-sugar (RC/LCS) products (Joe Derochowski, Nielsen, personal communication). The NPD Group is a marketing information company that conducts the National Eating Trends study, which has been continuously tracking the eating habits of Americans since 1980. The annual sample consists of 2000 households, representing ~5000 persons. The sample is demographically and geographically balanced to U.S. Census Bureau statistics each year at the household level. The sample is divided into 52 subsamples, and each week a group of nearly 50 households begins recording all of the foods and beverages consumed by all household members. Reporting is distributed evenly throughout the year to be sensitive to seasonal eating habits. Each household maintains a daily eating diary for 2 wk. The person most responsible for meal preparation is instructed to record the name and brand of each food and beverage consumed by any member of the household, including all additives, ingredients, and cooking aids. The diary consists of separate sections for each meal and snack situation and collects food names, flavor descriptors, brand names, package types, product forms, appliances used in preparation, and any special nutritional attributes, among other details. The same information is collected on ingredient and additive items used to create dishes or meals in the home. At the end of each day, the recorder is instructed to mail the daily diary to the NPD Group’s offices. After all 14 daily diaries are received from a household, they are coded and readied for data processing (32).

When asked, more than one-half of the survey population expected to consume an LCS product in the next 2 wk.

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**TABLE 1** Comparison of studies examining the association between use of LCSFB and disease state

<table>
<thead>
<tr>
<th>Category</th>
<th>CSFII (43)</th>
<th>NHANES (44)</th>
<th>ARIC (45)</th>
<th>FHS (72)</th>
<th>SAHS (73)</th>
<th>MESA (49)</th>
<th>HPF (74)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type of LCS</td>
<td>FB</td>
<td>FB</td>
<td>Soda</td>
<td>Soda</td>
<td>FB + B</td>
<td>Soda</td>
<td>B</td>
</tr>
<tr>
<td>Sample size, n</td>
<td>9087</td>
<td>4326</td>
<td>9514</td>
<td>6039</td>
<td>3371</td>
<td>6814</td>
<td>&gt;40K</td>
</tr>
<tr>
<td>LCS use, %</td>
<td>41</td>
<td>24</td>
<td>NA</td>
<td>NA</td>
<td>47.5</td>
<td>41</td>
<td>54</td>
</tr>
<tr>
<td>Study aim</td>
<td>DO</td>
<td>DO</td>
<td>MS</td>
<td>MS</td>
<td>Obesity</td>
<td>T2 DB/MS</td>
<td>T2DB</td>
</tr>
<tr>
<td>Food intake</td>
<td>2d</td>
<td>1 d</td>
<td>FFQ</td>
<td>FFQ</td>
<td>FFQ/1d</td>
<td>FFQ</td>
<td>FFQ/2, 7d</td>
</tr>
<tr>
<td>BMI any LCS</td>
<td>28</td>
<td>29.5</td>
<td>NA</td>
<td>NA</td>
<td>28</td>
<td>~29^3</td>
<td>~26</td>
</tr>
<tr>
<td>No LCS</td>
<td>27</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>27</td>
<td>~27</td>
<td>~25</td>
</tr>
</tbody>
</table>

1 ARIC, Atherosclerosis Risk In Communities; B, beverage; CSFII, Continuing Survey of Food Intakes by Individuals; DO, diet quality; F, food; FB, food and beverage; FHS, Framingham Heart Study; HPF, Health Professionals Follow-Up; LCS, low-calorie sweetened; LCSFB, low-calorie–sweetened food and beverage; MESA, Multi-Ethnic Study of Atherosclerosis; MS, metabolic syndrome; NA, information was not available for the measure; SAHS, San Antonio Heart Study; T2DB, type 2 diabetes.

2 Recall (1 or 2 days) vs. food frequency questionnaires.

3 ~ indicates a simple arithmetic means of one or more level of use. No statistical comparison could be made for these.
Currently, eating occasions of RC/LS products are ~10/y more than eating occasions recorded in 1999, although this number has reduced slightly since 2009. Despite this growth, RC/LS products still comprise a small fraction of the total diet. Although reported consumption of carbonated soft drinks and fruit juice, 2 of the most frequently consumed food categories, has declined over the past decade, this decrease was notably less pronounced for “diet” versions of these beverages. Applying cohort forecasting methodology, growth of light/diet/low-energy and low-sugar/sugar substitute/no-sugar-added products is anticipated to exceed population growth. Despite this forecasted growth, the majority of consumers (51–74%, depending on the brand) respond that they would not consider using branded artificial sweeteners.

Among the most frequent users (≥11 times in 2 wk) of RC/LS products, results skew toward women aged ≥35 y and men aged ≥55 y. This population segment tends to be the most interested in products that are “new” or have a “health” attribute. Consumption trends by children are similar to that of adults, but adults consume twice as many RC/LS products as children (157 annual eating occasions per capita vs. 80 annual eating occasions per capita, respectively). Each meal (breakfast, lunch, and dinner) is almost twice as many RC/LS products as children (157 annual eating occasions per capita vs. 80 annual eating occasions per capita, respectively). Each meal (breakfast, lunch, and dinner) is almost equally likely to include an RC/LS product (12–15% of meals), with lunch being the most common. Overall, the top categories of RC/LS products are carbonated soft drinks, tea, and yogurt for adults and carbonated soft drinks, fruit drinks, and fruit juice for children.

Observational Studies: Uses and Limitations

As discussed earlier, observational studies are often used to describe associations among foods, food components, and outcomes of interest. Therefore, to provide a better understanding of their use, this section addresses the following questions and points: 1) What are observational studies? 2) When do we need observational studies? 3) What is the fundamental limitation of observational studies? 4) How can the fundamental limitation be mitigated? 5) Why can’t the fundamental limitation be unequivocally eliminated? 6) What are common misleading statements made from observational studies? 7) What are common abuses of observational studies? and 8) How can we strengthen observational studies?

What are observational studies? Observational studies can be defined as studies in which units of observation (e.g., people, counties, mice, etc.) are not (randomly) assigned (by the experimenter) to levels of the independent variable. There can be some ambiguities of language here. For example, many methodologists would consider random assignment to levels of the independent variable to be the sine qua non of a true experiment, and there is clear agreement that studies in which the experimenter does randomly assign units of observation to levels of the independent variable do merit being termed experiments and not observational studies. There is also clear agreement that studies in which the experimenter does not manipulate levels of the independent variables and no process of random assignment is in play are observational studies. There is a zone in which language is less clear, e.g., when the investigator manipulates the independent variable but does not do so randomly or when there is a random process in play but not one controlled by the experimenter (53–55) (Jasjeet Sekhon, UC Berkeley and Rocio Titiunik, University of Michigan, personal communication). Observational studies are often categorized by the level of the unit of analysis (e.g., individual or ecological), time of exposure measurement (prospective or retroactive), or time course (longitudinal or cross-sectional) (56).

When do we need observational studies? Observational studies of dietary variables are designed to assess how one variable relates to another, with the goal of helping to inform conclusions about a causal relationship between the two. Observational studies only tell us about the associations among variables. Relative to true experiments, observational studies offer only weak information and they may suggest the plausibility of causation but cannot demonstrate causation.
Nevertheless, observational studies are warranted in multiple situations, including, but not necessarily limited to, the following: 1) situations in which it is impossible to assign participants to levels of the independent variable, such as to levels of weight loss to observe the effects of weight loss (one can only assign people to treatments that produce weight loss, to varying degrees); 2) situations in which it is unethical to assign participants to levels of the independent variable, such as assigning people to suspected toxins to find out if they are indeed dangerous; 3) situations in which one cannot yet specify the independent variable, because one is still exploring an area to generate hypotheses; and 4) situations in which conducting a randomized experiment would be prohibitively long, such as a study of the effects of a feeding practice in infants on cognition when those infants reached age 80 y.

What is the fundamental limitation of observational studies? There are multiple limitations to or challenges in observational studies, including measurement difficulties, sampling challenges, and difficulties obtaining a sufficient range of the independent variables. However, the fundamental limitation is the possibility of confounding. Loosely speaking, confounding is said to occur when some factor causes a hypothesized causal factor (the independent variable) and a hypothesized influenced outcome (the dependent variable) under study to be associated even when the independent variable does not have a direct or indirect causal effect on the dependent variable (57). Thus, even when an association is found in an observational study, it cannot be concluded that it demonstrates causation or, if it does, what the direction of causation is.

How can the fundamental limitation be mitigated? Removing the influence of variables that may cause confounding can help to mitigate it. These techniques include matching, stratification, and statistical adjustment. Typically, one postulates a set of potential confounding variables, measures them in the observational study along with the independent and dependent variables, and then statistically controls for them in the analysis. There are many complex variations. Performing such analyses is vital and often yields markedly different results than those that would have been obtained with such controls. For a striking example, see the work of Anderson et al. (58).

Why can’t the fundamental limitation of confounding be unequivocally eliminated? Confounding cannot be unequivocally eliminated, because we can only control for those variables that we think to measure, can measure well, and know how to statistically model appropriately. Unfortunately, knowledge is limited (if it were not, research would not be needed) and measurement capabilities for many potentially confounding factors such as diet, physical activity patterns, drug intake, acculturation, and social status are often quite limited. Therefore, there is no certainty that all confounders have been controlled for in observational studies (59,60).

What are common misleading statements made from observational studies? Three common examples of misleading statements are as follows. The first example arises from extrapolation beyond the range of the observed data. For instance, if it is found that people who run 5 mi/d (8.1 km/d) live 5 y longer on average than people who run 0 mi/d, the data cannot be extrapolated to suggest that if people run 50 mi/d, they would live 50 y longer. For a real-life extrapolation far beyond the range of the observed data, see the work of Sturm et al. (61). Second, misleading statements can arise from using language that indicates causation when only association has been demonstrated. As recently documented in an empirical analysis, this is a
far too common practice in the fields of nutrition and obesity (62). Finally, another common, misleading approach involves reporting estimates of the strength of associations (so-called effect sizes) in a way that exaggerates their magnitude (63).

**What are common abuses of observational studies?** One common misuse of observational studies is to conduct them long after the period in which they would be probative, i.e., capable of yielding new information that would help to decide an issue. In the early stages when a question is just being asked or developed, it is reasonable to conduct observational epidemiologic studies that may yield initial direction to guide further research. However, after passage of time, often multiple (M) observational studies have addressed a question and may either be convincing in showing an association, be convincing in not showing an association, or yield equivocal results. When contemplating conducting the (M+1)th study, one has to ask: “Is there reason to believe that that study will move the collective results from one category to another or settle the question of causation if that is under debate?” Often the answer is no, but the (M+1)th study is conducted nonetheless, perhaps more as a tool for rhetoric than to enhance understanding. Doing so is arguably an unethical waste of resources. In such cases, when randomized experiments can be done, these are the next logical step and can potentially be probative. Finally, another common abuse entails publication bias in which the probability that a study is published depends on its outcome (64,65).

**How can we strengthen observational studies?** One way to strengthen observational studies is to use designs that markedly reduce (but do not eliminate) the likelihood of confounding. These include longitudinal studies, sibling control studies (66), use of adoption as a form of pseudo-randomization to households (67), the randomization of roommates to study peer effects (68), and still other approaches (53,69). These types of studies, although often not as inferentially strong as traditional randomized experiments, can increase the rigor of observational research and represent a “bridge” between the 2 classes of evidence.

Ultimately, in many cases, it is only the conduct of large, well-designed RCT that will settle controversy and yield satisfactory evidence about causation. Yet in some domains, particularly in the area of health-related policy, it is often expressed that RCT are impossible. Although this is assuredly true in some cases, RCT may be far more feasible than many advocates of public health policies acknowledge. RCT have been conducted to include many thousands of people and to study issues as challenging as the effects of moving poor families to less poor neighborhoods (70) and the effects of supplemental income on long-term retention of guardianship for displaced children (71). If RCT can be conducted to address such challenging, expensive, and sensitive topics, then surely RCT of many nutrition-related practices and policies can be conducted. Long-term RCTs in free-living adult populations to separately address the role of LCS in weight loss or weight maintenance will ultimately help to clarify the role of LCS in assisting motivated individuals to achieve body weight goals and to inform policy makers.

**Conclusions**

We conclude that there is no evidence that LCS can be claimed to be a cause of higher body weights in adults. Similarly, evidence supporting a role for LCS in weight management is lacking. Due to the confounders in most observational studies, RCT are needed to advance understanding.

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