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## New horizons for glycemic index research

Dear Sir:

A recent editorial by Pereira (1) in the Journal presented several important perspectives on studies of the glycemic index (GI) and glycemic load in relation to weight status. Most of these perspectives related to the interpretation of findings reported thus far from epidemiologic studies, and Pereira looks forward to studies yet to be conducted. It is important also to recognize that, in addition to various analytic issues, numerous potentially serious methodologic problems exist with respect to the application of the GI to studies of usual diet; these problems have to do with the index itself. Such concerns were noted both during the 1980s (2) and more recently (3). They include, but are not limited to, the derivation of the underlying GI values for specific foods from studies of glucose excursion in response to ingestion of the food after an overnight fast, whereas much of the food consumed as part of a usual diet is consumed during the postprandial interval. And, as Pereira appropriately noted, habitual diets that have a low GI may simply be generally prudent diets, with frequent consumption of nutrient-rich and fiber-rich foods, as recently described (4). Dietary fiber, the type of carbohydrate, and the processing of carbohydrate-containing food do seem to matter to glucose and insulin metabolism and related health outcomes. It is extremely important that our understanding of these processes is advanced. Pereira noted inconsistencies in the literature and called for longer, high-quality, randomized controlled trials. I suggest that, before such trials are conducted, new work be conducted to address methodologic problems and to advance our understanding of the underlying construct of the GI. Without further work to better characterize aspects of carbohydrate-containing foods that affect health, we risk spending limited research dollars to produce studies that will continue to be sometimes positive and sometimes negative, but we will still lack the underlying knowledge required to understand those findings.

The author had no conflict of interest.

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## Reply to EJ Mayer-Davis

Dear Sir:

Mayer-Davis feels that further methodologic research is needed to better understand the glycemic index (GI) before moving forward with more definitive randomized trials on GI and body weight regulation and related health outcomes. As evidence that GI has questionable clinical importance in free-living settings, she refers to her null findings on associations between GI derived from a food-frequency questionnaire (FFQ) and measures of fasting and postprandial glycemia in a relatively small study of a multiethnic cohort (1). However, the use of glycemic endpoints, as attractive as they are for characterizing diabetes risk, does nothing to overcome the shortcomings of the FFQ that I pointed out in my editorial (2) on the study by Hare-Bruun et al (3). Whether the endpoint is body weight, serum glucose concentration, glycosylated hemoglobin, or frank diabetes or any other malady, if dietary intake is assessed with an instrument of dubious validity, a good chance exists that the finding will be null and uninformative. Indeed, the validation study of the FFQ used in the study described by Mayer-Davis revealed correlation coefficients for total carbohydrate, between the FFQ and eight 24-h dietary recalls, ranging from 0.25 to 0.64 across ethnic groups. Overall, a validity correlation of 0.37 was noted for energy-adjusted, log-transformed carbohydrate. That is, the FFQ-derived carbohydrate intake explained only 14% of the variance in the 24-h recall-derived carbohydrate intake (4). Bias toward the null and negative publication bias are rampant in secondary data analysis of existing cohort studies. Certainly, future studies should aim to test the validity of GI and glycemic load (GL) from FFQ- and diet history-based data. My strong suspicion is that the validity correlation will be similar to that for total carbohydrate—somewhere on the order of 0.4 to 0.6.

Several fruitful, well-controlled intervention studies on the topic of GI and body weight regulation have been conducted in the recent past (5–9). Although not entirely consistent in their findings, these studies laid the groundwork and provided the preliminary evidence in support of larger and longer studies. Whereas more contributions may come from basic food chemistry studies that attempt to learn more about the effect of specific starches, sugars, and fibers on postprandial glycemia, it would not be prudent to lose the momentum we have gained from the more applied, clinical intervention studies. A recent randomized controlled feeding trial conducted by McMillan-Price et al (5) examined daily variations in blood glucose

