CORRESPONDENCE

Sugar-Sweetened Beverages, Genetic Risk, and Obesity

TO THE EDITOR: In the Discussion section of their article regarding the cause of and responsibility for obesity, Qi et al. (Oct. 11 issue)[1] state that "persons with a greater genetic predisposition to obesity appeared to be more susceptible to the deleterious effects of sugar-sweetened beverages" on body-mass index (BMI). Their study, which used the "genetic-predisposition" score, provides support for our study[2] and other studies that use directly measured adiposity and show gene–environment (diet) interactions. In contrast to the self-reported anthropometric variables in the study by Qi and colleagues, such smaller studies allow accurate measurement of body composition (with the use of dual-energy x-ray absorptiometry) and prevent residual confounding. Furthermore, using twin modeling techniques, we found separate and shared genetic factors influencing both total and central adiposity.[3]

The finding by Qi et al. that greater consumption of sugar-sweetened beverages was related to an elevated BMI is most simply explained by common appetite-regulating genes, as shown in monogenic obesity disorders[4] and the fat-mass and obesity–related (FTO) genetic variant[5] in children. Public health policy should reflect the scientific basis of food intake in humans.

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No potential conflict of interest relevant to this letter was reported.

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TO THE EDITOR: Ebbeling et al. (Oct. 11 issue)[1] report that reducing the consumption of sugar-sweetened beverages was effective in changing the BMI and body weight in only a small number of Hispanics, and it had no significant effect in non-Hispanic whites. However, data suggest the public health impact will probably be minimal. Such a reduction overlooks a more likely culprit that pervades the food supply — high-fructose corn syrup. A common assumption is that high-fructose corn syrup is no different than table sugar (sucrose). However, sucrose has equal proportions of glucose and fructose joined by a glycosidic bond. High-fructose corn syrup comprises free fructose and glucose in varying and unregulated proportions. A recent study showed

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that popular sugar-sweetened beverages had almost twice as much fructose as glucose.[2] Head-to-head comparisons reveal that these differences matter.[3] Given the unique way in which it is metabolized, fructose may drive obesity and metabolic risk.[4] Rather than focusing on sugar-sweetened beverages, a broader "systems approach" to reduce the unnatural levels of free fructose from the use of high-fructose corn syrup in diets might be more effective.[5]

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No potential conflict of interest relevant to this letter was reported.

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TO THE EDITOR: The study by Ebbeling et al., which was designed to decrease consumption of sugar-sweetened beverages in overweight and obese adolescents, showed that the increase in BMI was smaller in the experimental group than in the control group after a 1-year intervention, but not at the 2-year follow-up.

We suggest that the similar BMI at the 2-year follow-up in the two groups, despite a lower energy intake and decreased television viewing, could be explained by a different adipose-tissue distribution that may be quantified by commonly used surrogate indexes of visceral adiposity.

Studies[1] have shown that a high intake of fructose, a key ingredient in many sugar-sweetened beverages, can increase the accumulation of triglycerides in visceral adipose tissue and lead to new lipogenesis and hepatic insulin resistance. Pollock et al.[2] have recently shown a correlation between dietary fructose and visceral adipose tissue, and they found an association with several markers of cardiovascular disease in a group of adolescents.

Therefore, in addition to the BMI, quantifying adipose-tissue distribution[3] with simple measures such as waist circumference and waist-to-height ratio could improve evaluation of the effectiveness of the educational intervention.

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DRS. QI AND QI REPLY: Greenfield et al. refer to their previous findings in a twin study suggesting gene–environment interactions in relation to body composition.[1] These findings provide support for the interactions between sugar-sweetened beverage intake and a genetic-predisposition score (derived from 32 BMI-associated genotypes) in relation to body adiposity and obesity risk observed in population-based cohorts. Subsequent to our article in the *Journal*, we also reported that sedentary behavior and physical activity might modify the genetic predisposition to elevated adiposity.[2]

The interpretation of underlying mechanisms of the observed gene–environment interactions is not straightforward. It is possible that common appetite-regulating genes may be involved, since many of the obesity genes are highly expressed in the brain, especially the hypothalamus; this suggests the potential roles of these genes in central regulation of energy intake and expenditure.[3] However, we could not rule out the involvement of other pathways, since the biologic functions of the most established obesity loci are largely unknown.[4] Nevertheless, our findings regarding gene–environment interactions suggest that diet and lifestyle modifica-

tions hold promise in reducing the risk of obesity attributed to genetic susceptibility.

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Since publication of their article, the authors report no further potential conflict of interest.

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DRS. EBBELING AND LUDWIG REPLY: Goran argues that the impact of public health measures targeting sugar-sweetened beverages will be minimal because high-fructose corn syrup differs metabolically from sucrose. However, sugar-sweetened beverages currently compose the primary source of dietary fructose (and total sugar) among adolescents.[1] Moreover, the physiological relevance of the chemical difference between fructose and glucose remains unclear. The most important natural source of fructose in human diets, whole fruit, is associated with a reduced risk of obesity and related metabolic disorders.[1,2] Moreover, glucose may stimulate hunger to a greater degree than fructose, as shown in classic studies by Spitzer and Rodin at Yale.[3] We would also argue that the larger intervention effect in Hispanics in our trial may have considerable public health importance, if confirmed in future studies, because of the increasing number of Hispanic Americans and their increased risk of obesity-related disease.[4]

We agree with Malavazos and colleagues that our experimental and control groups may have differed with respect to body-fat distribution (or, for that matter, body-fat proportion) at 2 years, even though BMI did not differ significantly at that time. We recognize that BMI is an imperfect indicator of body composition and provides no information regarding body-fat distribution. However, adipose-tissue depots are difficult to quantify in school-based studies.[5] Although waist circumference can be measured for minimal cost and used as a proxy for imaging methods to assess abdominal fat, these measurements do not differentiate between subcutaneous and visceral adipose tissue. High-resolution methods such as magnetic resonance imaging may be informative in future studies of sugar-sweetened beverages and health in adolescents and persons in other age groups.

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Peripheral-Blood versus Bone Marrow Stem Cells

TO THE EDITOR: Anasetti et al. (Oct. 18 issue)[1] report on an evaluation of bone marrow versus peripheral-blood stem cells for unrelated-donor transplantation. The overall outcomes were similar, but the incidence of chronic graft-versus-host disease (GVHD) was higher among recipients of peripheral-blood stem cells than among recipients of bone marrow, and patients who received bone marrow had a 9% incidence of graft failure. This rate is much higher than rates reported in studies from the 1990s.[2] Currently, many harvested products are shipped overseas and are often close to 20 hours old by the time they reach the transplantation center. In the case of major