Sweet Alternatives and Health: Guidance for the Clinician

Take Home Points:

- Low calorie sweeteners (LCS) can be used in certain patient populations. LCS contribute no calories or negligible calories in small quantities. LCS's may come directly from plants, industry produced from naturally occurring foods or be newly synthesized chemical compounds.
- Plant-based LCS's are preferential to synthetic. Chemically synthesized LCS's have the potential to be detrimental to human health. In contrast, plant-based LCS's may have a beneficial role in human health.
- Results of LCS and human health studies are mixed. Data primarily reflect animal models or human adult research. Adverse effects in children and pregnant women are not well understood with some evidence for harm from exposure *in utero*. Further research is needed to adequately inform dietary recommendations.

Background: Dietary sugars can be naturally occurring or added. To replace added sugars, low calorie sweeteners (nutritive and non-nutritive) are commonly used.

- Naturally occurring sugars are part of whole fruits and vegetables, and unsweetened dairy products (e.g. milk, yogurt).
- Added sugars include addition of sugars during food production. Pure (100%) honey, pure (100%) maple syrup, and other single-ingredient sugars, such as juice concentrates, contribute to the daily value of added sugars.
- Low calorie sweeteners—is an alternative product used to add sweetness that contains zero (non-nutritive) or very low amounts (nutritive) or carbohydrates.

Health Effects of Added Sugar.

- Added sugars increase the **risk** of chronic disease in adult and pediatric populations
- The U.S. Dietary Guidelines for Americans recommend limiting calories from added sugars to no more than 10% of total daily calories. These guidelines are supported by the Centers for Disease Control and Prevention, and World Health Organization.

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Low Calorie Sweeteners (LCS)

- Offer an opportunity to consume sweet tasting products without added calories.
- May support a healthy body weight, as well as diabetes and cardiovascular disease management in adult and pediatric populations, and during pregnancy.

LCS and Maternal-Fetal and Pediatric Implications:

- Studies primarily limited to animal and adult-human studies.
- American Academy of Pediatrics recommends more research to better understand possible health effects in children long-term.
- The American College of Obstetricians and Gynecologists have not made any statement on LCS consumption during pregnancy.
- Associations found in human studies, **LCS unspecified.**
    - Maternal intake of LCS-containing beverages during pregnancy **increased** risk of gestational diabetes and preterm delivery.
    - Maternal intake of LCS-containing beverages during pregnancy **increased** risk of childhood asthma.
    - Maternal consumption of LCS-containing beverages **increased** infant BMI and increased risk of being overweight at 1 year of age. In addition, a clinical trial demonstrated maternal consumption of LCS-containing beverages led to **unfavorable** shifts in infant gut microbiome.

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LCS may be further divided into the following categories, with clinical health impacts listed in the tables below. These Sweeteners are approved in the USA and meet GRAS classification (Generally Recognized as Safe) by the FDA.

Plant Based Sweeteners

Sweetener/Brand Names	Clinical health impacts
Stevia (Candyleaf plant)/ Truvia, Pure Via, Enliten	**Reduced** body weight, decreased plasma glucose, and improved insulin sensitivity. When compared to aspartame and sucrose, significantly **reduced** postprandial glucose. **Anticarcinogen** in human cancer cell lines.

Monk Fruit (Luo Han Guo plant)/ Monk Fruit in the Raw, PureLo, Nectresse	**Beneficial** for preventing hyperglycemia and insulin secretion. **Anticarcinogen** in human cancer cell lines.
Yacon (Yacon plant)	**Beneficial** for bowel function as a source of fructooligosaccharides. **Reduced** body weight, improved insulin sensitivity and satiety. **Anticarcinogen** in human cancer cell lines.
Thaumatin (West African Katemfe Fruit)/ Talin	Few long-term human studies. No significant effect on glycemic response for healthy individuals. **Decreased** blood glucose in Type 2 diabetics. **Reduced** H. pylori-induced pro-inflammatory cytokines in human parietal cells.

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Sweeteners Derived From Naturally Occurring Foods

Sweetener/Brand Names	Clinical health impacts
Tagatose	**Beneficial** effects for oral and colonic microbiome. Reduced circulating tagatose correlates with the development of inflammatory bowel disease.

	Antihyperglycemic, decreased postprandial glycemic response, and improved satiety. **Inhibitory** effects on colon cancer in human cell lines.
Allulose	**Improved** insulin sensitivity and lowered postprandial glycemic response. **Anticarcinogen** in human cancer cell lines.
Sugar alcohols (e.g. Erythritol, Mannitol, Isomaltitol, Lactitol, Sorbitol, Xylitol)	**Beneficial** effects on the microbiome possibly due to a prebiotic-like effect. In larger quantities, can increase blood glucose. In moderate amounts, **lowered** postprandial plasma glucose. Increased cancer **risk** (hepatocellular carcinoma). Studies of erythritol and xylitol show an association with incident major **adverse** cardiovascular events and thrombosis.

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New Chemical Compound Sweeteners

Sweetener/Brand Names	Clinical health impacts

Aspartame/ NutraSweet, Equal, Sugar Twin	Aspartame has demonstrated a **favorable** microbiome shift, **poorer** glucose control, and increased cancer **risk** with consumption in some studies. Aspartame has been associated with **risk** for cognitive deficits, mood disorders, headaches, and seizures. Association between autism in males and maternal aspartame intake in pregnancy.
Advantame	Neotame and advantame are derived from aspartame. Neither has been evaluated in human studies.
Neotame/ Newtame	
Acesulfame potassium "Ace-K"/ Sunett, Sweet One	Ace-K is commonly used in combination with other LCS (commonly Aspartame) — isolated effects are poorly understood. Has demonstrated a slightly higher **risk** of cancer overall, less than aspartame.
Saccharin/ Sweet and Low, Sweet N' Low, Sugar Twin, Necta Sweet	Both Saccharin and Sucralose have demonstrated **unfavorable** shifts in the microbiome and **poorer** glucose control for in some studies. Cancer risk not observed in humans (bladder cancer in rats).
Sucralose/ Splenda	
Combined Exposures	Maternal intake of Saccharin, Aspartame, Ace-K, and Sucralose during pregnancy contributes to gestational weight gain, **increased** childhood BMI, and **increased** insulin resistance. Combination sucralose and Ace-K containing beverages **lessen** BMI gain in adolescents. Intake of Aspartame, Ace-K, and Sucralose linked to higher **risk** of any cardiovascular problem, **risk** of stroke, and developing type 2 diabetes. Beverages containing sucralose or aspartame **do not raise** postprandial blood glucose or insulin levels to the same extent as sucrose.

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General Recommendations Given Current Knowledge:

- Consume sweet-tasting products in moderation with a focus on healthy eating.
- Use naturally occurring sugars in fruit as a sweetener. Examples:
    - Use mashed banana or unsweetened applesauce in home baked goods.
    - Use dried fruits with no added sugar (e.g. prunes, raisins and dates) to sweeten foods, baked goods, or as a snack to curb a sweet tooth.
    - Choose unsweetened yogurt with fruit over yogurt with added sugars.
- Look for products that use natural flavors derived from natural oils such as sparkling water without added sugars.
- When using LCS, consider choosing plant-based sweeteners, tagatose, or allulose.