SUMMARIES OF RECENT SCIENTIFIC PUBLICATIONS SUPPORTING THE USE OF NONNUTRITIVE SWEETENERS (2019 Update)

The research and evidence base for the safety and efficacy of nonnutritive sweeteners (NNS), also commonly known as low-calorie sweeteners (LCS), spans decades. Find a quick summary of the safety evaluation and regulatory review of LCS in the U.S. and globally on page 6. This bibliography includes key statements and brief abstracts of the more recent studies. (Publications are listed in reverse chronological order within each category.) Summaries of additional and older publications are available at SplendaProfessional.com/Studies-Science. This resource is provided by Heartland Food Products Group, LLC, the manufacturer of SPLENDA® Sweetener Products.

HEALTH ORGANIZATIONS AND PROFESSIONAL ASSOCIATIONS

American Diabetes Association (ADA) – Standards of Medical Care in Diabetes-2019.
Diabetes Care. S1-S183. Section 5. Lifestyle Management. S46-S60.
About NNS (abridged statement from Table 5.1): *"The use of nonnutritive sweeteners may have the potential to reduce overall calorie and carbohydrate intake if substituted for caloric (sugar) sweeteners and without compensation by intake of additional calories from other food sources."*
http://care.diabetesjournals.org/content/42/Supplement_1/S46

Diabetes UK Evidence-Based Nutrition Guidelines for the Prevention and Management of Diabetes.
Dyson PA, et al. Diabetic Medicine. 2018;35(5):541-547.
Summary: Diabetes UK is the British-based patient, healthcare professional and research association for diabetes. They reviewed and updated their nutrition guidelines in 2018 for the prevention and management of diabetes. Their statement on NNS is: *"Non-nutritive (artificial) sweeteners are safe and may be recommended."*
https://onlinelibrary.wiley.com/doi/full/10.1111/dme.13603

European Food Safety Authority (EFSA) Panel on Food Additives and Nutrient Sources added to Food. Statement on the Validity of the Conclusions of a Mouse Carcinogenicity Study on Sucralose (E 955) Performed by the Ramazzini Institute.
Aguilar F, et al. European Food Safety Authority Journal. 2017;15(5):4784.
Summary: In 2017, the European Food Safety Authority (EFSA) published a positive scientific opinion on the safety of sucralose with regard to carcinogenicity. The EFSA statement is consistent with myriad global scientific consensus and regulatory authorities' conclusions that sucralose is safe and does not cause cancer.
http://onlinelibrary.wiley.com/doi/10.2903/j.efsa.2017.4784/full

American Cancer Society: Guidelines on Nutrition and Physical Activity for Cancer Prevention and Physical Activity for Cancer Prevention. (Latest revision 2016)
About NNS: *"There is no proof that these sweeteners, at the levels consumed in human diets, cause cancer. Aspartame, saccharin, and sucralose are a few of the non-nutritive sweeteners approved for use by the FDA. Current evidence does not show a link between these compounds and increased cancer risk."*
http://www.cancer.org/healthy/eathealthygetactive/acsguidelinesonnutritionphysicalactivityforcancerprevention/acs-guidelines-on-nutrition-and-physical-activity-for-cancer-prevention-common-questions

Academy of Nutrition and Dietetics Position Paper: Interventions for the Treatment of Overweight and Obesity in Adults.
J Acad Nutr Diet. 2016;116(1):129-147.
Summary: The value of reducing sugar-sweetened beverages (SSBs) to reduce weight is discussed briefly. Data from two RCTs demonstrating greater weight loss with the replacement of low-calorie sweetened beverages for SSBs are detailed. These RCTs, by Tate et al. (2012) and Peters et al. (2014), are cited in summaries under Weight Management.
http://www.eatrightpro.org/~/media/eatrightpro%20files/practice/position%20and%20practice%20papers/position%20papers/weightmanagement.ashx

American Academy of Pediatrics Policy Statement from Council on School Health, Committee on Nutrition. Snacks, Sweetened Beverages, Added Sugars, and Schools.
Pediatrics. 2015;135(3):575-583.
About NNS: *"Additional improvements in nutrient density of sweet-tasting products could be obtained if nonnutritive sweeteners are used as a tool to replace added sugars and help lower caloric intake. Several nonnutritive sweeteners have been accepted by the US Food and Drug Administration as safe and have shown good safety over time. However, data are scarce on long-term benefits for weight management in children and adolescents or on the consequences of long-term consumption. Continued research is needed."*
http://pediatrics.aappublications.org/content/pediatrics/early/2015/02/17/peds.2014-3902.full.pdf

Academy of Nutrition and Dietetics Position Paper: Use of Nutritive and Nonnutritive Sweeteners.
J Acad Nutr Diet. 2012;112(5):739-758.
About NNS: *"It is the position of the Academy of Nutrition and Dietetics that consumers can safely enjoy a range of nutritive and nonnutritive sweeteners when consumed within an eating plan that is guided by current federal nutrition recommendations, such as the Dietary Guidelines for Americans and the Dietary Reference Intakes, as well as individual health goals and personal preference."*
https://jandonline.org/article/S2212-2672(12)00325-5/fulltext

Scientific Statement from the American Diabetes Association and the American Heart Association. Nonnutritive Sweeteners: Current Use and Health Perspectives.
Gardener C, et al. Diabetes Care. 2012;35(8):1798-1808 and Circulation: 2012;126:509-519.
Summary: This statement, which reviewed evidence published since 2005, concludes reducing the intake of added sugars is an important intervention to achieve a healthy weight and nutrient-dense dietary pattern. The statement also concludes that using NNS may result in small decreases in calorie intake and weight loss when used within a structured eating plan and without caloric compensation.
https://www.ahajournals.org/doi/full/10.1161/CIR.0b013e31825c42ee

META-ANALYSES, SYSTEMATIC AND LITERATURE REVIEWS

Association Between Intake of Non-Sugar Sweeteners and Health Outcomes: Systematic Review and Meta-Analyses of Randomised and Non-Randomised Controlled Trials and Observational Studies.
Toews I, et al. BMJ. 2019;364:1-13.
Summary: This systematic review, using Cochrane review methodology, set out to assess the association between intake of non-sugar sweeteners (NSS) and potential health benefits in generally healthy or overweight/obese adults and children. Studies included in the review allowed the direct comparison of no intake or lower intake of NSS with higher NSS intake. The NSSs had to be clearly named, and the intervention duration had to be at least seven days. Based on 56 studies, including 17 RCTs, evidence for several health benefits was found. This included a reduction in calorie consumption, not causing a rise in glucose levels and not contributing to tooth decay. Specifically in adults, mean calorie intake was about 250 calories lower in people consuming NSS vs. regular sweeteners (based on 4 RCTs) with no effect on feelings of hunger or appetite. There was a small benefit on BMI and fasting glucose (based on 5 RCTs). Based on the included studies, the authors noted the very low to moderate quality evidence and called for additional longer-term studies. However, based on the inclusion criteria, several often cited systematic reviews and/or RCTs were excluded including: Miller and Perez, 2014; Peters et al, 2016; and Rogers et al, 2016. (All of them are included in this bibliography. This publication was accompanied by the editorial below by Malik.) https://www.bmj.com/content/bmj/364/bmj.k4718.full.pdf

Non-Sugar Sweeteners and Health.
Malik VS. BMJ. 2018;363:1-2.
Summary: In a related editorial, Malik from Harvard T.H. Chan School of Public Health, offers a constructive analysis of the Toews, et al. systematic review. The author calls attention to the strengths and limitations of this review and notes, *"…use of NSS as a replacement for free sugars…could be a helpful strategy to reduce cardiometabolic risk among heavy consumers…"*
https://www.bmj.com/content/364/bmj.k5005.full

Stevia Leaf to Stevia Sweetener: Exploring its Science, Benefits, and Future Potential.
Samuel P, et al. J Nutrition. 2018;148(7):1186S-1205S.
Summary: This comprehensive report, written by internationally known experts on steviol glycosides, was based on a symposium held after the 2017 American Society for Nutrition meeting and published as a supplement. The extensive report is global in scope and covers the science, safety, acceptable daily intake (ADI) and potential health benefits of high-purity steviol glycosides. Regarding science and safety, the report states, *"All major global scientific and regulatory bodies have determined through their rigorous evaluation processes that high-purity steviol glycosides are safe for the general population."* In healthy individuals and those with diabetes, the use of steviol glycosides, in place of some carbohydrate and sugars, support reduction in postprandial glucose levels and reduced carbohydrate and sugar intake. This report also covers future research, application, global regulatory status, consumer insights and market trends. https://academic.oup.com/jn/article-abstract/148/7/1186S/5049670?redirectedFrom=fulltext

Critical Review of the Current Literature on the Safety of Sucralose.
Magnuson BA, et al. Food and Chemical Toxicology. 2017;106: 324-355.
Summary: Sucralose has been extensively studied and evaluated by researchers and regulatory agencies around the world. This publication offers an in-depth review of the broad array of studies conducted over the 40-year history, including the effects of sucralose on growth, development, reproduction, neurotoxicity, immunotoxicity, carcinogenicity and overall health status, as well as human studies on the effects of sucralose in people with diabetes. The review of more recent studies focused on carcinogenic potential and the effect of sucralose on the gut microflora and potential impact on glycemic control. The review concludes sucralose is safe for its intended use as an NNS. https://www.sciencedirect.com/science/article/pii/S0278691517302818
Due to the extensive length of this review, a "pocket guide" summary is available: https://www.splendaprofessional.com/sites/splenda_hcp/files/Magnuson_Pocket_Guide_2017.pdf

Does Low-Energy Sweetener Consumption Affect Energy Intake and Body Weight? A Systematic Review, Including Meta-Analyses of the Evidence from Human and Animal Studies.
Rogers PJ, et al. International J Obesity. 2016;40:381-394.
Summary: This systematic review covers a large and lengthy body of evidence, including numerous types of animal human studies using varied designs. Studies were conducted with various NNS, including several currently available or approved by the U.S. FDA. Conclusions are consistent with other systematic reviews of NNS that demonstrate decreased energy intake and body weight with consumption of NNS used in place of added sugars.
http://www.nature.com/ijo/journal/vaop/ncurrent/full/ijo2015177a.html

Substitution of Sugar-Sweetened Beverages with Other Beverage Alternatives: A Review of Long-Term Health Outcomes.
Zheng M, et al. J Acad Nutr Diet. 2015;115(5):767-779.
Summary: This systematic review culled studies from six different literature databases to identify prospective cohort studies (PCS) and randomized controlled trials (RCTs) in children and adults with four months or longer duration. Six PCS and 4 RCTs were included. Results showed that replacing sugar-sweetened beverages with a variety of low-calorie beverage alternatives demonstrate a favorable effect on long-term body weight.
http://www.andjrnl.org/article/S2212-2672(15)00112-4/fulltext

Intense Sweeteners, Appetite for the Sweet Taste, and Relationship to Weight Management.
Bellisle F. Current Obesity Report. 2015;4:106-110.
Summary: This paper, which analyzed research about how human NNS consumption may change the appetite for and intake of sweet-tasting products, draws three main conclusions: 1) No consistent relationship exists to demonstrate a heightened appetite for sweet foods; 2) Some research shows use of NNS is associated with consumption of less sweets; 3) Intervention studies in children and adults show use of NNS can reduce intake of caloric sweeteners and support weight loss efforts.
http://link.springer.com/article/10.1007%2Fs13679-014-0133-8#/page-1

Low-Calorie Sweeteners and Body Weight and Composition: A Meta-Analysis of Randomized Controlled Trials and Prospective Cohort Studies.
Miller PE, et al. Am J Clin Nutr. 2014;100:765-77.
Summary: This meta-analysis analyzed results from randomized control trials (RCTs) and prospective cohort studies on NNS and body weight, BMI, fat mass and waist circumference. It showed that in RCTs, NNS reduced body weight compared to placebo and modestly but "significantly" reduced BMI, fat mass and waist circumference. This meta-analysis was accompanied by the editorial referenced below by Hill.
http://ajcn.nutrition.org/content/early/2014/06/18/ajcn.113.082826.full.pdf+html

What Do You Say When Your Patients Ask Whether Low-Calorie Sweeteners Help with Weight Management?
Hill J. Am J Clin Nutr. 2014;100: 739-740.
Summary: This is a related editorial written by obesity expert James Hill.
http://ajcn.nutrition.org/content/early/2014/07/30/ajcn.114.094466.full.pdf

SAFETY AND CARCINOGENICITY

FDA Regulatory Approach to Steviol Glycosides.
Perrier JD, et al. Food and Chemical Toxicology. 2018;122:132-142.
Summary: This publication, authored by FDA employees, provides extensive detail on FDA's practices for filing and evaluating the Generally Recognized As Safe (GRAS) notices for high-purity steviol glycosides as sweeteners in foods. A table summarizes the data in the GRAS notices filed with FDA. To date, the FDA has not questioned the GRAS status of more than 50 GRAS applications for use of many steviol glycosides as general purpose sweeteners in foods, beverages and tabletop sweeteners.
https://ac.els-cdn.com/S0278691518307063/1-s2.0-S0278691518307063-main.pdf?_tid=67c-85faa-0d01-4bb3-b954-91a81105eb8f&acdnat=1549912118_38bc-f1ae06171c793b1bef23a386b266

Biological Fate of Low-Calorie Sweeteners.
Magnuson BA, et al, Nutrition Reviews. 2016; 74(11):670-689.
Summary: This comprehensive review covers commonly used NNS, including acesulfame potassium, aspartame, saccharin, stevia leaf extract (steviol glycoside) and sucralose. It details the biological fate of these NNS, including their absorption, distribution, metabolism and excretion pathways. The review also compares the chemical differences between these NNS and notes their global regulatory status. This article helps healthcare providers and their clients overcome potential concerns and hesitancy about using NNS to prevent and/or manage chronic health conditions.
https://academic.oup.com/nutritionreviews/search-results?page=1&q=Magnuson%20BA&fl_SiteID=5413&SearchSource-Type=1&allJournals=1

The Safety and Regulatory Process for Low-Calorie Sweeteners in the United States.
Roberts A. Physiology & Behavior, 2016;164, Part B, 439-444.
Summary: This article provides an in-depth review of the regulatory processes for NNS, including the food additive approval process and the Generally Recognized As Safe (GRAS) used by the U.S. FDA. The same level of scientific evidence is required to support safety and ensure a reasonable certainty of no harm in both review processes. This review covers potential safety concerns, including carcinogenicity, effects on body weight gain, glycemic control and effects on the gut microbiome.
http://www.sciencedirect.com/science/article/pii/S003193841630083X

Sucralose Non-Carcinogenicity: A Review of the Scientific and Regulatory Rationale.
Berry C, et al., Nutrition and Cancer. 2016 Nov-Dec;68(8):1247-1261.
Summary: This comprehensive safety review of sucralose includes independently conducted and industry-funded research on sucralose chemistry, pharmacokinetics, metabolism, toxicity, genotoxicity and long-term safety – including carcinogenicity. It concludes that sucralose is non-carcinogenic and safe for all consumers to use and supports four key points: 1) There is no evidence of chemical concerns or toxicity; 2) No metabolites in sucralose were found to be carcinogenic; 3) No changes to genes were observed to indicate any cancer-causing effects; 4) At doses thousands of times the maximum expected daily intake in humans, toxicity and long-term carcinogenicity studies showed no evidence of carcinogenic potential.
http://www.tandfonline.com/doi/full/10.1080/01635581.2016.1224366

GUT HEALTH, GLYCEMIC CONTROL, HUNGER AND APPETITE

Assessing the *in vivo* Data on Low/No-Calorie Sweeteners and the Gut Microbiota.
Lobach AR, et al. Food and Chemical Toxicology. 2019;124:385-399.
Summary: This systematic review was designed to find any published studies with gut microbiome measures in either animal or human subjects exposed to LNCSs and studies that investigated the general nature of the gut microbiome. The review determined that there is no credible evidence for LNCSs to adversely affect health through an effect on the gut microbiome. The authors found *"clear evidence that changes in the diet unrelated to LNCS consumption are likely the major determinants of change in gut microbiota numbers and phyla."* The authors also conclude that because the number and type of microbiome organisms change daily in response to normal dietary changes, it is virtually impossible to predict the clinical meaningfulness in the gut microbiome from LNCS research studies conducted to date.
https://www.sciencedirect.com/science/article/pii/S0278691518308780

Beverages Containing Low Energy Sweeteners Do Not Differ from Water in Their Effects on Appetite, Energy Intake and Food Choices in Healthy, Non-Obese French Adults.
Fantino M, et al. Appetite. 2018;125:557-565.
Summary: This two-arm RCT crossover design study was conducted in 166 healthy non-obese French adult men and women ages 18-45 naïve to regular NNS consumption. The study aimed to determine if beverages sweetened with LCS, when consumed with meals, would differ or not from plain water in their impact on mean energy intake, either before or after LCS habituation, in the laboratory or at home. Results showed there was no difference between the consumption of water and LCS-sweetened beverage in their effects on total energy intake, macronutrient intakes, selection of sweet foods and on motivational ratings. Results were similar in subjects who had not previously consumed LCS on a regular basis and those who consumed LCS on a habituated basis during the study.
https://www.sciencedirect.com/science/article/pii/S0195666318300667

Glycemic Impact of Non-Nutritive Sweeteners: A Systematic Review and Meta-Analysis of Randomized Controlled Trials.
Nichol AD, et al. Eur J Clin Nutr. 2018;72:796-804.
Summary: This systematic review and meta-analysis of 29 RCTs quantitatively synthesized existing research on the impact of four NNS (aspartame, saccharin, steviosides and sucralose) on glycemia in normoglycemic individuals and a subset of people with diabetes. Though all NNS differ in structure, sweetness intensity and in other ways, the results demonstrated no differences between the various NNS on glycemic impact. The NNS did not increase blood glucose levels over the observation period, but they were observed to gradually decrease over the observation periods. However, the impact of NNS on glycemia varied to some extent by the study subjects' age, body weight and whether they had diabetes or not.
https://www.nature.com/articles/s41430-018-0170-6

A 12-Week Randomized Clinical Trial Investigating the Potential for Sucralose to Affect Glucose Homeostasis.
Grotz VL, et al. Regulatory Toxicology and Pharmacology. 2017;88:22-33.
Summary: This 12-week RCT on the impact of sucralose on glucose control and other metabolic parameters was a double-blind, parallel design with 47 normoglycemic male volunteers. Study subjects consumed ~333.3 mg encapsulated sucralose or placebo three times a day at mealtimes, the equivalent to ~200 g of added sugars per meal. A1C, fasting glucose, insulin and C-peptide levels were measured weekly. Adherence was carefully measured. Results showed A1C, glucose, insulin and C-peptide levels were within normal ranges throughout the study. The findings support that sucralose has no effect on glycemic control. The discussion offers a valuable review of recent research on NNS, glucose control and the impact of gastrointestinal sweet taste receptors.
https://www.sciencedirect.com/science/article/pii/S0273230017301265?via%3Dihub

Impact of Diet Composition on Blood Glucose Regulation.
Russell WR, et al. Critical Reviews in Food Science and Nutrition, 2016;56(4):541-590.
Summary: This review explores human studies on a range of dietary components and their impact on blood glucose levels in prevention and management of type 2 diabetes. The review includes the impact of the major macronutrients, micronutrients, nonnutrient phytochemical, and low-calorie sweeteners [NNS]. It includes the range of research on various NNS related to glucose regulation, including impact on gut hormones and glucose, C-peptide and insulin levels. The article concludes the use of NNS in subjects with or without diabetes does not affect glucose levels and are tools that may help people reduce or control calorie consumption.
http://dx.doi.org/10.1080/10408398.2013.792772

Low Calorie Sweeteners: Evidence Remains Lacking for Effects on Human Gut Function.
Bryant C, McLaughlin J. Physiology & Behavior, 2016;164, Part B, 482-485.
Summary: This review covers cellular, animal and clinical studies and puts results into context with the gut-brain axis and its regulation of food intake. Authors conclude human studies do not support a clinically meaningful effect of ingested NNS on hormones involved in gut signaling. Sucralose, aspartame and Ace-K had no greater effect than water on secretion of GLP-1, insulin, PYY or ghrelin, nor any impact on appetite. In summarizing the literature in humans, the authors state studies have consistently not shown that activation of sweet taste receptors by NNS placed in the human gut replicate any of the effects on gastric motility, gut hormones or appetitive responses evoked by calorie-containing sugars.
http://www.sciencedirect.com/science/article/pii/S0031938416301627

Nonnutritive Sweeteners Are Not Supernormal Stimuli.
Antenucci RG, et al. International J Obesity. 2015;39(2):254-9.
Summary: Study participants were exposed to a series of taste tests with various caloric and nonnutritive sweeteners. Participants rated perceived sweetness. Results showed participants perceived the sweetness of NNS at lower concentrations than the caloric sweeteners and indicated caloric sweeteners all had higher sweetness ratings than NNS. Researchers concluded that results don't support the claim that NNS produce a negative effect by over-stimulating peoples' sweet taste receptors to produce supernormal stimuli.
http://www.nature.com/ijo/journal/v39/n2/full/ijo2014109a.html (abstract)

Non-Nutritive Sweeteners: No Class Effect on the Glycaemic or Appetite Responses to Ingested Glucose.
Bryant CE, et al. Eur J Clin Nutr. 2014;68:629-631.
Summary: This study examined the individual effect of acesulfame-K (Ace-K), aspartame and saccharin responses on glycemia and appetite in humans when consumed in combination with glucose in commonly used amounts. Results showed no additional effect of aspartame or saccharin on glucose response any time during the 60-minute post-ingestion period. No NNS individually had an effect on perceptions of hunger or fullness.
http://www.nature.com/ejcn/journal/v68/n5/full/ejcn201419a.html (abstract)

WEIGHT MANAGEMENT

The Role of Low-Calorie Sweeteners in the Prevention and Management of Overweight and Obesity: Evidence v. Conjecture.
Rogers PJ: Proceedings of the Nutrition Society. 2017;77(3):230-238.
Summary: This paper reviews evidence about the impact of LCS on energy intake and weight control and thoroughly examines three common claims about the effect of LCS on energy intake and preference for sweetness: 1) "Sweet Taste Confusion Hypothesis"; 2) the "Sweetness without Calories and Sweet Tooth Hypothesis"; and 3) the "Conscious Overcompensation Hypothesis." Utilizing the evidence, Rogers substantiates the lack of evidence for these claims and concludes that intervention studies generally show consumption of LCS in place of (some) sugar reduces energy intake and body weight.
https://www.cambridge.org/core/journals/proceedings-of-the-nutrition-society/article/role-of-lowcalorie-sweeteners-in-the-prevention-and-management-of-overweight-and-obesity-evidence-v-conjecture/7929AACDE02CFC525B02C12F2BA97BA7

Low Calorie Sweetener (LCS) Use and Energy Balance.
Peters, JC, Beck J. Physiology & Behavior, 2016;164, Part B, 524-528.
Summary: This review details over 30 years of research and reviews on NNS, energy balance and weight management. The authors summarize the observational longitudinal cohort studies that early on suggested the promotion of weight gain and others while more recent studies nearly uniformly show either weight loss or the prevention of weight gain. Two recent meta-analyses cited here are summarized (Miller, et al, Rogers, et al). The authors conclude: *"RCTs are consistent in showing a benefit of LCS which suggest that simple behavioral engagement by individuals attempting to control their weight is a sufficiently strong signal to overcome any potential mechanism that might act to promote energy intake and weight gain."*
http://www.sciencedirect.com/science/article/pii/S0031938416301111

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The Effects of Water and Non-Nutritive Sweetened Beverages on Weight Loss and Weight Maintenance: A Randomized Clinical Trial.
Peters JC, et al. Obesity. 2016;24(2):297-304.
Summary: The study group in this one-year behavioral weight control RCT was instructed to drink 24 fl. oz./day diet beverages (DB) and the control group 24 fl. oz./day of water and no diet beverages. At 12 weeks, results showed the DB group lost significantly more weight, an average of 13 pounds or 44 percent more than control group (average nine pounds). 64 percent of study group lost > 5 percent of body weight, compared with 43 percent of control group. DB group experienced significantly less hunger. After completing the 9-month maintenance phase, the DB group showed statistically significant greater weight loss (6.21 ± 7.65 kg) than subjects in the water treatment group (2.45 ± 5.59 kg).
http://onlinelibrary.wiley.com/doi/10.1002/oby.21327/epdf

Sugar- and Artificially Sweetened Beverages and Intrahepatic Fat: A Randomized Controlled Trial.
Campos V, et al. Obesity. 2015;23:2335-2339.
Summary: Over a 12-week study period, this RCT compared the impact of Artificially Sweetened Beverages (ASB) with Sugar-Sweetened Beverages (SSB) on intrahepatic fat among overweight adults who usually consumed two or more 22 fl. oz. of SSB daily. Results showed participants consuming ASB had significantly decreased total energy, carbohydrate, and sugar intakes. Subjects continuing to consume SSB showed no differences in intake. Dietary changes in the ASB group were accompanied by a significant decrease in intrahepatic fat.
http://onlinelibrary.wiley.com/doi/10.1002/oby.21310/abstract?userIsAuthenticated=false&deniedAccessCustomisedMessage=

Low/No Calorie Sweetened Beverage Consumption in National Weight Control Registry (NWCR).
Catenacci VA, et al. Obesity. 2014;22(10):2244-2251.
Summary: This study surveyed consumption of beverages with NNS in NWCR members with sustained weight loss for > seven years. Results showed 53 percent regularly consumed NNS beverages, and 10 percent regularly consumed sugar-sweetened beverages (SSB). 78 percent of NNS consumers reported they helped control calorie intake. Choice of beverage was "very important" for weight loss (42 percent) and weight maintenance (40 percent).
http://onlinelibrary.wiley.com/doi/10.1002/oby.20834/epdf

Replacing Caloric Beverages with Water or Diet Beverages for Weight Loss in Adults: Main Result of the Choose Healthy Options Consciously Everyday (CHOICE) Randomized Control Trial.
Tate D, et al. Am J Clin Nutr. 2012;95:555-563.
Summary: CHOICE was a six-month RCT with three groups: 1) diet beverage, 2) water or 3) control. Eligible subjects had to consume > 280 kcal/day sweetened beverages and commit to making a dietary change. Diet beverage and water groups substituted > two servings/day of sweetened beverage with a diet beverage or water, respectively. Results: At six months, diet beverage drinkers were more likely to achieve a 5 percent weight loss than water drinkers. A secondary analysis, Piernas, et al. (http://ajcn.nutrition.org/content/97/3/604.full.pdf+html), showed both study groups reduced total energy, carbohydrate and added sugars. Diet beverage group participants reduced dessert consumption more than water drinkers.
http://ajcn.nutrition.org/content/95/3/555.full.pdf+html

DIETARY PATTERNS AND QUALITY

Low-Calorie Beverage Consumption, Diet Quality and Cardiometabolic Risk Factor in British Adults.
Patel L, et al. Nutrients. 2018;10:1261.
Summary: This study aimed to determine that consumption of low-calorie sweetened beverages (LCB) did not negatively impact diet quality and cardiometabolic risk factor in British adults. Nearly two-thirds of adults in the U.K. are overweight or obese, and sugar-sweetened beverages (SSBs) are a significant source of added sugars. Data from over 5,000 individuals 16 years of age and older obtained from two waves of the National Diet and Nutrition Survey Rolling Programme (2008-2012 and 2013-2014) was analyzed. LCB consumption, compared with SSB consumption, was associated with lower energy consumption and lower free [added] sugar intake while consumption of other nutrients was not significantly different. No significant differences were observed in plasma glucose, total cholesterol, LDL, HDL or triglycerides. This study adds to existing evidence demonstrating that replacing LCB for SSB can positively impact diet quality and energy consumption.
https://www.mdpi.com/2072-6643/10/9/1261/htm

Low-/No-Calorie Sweeteners: A Review of Global Intakes.
Martyn D, et al. Nutrients. 2018;10(3):357.
Summary: This extensive review of studies conducted since 2008 determined the global intake of the seven most commonly used LCS, including aspartame, acesulfame-K, saccharin, sucralose, cyclamate, thaumatin and steviol glycosides. Intakes were calculated for the mean and high intake consumers. The broad review of studies raised no concern regarding excess intake among the general population and other subpopulations like children and people with diabetes. In addition, the data do not demonstrate any significant increase or decrease of LCS over this 10-year timeframe but do suggest a possible increase in the numbers of people consuming products containing LCS.
https://www.mdpi.com/2072-6643/10/3/357/htm

Low Calorie Beverage Consumption is Associated with Energy and Nutrient Intakes and Diet Quality in British Adults.
Gibson SA, et al. Nutrients. 2016;8,9:1-15 (e-pub).
Summary: This analysis of adults in the U.K. National Diet and Nutrition Survey (NDNS) observed associations between consumption of sugar-sweetened beverages (SSB), low-calorie sweetened beverages (LCB), non-consumers of soft drinks (NC) and consumers of both beverages (BB) with energy intake and diet quality. Results showed LCB and NC groups consumed less energy and sugars than consumers of SSB or BB. NC and LCB consumers had higher quality diets compared to SSB and BB consumers. They did not compensate for the sugar or energy deficit with more sugary foods.
http://www.mdpi.com/2072-6643/8/1/9

Consumption of LCS Among U.S. Adults is Associated with Higher Healthy Eating Index (HEI 2005) Scores and More Physical Activity.
Drewnowski A, et al. Nutrients. 2014;6:4389-4403.
Summary: This study analyzed NHANES data from over 22,000 participants between 1999-2008 who consumed beverages, foods and tabletop sweeteners with NNS. The USDA's Healthy Eating Index was used to measure diet quality. Results showed people who use NNS have a higher HEI than non-consumers, largely explained by lower calorie intake from solid fats, added sugars and alcohol. NNS users were found to practice other healthy lifestyle behaviors, such as physical activity and less tobacco and alcohol use.
http://www.mdpi.com/2072-6643/6/10/4389/htm

Quick Summary: Safety Evaluation and Regulatory Review of Low-Calorie Sweeteners in U.S. and Globally

United States: The U.S. Food and Drug Administration (FDA) regulates low-calorie sweeteners either through the Food Additive Approval Process or the Generally Recognized As Safe (GRAS) process.(1) Both processes follow established rigorous protocols and meet the FDA standard of safety.(1) Whether the LCS is evaluated as a Food Additive or GRAS ingredient, they are allowed for use by the entire population, including children, pregnant and lactating women and people with diabetes.

Food Additive Review Process: The manufacturer or entity submits a food additive petition for review to FDA. The petition must provide a complete safety assessment of the ingredient based on the principles of food toxicology.(5) The ingredient is not allowed to be used in foods until FDA completes their review and grants approval. Sucralose, the sweetening ingredient in SPLENDA® No Calorie Sweetener, is an example of an LCS that received FDA approval as a Food Additive.

GRAS Review Process: The general recognition of safety of these ingredients is based on data in the public domain; therefore, FDA does not require a safety assessment. Rather, the manufacturer or entity seeking to use the ingredient in foods obtains review from experts on the ingredient and submit the review as a "GRAS Notification" to FDA. In essence, this notifies the FDA of their intent to use the ingredient. FDA responds to a GRAS notification with either a No Objection letter, meaning FDA has no questions about the use of this ingredient, or notification that the ingredient does not provide a basis for use as a GRAS ingredient. To date, FDA has reviewed many GRAS notifications for steviol glycosides. Based on No Objection letters, these ingredients are allowed in foods.(6) As an example, the steviol glycosides Reb A and Reb D, the sweetening ingredients in SPLENDA® Naturals Stevia Sweetener, are GRAS.

Global: Sucralose, the sweetening ingredient in SPLENDA® No Calorie Sweetener, and steviol glycosides, the sweetening ingredients in SPLENDA® Naturals Stevia Sweetener, have been authorized or adopted for use across the globe by many regulatory bodies, including Health and Welfare Canada.(2,3)

The safety evaluation and regulatory processes to allow the use of LCS around the globe depends on the country or area of the world. Some have their country or area-based regulatory body. As examples, Canada has their regulatory body, Health and Welfare Canada, and countries in Europe look to the European Food Safety Authority (EFSA). Many countries use guidance from the Joint Expert Committees for Food Additives (JECFA) administered jointly by the Food and Agriculture Organization of the United Nations and the World Health Organization.(4)

References:

1. Roberts A: The safety and regulatory process for low-calorie sweeteners in the United States. Physiology & Behavior. 2016;164, Part B, 439-444..
2. International Food Information Council Foundation. What is Sucralose? https://foodinsight.org/what-is-sucralose. (Accessed February 19, 2019.)
3. Samuel P, Ayoob KT, Magnuson BA, Wolwe-Rieck U, Jeppesen PB, Rogers PJ, Rowland I, Mathews R: Stevia Leaf to Stevia Sweetener: Exploring its Science, Benefits and Future Potential. J Nutrition.
4. World Health Organization. Joint FAO/WHO Expert Committee on Food Additives (JECFA). https://www.who.int/foodsafety/areaswork/chemical-risks/jecfa/en. (Accessed February 19, 2019.)
5. Guidance for Industry and Other Stakeholders: Toxicological Principles for the Safety Assessment of Food Ingredients (Redbook). https://www.fda.gov/Food/GuidanceRegulation/GuidanceDocumentsRegulatoryInformation/ucm396147.htm. (Accessed February 19, 2019.)
6. Perrier JD, Mihalov JJ, Carlson SJ: FDA Regulatory Approach to Steviol Glycosides. Food and Chemical Toxicology. 2018;122:132-142.

The literature cited here is consistent with the extensive evidence base on NNS, which concludes that NNS can be used safely and efficaciously as part of a healthy eating pattern. Summaries of other and older publications are available at SplendaProfessional.com/Studies-Science. Using nonnutritive sweeteners can help people manage their weight and/or various aspects of metabolic health by reducing calories, total carbohydrate and added sugars.

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