sure glycemic index; however, nonstandard methods were used (2). Discarding means with inconsistent values is questionable; bootstrap analysis of our data (2) suggests, paradoxically, that the discarded means may be more reliable estimates of the true mean than the remaining ones.

Different blood sampling schedules influence the mean and variation of glycemic index values (3). Using our data (five foods tested by 47 subjects) (2), we found that the average SD of glycemic index values calculated from glucose results for the blood sampling times used by Alfenas and Mattes was 35, compared with 29 for the recommended seven blood samples. If a glucose meter is used to measure glycemic index the SD is increased by ~15% (4); thus, we estimate the SD of glycemic index values determined using Alfenas-Mattes methodology to be $35 \times 1.15 = 40$. With SD = 40 and $n = 3$, the 95% CI of a mean glycemic index value is ±99, and the chance of obtaining a mean within ±10 of the true mean is only ~33%. Thus, it is likely that the glycemic index category (high or low glycemic index) of many of the foods was misclassified. This is consistent with the failure to detect a difference in glucose response on day 1 of the period when subjects consumed only one food for breakfast.

Also, Alfenas and Mattes compared glycemic responses elicited by low– and high–glycemic index foods in different groups of subjects. Since large between-subject variation of glycemic responses exists, groups of normal subjects can have different means; e.g., the mean response after 50 g glucose in different groups of 10 subjects of similar ethnicity varied from 153 to 210 (2). Between-subject variation is a confounding variable the authors have not accounted for.

The combination of these several methodological problems seriously undermines the reliability of the results.

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Influence of Glycemic Index/Load on Glycemic Response, Appetite, and Food Intake in Healthy Humans

Response to Ludwig and Roberts and to Wolever and Brand-Miller

We are pleased to respond to the comments of Ludwig and Roberts (1) as well as Wolever and Brand-Miller (2). We will address the points raised by the former first.

Ludwig and Roberts state that we "conclude that the glycemic index values of individual foods do not predict glycemic response to mixed meals." Actually, we go beyond that and demonstrate that the glycemic index value of individual foods do not even reliably predict the glycemic response to that food alone. Indeed, Jenkins et al. (3) showed 15 years ago that the glycemic response to the gold-standard stimulus, glucose in water, depends on the timing of ingestion.

Second, Ludwig and Roberts state that "[b]ecause the observed glycemic response did not differ between diets, the lack of effect on appetite is not surprising." This assumes glucose or insulin is a key determinant of appetite. While both are correlated with hunger after meals, this is not evidence for causality. Euglycemic clamp studies demonstrate that independent manipulation of plasma glucose or insulin does not alter reported hunger (4).

Third, a question is raised about the adequacy of the methods used to select study foods. This concern was surprising because we considered this a study strength. We selected potential foods from the 2002 International Table of Glycemic Index and Glycemic Load Values (5). This table includes values verified as being determined by methods proposed by the Food and Agriculture Organization of the United Nations and the World Health Organization, as Ludwig and Roberts recommend. However, we then conducted a second round of testing, albeit less vigorous, to verify the values. Thus, the foods were more vigorously tested than in nearly any other published study. In addition, each food, not the combined mean, was comprised of comparable macronutrient composition, energy density, and palatability. This reduced several additional common confounds to study interpretation.

Interestingly, Ludwig and Roberts note that "the composition or manufacturing procedures of individual products may change over time, and shelf life and preparatory methods may also affect glycemic index." This is the very reason we question the utility of expected glycemic index influences on outcome measures. Given this agreed-upon fact, the concern with our test foods leads to an untenable argument that this variability does not negate the predicted responses of glycemic index diets in free-living consumers but does in more controlled clinical trials.

Fourth, Ludwig and Roberts state, "There are many studies demonstrating that the glycemic index of individual foods predicts response to mixed meals when appropriate methodology is utilized." We recognize there are studies finding associations, but to be fair to the literature, it should be acknowledged that there are also those that do not (6), and the latter are likely under-represented due to publication bias. It is in part this reason that glycemic index diets have not been endorsed for weight management by most biomedical societies and governmental agencies.

Wolever and Brand-Miller raise three points. The first reflects the same misunderstanding expressed by Ludwig and Roberts regarding the criteria we used for food selection. Their power analysis assumes the foods were only tested by 3

individuals when, in effect, they were tested in 13 (10 before their publication [5] and 3 more by us for verification), a level that exceeds any research recommendations, including their own (7).

Next, they state, "Discarding means with inconsistent values is questionable[. . .]." It is difficult to imagine that contrasting responses to foods with reliable glycemic index/glycemic load values is a methodological flaw. The fact that predictive power improves with inclusion of foods eliciting unreliable responses suggests that either a property other than glycemic index is responsible or that only a subset of individuals are responsive to the property. Both options undermine the utility of the glycemic index concept.

Finally, Wolever and Brand-Miller recognize that "large between-subject variation of glycemic responses exists." This recognition is completely consistent with our findings and undermines the predictive value of the glycemic index classification of foods. The glycemic index rating is a property of a food, not a response of an individual. There would be no point in testing foods and publishing their glycemic index values, as these authors have done, nor creating diets based on this property if individual responses to their ingestion are highly variable.

In the larger picture, our findings do not argue against the potential health benefits of a low–glycemic index diet. The balanced inclusion of fruits, vegetables, nuts, legumes, and whole grains that comprise such a diet are wholesome and may aid weight management through mechanisms independent of their glycemic index rating.

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Standards of Medical Care in Diabetes

Response to position statement of the American Diabetes Association

I write in reference to the recently updated and circulated "Standards of Medical Care in Diabetes," in particular part II, "Screening for Diabetes," which were recently updated and published in the American Diabetes Association (ADA) 2006 Clinical Practice Recommendations (1). I would like to take issue with the use of the phrase "standards of medical care in diabetes," which is used to title all the individual components of these recently updated ADA guidelines. I think this phrase is unhelpful for both the health care community and the public at large, in that it strongly suggests that these guidelines are the definitive source to inform a "standard of care" for diabetes. Any deviation from the guideline may then be interpreted as "substandard care."

A number of these guideline recommendations cite a level of evidence "E" (i.e., based on "[e]xpert consensus or clinical experience"). In most taxonomies, this is considered the weakest level of evidence available. The U.S. Preventive Services Task Force (USPSTF), in their most recently circulated guidelines, assigns an "I" ("inconclusive") rating to whether asymptomatic individuals should be routinely screened for type 2 diabetes and a "B" rating ("fair evidence that the services improve important health outcomes and concludes that benefits outweigh harms") to screening adults with hypertension or hyperlipidemia.

Given the importance of defining a standard of care for any disease management, I teach medical students that well-constructed guidelines developed by a nonpartisan group and based on a good level of evidence (such as the "B" rating by USPSTF) are the best informants of standard of care. Given the "I" rating by USPSTF, there clearly is room for clinical judgment when it comes to screening the general population. I respectfully suggest that it would be more helpful if the ADA guidelines, instead of being titled "Standard of Medical Care in Diabetes," were titled something like "ADA Consensus Panel Guidelines."

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Standards of Medical Care in Diabetes

Response to Power

We would like to thank Dr. Power for his letter (1) and allowing us to comment on the appropriateness of the title for our clinical practice guidelines, the evidence levels used in our guidelines, and specifically our recommendation regarding screening for type 2