Reply to RF Burton

Dear Sir:

The letter from Burton addresses an important issue regarding the use of a fat mass index (FMI). Similar to BMI, the goal of expressing fat mass relative to height is to have an index of body fat that is independent of overall body size. Burton proposes that (fat mass)/height^3 is a more appropriate formulation for FMI compared with (fat mass)/height^2. The changes in body proportions and body composition during childhood and adolescence are indeed complex, so the task of identifying the optimal index across the entire age range is challenging. There were multiple considerations in our selection of (fat mass)/height^2 rather than other indexes such as the one proposed by Burton.

The primary rationale for expressing fat mass relative to height squared in our article (1) was to generate reference data for fatness that could be readily compared with existing means of assessing adiposity in the pediatric population. BMI, calculated as (body mass)/height^2, is the most widely used method to screen for excess adiposity in children and adults. Because of the familiarity with BMI as a frame of reference across the research, clinical care, and public health spectrums, FMI is a meaningful measure.

It is important to note that BMI is a measure of body mass that is independent of height in adults (2), but this is not the case in the pediatric population in whom a positive correlation between height and BMI is generally seen (3, 4). The same is true for fat mass. The true value of p [as in the equation FMI = (fat mass)/height^p] necessary to eliminate the correlation between height and FMI and BMI has been investigated previously and found to vary across the pediatric age range (5, 6). Cross-sectional correlations between height and measures of adiposity including BMI, FMI [(fat mass)/height^2], and FMI3 [(fat mass)/height^3] at each age for children aged 8–20 y in our NHANES sample are shown in **Figure 1**. For all 3 measures, the correlations with height tend to be highest around the ages of the adolescent growth spurt and are lower at older ages. Although the correlation with height was lower for (fat mass)/height^3, the use of (fat mass)/height^3 did not eliminate the positive correlation with height seen among younger children and resulted in a larger negative correlation among older children.

Most important, it is unclear whether the ideal index of adiposity should be independent of height because this may mask biological associations between adiposity and height (7). Studies have found that height-independent formulations of body mass and fat mass may be inferior for the detection of cardiometabolic risk factors compared with traditional formulations of BMI and FMI (6, 8). To our knowledge, there are no studies that show that (fat mass)/height^3 is superior to FMI or BMI in identifying children at increased cardiometabolic risk.

Burton also maintains that curves for (fat mass)/height^3 are preferable to FMI because they more closely resemble those for percentage body fat (%BF). The rationale for using %BF as the gold standard comparator is unclear, because he acknowledges that %BF fails to take into account the independent contributions of fat and lean body mass. The decrease in the median %BF for boys aged 11–17 y is likely a result of the rapid accumulation of lean body mass during puberty. The use of FMI and lean body mass index allows for the independent evaluation of fat and lean body mass, and thereby would allow for an individual who has accumulated excessive fat mass in addition to lean mass to be identified for screening. That same individual with high fat and lean body mass would be missed if %BF were used as the screening tool.

In summary, the letter by Burton underscores many of the challenges in analyzing body composition in children. Reference curves for lean body mass index and FMI for children and adolescents are now available, so that future body composition studies have a frame of reference with which to evaluate lean and fat mass relative to height and age. Interested clinicians and researchers may use an online calculator to convert dual-energy X-ray absorptiometry measures of whole-body fat and lean body mass into age- and sex-specific z scores (http://www.research.chop.edu/web/zscore/). It is our hope that the scientific community will use this reference data in future studies aimed at the assessment of body composition in diverse patient populations and its relation to health outcomes.

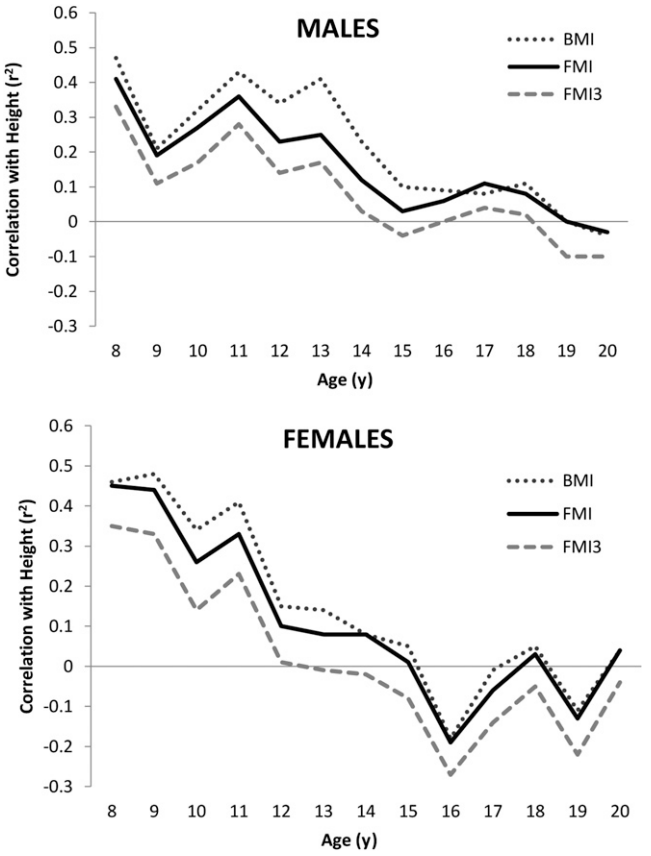

FIGURE 1. Cross-sectional correlations between height and BMI, FMI [(fat mass)/height^2], and FMI3 [(fat mass)/height^3] among 7336 NHANES participants aged 8–20 y. Pearson's correlation coefficients are shown. FMI, fat mass index.

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David R Weber

Department of Pediatrics
The Children's Hospital of Philadelphia
Philadelphia, PA

Reneé H Moore

Department of Statistics
North Carolina State University
Raleigh, NC

Mary B Leonard

Department of Pediatrics
The Children's Hospital of Philadelphia
Philadelphia, PA

Babette S Zemel

Department of Pediatrics
The Children's Hospital of Philadelphia
3535 Market Street
Philadelphia, PA 19104
E-mail: zemel@chop.edu

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Primate fructose study misses mark due to preventable design flaws

Dear Sir:

A recent article by Kavanagh et al (1) concluded that high exposure of fructose to primates (24% of total energy) induces hepatic lipidosis when consumed ad libitum for periods >1 y and significant liver damage brought about by inflammation when consumed under short-term, calorie-controlled conditions. Although the study aims to supply the primary mechanism by which high dietary fructose exposures provoke human metabolic disease, it misses the mark due to preventable design flaws.

First, the presentation of percentage of nutrients in the authors' Table 1 obscures critical differences in composition between control and high-fructose (HFr) diets. Perhaps for reasons of convenience, but inexplicable from a nutritional standpoint, the authors chose to formulate the purified HFr diet with different carbohydrate, protein, and fat sources than found in the Purina chow control diet. However, it has been known for nearly half a century that formulation choices can profoundly influence metabolic outcomes: the seminal work of Kritchevsky et al (2–5) thoroughly explored nutrient interactions in animals, including primates, and showed unequivocally that blood lipids and the course of atherosclerosis are materially affected by interactions between type and amount of protein, carbohydrate (including fructose), and nonnutritive fiber.

Second, the authors offer a meaningless comparison of extreme fructose amounts, both too low (control) and too high (HFr) to be within the normal range of human, and surely primate, consumption. Low fructose amounts comparable to the control group ($\leq$0.5% of energy as fructose) would be achievable only by those subsisting on a diet of starches, protein, and fat; no fruit or vegetables and no added sugars. The high fructose value in the HFr diet (24% of energy) may have arisen from a misreading of Marriott et al's (6) fructose exposure data: the authors appear to have selected the 95th percentile of fructose intake as a percentage of carbohydrate intake for adolescent US males (24.6%; Marriott et al's Supplemental Table 3) instead of the correct 95th percentile fructose intake as a percentage of energy intake (14.6%; Marriott et al's Supplemental Table 2). For clarification, the population subgroup identified by Marriott et al with the highest fructose intake was young adult women (19–22 y), with 17.9% of energy as fructose. As a result of this oversight, the HFr monkey group was exposed to an amount of fructose >30% above the most extreme human consumers of fructose.

Finally, it is disconcerting to find errors in the article and in the accompanying press release (7) mischaracterizing the composition of experimental and common ingredients and exaggerating the dietary prominence of fructose. According to the authors' Table 1, protein in the control group diet was composed of whey, grain, and fish meals, not soy protein. Fructose is not the main sugar in corn syrup, a fructose-free food ingredient composed entirely of glucose and glucose oligosaccharides. And whereas fructose is certainly 1 of the 2 most commonly added sugars (with comparable glucose) in the American diet, its metabolic influence is surely diminished by the 5-fold surplus of glucose from all dietary sources (8).

In summary, the study by Kavanagh et al (1) aiming to explain how high dietary fructose provokes human metabolic disease misses the mark. Preventable design flaws in diet formulation and fructose dosing leave the study with little relevance to human health.

As a consultant and advisor to the food and beverage industry in the area of nutritive sweeteners, the author receives compensation from scientific societies, research institutes, food industry councils, trade organizations, and individual companies. Clients have an ongoing interest in nutritive sweetener research, development, production, applications, safety, nutrition, and education.

John S White

White Technical Research
8895 Hickory Hills Drive
Argenta, IL 62501
E-mail: white.tech.res@gmail.com

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