

Liquid calories, sugar, and body weight¹⁻³

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ABSTRACT

The consumption of sugar-sweetened beverages has been linked to rising rates of obesity in the United States. The standard explanation is that energy-containing liquids are less satiating than are solid foods. However, purely physiologic mechanisms do not fully account for the proposed links between liquid sugar energy and body weight change. First, a reevaluation of published epidemiologic studies of consumption of sweetened beverages and overweight shows that most such studies either are cross-sectional or are based on passive surveillance of temporal trends and thus permit no conclusions about causal links. Second, research evidence comparing the short-term satiating power of different types of liquids and of solids remains inconclusive. Numerous clinical studies have shown that sugar-containing liquids, when consumed in place of usual meals, can lead to a significant and sustained weight loss. The principal ingredient of liquid meal replacement shakes is sugar, often high-fructose corn syrup, which is present in amounts comparable to those in soft drinks. Far from suppressing satiety, one such liquid shake is marketed on the grounds that it helps control hunger and prevents hunger longer when consumed for the purpose of weight loss. These inconsistencies raise the question whether the issue of sugars and body weight should continue to be framed purely in metabolic or physiologic terms. The effect of sugar consumption on body weight can also depend on behavioral intent, context, and the mode of use, availability, and cost of sweetened liquids. *Am J Clin Nutr* 2007;85:651-61.

KEY WORDS Sweetened beverages, meal replacement shakes, weight gain, weight loss, satiety, cost

INTRODUCTION

Regular consumption of sugar calories in liquid form is said to be responsible for body weight gain (1-4). That is the conclusion of some epidemiologic and experimental studies that have linked the consumption of sweetened beverages in the United States to the rising rates of obesity and overweight (2, 5, 6). Sugar-sweetened beverages are said to promote obesity by virtue of their low satiety and high added sugar content (4).

In evidence-based medicine, one of the criteria for establishing causality is a biologically plausible mechanism (7). The reported links between sweetened beverage consumption and weight gain (4) rest largely on temporal parallels (1, 3) and cross-sectional studies (8). The similarity in time trends between growing beverage consumption (9, 10) and rising obesity rates in

the United States (11-13) is indeed striking and cannot be denied. However, temporal associations are confounded by myriad factors, including dietary and secular trends, and by more sedentary lifestyles (14). Cross-sectional studies, based on a single point in time, do not allow the drawing of conclusions about causal links between sugar intake and the dynamics of weight change.

The search for a biologically plausible mechanism has come to focus on the notion that liquid calories are not perceived by the body. Despite the fact that short-term satiety signals may have little to do with the long-term homeostatic mechanisms regulating body weight, putative satiety deficits are routinely invoked to bolster associations found in epidemiologic studies (1, 4, 6, 15, 16). In fact, the entire debate about beverages and body weight gain has been framed in physiologic terms, and much attention has been paid to satiety (4, 15, 16), energy compensation (4, 17), glycemic index (18), and the vitamin and micronutrient content of beverages (6). When it comes to soft drinks consumption and body weight change, most researchers have opted to implicate human physiology (1, 4, 6, 15, 16, 18) rather than to explore human dietary behavior or the economics of food choice.

Sugar-containing beverages include still and carbonated soft drinks, juice-based beverages, 100% juices, and flavored milk. The overwhelming emphasis has been on soft drinks, and beverages sweetened with high-fructose corn syrup (HFCS) rather than sucrose have come under particular scrutiny (1, 3). In animal models, the consumption of pure fructose or a fructose-rich diet is reported to suppress insulin secretion and leptin production (19, 20), thereby promoting weight gain. One hypothesis is that fructose, whether consumed in solid or in liquid form, does not stimulate insulin secretion or leptin production in humans and may potentially contribute to weight gain (21). However, the question of whether HFCS promotes human obesity (1) requires further study (4). This review will distinguish between different

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types of sweetened beverages by using the terms and definitions provided by the authors of the studies referenced.

Despite its popularity, the notion that liquid calories are not perceived by the body (17, 22) rests on inconclusive evidence. As documented in a review, some studies showed that liquids were less satiating than were solids, whereas other studies showed the exact opposite (23). In one study, jelly beans led to energy compensation, but beverages did not (19); in another study, cookies and cola had identical effects on hunger ratings and energy intakes (EIs) at lunch (24). The argument that humans are ill-adapted to liquids (17) has now been extended to some solid foods (21, 25). Solid fast foods of high energy density are reported to have low satiating power (25).

The notion that the consumption of sugared beverages must result in weight gain (17, 22) runs counter to a large body of clinical literature on the consumption of sugared beverages for the purpose of weight loss (26). Not everyone fully appreciates that the principal ingredient of liquid meal replacement (MR) shakes is sugar, which is present in quantities comparable to those in caloric soft drinks (36–72 g sugar/d). As the name implies, liquid MR shakes are sugared beverages consumed for the specific purpose of weight loss. In randomized clinical trials with overweight adults, daily consumption of liquid MR shakes, some containing HFCS, led to a sustained and significant weight loss (26, 27). Sugared liquid shakes were reported to be more effective in promoting weight loss than were low-fat diets that included plenty of vegetables and fruit (26).

Clearly, additional insights should come from studies in behavior and the economics of food selection. Depending on who uses them, in what context, and for what purpose, sugar-containing liquids can lead either to weight gain or to weight loss (26). Price may be one issue (28). Sweetened beverages are the largest source of inexpensive added sugars in the US diet (28). Liquid MR shakes provide the same sugar energy as do sugar-sweetened beverages, but for different population subgroups, in a different context, and at a higher cost. The links between sugar consumption and body weight change may well depend on the purpose, context, and mode of use of liquid sugar calories and on the beverages' availability and price. A critical reexamination of the role of liquid sugar energy in weight control is the focus of this report.

SUGARS AND BODY WEIGHT

The consumption of sweetened beverages in the United States has increased sharply over the last 2 decades (9, 10). Analyses of the data from the third National Health and Nutrition Examination Survey (NHANES III; from 1988–1994) showed that beverages (including milk) provided 20%–24% of dietary energy across all age groups, and that soft drinks accounted for 8% of energy in the adolescents' diet (8). By 2001, soft drinks accounted for 9.2% of daily energy intake in persons >2 y old, and another 7.3% of energy was supplied by fruit juices and milk (10). Analyses of the 1994–1996 Continuing Survey of Food Intake by Individuals (CSFII) data found that added sugars accounted for 15.8% of daily EIs; more than one-third of sugar energy was provided in liquid form (28). Soft drinks have become the leading source of sugar in the adolescent diet, contributing 36.2 g sugar/d for girls and 57.7 g sugar/d for boys (28). Other analyses of 1994 CSFII data for those aged 2–18 y (29) found that those subjects who consumed an average of 9 oz/d of

caloric sodas had higher total EIs than did those who consumed none (2018 and 1830 kcal, respectively) and tended to consume less fruit juice and less fluid milk.

Numerous studies reported associations between soft drink consumption and body weight or body weight gain. Among these studies were those based on nationally representative cross-sectional surveys (8, 30), longitudinal cohorts (2, 5, 15, 31, 32), and between-group comparisons (33, 34). The data, as shown in **Table 1**, were mixed. Despite a dramatic rise in adolescent obesity rates, an analysis of NHANES III data showed that mean total EIs of youth aged 2–19 y changed little, except for a significant increase in adolescent females (8). In this age group, overweight youths consumed a significantly greater proportion of energy from beverages than did the nonoverweight youths (8). On the other hand, reanalyses of the nationally representative 1994–1996 CSFII dataset for 6–19-y-olds found that the consumption of caloric carbonated beverages, fruit drinks, and milk was unrelated to body weight (30). Instead, beverage choices and total beverage consumption were strongly linked to age, sex, and race (30).

Although cross-sectional studies can provide a fertile ground for speculation, they do not show causality. EIs, measured at a single point in time, can provide no indication of the direction of the association or of its possible relation to the dynamics of body weight. For example, epidemiologic studies generally show an inverse relation between the intake of sucrose (in any form) and the body weights of children (41–43) and adults (44, 45). That does not mean, however, that consuming more sugar will lead to weight loss. Given that sugar consumption declines with age, higher sugar intakes are usually associated with younger age, lower weight, and greater physical activity (46). Even when age is not a factor, cross-sectional studies may be confounded by activity patterns and energy needs, not to mention severe under-reporting. In a study of 16 882 subjects aged 9–14 y, overweight participants reported consuming significantly less energy than did their normal-weight peers (47).

Between-group comparisons suggest that other dietary factors may also be involved. A study of 91 obese and 90 nonobese children and adolescents (aged 4–16 y) found that the obese group consumed significantly more sugar-sweetened drinks (excluding 100% fruit juice) than did the nonobese group (34). However, the obese group also consumed significantly more meat, grain products, potato chips, and total sugar, as determined by the dietary history method, whereas the consumption of many other sugar-rich foods (ie, cookies, candy, chocolate, doughnuts, and ice cream) did not differ significantly between the 2 groups. Another study, based on 14-d food records, showed no significant difference in soda consumption between 21 obese and 22 normal-weight adolescents (33). The normal-weight adolescents consumed twice the amount of high-calorie foods as did the obese adolescents (33). In a study of 928 men and 889 women aged 18–99 y in rural communities (36), overweight was associated with significantly more frequent consumption of soft drinks—but also with ordering super-sized portions, eating when watching TV, and not exercising enough.

A report based on the Nurses Health Study noted that the highest consumers of sugar-sweetened soft drinks were less physically active and were twice as likely to be current smokers than were the lowest consumers of soft drinks—21% compared with 10.9% (6). Physical activity is associated with socioeconomic status, which is in turn predictive of improved diet quality



TABLE 1
Liquid sugar calories and overweight¹

Study (reference)	Subjects	Age	Study duration	Intake measures	Height and weight data ²	Association found	Comment
	<i>n</i>	<i>y</i>					
Cross-sectional							
Troiano et al (8)	10 371	2–19	NA	24-h recall	M	Yes	NHANES III
Forshee and Storey (30)	3311	6–19	NA	Questionnaire	SR	No	1994–1996 CSFII
Giammattei et al (35)	385	12–13	NA	Questionnaire	M	Yes	Only for >3 servings/d
Liebman et al (36)	1817	18–99	NA	Questionnaire	SR	Yes	Also other foods, television
Rodriguez et al (37)	1112	6–7	NA	Proxy FFQ ³	M	No	
Cohort							
Ludwig (15)	548	11–12	19 mo	Youth FFQ	M	Yes	Planet Health Study
Berkey et al (2)	10 000	9–14	2 12-mo phases	FFQ	SR	Yes	NS when adjusted for energy
Welsh et al (5)	10 904	2–3	12 mo	Proxy FFQ ³	M	Yes	Overweight or obese only
Blum et al (31)	164	9.5	24 mo	24-h recall	M	No	Diet soda associated with BMI <i>z</i> scores
Rajeshwari et al (38)	1548	10	21 y	24-h recall	M	No	Bogalusa Heart Study
Schulze et al (6)	51 603	26–46	4 y	FFQ	SR	Yes	Also for fruit juice
Kvaavik et al (39)	422	15–33	18–20 y	Self-report	M, SR	No	Norway; 18–20 y follow-up
Bes-Rastrollo et al (32)	7194	41	28.5 mo	FFQ	SR	Limited	Only in subjects who gained 3–5 kg in 5 y before study
Case-control							
Bandini et al (33)	43	12–18	NA	14-d diary	M	Yes	Also for fruit juice
Gillis and Bar-Or (34)	181	4–16	NA	Dietary history	BI	Yes	Also other foods
Intervention							
James et al (40)	644	7–11	12 mo	Beverage diary	M	No	No drop in soda intake

¹ NA, not available; NHANES III, third National Health and Nutrition Examination Survey; CSFII, Continuing Survey of Food Intakes by Individuals; FFQ, food-frequency questionnaire.

² Data were from measurements (M), self-reporting (SR), or bioelectrical impedance (BI).

³ Completed by the child's parent or guardian.

(48) and better access to health care. Hence, it is difficult to establish links between obesity and the consumption of a single food, independent of economic variables that may also affect diet choice (48, 49).

BEVERAGES AND BODY WEIGHT CHANGE

Longitudinal cohort studies that address soft drink consumption and body weight change are extremely limited. Researchers have argued that longitudinal data, based on 2 points in time, permit better-informed speculation about causal links than do data from cross-sectional studies (15). Although such observations do provide evidence of parallel temporal trends, they still fall short of showing causality.

The most frequently cited study is one by Ludwig et al (15), which was based on a prospective 19-mo follow-up of 548 schoolchildren ($\bar{x} \pm SD$ age: 11.7 \pm 0.8 y). Sugar-containing drinks were sodas, Hawaiian Punch (Dr. Pepper/Seven-Up, Plano, TX), lemonade, Kool-Aid (Kraft Foods, Northfield, IL), sweetened fruit drinks and iced tea, but not 100% fruit juice. Soft drink consumption at baseline was associated with BMI gains at follow-up (0.18/daily serving). For each additional daily serving during the study period, the children's BMI increased by 0.24, after adjustment for anthropometric, demographic, dietary, and lifestyle variables. Whereas the consumption of sugar-sweetened drinks increased from 1.22 to 1.44 daily servings, fruit juice consumption declined from 1.28 to 1.08 daily servings, so that mean sugar consumption remained approximately the same.

Despite the reported 37 new cases of obesity, the overall prevalence rate did not increase during the study period (27.4% compared with 27.7%). It can therefore be deduced that 35 children who were obese at baseline were no longer classified as obese at follow-up. Their beverage consumption was not mentioned (5).

Berkey et al (2) examined longitudinal changes in beverage consumption and BMI values in a large sample of 9–14-y-olds over 2 successive 1-y periods. Diets were assessed by using food-frequency questionnaires (FFQs), and BMI values were computed from self-reported heights and weights (2). At baseline, 23.2% of the boys and 17.5% of the girls were classified as overweight. In regression analyses, each additional daily serving of sugar-containing beverages (ie, soda, iced tea, and fruit drinks) was associated with a small gain (0.03–0.04) in BMI over 1 y. In other words, each additional 144 kcal of liquid sugar energy consumed per day (ie, 52 560 kcal/y) was associated with a body weight gain of only 100 g at the year's end. Adjustment for total EIs further reduced the associations, which became nonsignificant. Whereas the data seemed to show that sugar-containing beverages had virtually no effect on body weight gain in growing children, that finding was at odds with the title of the study (2).

Welsh et al (5) studied 10 904 low-income children aged 2–3 y by using a retrospective cohort design. Dietary intakes at baseline were assessed by proxy report using FFQs. Heights and weights were measured at baseline and 1 y later. In normal-weight children, no association was found between soft drink



consumption at baseline and later weight gain. In contrast, children at risk (85th–95th percentile) and those already overweight (>95th percentile) who consumed >1 drink/d were twice as likely to become or remain overweight than were children in the referent group (<1 drink/d). That relation persisted after soda drinks were removed from the model. However, no dose-response relation was observed and, if anything, the highest consumption was associated with slightly lower risk.

Blum et al (31) examined the intakes of sugar-sweetened drinks, diet soda, 100% juice, and milk in 99 normal-weight and 48 overweight children (aged \approx 9.5 y) over a period of 2 y. The consumption of sugar-sweetened drinks was not linked either to baseline BMI or to a change in BMI over the 2-y period, contrary to the previous report of Ludwig et al (15). Two recent studies using long follow-up periods (18–21 y) also failed to show the effect of sweetened beverages on body weight gain. One of these studies was based on data from the Bogalusa Health Study (38), and the other was based on a population of young adults in Norway (39).

Longitudinal data in adults are even more limited (6). One report, based on data from the Nurses Health Study, examined sharp changes in the consumption of different beverages in relation to body weight change over a 4-y period. Women who increased their beverage consumption from \leq 1 serving/wk to \geq 1 serving/d were compared with the referent group of women who decreased consumption from \geq 1 serving/d to \leq 1 serving/wk, a major shift. For soft drinks, body weight gain was 4.7 kg versus 1.3 kg for the referent group. For 100% fruit juice, body weight gain was 4.0 kg versus 2.3 kg for the referent group, and for fruit punch the gain was 3.7 kg versus 2.4 kg. All 3 differences were significant ($P < 0.001$). Greater consumption of soft drinks and fruit punch (but not of 100% juice) was also associated with a higher risk of diabetes (6).

A recent study examined the potential effect of soft drinks and fast foods on weight gain in a Spanish cohort of 7194 adult men and women (\bar{x} age: 41 y) over a 28.5-mo period (32). Dietary intakes were based on a 136-item FFQ. Data analyses showed that soft drink consumption was linked to self-reported weight gain—but only in those participants who had gained 3–5 kg in the 5 y before the study. Soft drink consumption was unrelated to weight gain in persons whose prestudy weights were stable. In contrast, the consumption of fast foods (eg, hamburgers, pizza, and sausages) was associated with body weight gain, independent of weight history. These data suggest that the trajectory of body weight gain may be another important, and rarely measured, variable. Although soft drink consumption may exacerbate the problem in an already vulnerable population, other aspects of the diet may be important as well.

DIETARY INTERVENTIONS

Data on the success of interventions are equally sparse. One attempt to reduce soft drink consumption by 7–11-y-olds was based on a randomized, controlled study design (40). The educational program discouraged the consumption of caloric and diet carbonated soft drinks over the period of 1 school year in 6 primary schools. All children were encouraged to drink plain water. A 1-h educational session was assigned for each class each term, and additional support was available on the project's website. The control group was not exposed to the program.

Consumption of carbonated soft drinks was measured in glasses per day (average glass size, 250 mL). At the end of 1 y, the intervention group consumed a smaller amount of caloric and diet carbonated soft drinks (0.6 glass/3 d), whereas the control group consumed slightly more (0.2 glass/3 d). (Because the reported drop in consumption included caloric and diet (0.3 glass for each) carbonated soft drinks, the decline in sugar energy can be estimated at 10 kcal/d. The drop in caloric soda consumption was not significant, and only the cumulative difference (caloric and diet sodas) reached $P = 0.02$. No significant group differences in BMI change were observed. The rates of overweight increased by 7.5% in the control group and decreased slightly (0.2%) in the intervention group. However, those differences cannot be attributed to a decline in the consumption of caloric sodas, because no significant decline was, in fact, observed.

A recent pilot study of 103 middle- to low-income adolescents aged 13–18 y tested the effect of replacing caloric beverages with diet beverages (50). Whereas the intervention group ($n = 53$) received free home delivery of diet beverages over a period of 25 wk, the control group ($n = 50$) continued their usual beverage consumption. Although EIs from the caloric beverages dropped by 82% (1201 kJ/d) in the intervention group, the difference in BMI gain was not significant (0.07 compared with 0.21). The effects of the intervention on BMI were significant only for those 18 adolescents (12 intervention and 6 control) whose baseline BMIs were >30 . Adolescents in the top tertile of BMIs who were in the intervention group showed a modest weight loss (BMI decrease of 0.63 or weight loss of \approx 1.75 kg), whereas those in the control group continued to gain weight (BMI increase of 0.12). In this study, diet beverages had the greatest effect on body weight in the group that needed them the most. The study was also one of the few that took economic factors into account (50).

CONTEXT AND BEHAVIORAL INTENT

Observational studies, whether cross-sectional or longitudinal, provide no information as to why people consume a given food or beverage. This point can be illustrated with reference to the consumption of zero-calorie diet soft drinks, for which the data are highly inconsistent. For example, at baseline, Ludwig et al (15) found no association between diet soda consumption and BMI. In contrast, Berkey et al (2) found a positive association at baseline, but only in boys. Analyses of the cross-sectional 1994–1996 CSFII dataset for 2–19-y-olds found a weakly positive association between diet soda consumption and BMI (30); it was the overweight youth who consumed more diet sodas.

The effect of diet soda consumption on body weight change was not clear. Whereas one study found that diet soda consumption was associated with lower obesity risk (15), another study found that diet soda consumption was associated with higher obesity risk (2). In the second study, the association between diet cola consumption and higher obesity risk was significant in boys but not in girls. In other words, the same studies that linked the consumption of caloric sodas to weight gain (2, 15) linked diet soda consumption to weight gain (2) or to weight loss (15). The authors attributed this discrepancy to the heavier participants' presumed intent to lose weight (2). However, in the absence of information on dieting practices, behavioral intent should not be imputed post hoc from purely observational data. On the basis of



the observed association between increased soft drink consumption and increased EIs from other foods, Schulze et al (6) suggested post hoc that the consumption of caloric beverages may have induced hunger and thus food intake. An alternative hypothesis—that the increased consumption of solid foods induced thirst—was not examined.

LABORATORY STUDIES OF SUGAR AND WEIGHT GAIN

Experimental evidence linking daily soft drink consumption with increased EIs and body weight gain is provided by 3 studies (Table 2). Two were conducted with normal-weight adults who were asked to consume large volumes of sugar-sweetened beverages in addition to their usual diet (51, 52). The third was conducted with overweight adults, who were provided with sucrose- or sweetener-containing beverages and foods in addition to their usual diets for a period of 10 wk (53).

One study provided normal-weight participants with 1135 g of beverages sweetened with either HFCS (530 kcal or 2215 kJ) or aspartame (51). The consumption of caloric and diet sodas reduced the intake of energy from the diet by a nonsignificantly different amount (179 and 195 kcal/d, respectively), which suggests only a partial compensation. As a result, total EIs (including sodas) were higher in the HFCS condition, leading to body weight gain.

Raben et al (53) provided overweight adults with sodas and juices and with solid foods (ie, yogurt, marmalade, ice cream, and stewed fruits) containing either sucrose or intense sweeteners, mostly aspartame. Minimum mandatory consumption of sucrose was set at $2 \text{ g} \cdot \text{kg}^{-1} \cdot \text{d}^{-1}$. Persons in the 60–75 kg weight range consumed 125 g sucrose/d, those in the 75–90 kg weight range consumed 150 g/d, and those weighing >90 kg consumed 170 g/d. The sucrose condition provided an average of 28% of energy from sucrose, or $\approx 152 \text{ g/d}$, 70% of which came from beverages. The energy density of the diet was higher in the sucrose than in the sweetener condition.

Mandatory consumption of sucrose in addition to the usual diet led to higher EIs and to body weight gain. After 10 wk, the sucrose group had higher EIs (1.6 MJ/d), body weight (1.6 kg), fat body mass (1.3 kg), and blood pressure, whereas no change or a decrease was observed in the sweetener group. The likely reason for these differences, according to the authors, was that the provision of sucrose in largely liquid form failed to promote satiety (53).

Using a crossover study design, Van Wymelbeke et al (52) asked young normal-weight subjects to consume 2 L/d (2000 mL or 68 oz) of a distinctively flavored sucrose-sweetened or sugar-free beverage. Food consumption was measured over 2 d. No downward adjustment in diet energy was observed, so that total EIs over 2 d were higher in the sucrose than in the sweetener condition. The participants were then habituated for 4 wk to the distinctive tastes of the caloric and noncaloric drinks, in an effort to promote associative learning. Nonetheless, at the end of 4 wk, they still ingested more energy in the sucrose than in the sweetener condition. In all 3 studies (51–53), mandatory consumption of sugar-sweetened beverages in addition to the usual diet led to higher EIs, a situation that was not corrected after habituation and learning.

CLINICAL STUDIES OF LIQUID SUGAR AND WEIGHT LOSS

Liquid MR products used in clinical studies were sugar solutions supplemented with small amounts of protein and fiber. A typical 325-mL Slim Fast liquid MR shake (Unilever, Rotterdam, Netherlands) contained 36 g sugar (144 kcal out of a total of 220 kcal), 10 g protein, and <2 g fat. The amount of liquid sugar calories was comparable to that in 12-oz caloric soft drinks (34 g/12 oz). In some product formulations, HFCS was listed as the principal sweetener. Although the sugar content of most MR shakes has since been reduced, virtually all studies published in peer-review literature were based on the full-sugar version (26).

The success of HFCS-sweetened liquid sugar shakes in promoting weight loss has been documented in several clinical trials (26). Some of the published studies were based on randomized controlled clinical trials, the gold standard of evidence-based medicine. The partial MR (PMR) program was a low-calorie diet (800–1600 kcal/d) in which up to 2 meals were replaced with liquid MR shakes or with solid bars. The shakes typically provided 30–72 g/d of liquid sugar energy. One 220-kcal solid MR bar contained 20–24 g sugar (average: 22 g), 8 g protein, and 5 g fat. Other products contained $\approx 20 \text{ g}$ of sugar, 1–3 g fat, 7–10 g protein, and up to 5 g fiber (26).

Uniformly described as palatable, inexpensive, and convenient (26, 54), sweetened liquid shakes provided a daily sugar dose (30–72 g/d) that often exceeded the one now associated with soft drinks (30–60 g/d). In one study (55), the MR group was instructed to replace 3 meals/d with a 220-kcal liquid shake, for a total of 108 g sugar/d. In another study (56, 57), 2 of 3 main meals were replaced with liquid shakes, soups, or hot chocolate. Each liquid shake contained 0.84–1.05 MJ, including 27–33.5 g carbohydrate, most of which was sugar. In addition, 2 daily snacks were replaced with solid snack replacement bars that contained 0.38–0.46 MJ energy and 16.1–18.1 g carbohydrate, mostly sugar. HFCS was a key ingredient. Daily sugar consumption, both as liquid and solid, was therefore on the order of 90 g. Ashley et al (58, 59) instructed participants to replace 2 of 3 main meals with liquid shakes containing 35–41 g carbohydrate or with solid bars containing 31–34 g carbohydrate for a total of $\approx 70 \text{ g}$ added sugar/d. The proportion of energy from sugars was $\approx 25\text{--}33\%$, which is comparable to the 28% reported by Raben et al (53), and most of the sugar energy was provided in liquid form. The efficacy of these sugared liquids in promoting weight loss was then compared with that of conventional reduced-calorie diets.

Heysmsfield et al (26) conducted a useful meta-analysis and pooling analysis of randomized controlled PMR interventions lasting $\geq 12 \text{ wk}$ in subjects aged >18 y and with a BMI > 25. Studies with self-reported weights and heights were excluded. Of 30 studies conducted between 1960 and 2001, only 6 met all the inclusion criteria in using liquid MR products and a control condition with an associated diet plan (see Table 2).

All analyses pointed to a significantly greater weight loss in subjects who consumed liquid sugar energy than in those following isoenergetic conventional diets. At 3 mo, 72% of the PMR group lost >5% of body weight, whereas only 34% of subjects on the conventional diet did so. Mean weight loss in the PMR group was 2.5 kg greater at 12 wk and 2.4 kg greater at 12 mo than that in the conventional diet group. Pooling analysis



TABLE 2
Laboratory studies and randomized controlled clinical trials of the effects of sugar solutions on weight change¹

Study (reference)	Subjects	Age	Intervention	Active phase	Estimated sugar intake	Paid for by subjects? ²	Control group intake	Paid for by subjects? ²	Contact	Weight change
Laboratory										
Tordoff and Alleva (51)	30	22–30	2.2 MJ/d	3 wk	133 g/d	Yes	Aspartame; no beverage	Yes	10 Visits	Gain with HFCS
Raben et al (53)	41	20–50	3.4 MJ/d	10 wk	152 g/d	Yes	Intense sweeteners	Yes	11 Visits	Gain (1.3–1.6 kg)
Clinical										
Ditschuneit et al (56)	100	18–65	2 MR, 2 SR (5.0–6.2 MJ/d)	12 wk	102 g/d	Yes	5.0–6.2 MJ/d	No	12 Visits	Loss (7.1 versus 1.3 kg)
Rothacker et al (55)	75	18–55	3 MR (5.0 MJ/d)	12 wk	108 g/d	Yes	5.0 MJ/d	No ²	None	Loss (6.3 versus 3.8 kg)
Yip et al (60)	57	>30	2 MR (2.0 MJ/d)	12 wk	11–72 g/d	NA	ADA diet: 2.0 MJ/d	No	5 Visits	Loss (6.1 versus 4.2 kg)
Ashley et al (58, 59)	113	25–50	2 MR/d (shake or bar)	12 mo	72 g/d	Yes	Lifestyle group	No	26 Visits	Loss (3.5–7.7 versus 3.4 kg)
Allison et al (61)	74	35–65	MR (5.0 MJ/d)	12 wk	75 g Carbohydrate/d	NA	1200 kcal/d	NA	1 Visit	Loss (7.0 vs 2.9 kg)
Noakes et al (62)	66	20–65	2 MR (6.0 MJ/d)	12 wk	72 g/d	Yes	Structured meal	Yes ³	6 Visits; monthly records	Loss (6 versus 6.6 kg); NS
Poston et al (63)	100	33–55	MR (5.0–6.2 MJ/d)	24 wk	MR	NA	MR and snacks	Yes	NA	Loss in all conditions
Ebbeling et al (50)	103	13–18	Diet beverages	25 wk	Decrease of 1.2 MJ/d	Yes	Regular beverages	No	6 Telephone calls	Loss only for subjects with BMI >30

¹ HFCS, high-fructose corn syrup; MR, meal replacement; SR, snack replacement; NA, not available; ADA, American Diabetes Association.

² \$400 Honorarium for each participant.

³ Payment of \$50 Australian/2wk.

strengthened these effects. Overall, the magnitude of the weight-loss effect induced by drinking liquid sugar shakes (ie, 36–72 g sugar/d) was said to be in the range observed in pharmacologic studies (26).

These clinical data stand in stark contrast to the prevailing notion that the consumption of liquid sugar energy has inevitable metabolic consequences leading to weight gain (1, 4, 17, 20). Rather, the studies indicate that sugared MR shakes can safely and effectively produce a significant weight loss (26). The shakes were undoubtedly liquid, they supplied significant sugar energy, and, in some cases, they contained HFCS.

Later studies confirmed the efficacy of liquids in promoting weight loss. Using soy-based liquid shakes with a higher protein and lower sugar content (13 g), Allison et al (61) found that the PMR group lost significantly more weight than did the control conventional diet group (7.0 and 2.9 kg, respectively). In a recent study (63), 100 participants were randomly assigned to 1200–1500 kcal/d diets and asked to consume 2 MR products/d with or without snacks. By 24 wk, mean weight loss across the 2 groups was 4.6 kg. The literature provides further examples of liquid weight-loss diets. In one study, a weight-reducing diet composed only of milk (5.6 MJ/d) led to a loss of 9.4 kg over 16 wk (64). None of the studies reported significant problems with satiety that were specifically due to the consumption of liquid foods. Indeed, liquid sugar shakes were said to be more effective in promoting weight loss than were diets high in vegetables and fruit (26).

The high sugar content of MR shakes used to treat obese diabetic patients has been a concern for some investigators. Yip et al (60) compared the effects of canned liquid shakes containing lactose (11 g), fructose (13 g), and sucrose (8.5 g) on weight loss with the effects of sugar-free shakes containing equivalent concentrations of maltodextrins. Weight losses in the 2 PMR groups were similar and significantly higher than those in subjects following the American Diabetes Association exchange diet. Short-term tests of glucose and insulin responses over time found no differences in the area under the curve after the consumption of a canned (liquid) shake or a solid breakfast. In other words, no evidence for a differential physiologic response to liquid and solid calories was observed in diabetic patients (60).

Only one study did not observe a difference between the PMR strategy and the conventional diet (62). That study randomly assigned 66 subjects to a 6000-kJ/d intervention for 12 wk. The PMR group was supplied with MR shakes and bars (1800 kJ/d) and consumed a low-fat evening meal and fruit as snacks, whereas the control group followed a low-energy, low-fat diet. The magnitude of weight loss did not differ between the 2 groups: 6.0 and 6.6 kg, respectively, at 12 wk and 9.0 and 9.2 kg, respectively, at 6 mo. However, convenience and compliance were viewed more favorably by the PMR group.

THE ROLE OF CLINICAL CONTEXT

If daily consumption of liquid sugar energy (30–60 g/d) can lead either to weight gain or to weight loss, then the discussion needs to shift from human physiology to human dietary behavior. In principle, weight-loss trials with obese patients should have involved motivated patients, a clinical setting, a defined health outcome, and close professional supervision. However, an examination of the literature shows that this was not always the case. Whereas some studies reported that participant meetings

were held weekly, biweekly, or monthly (58, 59), other studies viewed the lack of supervision as a positive therapeutic advantage. Published studies repeatedly noted that no nutrition information was given (65), no advice was provided (62, 65), compliance with diet was not monitored (65) and professional intervention was kept to a minimum (55, 66). One 12-wk study showed that unsupervised patients provided with liquid shakes outside the clinical setting still managed to lose weight (65). The consumption of liquid MR products, whether unsupervised (62) or in a pharmacy setting (67), was just as effective in weight management as the conventional reduced-calorie diets (62, 67).

One study was based on the provision of MR products, free of charge, to 141 overweight participants in rural Wisconsin for a period of 5 y (66). At the end of the study, the sample of 50 men lost a mean of 5.8 ± 5.4 kg, and the 84 women lost 4.2 ± 6.9 kg. In contrast, 142 men in the control group (selected post hoc) gained 6.7 ± 10.2 kg, and 247 women gained 6.5 ± 10.7 kg (66).

The literature repeatedly noted that the shakes were palatable, convenient, and readily accepted by the patients (26). No mention was made of hunger or satiety deficits, and no suggestion was made that liquid calories were not perceived by the body. On the contrary, participants in the PMR group reported a high level of hunger satisfaction (65).

LIQUID CALORIES AND SATIETY

The notion that liquid calories fail to trigger satiety mechanisms (17, 22) is routinely cited to support associations found in epidemiologic studies (1, 4, 6). Yet, a review of the satiety literature found much of it to be inconclusive (23). For the most part, studies of beverages and satiety have measured the short-term effect of a caloric preload, ingested in the laboratory, on hunger and satiety ratings and on EIs at the next meal. Those mechanisms may not translate to dietary patterns measured in the long term. Furthermore, in many of those studies, energy adjustments after ingestion of a preload were influenced by subject characteristics, preload volume, and nutrient composition and by the interval between the preload and the test meal. These factors were often more important than whether the preload was liquid or solid (23).

Despite claims that all liquid calories are not perceived by the body (17), nutritionists have encouraged replacing sodas with 100% fruit juices and with low-fat milk (68). One important question, therefore, is whether the satiating power of soft drinks is the same as that of 100% fruit juices and milk (23, 69, 70). The latter 2 beverages were described as “foods that you drink,” which are capable of triggering physiologic satiety (69, 70). Although their sugar content does vary, caloric cola, orange juice, and milk (1% fat) have equivalent energy density— ≈ 0.4 kcal/g. In one study, the 3 beverages (250 kcal) had identical effects on the temporal profiles of hunger, fullness, and desire to eat for up to 2 h after ingestion (69). However, no energy adjustment at lunch was observed, so that total EIs were higher than those in the sparkling water control condition. Virtually identical results were obtained when 150 kcal caloric cola, orange juice, and 1% milk was consumed with a meal and before a meal (71). Although both studies showed that caloric beverages had little effect on the next meal, there were no major differences between sugared cola, 100% fruit juice, and low-fat (1%) milk (23). Another study, also based on the preload paradigm, failed to show significant differences in satiety profiles of a cola beverage and

an isocaloric amount of solid cookies (24). Both suppressed intake when consumed immediately before lunch (24).

Arguably, the effect of milk or juices on satiety may be modulated by the protein or fiber content of these beverages. MR shakes typically contain protein (13.5 g) and some fiber (5 g), both of which are known to have an effect on satiety, whereas soft drinks generally contain neither. MR shakes and 1% milk have similar protein content (2.9 g/100 g for an MR shake and 3.0 g/100 g for milk). MR shakes contain 5 g fiber/350 mL (1.4 g/100 g), whereas milk and orange juice contain none.

The evidence for the satiating power of protein when administered in beverage form is extremely limited. Although protein is reputed to be more satiating than either sugar or fat, studies have failed to show a strong satiety effect of 1% fat milk (23, 71). On the other hand, drinkable yogurt containing 17.1 g protein/378 g was more satiating than a dairy fruit drink (2.6 g protein/400 mL) or a fruit drink (0 g protein), that were matched for both volume and energy content (72). It may be that protein's satiating effects are threshold dependent or related to protein type, or that they are simply too elusive for the conventional preload study design. Anderson et al (73) found that participants who consumed liquid preloads of milk-based protein (whey) ate more at the next meal than those who consumed liquid preloads of egg-albumen protein.

Dietary fiber has also been associated with greater satiety (74). However, most studies on fiber and satiety have been conducted not with beverages but with solid or semi-solid foods (75, 76), although some studies were conducted with beverages (77). In one study, fiber (< 0.1 g microcrystalline cellulose) added to a beverage increased viscosity and led to higher satiety ratings (78). Participants reported significantly greater satiety when fiber was present in a fruit puree or was added to the stimulus as soluble plant fibers than when it was not present (79). The physiologic mechanisms proposed for the satiating effects of fiber include slowed ingestion time because of the need for chewing, increased gastric distention (signaling fullness), and delayed gastric emptying (74). As yet, no data clarify whether the supposed satiety deficit after the ingestion of sugar-containing liquids can be counteracted by the ingestion of fiber.

The supposed contribution of fructose to weight gain is largely based on extrapolations from animal studies (22). Whereas, in many such studies, the animals were fed pure fructose, HFCS used in soft drinks contains 55% fructose and 45% glucose. Differences in fructose metabolism are minimized when small amounts of glucose are present (80). Almost no studies on fructose and weight gain in humans have been published (21).

THE COST OF LIQUID SUGAR

MR shakes were consistently described as a less costly alternative to very-low-calorie diets (VLCDs) and to prepared foods (62). The point has frequently been made that such shakes cost less than the meal they replace (81). Furthermore, in most clinical studies, shakes and snack bars were provided to the dieting patients at no cost. Ashley et al (58, 59) provided coupons to be redeemed at local stores and distributed snack bars at scheduled group sessions. Winick et al (65) used weekly delivery of 14 powder shakes and 12 snack bars to participants who needed only to buy skim milk. Rothacker (66) provided free MR products for 5 y to 141 overweight adults in rural Wisconsin. In contrast, the

instructions to follow a low-fat diet with plenty of vegetables and fruit were not accompanied by any financial incentive. A few studies either paid all participants \$25/wk over 12 wk (54) or provided \$600 stipends and some free groceries to all participants (82).

Ebbeling et al (50) also provided an economic incentive by supplying sugar-free products to a sample of 103 nondieting adolescents, one-third of whom were obese. Bottled water and sugar-free diet beverages were delivered to each subject's home over a 25-wk period. Each household received the equivalent of four 12-oz servings of noncaloric beverages per day for the study participant and 2 servings/d for each additional household member. A supermarket delivery service filled the orders, delivering 3–5 times/wk. Participants were contacted monthly by telephone to discuss satisfaction and provide motivational counseling, but no other professional intervention was provided. At the end of the study, all participants, including the control group, received a \$100 gift certificate for use at a local shopping mall (50).

Although monetary incentives are known to improve dietary compliance (83, 84), few studies have explored the effect of providing free food to study participants. Providing foods with up to 660 kcal/d free of charge could not have been an insignificant factor for subjects whose reported mean annual income was \$10 420 (66). Receiving beverages worth \$1.50–\$2.00 a day (50), whether caloric or not, may have represented a substantial saving in the food budget of minority families living in subsidized housing in Boston. The population in that study was 66% nonwhite, and 40% had a household income <\$30 000 (50). It is interesting that the reported outcome was weight loss, regardless of whether the supplied beverages were sugared (26) or sugar-free (50).

It may be that the influence of liquid sugar calories on weight control involves economics more than it does human physiology. According to Keogh and Clifton (27), studies that showed the superiority of liquid shakes over conventional diets were those in which the MR shakes were provided for free, but subjects had to pay for the conventional diets. Only one study provided control participants with shopping vouchers with a financial value similar to that of the MR products (62). When equivalent financial incentives were provided to controls, the 2 conditions no longer differed significantly.

Obesity in the United States is associated with limited resources (48). Sugar-sweetened beverages are an inexpensive source of energy in the typical US diet (28). Soft drinks, 100% fruit juices, and MR shakes have roughly the same sugar content per 100 g, as shown in **Table 3**. The sugar content of colas, soft drinks, fruit punches, 100% fruit juices, and liquid shakes is ≈ 10 – 12 g/100 g, which is close to the hedonic optimum for sweet taste. Although some of the currently available liquid shakes have reduced their sugar content by 50%, higher-sugar versions that provide as much sugar as do soft drinks are still available. On the other hand, soft drinks, juices, and MR shakes differ sharply in their energy cost (\$/MJ). Whereas soft drinks cost \approx \$2.50/MJ, the cost per MJ of 100% fruit juices was several times higher. At the high end of the scale, liquid MR shakes cost up to 10 times as much per MJ. Even though the sugar content of all beverages was approximately the same, it was the lower-cost beverages that have been most consistently associated with weight gain (1, 3, 4).



TABLE 3
The price of sweetened beverages¹

Beverages	Sugar content	Cost
	<i>g/100 g</i>	<i>\$/MJ</i>
Tampico Tropical Punch ²	10.8	0.25
Safeway Select Cola ³	12.1	0.32
Reduced-fat Chocolate Milk ⁴	12.3	0.38
A&W Root Beer ⁵	12.9	0.40
Coca-Cola Classic ⁶	11.3	0.44
Sunny D Tangy Original (5% juice) ⁷	11.3	0.44
Hi-C Blast Fruit Pow (10% juice) ⁶	12.7	0.66
Safeway White Grape Juice (100% juice) ³	15.8	0.77
Welch's Grape Juice (100% juice) ⁸	16.7	0.82
Ocean Spray Cranberry Juice Cocktail (27% juice) ⁹	13.8	0.89
Minute Maid Orange Juice (100% from concentrate) ⁶	10.0	0.94
Tropicana Orange Juice (100% pure squeezed) ¹⁰	9.2	1.08
V8 Fusion Fruit & Vegetable Juice ¹¹	11.2	1.49
Slim Fast Optima French Vanilla (low sugar) ¹²	4.8	1.59
Slim Fast French Vanilla Classic (original formula) ¹²	10.8	1.59
Odwalla Orange Juice (100% juice squeezed) ⁶	10.0	2.92

¹ All prices were obtained from www.safeway.com (accessed 23 March 2006).

² Heartland Farms, City of Industry, CA.

³ Safeway Inc, Pleasanton, CA.

⁴ Darigold Dairies, Seattle, WA.

⁵ Dr. Pepper/SevenUp Inc, Plano, TX.

⁶ Coca-Cola Company, Atlanta, GA.

⁷ Sunny Delight Beverages, Cincinnati, OH.

⁸ Welch Foods Inc, Concord, MA.

⁹ Ocean Spray Cranberries Inc, Lakeville-Middleboro, MA.

¹⁰ PepsiCo Inc, Purchase, NY.

¹¹ Campbell's, Camden, NJ.

¹² Unilever, Vlaardingen, Netherlands.

CONCLUSIONS

The argument that liquid calories are not detected by the body (17) has been used to establish a causal connection between the consumption of sweetened beverages and body weight gain. For the most part, the debate about soft drinks and overweight has been couched in biomedical terms, and much attention has been paid to short-term satiety deficits, energy compensation, and sugar metabolism (1, 4, 6, 20, 21). Even though short-term satiety and the long-term regulation of body weight are distinct mechanisms, beverages are said to contribute to obesity by virtue of being liquid and having a high sugar content (4, 6).

However, regular daily consumption of sugared liquids need not automatically result in weight gain. Clinical evidence has shown that regular consumption of sugar-containing liquid MR products by overweight patients can lead to a significant and sustained weight loss (26). Liquid MR shakes, provided free of charge, are the preferred treatment modality in the Look AHEAD (Action for Health in Diabetes) Study (85), a multicenter, randomized controlled trial of 5145 participants undergoing intentional weight loss. Liquid MRs were included in the 1200–1500 kcal diet because they simplified food choices (85), improved

glycemic control (85), and led to a significantly greater weight loss as compared with isocaloric diets composed of conventional foods (85).

Given that the consumption of sugared liquids can be linked to loss as well as to weight gain, it may be time to focus on dietary behavior (86). Whereas sugar-sweetened soft drinks are consumed with meals, sugar-sweetened MR shakes are consumed instead of meals (26, 85). Evidently, the critical issue is not sugar metabolism but the way that sugar is used by the consumer. In a departure from the notion that all liquids fail to promote satiety (17, 22), one brand of canned liquid MR shakes is marketed with such slogans as “helps control hunger” and “prevents hunger longer” (87), which presumably had been approved by the Federal Trade Commission.

The current advice would be to focus on the psychological as well as the physiologic aspects of weight management. Successful weight management requires cognitive control of EI, a healthy lifestyle, and successful adherence to low-energy diets (85). And if context and dietary behavior become the key issues, then the notion of a physiologic satiety deficit after liquid sugar consumption (17) loses much of its popular appeal.

At this time, the epidemiologic evidence linking beverage consumption to the global obesity epidemic is still weak (88). Given that most of the studies were conducted in the United States (1, 3, 8), a clear need exists for additional international comparisons. For example, although France has experienced a sharp rise in childhood obesity rates (89), the consumption of sugars has traditionally been low (10–15 g/d), HFCS has not entered the food supply in significant amounts, and the consumption of soft drinks is far lower than in other European countries (89). Because of a trade dispute, Mexico instituted in 2003 an internal tax on US-manufactured HFCS, which resulted almost immediately in the near-total replacement of HFCS in soft drinks with sucrose (90). Whether this measure will reduce the high prevalence of overweight and obesity in Mexican children (91) remains to be seen.

The cost of sweetened beverages, documented in Table 3, is another unexplored issue. It would appear that the obesity-promoting capacity of different beverages is linked not so much to their sugar content (which is the same) but to their low price. Obesity has been linked to limited economic resources (48) and may involve preferential selection of low-cost beverages and foods (49). Studies of diet sugar content, dietary choices, and health outcomes should take diet costs into account (48, 49).

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