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Artificial sweeteners are not the answer to childhood obesity

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ABSTRACT

While no single factor is responsible for the recent, dramatic increases in overweight and obesity, a scientific consensus has emerged suggesting that consumption of sugar-sweetened products, especially beverages, is casually linked to increases in risk of chronic, debilitating diseases including type 2 diabetes, cardiovascular disease, hypertension and stroke. One approach that might be beneficial would be to replace sugar-sweetened items with products manufactured with artificial sweeteners that provide sweet tastes but with fewer calories. Unfortunately, evidence now indicates that artificial sweeteners are also associated with increased risk of the same chronic diseases linked to sugar consumption. Several biologically plausible mechanisms may explain these counterintuitive negative associations. For example, artificial sweeteners can interfere with basic learning processes that serve to anticipate the normal consequences of consuming sugars, leading to overeating, diminished release of hormones such as GLP-1, and impaired blood glucose regulation. In addition, artificial sweeteners can alter gut microbiota in rodent models and humans, which can also contribute to impaired glucose regulation. Use of artificial sweeteners may also be particularly problematic in children since exposure to hyper-sweetened foods and beverages at young ages may have effects on sweet preferences that persist into adulthood. Taken as a whole, current evidence suggests that a focus on reducing sweetener intake, whether the sweeteners are caloric or non-caloric, remains a better strategy for combating overweight and obesity than use of artificial sweeteners.

Introduction

It is widely acknowledged that rates of overweight and obesity among adults have risen significantly not only within the U.S., but also worldwide, over the past several decades (Flegal, Carroll, Kit, & Ogden, 2012). At the same time, rates of excess body weight have also risen dramatically among children and adolescents; for example, it is estimated that almost 35% of children between the ages of 12 and 19 in the U.S. are overweight, with a body mass index (BMI) above the 85th percentile (Ogden, Carroll, Kit, & Flegal, 2014). From a public health perspective, overweight and obesity are of particular concern because they are associated with increased risk for a variety of chronic and debilitating diseases including cancers, cardiovascular disease and diabetes (Ng et al., 2014). The full magnitude of the effects of overweight and obesity during childhood on health outcomes will take years to emerge. However, current data suggest that not only is overweight during childhood a strong predictor of overweight during adulthood (e.g. Clarke & Lauer, 1993; Freedman et al., 2005; Serdula et al., 1993), but that diseases once confined to adulthood, such as type 2 diabetes, are now diagnosed in increasing numbers in children and adolescents (Dabelea et al., 2014; Demmer, Zuk, Rosenbaum, & Desvarieux, 2013). Thus, formulating effective strategies to reduce the prevalence of overweight, obesity, and attendant health consequences in childhood is important not only for improving the quality of life for children now, but for preventing the emergence of life-long problems, including cognitive deficits as described in other papers in this volume.

The goal of the present paper is to consider scientific evidence related to one approach that has been advocated as a possible strategy to reduce overweight and obesity in children, replacing caloric sugars like sucrose or high-fructose corn syrup with sweeteners that satisfy the desire for sweet tastes without the detrimental effects strongly associated with sugar intake. Currently, in the U.S., six such sweeteners are approved for use in foods and beverages, including aspartame, sucralose, saccharin, and acesulfame potassium, with another two plant-derived sweeteners receiving Generally Regarded as Safe designations (US Food and Drug Administration, 2014). While these sugar substitutes are referred to by a number of names, including artificial, high-intensity, low-calorie, or non-caloric sweeteners, in the present paper the term artificial sweetener will be used. Each provides little or no energy, in most cases because it activates sweet taste receptors at very low concentrations relative to sugar, with estimates of the potency of artificial sweeteners currently approved in the U.S. ranging from about 200 times to up to 20,000 times the sweetness of sugar (US Food and Drug Administration, 2014). Because they provide little or no energy, so

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goes the argument, the number of calories consumed will be reduced when artificial sweeteners are used in place of caloric sugars. However, it is not clear that scientific evidence actually supports such a belief. Instead, as described below, artificial sweeteners may actually contribute to increasing the negative outcomes they have been employed to mitigate.

Obesity, sugary drinks and disease

The causes of overweight and obesity are multifactorial, and the focus on any single factor no doubt oversimplifies the issue. Nevertheless, with regard to recent and rapid increases in the prevalence of obesity, scientific evidence has implicated a number of dietary factors as likely contributors. Most recently, special attention has been focused on the extremely high levels of consumption of sugars in general, and sugar-sweetened beverages in particular. For example, in the U.S. overall consumption of sugar-sweetened soft drinks in 2001 was roughly 37 gallons per capita (USDA, Economic Research Service, 2008). In 2012 over 70% of adults reported that they consumed sugar-sweetened beverages (SSB; soft drinks or fruit drinks with added sugar; Kumar et al., 2014), with over 25% reporting daily intake. A recent meta-analysis also showed strong links between SSB consumption and increased body weight (Malik, Pan, Willett, & Hu, 2013). Further, regular consumption of SSB in adults has been directly associated with a variety of negative outcomes. For example, a number of long-term prospective cohort studies have documented increased risk for overweight and obesity, cardiovascular disease, hypertension and stroke, type 2 diabetes, and metabolic syndrome in adults who regularly consume SSB (typically one serving or more per day; see Malik et al., 2013).

Intake of sweetened foods and beverages is problematic not only for adults but may be even more of an issue for children and adolescents, as data suggest that exposure to foods during early development can have effects on food choices and preferences that persist throughout life (e.g. Mennella & Castor, 2012). From very early in life, sweet tastes elicit behavioral responses suggesting they are highly pleasant, and newborns of many mammalian species display strong preferences for sweet tastes relative to water (for review, see Mennella, 2014). While strong preferences may not always translate into high levels of intake, current data indicate that children and adolescents do consume high levels of sweetened beverages, including sweetened milks, fruit-flavored drinks, soda and sports drinks. For example, roughly 70% of children aged 2–19 years currently consume sugar-sweetened beverages daily (Han & Powell, 2013; Mesirow & Welsh, 2015). Even among young children, sweetened beverage is highly prevalent, with intake of at least one type of sweetened beverage reported in more than 90% of children aged 3–5 (e.g. Nickelson, Lawrence, Parton, Knowlden, & McDermott, 2014) and one study reporting *daily* SSB consumption among approximately 10% of *2-year-olds* (DeBoer, Scharf, & Demmer, 2013). As seen in adults, regular consumption of SSB in children and adolescents is associated with increased risk for overweight and obesity (DeBoer et al., 2013; Fiorito, Marini, Francis, Smiciklas-Wright, & Birch, 2009; Zheng et al., 2014, 2015).

Artificial sweeteners, obesity, and disease

The strong and consistent associations among SSB intake, obesity, and diseases like diabetes have led to increasing emphasis on reducing the availability and consumption of sugars and sugar-sweetened beverages among children and adults (Hu, 2013). But reducing intake of sugary foods and beverages has not proved simple, as evidenced by persistently high levels of intake. While the promise has been that artificial sweeteners will promote healthy outcomes like reductions in overweight and obesity this is a promise that lacks clear and consistent supporting evidence. It is critical to recognize that even if diet soda consumption can produce weight loss compared to SSB, this does not necessarily indicate that artificial sweeteners are healthy, only that they may be less problematic than SSB. Among interventional studies in which sugar-sweetened versions of foods or beverages have been replaced by artificially-sweetened versions, results do not consistently indicate that artificial sweeteners themselves play any specific role in promoting weight loss in overweight individuals. For example, one early study compared weight loss in overweight women who were encouraged to increase their consumption of the artificial sweetener aspartame to those who were advised to eliminate aspartame from their diets (Blackburn, Kanders, Lavin, Keller, & Whatley, 1997). The results clearly illustrated identical weight loss in the two groups; women who virtually eliminated aspartame from their diets lost the same amount of weight as women who significantly increased their aspartame intake, suggesting that artificial sweeteners are not specifically helpful at aiding weight loss. More recently, an interventional study in overweight adults examined daily consumers of SSB who were encouraged to replace the SSB with either diet soda or water; both groups demonstrated weight loss that was not different from that observed in an attentional control group given no specific advice about beverage intake (Tate et al., 2012). This again suggests that little effectiveness is specifically added by the use of artificial sweeteners. In other words, adults can lose weight over the short term by paying attention to what they eat and drink, but including artificial sweeteners does not appear to produce better outcomes than not including artificial sweeteners. Reviews of the results of studies examining artificial sweeteners and weight have also produced inconsistent conclusions (Blundell & Green, 1996; Mattes & Popkin, 2009). While a recent food-industry sponsored meta-analysis appears to suggest that artificial sweeteners may be beneficial for short-term weight loss (Miller & Perez, 2014), concerns regarding the selection strategy of trials included in this work have been raised (Pan & Hu, 2014). Further, within some of the trials that were included, only select groups were considered. For example, in the Tate et al. (2012) study, only the attentional control and artificial sweetener groups appear to have been considered, while results from the water group were excluded.

Outcomes of long-term prospective cohort studies that examine body weight effects also do not clearly support the utility of artificial sweeteners. For example, in a multi-ethnic prospective cohort study, consumption of artificially-sweetened beverages was associated with significantly increased risk of overweight after 7–8 year follow-up in people who were at a healthy weight at baseline, and significantly increased risk of obesity in those who were overweight at baseline (Fowler et al., 2008). In contrast, other cohort data have indicated that replacement of SSB with artificially-sweetened versions is associated with weight loss (Mozaffarian, Hao, Rimm, Willett, & Hu, 2011; Pan et al., 2013). As described above, some of these contradictory results may reflect differences in comparison groups, with artificially-sweetened beverages producing better outcomes than SSB, but worse outcomes compared to no sweetened beverages at all.

Thus, in adults evidence that artificial sweeteners are particularly useful for promoting weight loss is mixed at best. Despite this fact, their availability and consumption continues to increase, even in children (Ng, Slining, & Popkin, 2012; Sylvetsky, Welsh, Brown, & Vos, 2012). For example, approximately 15% of children in the U.S. aged 2–17 years old reported daily intake of artificially sweetened beverages in 2007–2008 (Sylvetsky et al., 2012). A positive impact of artificially-sweetened beverage intake on body weight outcomes is no more obvious in children than it is in adults, and again likely depends on whether the comparison group is one that is consuming SSB or not. One recent interventional study in overweight adolescents indicated that reduction of SSB intake among those who regularly consumed them did result in decreased body weight gain

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relative to a control group (Ebbeling et al., 2012). However, this intervention emphasized consumption of unsweetened beverages over artificially-sweetened beverages; the biggest behavioral difference between the groups was a greater increase in the quantity of unsweetened beverages consumed in the intervention group. Again, this means that drawing a conclusion that artificial sweeteners played any role is not warranted. In another study, diet soda intake in adolescent girls, but not boys, was associated with increased weight gain and percent body fat in cross-sectional data, but these effects were not statistically significant in longitudinal data (Laska, Murray, Lytle, & Harnack, 2012). Another recent clinical trial examined the effects of masked replacement of one SSB with an artificially sweetened beverage in primarily lean Dutch children aged 4–11 who reported consuming at least one SSB daily (de Ruyter, Olthof, Seidell, & Katan, 2012). These results indicated that in this cohort, children in the ASB group did have lower rates of weight gain compared to those who continued to consume SSB. No group that did not drink a sweetened beverage daily was included. Earlier studies in children also produced inconsistent outcomes with some indicating better weight outcomes while others showed that diet soft drinks were associated with greater weight gain (for review see Brown, de Banate, & Rother, 2010).

Exposure and experience

At present, the weight of the evidence suggests that consuming sugar-sweetened beverages is problematic, but the data regarding whether artificially-sweetened beverages are particularly useful as replacements is ambiguous. Even if these data were clear, it's important to consider some broader issues, particularly given data suggesting that outcomes are worse if artificially-sweetened beverages are consumed compared to unsweetened beverages like water. For example, it seems troubling that our cultural norms now sufficiently permit children's daily consumption of beverages. That we can even address a question like whether SSB or their artificially-sweetened counterpoints is more unhealthy underscores how pervasive these beverages have become, despite the fact that they are empty of any nutritional value at all; they are essentially candy in a can. It is now routine for children as young as 3 years of age to consume at least one serving of a sweetened drink every day (e.g. Nickelson et al., 2014). In the context of development, persistent consumption of even sweeteners that provide no calories is problematic because childhood represents a time during which experiences with foods and beverages have special relevance for long-term preferences and intake decisions (e.g. Mennella, 2014). Children already show enhanced preferences for sweet tastes from very early in life, and prolonged exposure to hyper-sweetened foods and beverages has the capacity to set the stage for persistence of heightened sweet preferences. In animal models, for example, neonates exposed to artificial sweeteners directly or through their mother's milk have persistent alterations in the development of gustatory pathways along with altered preferences and thresholds for artificial sweeteners and sugars that persist into adulthood (Chen et al., 2013; Li et al., 2013; Zhang et al., 2011). Effects of experience with foods and fluids both pre- and post-natally on later food preferences are seen in children as well (e.g. Mennella, 2014; Mennella & Castor, 2012; Mennella, Jagnow, & Beauchamp, 2001), with childhood functioning as a time during which information about how sweet foods are "supposed" to taste is acquired (e.g. Beauchamp & Cowart, 1985; Birch & Anzman-Frasca, 2011). Thus, even if artificially-sweetened beverages are less unhealthy than sugar-sweetened versions, children who consume them frequently may be set up to have enhanced levels of sweetener intake that persist into adulthood.

Further, data suggest that in the real world, artificial sweeteners are not specifically helpful at reducing sugar intake. Overweight adults involved in a clinical trial to switch from SSB to artificially-sweetened beverages showed the same amount of sugar intake at the conclusion of the intervention as those who switched from SSB to water (Piernas, Tate, Wang, & Popkin, 2013), despite drinking over 900 ml of diet soda a day. Thus, introducing artificial sweeteners in an attempt to minimize the negative consequences of sugars in children may have no special ability to reduce sugar intake.

Data from studies in adults and children provide little consistent evidence that artificially-sweetened beverages are likely to produce positive results with regard to body weight regulation. In fact, according to the most recent consensus statement from the American Heart Association and American Diabetes Association, "At this time, there are insufficient data to determine conclusively whether the use of NNS to displace caloric sweeteners in beverages and foods reduces added sugars or carbohydrate intakes, or benefits appetite, energy balance, body weight, or cardiometabolic risk factors" (Gardner et al., 2012). Thus, despite the fact that the food and beverage industry has led consumers to believe that artificial sweeteners will promote weight loss, the data regarding artificial sweeteners and weight gain or loss are at best inconclusive.

Of greater concern than the lack of apparent beneficial effects on body weight, recent long-term (up to 28 years follow-up) prospective cohort studies have shown that people who consistently drink diet sodas have significantly increased risks for the development of the very diseases people are trying to avoid. For example, compared to those who report that they do not consume diet soda, diet soda drinkers have elevated risks for type 2 diabetes, metabolic syndrome, cardiovascular disease, high blood pressure and stroke, and declines in kidney function (Bernstein, de Koning, Flint, Rexrode, & Willett, 2012; Bhupathiraju et al., 2013; Cohen, Curhan, & Forman, 2012; Dhingra et al., 2007; Duffey, Steffen, Van Horn, Jacobs, & Popkin, 2012; Fagherazzi et al., 2013; Fowler et al., 2008; Fung et al., 2009; Gardener et al., 2012; Lin & Curhan, 2011; Lutsey, Steffen, & Stevens, 2008; Nettleton, Polak, Tracy, Burke, & Jacobs, 2009; Romaguera et al., 2013; Sakurai et al., 2013; for review see Swithers, 2013). In many cases, these risks persist even after adjustments for the fact that those who choose to consume diet sodas differ from those who do not. So while people may be getting the message that scientific evidence demonstrates clear links between consumption of SSB and disease, these recent data show that switching to artificially-sweetened beverages may not represent a healthy option since consumption of even "diet" soft drinks has been linked to increases in risks for the very same diseases.

Mechanisms that might underlie counterintuitive consequences of artificial sweeteners

One explanation for the popularity of artificial sweeteners has been a common-sense point of view in which they must be healthy options because they do not provide appreciable energy. However as described above, data showing that artificial sweeteners actually promote weight loss or result in positive health outcomes are contradictory at best. Correlational associations between artificial sweetener intake and increased risk diseases like diabetes and hypertension have often been dismissed as examples of reverse causation, in which those who are already overweight or unhealthy are more likely to consume artificial sweeteners. However, experimental work in animal models and humans provide evidence for multiple, plausible biological mechanisms that suggest that consumption of artificial sweeteners actually contributes to weight gain and negative health outcomes.

One hypothesis to explain this causal link between consumption of artificial sweeteners and negative outcomes is that artificial sweeteners interfere with basic conditioning mechanisms that typically permit animals to anticipate the consequences of consuming food. Since the work of Pavlov and Anrep (1960), it has been clear that cues in the environment can come to control physiological responses related to digestion and metabolism. Now commonly referred to as cephalic phase responses, these anticipatory responses contribute to efficient and effective energy utilization. Animals, including humans, are exposed to sweet tastes from very early in life (pre-natally, in fact) and activation of sweet taste receptors in the mouth would be a strong and consistent predictor that energy and sugar would be arriving in the gut. As a result, anticipatory responses, such as the release of hormones or increases in energy expenditure, are elicited at the first taste of sweet, prior to actual absorption or metabolism of food. Based on principles of Pavlovian conditioning, one method to diminish the strength of conditioned responses is to present the conditioned stimulus without presenting its consequences. Artificial sweeteners do just this; they provide very sweet tastes but without the energy or sugar that has been associated with sweet. Following such experience, physiological responses become blunted even when real sugars are consumed because sweet tastes no longer provide reliable cues about what will happen.

Work from rodent models has provided evidence that in fact artificial sweeteners interfere with learned relations between sweet tastes and energy. For example, one set of studies took advantage of the fact that previous work on classical conditioning had shown that if multiple cues predict a particular outcome, they compete with each other for associative strength. One way to enhance learning about one of the cues is to present the alternative cue without the intended outcome (Bills, Dopheide, Pineno, & Schachtman, 2006). In the context of sweet tastes, it is known that animals will learn to prefer a neutral flavor, like cherry, that is presented along with energy. If the energy is provided in the form of sugar, the cherry flavor must compete with the sweet taste of sugar because the sugar already predicts energy. One method to increase learning about the novel flavor would be to first weaken the association between sweet tastes and energy – for example by providing artificial sweeteners prior to conditioning with the novel flavor. And results from studies in adult and pre-weanling rats support this hypothesis. Greater preferences are shown for novel flavors paired with sugar if animals have previously been exposed to artificial sweeteners (Davidson, Martin, Clark, & Swithers, 2011; Swithers, Ogden, Laboy, & Davidson, 2012). Additional work has shown that animals given artificial sweeteners not only show evidence of changes in learned responses, but that these effects translate into overeating, excess weight gain, and altered physiological responses (Davidson et al., 2011; Davidson & Swithers, 2004; Feijo et al., 2013; Mitsutomi et al., 2014; Swithers, Baker, & Davidson, 2009; Swithers & Davidson, 2008; Swithers, Laboy, Clark, Cooper, & Davidson, 2012; Swithers, Martin, Clark, Laboy, & Davidson, 2010; Swithers, Martin, & Davidson, 2010; Swithers, Sample, & Davidson, 2013; Swithers, Sample, & Katz, 2013). Among the physiological alterations observed is a decrease in the release of the incretin hormone GLP-1 (Swithers et al., 2012), which has been implicated in regulation of food intake, blood sugar levels and protection of the cardiovascular system (e.g. Sivertsen, Rosenmeier, Holst, & Vilsboll, 2012). If GLP-1 levels are persistently reduced by consumption of artificial sweeteners, then over the long term risks for outcomes like diabetes, cardiovascular disease and stroke would be elevated, the exact pattern that has been observed in long-term cohort studies.

More recently, artificial sweeteners including saccharin, sucralose and aspartame have been documented to alter gut microbiota in rodent models and lead to overeating, weight gain and impaired blood glucose regulation (Abou-Donia, El-Masry, Abdel-Rahman, McLendon, & Schiffman, 2008; Palmnas et al., 2014; Suez et al., 2014). Further, in a small human study, saccharin led to changes in gut microbiota along with blood glucose dysregulation in a subset of participants (Suez et al., 2014). Given our increasing understanding of the many roles the gut microbiome plays in health and disease (Nicholson et al., 2012), if artificial sweeteners persistently alter the composition of gut bacteria, then effects such as weight gain and glucose intolerance may derive from this type of disruption.

Sweeteners during childhood

Slowing and reversing the high levels of childhood overweight and obesity clearly needs to be a high public health priority. Overweight and obesity in childhood predict not only overweight and obesity, but also diseases like diabetes in adulthood. In many cases, the message that reduction of sugar intake is important has been received, and consumption of some types of sweetened beverages does appear to be decreasing in children (Han & Powell, 2013). However, messages need to be clearer that sweetened beverages including fruit juices, sweetened milks, and soft drinks, do not represent healthy options to be served on a daily basis, and that artificially-sweetened beverages may be no more appropriate for routine consumption than sugar-sweetened versions. Long-term epidemiological data link both sugar-sweetened and artificially-sweetened beverages to negative health outcomes. Experimental data provide multiple plausible mechanisms by which these links could reflect causal relationships. Eating habits established during infancy and childhood can have persistent effects on adult eating habits, through cultural acclimatization, learning, and shaping of taste pathways. As a result, reinforcing sweet preferences in children by exposing them to high quantities of sweeteners, whether caloric or non-caloric, may remain problematic for a lifetime.

Parents need to be a part of any solution to the excessive consumption of sweetened beverages in children, and many parents indicate that they prefer to avoid products that contain artificial sweeteners. However, parents currently face the burden of being able to identify both caloric and artificial sweeteners in the products they purchase. Data suggest that even parents who indicate concern about artificial sweeteners end up purchasing foods and beverages that contain artificial sweeteners (Sylvetsky, Greenberg, Zhao, & Rother, 2014). Parents also have to counter extraordinary levels of food and beverage marketing, much of it directed toward children (Hansen, Friis Hansen, Krych, & Nielsen, 2014; Lioutas & Tzimitra-Kalogianni, 2014; Scully et al., 2015).

Most disturbingly, a significant amount of marketing of sweetened beverages occurs outside the control of parents, in locales where promotion of healthy eating and drinking habits ought to be expected, namely inside schools. In the U.S., significant numbers of children are exposed to food and beverage marketing materials at school; over 70% of students in elementary through high schools attend a school that contains food and beverage marketing in the form of vending, advertising, and/or use of coupons as incentives. The highest prevalence of this marketing targeted at lower-income students, among whom the prevalence of sweetened beverage intake is the highest (Han & Powell, 2013; Johnston, Delva, & O'Malley, 2007; Terry-McElrath, O'Malley, & Johnston, 2013; Terry-McElrath, Turner, Sandoval, Johnston, & Chaloupka, 2014). Food and beverage advertising is known to influence food selection and consumption among children and the availability of food and beverage products in schools is related to greater consumption, at least in some groups of students (Blum et al., 2008; Johnston et al., 2007; Terry-McElrath et al., 2013). Thus far, a principal focus has been to decrease or eliminate vending of SSB in schools. However, given the lack of clear data supporting positive effects of so-called "diet" sodas as well and mounting evidence suggesting negative consequences over the longer term, it seems prudent that additional efforts be expended to eliminate marketing of hyper-sweetened foods and beverages to children both within and outside of schools.

Childhood obesity has no simple cause, and no single intervention will eliminate childhood obesity. But the recent focus on reducing the high levels of consumption of sugar-sweetened

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beverages by children represents an approach strongly supported by the science illustrating the negative health impact of prolonged intake of these products. It is important to continue to reinforce this message, but it is also important to consider what is promoted as the alternative to sugar-sweetened beverages. Our current scientific knowledge indicates that artificially-sweetened beverages may be better than sugar-sweetened versions, but that does not mean that they are healthy options. Instead, there are reasons to be concerned that exposing children to highly-sweetened beverages, even if they do not provide calories themselves, can contribute to negative outcomes. First, exposure to artificial sweeteners could persistently alter sweet preferences, leading to enhanced intake of sugars throughout adulthood. Second, exposure to artificial sweeteners could interfere with learning of basic relations between sweet tastes and the delivery of calories, which in turn could negatively affect regulation of metabolic processes. Third, artificial sweeteners could alter the composition of the gut microbiota, which in turn can contribute to metabolic dysregulation. Thus, the best approach to improving health outcomes in childhood would seem to be an emphasis on the intake of foods and beverages without added sweeteners, regardless of whether sugars or artificial sweeteners are used.

References

Abou-Donia, M. B., El-Masry, E. M., Abdel-Rahman, A. A., McLendon, R. E., & Schiffman, S. S. (2008). Splenda alters gut microflora and increases intestinal p-glycoprotein and cytochrome p-450 in male rats. *Journal of Toxicology and Environmental Health. Part A*, *71*(21), 1415–1429. doi:10.1080/15287390802328630.

Beauchamp, G. K., & Cowart, B. J. (1985). Congenital and experiential factors in the development of human flavor preferences. *Appetite*, *6*(4), 357–372.

Bernstein, A. M., de Koning, L., Flint, A. J., Rexrode, K. M., & Willett, W. C. (2012). Soda consumption and the risk of stroke in men and women. *The American Journal of Clinical Nutrition*, *95*(5), 1190–1199. doi:10.3945/ajcn.111.030205.

Bhupathiraju, S. N., Pan, A., Malik, V. S., Manson, J. E., Willett, W. C., van Dam, R. M., et al. (2013). Caffeinated and caffeine-free beverages and risk of type 2 diabetes. *The American Journal of Clinical Nutrition*, *97*(1), 155–166. doi:10.3945/ajcn.112.048603.

Bills, C. H., Dopheide, M., Pineno, O., & Schachtman, T. R. (2006). Effects of an extinguished CS on competition with another CS. *Behavioural Processes*, *72*(1), 14–22. doi:10.1016/j.beproc.2005.11.009.

Birch, L. L., & Anzman-Frasca, S. (2011). Learning to prefer the familiar in obesogenic environments. *Nestle Nutrition Workshop Series. Paediatric Programme*, *68*, 187–196, discussion 196-189. doi:10.1159/000325856.

Blackburn, G. L., Kanders, B. S., Lavin, P. T., Keller, S. D., & Whatley, J. (1997). The effect of aspartame as part of a multidisciplinary weight-control program on short- and long-term control of body weight. *The American Journal of Clinical Nutrition*, *65*(2), 409–418.

Blum, J. E., Davee, A. M., Beaudoin, C. M., Jenkins, P. L., Kaley, L. A., & Wigand, D. A. (2008). Reduced availability of sugar-sweetened beverages and diet soda has a limited impact on beverage consumption patterns in Maine high school youth. *Journal of Nutrition Education and Behavior*, *40*(6), 341–347. doi:10.1016/j.jneb.2007.12.004.

Blundell, J. E., & Green, S. M. (1996). Effect of sucrose and sweeteners on appetite and energy intake. *International Journal of Obesity and Related Metabolic Disorders: Journal of the International Association for the Study of Obesity*, *20*(Suppl. 2), S12–S17.

Brown, R. J., de Banate, M. A., & Rother, K. I. (2010). Artificial sweeteners. A systematic review of metabolic effects in youth. *International Journal of Pediatric Obesity*, *5*(4), 305–312. doi:10.3109/17477160903497027.

Chen, M. L., Liu, S. S., Zhang, G. H., Quan, Y., Zhan, Y. H., Gu, T. Y., et al. (2013). Effects of early intraoral acesulfame-K stimulation to mice on the adult's sweet preference and the expression of alpha-gustducin in fungiform papilla. *Chemical Senses*, *38*(5), 447–455. doi:10.1093/chemse/bjt001.

Clarke, W. R., & Lauer, R. M. (1993). Does childhood obesity track into adulthood? *Critical Reviews in Food Science and Nutrition*, *33*(4–5), 423–430. doi:10.1080/10408399309527641.

Cohen, L., Curhan, G., & Forman, J. (2012). Association of sweetened beverage intake with incident hypertension. *Journal of General Internal Medicine*, *27*(9), 1127–1134. doi:10.1007/s11606-012-2069-6.

de Ruyter, J. C., Olthof, M. R., Seidell, J. C., & Katan, M. B. (2012). A trial of sugar-free or sugar-sweetened beverages and body weight in children. *The New England Journal of Medicine*, *367*(15), 1397–1406. doi:10.1056/NEJMoa1203034.

Dabelea, D., Mayer-Davis, E. J., Saydah, S., Imperatore, G., Linder, B., Divers, J., et al. (2014). Prevalence of type 1 and type 2 diabetes among children and adolescents from 2001 to 2009. *JAMA: The Journal of the American Medical Association*, *311*(17), 1778–1786. doi:10.1001/jama.2014.3201.

Davidson, T. L., Martin, A. A., Clark, K., & Swithers, S. E. (2011). Intake of high-intensity sweeteners alters the ability of sweet taste to signal caloric consequences. Implications for the learned control of energy and body weight regulation. *Quarterly Journal of Experimental Psychology*, *64*(7), 1430–1441. doi:10.1080/17470218.2011.552729.

Davidson, T. L., & Swithers, S. E. (2004). A Pavlovian approach to the problem of obesity. *International Journal of Obesity and Related Metabolic Disorders: Journal of the International Association for the Study of Obesity*, *28*(7), 933–935. doi:10.1038/sj.ijo.0802660.

DeBoer, M. D., Scharf, R. J., & Demmer, R. T. (2013). Sugar-sweetened beverages and weight gain in 2- to 5-year-old children. *Pediatrics*, *132*(3), 413–420. doi:10.1542/peds.2013-0570.

Demmer, R. T., Zuk, A. M., Rosenbaum, M., & Desvarieux, M. (2013). Prevalence of diagnosed and undiagnosed type 2 diabetes mellitus among US adolescents. Results from the continuous NHANES, 1999–2010. *American Journal of Epidemiology*, *178*(7), 1106–1113. doi:10.1093/aje/kwt088.

Dhingra, R., Sullivan, L., Jacques, P. F., Wang, T. J., Fox, C. S., Meigs, J. B., et al. (2007). Soft drink consumption and risk of developing cardiometabolic risk factors and the metabolic syndrome in middle-aged adults in the community. *Circulation*, *116*(5), 480–488. doi:10.1161/CIRCULATIONAHA.107.689935; CIRCULATIONAHA.107.689935 [pii].

Duffey, K. J., Steffen, L. M., Van Horn, L., Jacobs, D. R., Jr., & Popkin, B. M. (2012). Dietary patterns matter. Diet beverages and cardiometabolic risks in the longitudinal Coronary Artery Risk Development in Young Adults (CARDIA) Study. *The American Journal of Clinical Nutrition*, *95*(4), 909–915. doi:10.3945/ajcn.111.026682.

Ebbeling, C. B., Feldman, H. A., Chomitz, V. R., Antonelli, T. A., Gortmaker, S. L., Osganian, S. K., et al. (2012). A randomized trial of sugar-sweetened beverages and adolescent body weight. *The New England Journal of Medicine*, *367*(15), 1407–1416. doi:10.1056/NEJMoa1203388.

Fagherazzi, G., Vilier, A., Saes Sartorelli, D., Lajous, M., Balkau, B., & Clavel-Chapelon, F. (2013). Consumption of artificially and sugar-sweetened beverages and incident type 2 diabetes in the Etude Epidemiologique aupres des femmes de la Mutuelle Generale de l'Education Nationale-European Prospective Investigation into Cancer and Nutrition cohort. *The American Journal of Clinical Nutrition*, *97*(3), 517–523. doi:10.3945/ajcn.112.050997.

Feijo, F. M., Ballard, C. R., Foletto, K. C., Batista, B. A., Neves, A. M., Ribeiro, M. F., et al. (2013). Saccharin and aspartame, compared with sucrose, induce greater weight gain in adult Wistar rats, at similar total caloric intake levels. *Appetite*, *60*(1), 203–207. doi:10.1016/j.appet.2012.10.009.

Fiorito, L. M., Marini, M., Francis, L. A., Smiciklas-Wright, H., & Birch, L. L. (2009). Beverage intake of girls at age 5 y predicts adiposity and weight status in childhood and adolescence. *The American Journal of Clinical Nutrition*, *90*(4), 935–942. doi:10.3945/ajcn.2009.27623.

Flegal, K. M., Carroll, M. D., Kit, B. K., & Ogden, C. L. (2012). Prevalence of obesity and trends in the distribution of body mass index among US adults, 1999–2010. *JAMA: The Journal of the American Medical Association*, *307*(5), 491–497. doi:10.1001/jama.2012.39.

Fowler, S. P., Williams, K., Resendez, R. G., Hunt, K. J., Hazuda, H. P., & Stern, M. P. (2008). Fueling the obesity epidemic? Artificially sweetened beverage use and long-term weight gain. *Obesity*, *16*(8), 1894–1900. doi:10.1038/oby.2008.284; oby2008284 [pii].

Freedman, D. S., Khan, L. K., Serdula, M. K., Dietz, W. H., Srinivasan, S. R., & Berenson, G. S. (2005). The relation of childhood BMI to adult adiposity. The Bogalusa Heart Study. *Pediatrics*, *115*(1), 22–27. doi:10.1542/peds.2004-0220.

Fung, T. T., Malik, V., Rexrode, K. M., Manson, J. E., Willett, W. C., & Hu, F. B. (2009). Sweetened beverage consumption and risk of coronary heart disease in women. *The American Journal of Clinical Nutrition*, *89*(4), 1037–1042. doi:10.3945/ajcn.2008.27140.

Gardener, H., Rundek, T., Markert, M., Wright, C. B., Elkind, M. S., & Sacco, R. L. (2012). Diet soft drink consumption is associated with an increased risk of vascular events in the Northern Manhattan Study. *Journal of General Internal Medicine*, *27*(9), 1120–1126. doi:10.1007/s11606-011-1968-2.

Gardner, C., Wylie-Rosett, J., Gidding, S. S., Steffen, L. M., Johnson, R. K., Reader, D., et al. (2012). Nonnutritive sweeteners. Current use and health perspectives. A scientific statement from the American Heart Association and the American Diabetes Association. *Circulation*, *126*(4), 509–519. doi:10.1161/CIR.0b013e31825c42ee.

Han, E., & Powell, L. M. (2013). Consumption patterns of sugar-sweetened beverages in the United States. *Journal of the Academy of Nutrition and Dietetics*, *113*(1), 43–53. doi:10.1016/j.jand.2012.09.016.

Hansen, A. K., Friis Hansen, C. H., Krych, L., & Nielsen, D. S. (2014). Impact of the gut microbiota on rodent models of human disease. *World Journal of Gastroenterology*, *20*(47), 17727–17736. doi:10.3748/wjg.v20.i47.17727.

Hu, F. B. (2013). Resolved. There is sufficient scientific evidence that decreasing sugar-sweetened beverage consumption will reduce the prevalence of obesity and obesity-related diseases. *Obesity Reviews*, *14*(8), 606–619. doi:10.1111/obr.12040.

Johnston, L. D., Delva, J., & O'Malley, P. M. (2007). Soft drink availability, contracts, and revenues in American secondary schools. *American Journal of Preventive Medicine*, *33*(4 Suppl.), S209–S225. doi:10.1016/j.amepre.2007.07.006.

Kumar, G. S., Pan, L., Park, S., Lee-Kwan, S. H., Onufrak, S., & Blanck, H. M. (2014). Sugar-sweetened beverage consumption among adults. 18 states, 2012. *MMWR. Morbidity and Mortality Weekly Report*, *63*(32), 686–690.

Laska, M. N., Murray, D. M., Lytle, L. A., & Harnack, L. J. (2012). Longitudinal associations between key dietary behaviors and weight gain over time. Transitions through the adolescent years. *Obesity*, *20*(1), 118–125. doi:10.1038/oby.2011.179.

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Li, W. L., Chen, M. L., Liu, S. S., Li, G. L., Gu, T. Y., Liang, P., et al. (2013). Sweet preference modified by early experience in mice and the related molecular modulations on the peripheral pathway. *Journal of Molecular Neuroscience*, *51*(1), 225–236. doi:10.1007/s12031-013-0011-y.

Lin, J., & Curhan, G. C. (2011). Associations of sugar and artificially sweetened soda with albuminuria and kidney function decline in women. *Clinical Journal of the American Society of Nephrology*, *6*(1), 160–166. doi:10.2215/cjn.03260410.

Lioutas, E. D., & Tzimitra-Kalogianni, I. (2014). 'I saw Santa drinking soda!' Advertising and children's food preferences. *Child: Care, Health and Development*, doi:10.1111/cch.12189.

Lutsey, P. L., Steffen, L. M., & Stevens, J. (2008). Dietary intake and the development of the metabolic syndrome. The Atherosclerosis Risk in Communities study. *Circulation*, *117*(6), 754–761. doi:10.1161/CIRCULATIONAHA.107.716159; CIRCULATIONAHA.107.716159 [pii].

Malik, V. S., Pan, A., Willett, W. C., & Hu, F. B. (2013). Sugar-sweetened beverages and weight gain in children and adults. A systematic review and meta-analysis. *The American Journal of Clinical Nutrition*, *98*(4), 1084–1102. doi:10.3945/ajcn.113.058362.

Mattes, R. D., & Popkin, B. M. (2009). Nonnutritive sweetener consumption in humans. Effects on appetite and food intake and their putative mechanisms. *The American Journal of Clinical Nutrition*, *89*(1), 1–14. doi:10.3945/ajcn.2008.26792.

Mennella, J. A. (2014). Ontogeny of taste preferences. Basic biology and implications for health. *The American Journal of Clinical Nutrition*, *99*(3), 704S–711S. doi:10.3945/ajcn.113.067694.

Mennella, J. A., & Castor, S. M. (2012). Sensitive period in flavor learning. Effects of duration of exposure to formula flavors on food likes during infancy. *Clinical Nutrition (Edinburgh, Scotland)*, *31*(6), 1022–1025. doi:10.1016/j.clnu.2012.05.005.

Mennella, J. A., Jagnow, C. P., & Beauchamp, G. K. (2001). Prenatal and postnatal flavor learning by human infants. *Pediatrics*, *107*(6), E88.

Mesirow, M. S., & Welsh, J. A. (2015). Changing beverage consumption patterns have resulted in fewer liquid calories in the diets of US children. National health and nutrition examination survey 2001–2010. *Journal of the Academy of Nutrition and Dietetics*, *115*(4), 559–566. doi:10.1016/j.jand.2014.09.004.

Miller, P. E., & Perez, V. (2014). Low-calorie sweeteners and body weight and composition. A meta-analysis of randomized controlled trials and prospective cohort studies. *The American Journal of Clinical Nutrition*, *100*(3), 765–777. doi:10.3945/ajcn.113.082826.

Mitsutomi, K., Masaki, T., Shimasaki, T., Gotoh, K., Chiba, S., Kakuma, T., et al. (2014). Effects of a nonnutritive sweetener on body adiposity and energy metabolism in mice with diet-induced obesity. *Metabolism: Clinical and Experimental*, *63*(1), 69–78. doi:10.1016/j.metabol.2013.09.002.

Mozaffarian, D., Hao, T., Rimm, E. B., Willett, W. C., & Hu, F. B. (2011). Changes in diet and lifestyle and long-term weight gain in women and men. *The New England Journal of Medicine*, *364*(25), 2392–2404. doi:10.1056/NEJMoa1014296.

Nettleton, J. A., Polak, J. F., Tracy, R., Burke, G. L., & Jacobs, D. R., Jr. (2009). Dietary patterns and incident cardiovascular disease in the Multi-Ethnic Study of Atherosclerosis. *The American Journal of Clinical Nutrition*, *90*(3), 647–654. doi:10.3945/ajcn.2009.27597; ajcn.2009.27597 [pii].

Ng, M., Fleming, T., Robinson, M., Thomson, B., Graetz, N., Margono, C., et al. (2014). Global, regional, and national prevalence of overweight and obesity in children and adults during 1980–2013. A systematic analysis for the Global Burden of Disease Study 2013. *Lancet*, *384*(9945), 766–781. doi:10.1016/s0140-6736(14)60460-8.

Ng, S. W., Slining, M. M., & Popkin, B. M. (2012). Use of caloric and noncaloric sweeteners in US consumer packaged foods, 2005–2009. *Journal of the Academy of Nutrition and Dietetics*, *112*(11), 1828–1834, e1821-1826. doi:10.1016/j.jand.2012.07.009.

Nicholson, J. K., Holmes, E., Kinross, J., Burcelin, R., Gibson, G., Jia, W., et al. (2012). Host-gut microbiota metabolic interactions. *Science*, *336*(6086), 1262–1267. doi:10.1126/science.1223813.

Nickelson, J., Lawrence, J. C., Parton, J. M., Knowlden, A. P., & McDermott, R. J. (2014). What proportion of preschool-aged children consume sweetened beverages? *The Journal of School Health*, *84*(3), 185–194. doi:10.1111/josh.12136.

Ogden, C. L., Carroll, M. D., Kit, B. K., & Flegal, K. M. (2014). Prevalence of childhood and adult obesity in the United States, 2011–2012. *JAMA: The Journal of the American Medical Association*, *311*(8), 806–814. doi:10.1001/jama.2014.732.

Palmnas, M. S., Cowan, T. E., Bomhof, M. R., Su, J., Reimer, R. A., Vogel, H. J., et al. (2014). Low-dose aspartame consumption differentially affects gut microbiota-host metabolic interactions in the diet-induced obese rat. *PLoS ONE*, *9*(10), e109841. doi:10.1371/journal.pone.0109841.

Pan, A., & Hu, F. B. (2014). Question about a recent meta-analysis of low-calorie sweeteners and body weight. *The American Journal of Clinical Nutrition*, *100*(6), 1604. doi:10.3945/ajcn.114.098772.

Pan, A., Malik, V. S., Hao, T., Willett, W. C., Mozaffarian, D., & Hu, F. B. (2013). Changes in water and beverage intake and long-term weight changes. Results from three prospective cohort studies. *International Journal of Obesity (2005)*, *37*(10), 1378–1385. doi:10.1038/ijo.2012.225.

Pavlov, I. P., & Anrep, G. V. E. (1960). G. V. Anrep (Ed.), *Conditioned reflexes. An investigation of the physiological activity of the cerebral cortex*. Dover Publications. Translated [from Russian].

Piernas, C., Tate, D. F., Wang, X., & Popkin, B. M. (2013). Does diet-beverage intake affect dietary consumption patterns? Results from the Choose Healthy Options Consciously Everyday (CHOICE) randomized clinical trial. *The American Journal of Clinical Nutrition*, *97*(3), 604–611. doi:10.3945/ajcn.112.048405.

Romaguera, D., Norat, T., Wark, P. A., Vergnaud, A. C., Schulze, M. B., van Woudenbergh, G. J., et al. (2013). Consumption of sweet beverages and type 2 diabetes incidence in European adults. Results from EPIC-InterAct. *Diabetologia*, *56*, 1520–1530.

Sakurai, M., Nakamura, K., Miura, K., Takamura, T., Yoshita, K., Nagasawa, S. Y., et al. (2013). Sugar-sweetened beverage and diet soda consumption and the 7-year risk for type 2 diabetes mellitus in middle-aged Japanese men. *European Journal of Nutrition*, *53*(4), 1137–1138. doi:10.1007/s00394-013-0523-9.

Scully, P., Macken, A., Leddin, D., Cullen, W., Dunne, C., & Gorman, C. O. (2015). Food and beverage advertising during children's television programming. *Irish Journal of Medical Science*, *184*(1), 207–212. doi:10.1007/s11845-014-1088-1.

Serdula, M. K., Ivery, D., Coates, R. J., Freedman, D. S., Williamson, D. F., & Byers, T. (1993). Do obese children become obese adults? A review of the literature. *Preventive Medicine*, *22*(2), 167–177. doi:10.1006/pmed.1993.1014.

Sivertsen, J., Rosenmeier, J., Holst, J. J., & Vilsboll, T. (2012). The effect of glucagon-like peptide 1 on cardiovascular risk. *Nature Reviews Cardiology*, *9*(4), 209–222. doi:10.1038/nrcardio.2011.211.

Suez, J., Korem, T., Zeevi, D., Zilberman-Schapira, G., Thaiss, C. A., Maza, O., et al. (2014). Artificial sweeteners induce glucose intolerance by altering the gut microbiota. *Nature*, *514*(7521), 181–186. doi:10.1038/nature13793.

Swithers, S. E. (2013). Artificial sweeteners produce the counterintuitive effect of inducing metabolic derangements. *Trends in Endocrinology and Metabolism*, *24*(9), 431–441. doi:10.1016/j.tem.2013.05.005.

Swithers, S. E., Baker, C. R., & Davidson, T. L. (2009). General and persistent effects of high-intensity sweeteners on body weight gain and caloric compensation in rats. *Behavioral Neuroscience*, *123*(4), 772–780. doi:10.1037/a0016139.

Swithers, S. E., & Davidson, T. L. (2008). A role for sweet taste. Calorie predictive relations in energy regulation by rats. *Behavioral Neuroscience*, *122*(1), 161–173. doi:10.1037/0735-7044.122.1.161; 2008-01943-017 [pii].

Swithers, S. E., Laboy, A. F., Clark, K., Cooper, S., & Davidson, T. L. (2012). Experience with the high-intensity sweetener saccharin impairs glucose homeostasis and GLP-1 release in rats. *Behavioural Brain Research*, *233*(1), 1–14. doi:10.1016/j.bbr.2012.04.024.

Swithers, S. E., Martin, A. A., Clark, K. M., Laboy, A. F., & Davidson, T. L. (2010). Body weight gain in rats consuming sweetened liquids. Effects of caffeine and diet composition. *Appetite*, *55*(3), 528–533. doi:10.1016/j.appet.2010.08.021.

Swithers, S. E., Martin, A. A., & Davidson, T. L. (2010). High-intensity sweeteners and energy balance. *Physiology and Behavior*, *100*(1), 55–62. doi:10.1016/j.physbeh.2009.12.021.

Swithers, S. E., Ogden, S. B., Laboy, A. F., & Davidson, T. L. (2012). Saccharin pre-exposure enhances appetitive flavor learning in pre-weanling rats. *Developmental Psychobiology*, *54*(8), 818–824. doi:10.1002/dev.21047.

Swithers, S. E., Sample, C. H., & Davidson, T. L. (2013). Adverse effects of high-intensity sweeteners on energy intake and weight control in male and obesity-prone female rats. *Behavioral Neuroscience*, *127*(2), 262–274. doi:10.1037/a0031717.

Swithers, S. E., Sample, C. H., & Katz, D. P. (2013). Influence of ovarian and non-ovarian estrogens on weight gain in response to disruption of sweet taste. Calorie relations in female rats. *Hormones and Behavior*, *63*(1), 40–48. doi:10.1016/j.yhbeh.2012.11.003.

Sylvetsky, A. C., Greenberg, M., Zhao, X., & Rother, K. I. (2014). What parents think about giving nonnutritive sweeteners to their children. A pilot study. *International Journal of Pediatrics*, *2014*, 819872. doi:10.1155/2014/819872.

Sylvetsky, A. C., Welsh, J. A., Brown, R. J., & Vos, M. B. (2012). Low-calorie sweetener consumption is increasing in the United States. *The American Journal of Clinical Nutrition*, *96*(3), 640–646. doi:10.3945/ajcn.112.034751.

Tate, D. F., Turner-McGrievy, G., Lyons, E., Stevens, J., Erickson, K., Polzien, K., et al. (2012). Replacing caloric beverages with water or diet beverages for weight loss in adults. Main results of the Choose Healthy Options Consciously Everyday (CHOICE) randomized clinical trial. *The American Journal of Clinical Nutrition*, *95*(3), 555–563. doi:10.3945/ajcn.111.026278.

Terry-McElrath, Y. M., O'Malley, P. M., & Johnston, L. D. (2013). School soft drink availability and consumption among U.S. secondary students. *American Journal of Preventive Medicine*, *44*(6), 573–582. doi:10.1016/j.amepre.2013.01.026.

Terry-McElrath, Y. M., Turner, L., Sandoval, A., Johnston, L. D., & Chaloupka, F. J. (2014). Commercialism in US elementary and secondary school nutrition environments. Trends from 2007 to 2012. *JAMA Pediatrics*, *168*(3), 234–242. doi:10.1001/jamapediatrics.2013.4521.

US Food and Drug Administration (2014). Additional information about high-intensity sweeteners permitted for use in food in the United States. SummaryTable. <http://www.fda.gov/Food/IngredientsPackagingLabeling/FoodAdditivesIngredients/ucm397725.htm> Last accessed 03.01.15.

USDA, Economic Research Service (2008). Beverages. Per capita consumption. <http://www.ers.usda.gov/data/foodconsumption/spreadsheets/beverage.xls> Last accessed 26.10.08.

Zhang, G. H., Chen, M. L., Liu, S. S., Zhan, Y. H., Quan, Y., Qin, Y. M., et al. (2011). Effects of mother's dietary exposure to acesulfame-K in pregnancy or lactation on the adult offspring's sweet preference. *Chemical Senses*, *36*(9), 763–770. doi:10.1093/chemse/bjr050.

Zheng, M., Rangan, A., Olsen, N. J., Andersen, L. B., Wedderkopp, N., Kristensen, P., et al. (2015). Substituting sugar-sweetened beverages with water or milk is inversely associated with body fatness development from childhood to adolescence. *Nutrition (Burbank, Los Angeles County, Calif.)*, *31*(1), 38–44. doi:10.1016/j.nut.2014.04.017.

Zheng, M., Rangan, A., Olsen, N. J., Bo Andersen, L., Wedderkopp, N., Kristensen, P., et al. (2014). Sugar-sweetened beverages consumption in relation to changes in body fatness over 6 and 12 years among 9-year-old children. The European Youth Heart Study. *European Journal of Clinical Nutrition*, *68*(1), 77–83. doi:10.1038/ejcn.2013.243.