Dietary Sugar and Body Weight: Have We Reached a Crisis in the Epidemic of Obesity and Diabetes?

We Have, but the Pox on Sugar Is Overwrought and Overworked

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In the preceding point narrative, Drs. Bray and Popkin provide their opinion and review data that suggest to them that we need to reconsider the consumption of dietary sugar based on the growing concern of obesity and type 2 diabetes. In the counterpoint narrative below, we argue that there is no clear or convincing evidence that any dietary or added sugar has a unique or detrimental impact relative to any other source of calories on the development of obesity or diabetes. Sugar is purely a highly palatable source of energy; because it has no other property that appears to contribute to our nutritional well-being, it is not an essential food for most of us. For those who wish to reduce energy consumption, ingesting less sugar is a good place to start. However, doing so does not automatically portend any clinical benefit.

In this counterpoint discussion, we use the phrase "dietary sugar" or "added sugar" to mean sucrose or high-fructose corn syrup (HFCS). Almost all dietary or added sugar used as an ingredient in either solid (e.g., desserts, snacks) or liquid (e.g., sugar-sweetened beverages [SSB]) foods is in the form of these two disaccharides. Although we will discuss evidence from feeding studies in which fructose itself was used as the sole added sweetener, it should be noted that fructose rarely occurs alone in foods commonly consumed by humans. Also of importance is the fact that sucrose and HFCS are both composed of glucose and fructose. Whereas the ratio of glucose to fructose is equal in sucrose, in HFCS the ratio is usually 55% fructose, 42% glucose, and 3% glucose polymers; other forms of HFCS have a lower proportion of fructose. In addition, the glucose and fructose in HFCS are free in solution; in sucrose they are initially bound together. But when sucrose is used in processed or prepared foods/beverages an appreciable amount is broken down to free fructose and glucose prior to consumption. Finally, whereas glucose and fructose are metabolized differently, the belief that sucrose is metabolized differently than HFCS is a myth. No study has shown any difference between the two when each is given isocalorically, nor is there any difference in sweetness or caloric value (1–3).

Much of the condemnation of sugar in the last few years owes its origin to an article by Bray et al. (4) showing an ecological relationship between sugar availability (a crude measure of intake) and obesity, which has now been expanded to explain a myriad of metabolic abnormalities (5–7). Table 1 shows that the rise in the prevalence of overweight/obesity in the early 1980s does indeed appear to be related to an increase in the availability of added sugars. However, starting around 2000, sugar

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Table 1—Prevalence of overweight/obesity and its relationship to estimated dietary sugar consumption

Years	Prevalence of overweight/ obesity (%)*	Estimated intake of added sugars (% daily energy)	Estimated intake of caloric sweeteners (kcal/day)****	Estimated intake of HFCS (kcal/day)****
1971–1974	46.5	NA	411	7
1976–1980	46.5	13.1**	409	36
1988–1994	55.9	13.5**	448	170
1999–2000	64.5	18.1***	502	211
2007–2008	68.0	14.6***	457	189
2009–2010	68.7	NA	440	169

*Data obtained from references 64–67. **Data obtained from reference 68. ***Data obtained from reference 69. ****Data obtained from reference 70.

consumption appears to have declined considerably, but the prevalence of obesity (and diabetes, data not shown) has continued to rise. Such ecological findings are certainly intriguing, but because obesity appears related to many changes in our environment (8), including a rise in the consumption of bottled water (9), they are only hypothesis-generating.

The preferred methodology to determine whether sugar itself causes weight gain would be to conduct a randomized controlled trial (RCT), in which the consumption of sugar is the only variable between otherwise identical groups. RCTs are, of course, the strongest form of evidence (10,11) because they eliminate the possibility of confounding from prerandomization factors and can determine the effect of sugar independent of other dietary components.

RCTs ON THE EFFECT OF SUGAR ON BODY WEIGHT

Over the last decade, numerous RCTs on the effects of sugar consumption have been performed. Very recently, four independent groups have performed systematic reviews and meta-analyses of these published trials (9,12–14). Each of these studies used different inclusion and exclusion rules but in all four the outcome of interest was weight change. Although each of the four meta-analyzed many of the same trials, they often grouped them differently and each used different exclusion/inclusion rules and reported different summary point estimates.

Te Morenga et al. (13) and Sievenpiper et al. (12) examined whether an isocaloric exchange of added sugar or purified fructose with other macronutrients (mostly other carbohydrates) would affect body weight in adults. In both analyses the forest plot summary estimates showed no significant effect of sugar or pure fructose on body weight (relative risk [RR] 0.26 [95% CI −0.26 to 0.83] and RR −0.18 [95% CI −0.47 to 0.23], respectively). No isocaloric trials have been performed in children.

Another approach in RCTs has been to examine the effect on weight when calories from sugar are *reduced* relative to consumption in the control group. Te Morenga et al. (13) meta-analyzed five such trials in children and the summary point estimate was not significant. Kaiser et al. (9) also found no significant change in weight with a reduction in calories from sugar when eight trials in children and adults were meta-analyzed together. However, a meta-analysis by Malik et al. (14) identified two of five trials that showed a significant loss of weight with a reduction in calories from sugar, and the summary point estimate was significant when a fixed-effects model was used but not with a random-effects model. Te Morenga et al. (13) also meta-analyzed trials conducted in adults and found that the summary point estimate significantly favored a reduction in body fat/weight resulting from a reduction in calories from sugar consumption. However, when three of five studies were removed from the analysis because they had a high risk of bias, the summary point estimate was no longer significant. All three meta-analyses (9,13,14) found major interstudy heterogeneity ($I^2 > 50\%$).

Of note, in all the individual trials in which subjects consumed less calories from sugar they also consumed less total energy, and therefore it is unclear if any weight loss was due to some unique property of sugar, or simply because total energy consumption in the intervention was less than in control subjects.

Finally, all four research groups (9–12) meta-analyzed trials in which an *increased* amount of calories from sugar were given to adults (there were no studies in children) as a supplement to their normal diet. The summary point estimates in all four reports showed a modest but significant weight gain even though in most of the individual studies the CI crossed unity. Again, whether the change in weight was due to the increase in energy consumed (as would be expected in the absence of complete compensation) or to some unique property of sugar is unknown.

Overall, therefore, when sugar was replaced in an isocaloric exchange, there was no change in body weight. When subjects were randomized to receive fewer calories from sugar and thus consumed less total energy, the studies generally showed no significant weight loss or were sufficiently confounded to preclude reaching any conclusions. Conversely, adults given added energy in the form of sugar gained weight. As weight gain or loss only occurred when sugar (energy) was added to, or reduced from, the usual background diet, and there was no change in weight from an isocaloric exchange, it seems likely that any effect of sugar on weight is because of the energy it supplies and not because it has any unique property.

Unfortunately, virtually all the individual trials meta-analyzed in the four reports discussed above, recruited few subjects (<100) and the intervention was of short duration (<1 year). Publication bias was also noted in the trials conducted in adults (11,12). The only exceptions to these design issues were two recent trials (15,16), where a large number of children (224 and 641, respectively) were randomized to reduced reduction in calories from sugar consumption relative to control subjects and the interventions were carried out for 12 and 24 months, respectively. Although both trials were included in two of the above meta-analyses (9,14), their individual results may be instructive. Both trials (15,16) reported significant weight reduction when the consumption of calories from SSBs was reduced. However, in one study (15) weight loss was quite modest after 12 months

(mean difference between groups −0.13 [95% CI −0.20 to −0.06]). In the other (16), the prespecified primary body weight end point was not significant, but was so ($P = 0.045$) at an interim 1-year analysis. In a subgroup analysis, the positive effect for the primary end point occurred only in Hispanic children. Thus, these larger and longer duration trials show no definitive adverse effect of sugar on body weight, despite the fact that the intervention groups consumed less total energy throughout the follow-up period, which would be expected to favor weight loss.

PROSPECTIVE STUDIES ON THE EFFECT OF SUGAR ON BODY WEIGHT

As RCTs do not indicate that sugar consumption itself causes weight gain, why do some investigators believe otherwise? One possibility is that they focus instead on the results of prospective cohort studies. In the latter, subjects are asked to complete a semiquantitative food frequency questionnaire to ascertain the consumption of specific foods. Participants are then followed, often for years, and many outcomes are recorded.

Te Morenga et al. (13) and Malik et al. (14) also conducted a systematic review and meta-analysis of such cohort studies. Their results indicated that a majority of the studies found a significantly positive association between sugar intake and various measures of body weight. Te Morenga et al. (13), however, noted that because a wide variety of measures of adiposity were used (e.g., BMI, skinfold thickness, incident overweight or obesity, weight, percent body fat), it was difficult to draw a definitive conclusion because in many studies some measures were significant whereas others were not. In the Malik et al. (14) meta-analysis, the studies considered displayed high heterogeneity and publication bias.

Of importance, while all of the prospective cohort studies examining the relationship between sugar and weight adjusted for various potentially confounding variables, almost none adjusted for energy consumption. Thus, in these studies, as in the RCTs, the positive association between increased sugar consumption and weight could well be due to excess energy intake and not to a unique effect of sugar. Indeed, Malik et al. (14) showed that when adjusted for total energy consumed the once positive relationship was no longer significant.

Supporting our claim that there is nothing special about calories from sugar, many other sources of highly palatable calories can also increase body weight. For example, in a pooled analysis of three of the well-known Harvard cohorts (which are often cited [5–7,17] as showing that sugar causes obesity and diabetes) an increase in one serving of French fries (+3.35 lbs), potato chips (+1.69 lbs), unprocessed meat (+0.93 lbs), or boiled, baked or mashed potatoes (+57 lbs) resulted in greater or similar weight gain as did sugary beverages (+1.0 lbs) for every 4 years of follow-up, when intake was not adjusted for total energy consumption (18).

Of note, there are many methodological problems with the prospective cohort studies that are related to sugar consumption. First, they obviously suffer from the inability to control for all the variables that could lead to residual confounding; indeed, the vast majority do not adjust for caloric intake. Second, they did not publicly prespecify how exposure would be defined (e.g., quartile- or tertile-defined categories, highest vs. lowest), the number of analyses that would be performed, or the statistical tests to be used, and the results were not adjusted for repeated tests of significance. Any of these problems could have easily led to spurious results.

Finally, the essence of prospective cohort studies in nutrition is their reliance on the ability of subjects to recall accurately exactly what they ingested. In the context of meals consisting of a variety of foods assembled in a myriad of ways and that often vary over time, along with changing tastes, lifestyles, and the constant introduction of new products and packaging—it should not be surprising that many studies have shown that such questionnaires have substantial biases and inaccuracies (19–25). Moreover, even when focusing on a specific food such as SSBs, such single nutrient analyses may be confounded by dietary pattern; over- or underreporting of intake can also be different depending on the demographic characteristics of the population (26–33). For all these reasons as well as the others mentioned above, the claim that sugar itself promotes weight gain based on the results from prospective cohort studies appears very problematic.

EFFECTS OF SUGAR ON APPETITE AND SATIETY

Some investigators argue that an adverse effect of sugar, particularly when consumed as SSBs, is that it stimulates appetite or reduces satiety (4,6,34). Many investigators have pursued this hypothesis and the results have been conflicting. Recently, Almiron-Roig et al. (35) performed a systematic review and meta-analysis of the studies on this topic. The question they addressed is whether energy given before a meal (i.e., preload) will affect the energy consumed at a meal. Their analyses showed that overeating was much greater with liquid preloads than with solid or semisolid preloads. Whereas this finding might support the claim that SSBs increase energy consumption, the authors also found that the effect of liquids did *not* correlate significantly with their energy content. That is, it was the liquid nature of the preload, rather than the energy within it, that influenced subsequent food consumption. Therefore, the hypothesis that sugar per se leads to excess food consumption is not supported by the totality of the evidence.

The Almiron-Roig et al. (35) review focused only on compensatory energy intake after a preload. All the studies they examined did not report whether overeating translated into persistent weight gain. There appears to be, however, only two studies that examined the effect of liquid versus solid energy on weight, and both showed no significant effect of food form on weight change (36,37).

All told, therefore, we have no persuasive clinical evidence that sugar in beverages enhances energy consumption or that liquid energy is weight-promoting any more so than solid energy. Liquids (e.g., SSBs, milk) ingested around or shortly before a meal in experimental conditions do seem to stimulate overeating more so than energy in other forms, but whether that translates into long-term weight gain is unknown.

WHAT ABOUT FRUCTOSE OR HFCS?

Some investigators have focused on the fructose component of sucrose/HFCS as the "evildoer" of sugar consumption as

glucose and fructose are absorbed and metabolized differently (2). The impact of fructose on body weight was reviewed above and the evidence suggests no difference between fructose and any other monosaccharide (12,38). In addition, as concluded above, if there is an effect of any sugar on weight, it appears to be because of its contribution to total energy consumed. Additional evidence for that assertion comes from weight-loss trials, where changes in the macronutrient composition of the diet (high or low carbohydrate, high or low fat) in the setting of equally hypocaloric diets result in an equivalent weight loss (39).

In conclusion, there is no evidence that fructose or HFCS per se causes obesity or even weight gain. Sugar obviously contains energy, and there is some evidence, albeit conflicting, incomplete, and inconclusive, that excess energy consumption in the form of any sugar may contribute to weight gain. If the excess energy in sugar is the culprit, it is reasonable to conclude that any food consumed in excess is just as likely to alter energy balance as would an equal caloric amount of sugar. On the other hand, sugar contains no essential micronutrient and therefore if a reduction in energy intake is desirable, reducing sugar consumption is obviously the place to start.

SUGAR AND DIABETES

It is well accepted that weight gain is a major risk factor for the development of diabetes. As dietary sugar itself does not appear to have a significant role in weight gain, it is possible that sugar alters metabolism in some other regard thereby causing diabetes. From a clinical perspective, there are no RCTs examining whether sugar consumption in subjects with normoglycemia results in diabetes or even prediabetes. Prospective cohort studies have generated conflicting results. For example, Malik et al. (40) performed a meta-analysis of large, long-term cohort studies and found a significant association between SSBs and incident diabetes. A close examination of the eight studies included reveals that four did not find a significant association between SSBs and diabetes. Moreover, five of the eight did not adjust their findings for energy intake or even body weight. Interestingly, another large cohort study published earlier by the same research group, but not included in the meta-analysis, found no association between total sugar intake and diabetes (41). Also, one of the studies included in the meta-analysis (42) showed no significant association between intake of SSB and the development of diabetes when the data were adjusted for energy intake, but that finding was not mentioned in the meta-analysis. In that study (42), the consumption of artificially sweetened beverages was significantly associated with diabetes when adjusted for total energy intake, which is similar to a recent report (43) showing that both SSBs and artificially sweetened beverages conveyed equally significant risk.

Finally, other prospective cohort studies have shown a significant negative association for total sugars (44) or sucrose (45) with diabetes and no significant positive association for total sucrose or fructose (41,44,46), and one study showed a positive association for total fructose and a negative association for sucrose (45). All told, therefore, there is no persuasive evidence for a role of sugar in the development of diabetes.

Other studies have examined surrogate measures of diabetes risk, also with mixed results. Most (47–53) but not all (54) controlled trials showed that fructose or sucrose had no adverse effect on fasting plasma glucose, postprandial glucose, or insulin levels. Similar inconsistent results have been reported on measures of insulin resistance regardless if the sugar is sucrose or fructose (51–57). In addition, meta-analyses of controlled trials have shown that fructose administration improves glycemia in people with diabetes (58,59). There appears to be no study on the effect of sugar on β-cell function, which is as important in the development of diabetes as is insulin resistance.

Johnson et al. (60) recently reviewed the literature on the effect of fructose consumption on the development of diabetes and obesity. Despite some conflicting evidence, they hypothesized that fructose induces hyperuricemia, which then results in the development of the metabolic syndrome. Although there has been no RCT that has tested that hypothesis, the Malik et al. (40) article discussed above performed a second meta-analysis and concluded that SSBs were associated with the development of metabolic syndrome. Of note, however, Malik et al. (40) identified only three cohort studies that had metabolic syndrome as the outcome of interest. In two of the three, the relative risk between the extreme quartiles of SSB consumption was not significant, and in the remaining study where the relative risk cited was significant (61), that result pertained the consumption of any soft drink (regular or diet) and the data were not adjusted for smoking, body weight, or energy intake. Moreover, a closer examination of the results of the latter study (61) indicate that the risk of metabolic syndrome was the same when regular soda consumption was compared with diet soda and at any level of consumption.

The hypothesis that fructose-induced hyperuricemia is harmful was recently tested in a double-blind RCT (62). High fructose consumption in an overall isocaloric diet did indeed result in an increase in serum uric acid when compared with an isocaloric high-glucose diet. Yet the high-fructose diet had no significant effect on a wide variety of hepatic biomarkers, including triacylglyerol. On the other hand, when either sugar was given in an overall hypercaloric diet, they both produced similar significant changes in biomarkers of nonalcoholic fatty liver disease. These results suggest, once again, that any adverse effect of a sugar—particularly fructose—is due to the excess energy it provides and not the molecule itself.

Even if one believes that sucrose or fructose adversely affects some aspect of metabolism related to the development of diabetes, all of the surrogate outcome studies were conducted over days or at most a few weeks and therefore any adverse effect of sugar certainly does not mean the diabetes would eventually develop. Also, the vast majority of feeding studies showing an adverse effect of sugar on a metabolic parameter related to diabetes gave subjects sucrose or fructose in a hypercaloric exchange with other sources of energy, or in addition to a background diet, or (particularly when studying fructose) in amounts usually exceeding the 95th percentile of consumption (3,63). Conversely, when

Table 2—Putative effects of sugar*

Adverse outcome	Strength of the evidence
Increases weight in an isocaloric exchange with other macronutrients	None
Increases weight in a hypercaloric diet**	Moderate/inconsistent
Decreases weight in a hypocaloric diet**	Weak/inconsistent
Increases appetite resulting in weight gain	None
Causes diabetes	None
Provides unnecessary energy	Strong

*Sugar defined as sucrose, glucose, fructose, or HFCS. **A hypercaloric diet is defined as a diet in which energy intake exceeds energy expenditure, and a hypocaloric diet is defined as a diet in which energy intake is less than energy expenditure, thereby favoring weight gain and weight loss, respectively.

sucrose or fructose was given in an overall isocaloric diet or at the 50th percentile of consumption adverse effects have rarely been reported (3,12,63). Therefore, whether sugar consumption has even an indirect effect on the development of diabetes is quite unclear.

CONCLUSIONS

Table 2 summarizes what we believe is known about the role of sugar in the development of obesity and diabetes. Although no one would take issue that we are indeed in the midst of an obesity and diabetes epidemic, placing the blame on sugar consumption lacks persuasive evidence and is misguided. Although calories from sugar (sucrose, fructose, or HFCS in any form—solid or liquid) have been shown to increase weight in a hypercaloric diet and decrease weight in a hypocaloric diet, when consumption is corrected for energy intake, sugar has no effect on body weight. Finally, there is no direct evidence that sugar itself, in liquid or solid form, causes an increase in appetite, decreases satiety, or causes diabetes.

If there are any adverse effects of sugar, they are due entirely to the calories it provides, and it is therefore indistinguishable from any other caloric food. Excess total energy consumption seems far more likely to be the cause of obesity and diabetes. Although many individuals can lose a substantial amount of weight and thereby also delay the onset of diabetes, to do so has relied on an overall reduction in energy consumption. Thus, if reduced energy intake is desirable, all caloric foods are candidates. A reduction in consumption of added sugars should head the list because they provide no essential nutrients.

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