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 Presenter: Alan W Barclay, PhD- Speaker's Bureau: C3, Coca Cola; Diabetes Australia, GI Foundation, Fonterra, ILSI, Novo Nordisk Advisory Board: Roche Diagnostic; Nestle Australia; Consultancy: GI Foundation, Merisant (Australia)
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Objectives

1. To define Added and Free sugars
2. To review approved Nonnutritive Sweeteners
3. To review evidence and safety of the use of Sweeteners in Weight Management and Diabetes control

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The screenshot shows a webpage from Natural News. The main headline reads: "Aspartame is linked to leukemia and lymphoma in new landmark study on humans". Below the headline, it says "Wednesday, October 21, 2015 by Ethan Evans" and "Tags: aspartame, leukemia, lymphoma". There is a search bar and navigation links at the top. The article text is partially visible, mentioning "As few as one diet soda daily may increase the risk for leukemia in men and women, and for multiple myeloma and non-Hodgkin lymphoma in men, according to new results from the longest-ever running study on aspartame as a carcinogen in humans. Incredibly, this is the most..."

FACT VS. FICTION

Common Myths About Sweeteners

- ☠️ Sugar is addictive, toxic and causes disease
- 💪 "Natural sugars" are healthier
- 😬 "Artificial sugars" causes disease, obesity, increases hunger, appetite etc.
- 🔍 Eating sugar(s) causes diabetes

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What are sugars?

Class (DP *)	Subgroup	Principal components
Sugars (1-2)	Monosaccharides	Glucose, fructose, galactose
	Disaccharides	Sucrose, lactose, maltose, trehalose
	Polyols (sugar alcohols)	Sorbitol, mannitol, lactitol, xylitol, erythritol, isomalt, maltitol

* Degree of polymerization or number of monomeric (single sugar) units.
Based on Food and Agriculture Organization/World Health Organization 'Carbohydrates in Human Nutrition' report (1998), and Cummings et al. (1997).

Allulose- Brand name: Dolcica Prima

2015 GRAS
Not approved in Europe
low calorie sweetener –
90% fewer calories than sugar
70% as sweet as sugar
Texture and bulk of regular sugar when added to food by manufacturer
Not available as table sugar

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Cummings and Stephen, EJCN, 2007

Added Sugars

- US pop intake AS 268 cal/day = 13.4% = 17 tsp/d
- Sugars added during processing of foods
 - include sugars (free, mono and disaccharides), syrups, naturally occurring sugars that are isolated from a whole food and concentrated so that sugar is the primary component (e.g. fruit juice concentrates), other caloric sweeteners.
 - 39% US added sugar intake is in beverages!

US Scientific Report of the 2015 Dietary Guidelines Advisory Committee

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Ingredients that mean “Added Sugars” on Food Labels

*Percent Daily Values are based on a 2,000 calorie diet. Your Daily Values may be higher or lower depending on your calorie needs.

Ingredients: Dextrose, fructose, honey, invert sugar, raw sugar, malt syrup, rice syrup, sucrose, xylose, molasses, corn sweetener, fruit juice concentrate, high-fructose corn syrup, brown sugar, corn syrup, glucose, lactose, maltose, sucrose, evaporated cane juice, agave nectar, cane crystals, cane sugar, crystal-line fructose, barley malt, beet sugar, caramel.

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Free sugars

- ‘Added to foods by manufacturer, cook, or consumer, plus sugars naturally present in honey, syrups and fruit juices’.
- Does not include fruit and dairy products such as milk and yoghurt which naturally contain unrefined sugars and are a source of essential nutrients.

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WHO, 2015

Non-nutritive sweeteners

- US FDA has approved the use of: Acesulfame-K, Aspartame, Neotame, Saccharin, Sucralose and Stevia
- Nonnutritive sweeteners are zero- or low-calorie alternatives to nutritive sweeteners, such as table sugar.
- Much sweeter than sugar so only small amounts are needed.
- Labeled low-calorie, non-caloric, nonnutritive, artificial and diet

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<https://fnic.nal.usda.gov/food-composition/nutritive-and-nonnutritive-sweetener-resources>

Table D6.2. Recommendations or statements related to added sugars or sugar-sweetened beverages from international and national organizations

Organization	Recommendation/Statement Related to Added Sugars and/or Sugar-Sweetened Beverages
World Health Organization (WHO) ⁶⁸	<ul style="list-style-type: none"> • WHO recommends reduced intake of free sugars throughout the life-course (strong recommendation). • For both adults and children, WHO recommends that intake of free sugars not to exceed 10% of total energy (strong recommendation). • WHO suggests further reduction to below 5% of total energy (conditional recommendation).
American Heart Association (AHA) ⁶⁹	The AHA recommends reductions to added sugars with an upper limit of half of the discretionary calorie allowance that can be accommodated within the appropriate energy intake level needed for a person to achieve or maintain a healthy weight based on the USDA food intake patterns. Most American women should eat or drink no more than 100 calories per day from added sugars (about 6 teaspoons), and most American men should eat or drink no more than 150 calories per day from added sugars (about 9 teaspoons).
HealthyPeople 2020 ⁷⁰	Objective NWS-17.2: Reduce consumption of calories from added sugars (Target: 10.8%)
American Academy of Pediatrics (AAP) ⁷¹	<p>Limit consumption of sugar-sweetened beverages (strongest evidence)</p> <p>Pediatricians should seek to eliminate recreational drinks in schools</p> <p>Note: Due to limited studies on children, the American Academy of Pediatrics (AAP) has no official recommendations regarding the use of non-caloric sweeteners.</p>
American Diabetes Association (ADA) ^{72,73}	<p>Prevention</p> <p>Research has shown that drinking sugary drinks is linked to type 2 diabetes, and the American Diabetes Association recommends that people limit their intake of sugar-sweetened beverages to help prevent diabetes.</p> <p>Diabetes Management</p> <p>People with diabetes should limit or avoid intake of sugar-sweetened beverages (from any calorie sweetener including high fructose corn syrup and sucrose) to reduce risk for weight gain and worsening of cardiovascular risk profile. (Evidence rating: B)</p>
NHLBI Expert Panel Guidelines for Cardiovascular Health and Risk Reduction in Children ⁷⁴	Reduced intake of sugar-sweetened beverages is associated with decreased obesity measures (Grade: B)

Scientific Report of the 2015 Dietary Guidelines Advisory Committee
Part D, Chapter 6: Cross-Cutting Topics of Public Health Importance.

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2015 Dietary Guidelines for Americans

- “Reexamined evidence on “Added Sugar” because it has been associated with negative health outcomes when over-consumed”.
- “To avoid an unintended replacement of added sugars with low-calorie sweeteners by food manufacturers, evidence on low-calorie [NNS] sweeteners was also examined”.

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Part D, Chapter 6: Cross-Cutting Topics of Public Health Importance, <http://health.gov/dietaryguidelines/2015-scientific-report/11-chapter-6d6-3.asp>

DGAC 2015 NS Findings

- The recommendation to limit added sugars is consistent with recommendations from national and international organizations AAP, WHO, AHA, CDC, ADA, Academy
- Additional information on labels is needed to assist informed dietary decisions



<http://www.fda.gov/downloads/food/guidance/regulatory/guidance/documents/regulatoryinformation/ucm502019.pdf>

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DGAC 2015 NS Findings

- Strong evidence to limit added sugar intake <10% total daily energy
- Strong evidence risk of T2DM in adults is increased by higher consumption of added sugars (from sugar sweetened beverages)
- Moderate evidence higher consumption of added sugars associated with increased risk in adults for HTN, CHD, CVA

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GRAS- evaluated by experts as safe under conditions of intended use. Companies can determine GRAS with or without notifying FDA.

<http://www.diabetesforecast.org/2016/jan-feb/5-must-know-facts-about-sweeteners>

Brand Name	Each Packet Size	Calories Per Packet	Number of Packets in 16.025*
Aspartame (NutraSweet)	0	0	23
Advantame (0.02, 0.05, 0.10, 0.20, 0.40, 0.80, 1.60, 3.20, 6.40, 12.80, 25.60, 51.20, 102.40, 204.80, 409.60, 819.20, 1638.40, 3276.80, 6553.60, 13107.20, 26214.40, 52428.80, 104857.60, 209715.20, 419430.40, 838860.80, 1677721.60, 3355443.20, 6710886.40, 13421772.80, 26843545.60, 53687091.20, 107374182.40, 214748364.80, 429496729.60, 858993459.20, 1717986918.40, 3435973836.80, 6871947673.60, 13743895347.20, 27487790694.40, 54975581388.80, 109951162777.60, 219902325555.20, 439804651110.40, 879609302220.80, 1759218604441.60, 3518437208883.20, 7036874417766.40, 14073748835532.80, 28147497671065.60, 56294995342131.20, 112589990684262.40, 225179981368524.80, 450359962737049.60, 900719925474099.20, 1801439850948198.40, 3602879701896396.80, 7205759403792793.60, 14411518807585587.20, 28823037615171174.40, 57646075230342348.80, 115292150460684697.60, 230584300921369395.20, 461168601842738790.40, 922337203685477580.80, 1844674407370955161.60, 3689348814741910323.20, 7378697629483820646.40, 14757395258967641292.80, 29514790517935282585.60, 59029581035870565171.20, 118059162071741130342.40, 236118324143482260684.80, 472236648286964521369.60, 944473296573929042739.20, 1888946593147858085478.40, 3777893186295716170956.80, 7555786372591432341913.60, 15111572745182864683827.20, 30223145490365729367654.40, 60446290980731458735308.80, 120892581961462917470617.60, 241785163922925834941235.20, 483570327845851669882470.40, 967140655691703339764940.80, 1934281311383406679529881.60, 3868562622766813359059763.20, 7737125245533626718119526.40, 15474250491067253436239052.80, 30948500982134506872478105.60, 61897001964269013744956211.20, 123794003928538027489912422.40, 247588007857076054979824844.80, 495176015714152109959649689.60, 990352031428304219919299379.20, 1980704062856608439838598758.40, 3961408125713216879677197516.80, 7922816251426433759354395033.60, 15845632502852867518708790067.20, 31691265005705735037417580134.40, 63382530011411470074835160268.80, 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NNS effect on Appetite and Weight

A review of observational studies, experimental laboratory studies, randomized controlled trials, and brain imaging studies concluded

- **No** consistent association of NNS with a heightened appetite for sugar or sweet products
- Intervention studies **suggest use NNS reduce** intake of foods made with sugar
- **Suggest use NNS** in food facilitate weight loss.

Bellisle F. Curr Obes Rep. 2015;4:106-110

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Exploring the Evidence NNS Useful Tool

- Prospective cohort studies suggest association between NNS and weight gain
 - Mattes and Popkin 2009 comprehensive review of potential mechanisms concluded existing human **evidence does not support proposed mechanisms for NNS affecting energy balance**
- RCT show net benefit of weight loss or no change
 - Peters and Beck 2016 RCT comparing NNS beverage with greater weight loss (5.95kg) to water (4.09kg/) $p < .0001$
 - Wt loss at least 5% total weight in NNS bev 64% vs 43% water group $p < .0002$
 - Reduced hunger ratings in NNS bev group

J.C. Peters, J. Beck. Low Calorie Sweetener use and energy balance, Physiol Behav. (2016), <http://dx.doi.org/10.1016/j.phybeh.2016.03.024>

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Liver Metabolic Health

- RCT compared impact from NNS beverages with NS beverages on intrahepatic fat

Campos V, et al. Obesity (2015) 23, 2335-2339. doi:10.1002/oby.21310

- 31 healthy men/women, BMI > 25, who drank 2+ NS beverages/day replaced with NNS beverages. 27 completed the study
- Fasting BG metabolic markers measured before & after 4 week run in period, 12 week intervention
- Results – NNS ↓ intrahepatic fat 74%

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Sweeteners, overweight and obesity

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WHO sugars recommendations



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WHO review of sugars and overweight/obesity

- SLR and meta-analysis of 30 trials and 38 cohort studies
- ↓ intake of dietary sugars was associated with ↓ body weight (0.80 kg, 95% confidence interval 0.39 to 1.21; P<0.001)
- ↑ sugars intake was associated ↑ weight (0.75 kg, 0.30 to 1.19; P=0.001)

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Te Morenga et al. BMJ 2013.

WHO review of sugars and overweight/obesity

- Isoenergetic exchange of dietary sugars with other carbohydrates showed no change in body weight (0.04 kg, -0.04 to 0.13).
- The overall meta-regression of randomised trials ... showed no evidence of a dose-response association between sugar as a percentage of total energy intake and body weight (0.02 kg, -0.03 to 0.08).

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Te Morenga et al. BMJ 2013.

Free sugars

- In both adults and children, WHO recommends reducing the intake of free sugars to less than 10% of total energy intake (strong recommendation).
- WHO suggests a further reduction of the intake of free sugars to below 5% of total energy intake (conditional recommendation).

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WHO, 2015.

Free sugars

- The recommendation to limit free sugars intake to less than **10%** of total energy intake is based on **moderate quality evidence** from observational studies of **dental caries**.
- The recommendation to further limit free sugars intake to less than **5%** of total energy intake is based on **very low quality evidence** ... relationship between free sugars intake and **dental caries**...

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WHO, 2015

10 percent sugars looks like this:

Breakfast	Lunch	Dinner
2/3 cup rolled oats 1 cup reduced-fat (1-2%) milk 1 tablespoon (3 teaspoons) wildflower honey ½ grapefruit	2 slices of hearty whole grain bread 2 teaspoons olive oil margarine 3½ ounces (100 g) canned red salmon ½ cup mixed salad (lettuce, cucumber, and tomato) One 7-ounce (200 g) container low-fat vanilla yogurt ½ banana Diet soft drink	2 ounces (60 g) beef strips 1½ cups Asian-style stir-fry noodles 2 cups Asian-style stir-fry vegetables 1 tablespoon sesame oil ½ cup Asian stir-fry sauce ½ cup reduced-fat vanilla ice cream ½ cup strawberries 1 piece (8 g) milk chocolate

2040 calories (8,400 kJ); 105 g protein; 62 g fat; 16 g saturated fat; 162 mg cholesterol; 250 g total carbohydrate; 104 g total sugars; 50 g added sugars; 25g fibre; 1742mg sodium

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Ultimate Guide S&S, 2014

5 percent added sugars looks like this:

Breakfast	Lunch	Dinner
2/3 cup rolled oats 1 cup reduced-fat (1-2%) milk 2 teaspoons wildflower honey ½ grapefruit	2 slices of hearty whole grain bread 2 teaspoons olive oil margarine 3½ ounces (100 g) canned red salmon ½ cup mixed salad (lettuce, cucumber, and tomato) One 7-ounce (200 g) NNS sweetened yogurt ½ banana	2 ounces (60 g) beef strips 1½ cups Asian-style stir-fry noodles 2 cups Asian-style stir-fry vegetables 1 tablespoon sesame oil ½ cup Asian stir-fry sauce Small glass (100 ml) white wine ½ cup reduced-fat vanilla ice cream ½ cup strawberries with NNS sprinkled on top

2000 calories (8,400kJ); 106 g protein; 60 g fat; 15 g saturated fat; 160 mg cholesterol; 228 g total carbohydrate; 82 g total sugars; 25 g added sugars; 25 g fibre; 1765 mg sodium

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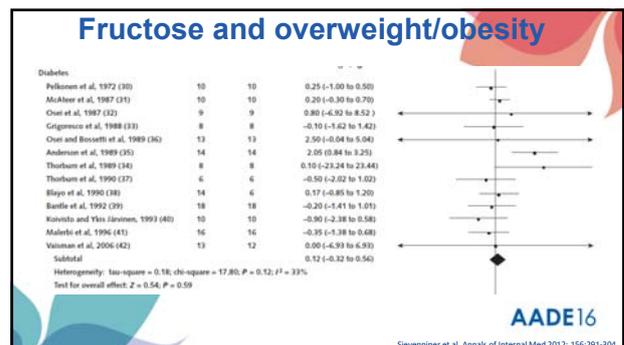
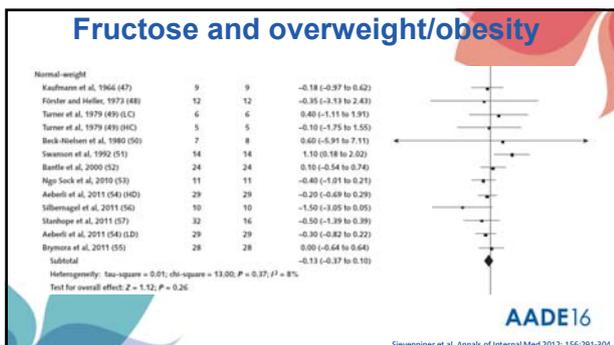
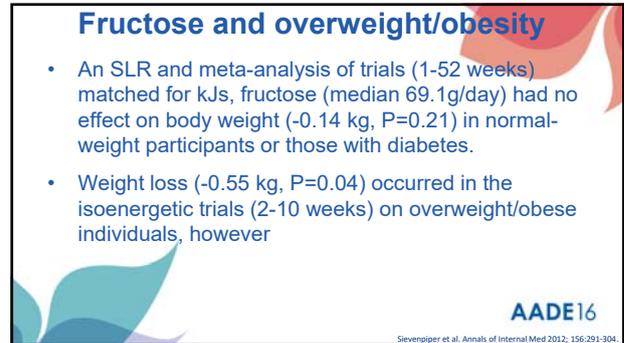
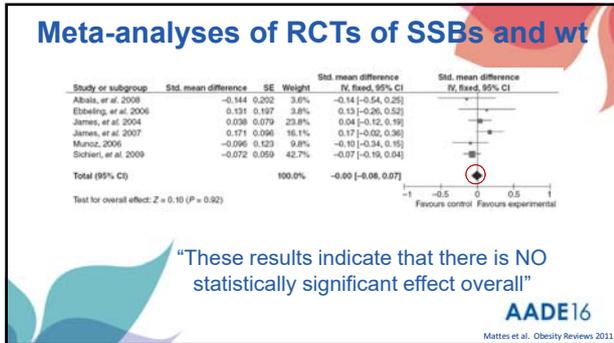
Ultimate Guide S&S, 2014

Sugar sweetened beverages and overweight/obesity

- 20+ systematic literature reviews published
- Some include observational studies and RCTs
Others include only randomised controlled trials
- The SLRs that include both generally conclude that SSBs contribute to weight gain
- The SLRs that only include RCTs generally find more equivocal results

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Hu, Obes Rev, 2013





Fructose and overweight/obesity

- Hypercaloric trials (1-10 weeks) of controlled diets supplemented with excess kJs from high doses of fructose (104-250 g/d or 18% to 97% of energy) found that body weight increased modestly overall (0.53 kg).
- The authors concluded that this was likely due to the additional kilojoules (~1,700 – 4,000 kJ/d), not any unique property of fructose per se.

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 Sievenpiper et al. Annals of Internal Medicine 2012; 156:291-304.



NNS and overweight/obesity

- Randomised controlled trials in humans (15 studies) of 3 – 78 weeks duration, using non-nutritively sweetened foods and beverages compared to added sugar
- Body weight (-0.80 kg), body mass index (-0.24 kg/m²), fat mass (-1.10 kg), and waist circumference (-0.83 cm) all decreased when consuming NNS foods and beverages.

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 Miller and Perez. AICN, 2014

NNS and overweight/obesity

- Among prospective cohort studies, NNS intake was **not associated** with **body weight** or **fat mass**, but **was significantly associated** with **slightly higher BMI** (0.03 kg/m²).

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Miller and Perez. AICN, 2014

NNS and the microbiome

- Microbiome is a collection of around 100 trillion bacteria (mostly), fungi and viruses that live both on the surface of our body's and inside our gastrointestinal tracts.
- Very high doses of saccharin (5 mg/kg/day) and sucralose (100+ mg/kg/day) may adversely affect the microbiome of rodents.

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Suez. Nature, 2014

NNS and the microbiome

- Aspartame is completely digested to aspartic acid, phenylalanine and methanol in the upper small intestine, and absorbed into the blood, it is not likely that it will adversely affect the microbiome.

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Suez. Nature, 2014

Evidence About Sweeteners And Diabetes



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DGAC 2015 NS Findings

- **Grade: Strong**
 - Higher consumption of added NS, especially sugar-sweetened beverages, increases the risk of T2DM among adults and this relationship is not fully explained by body weight.
 - Insufficient high-quality data to determine a dose-response between consumption and T2DM risk

References 33, 61-63 and Appendices E-2.47 (body weight) and E-2.48 (type 2 diabetes)
<http://health.gov/dietaryguidelines/2015-scientific-report/14-appendix-e2/e2-45.asp>

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DGAC 2015 NNS Findings

- Moderate and generally consistent evidence from short-term RCTs conducted in adults and children supports that **replacing NS with NNS reduces calorie intake, body weight, and adiposity. Grade: Moderate**
- Inconsistent evidence of an association between NNS and body weight as compared to NS. **Grade: Limited**
- Inconsistent evidence of an association between NNS and risk of T2DM. **Grade: Limited**

<http://health.gov/dietaryguidelines/2015-scientific-report/11-chapter-6/d6-3.asp>

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Soft drinks and type 2 diabetes

- SLR and meta-analysis of over 280,000 participants and 22,000 cases of type 2 diabetes
- For every 330 mL of sugar sweetened soft drink consumed there was a 20% increase in risk
- For every 330 mL of artificially sweetened soft drink consumed there was a 13% increase in risk

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Greenwood et al. BMJ. 2014.

May be guilty by association...



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GLP-1 and Glycemic Response

- Brown et al NNS (sucralose and Ace-K) in diet soda stimulated GLP-1 release
- Pepino et al, Ford et al, Ma et al and Ma et al, all found no effect when sucralose was the NNS
- ? GLP-1 effect due to Ace-K ?

Brown RJ et al. Diabetes Care. 2009;32:2184-2186
Pepino et al. Diabetes Care. 2013
Ford et al. Eur J Clin Nutr. 2011
Ma et al. Br J Nutr. 2010
Ma et al. Am J Physiol Gastrointest Liver Physiol. 2009

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Gastric Emptying, GLP-1, Glycemic Response

- Wu et al results were NNS have no effect
 - N=10 healthy men
 - 4 Drinks with NNS
 - water,
 - water with 46mg sucralose
 - water with 26mg Ace-K
 - water with sucralose and Ace-K
 - Glucose, insulin, GLP-1 measured before and 4 hrs post ingestion

Wu T, et al. Diabetes Care. 2013;36:e202-e203

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Glycemic and Appetite Response

- Bryant et al results were NO response NNS on glucose response 60 min post ingestion (Aspartame or Saccharine) with unclear significance from Ace-K
 - N=10 healthy subjects
- NO effect of individual NNS on hunger or fullness (Ace-K, Aspartame or Saccharine)

Bryant, CE et al. European Journal of Clinical Nutrition, 2014;68:629-631

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Summary

- Focus on Healthy Dietary Patterns with <10% added / free sugars
- The evidence shows reducing NS reduces certain health risks
- The evidence does not prove that NNS cause diabetes, weight gain or changes in appetite
- The evidence does show NNS help weight loss if other calories eaten don't make up for calories saved
- Understand information on new US Nutrition Fact labels to make healthier choices

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