Glycemic index is as reliable as macronutrients on food labels[1]

Dear Editor:

In a recent article, Matthan et al. (1) measured glucose and insulin responses elicited by 50-g available carbohydrate portions of white bread and glucose in 63 subjects. They concluded that the substantial variability in individual responses to glycemic index (GI) value determinations makes GI an unreliable approach to guiding food choices. This conclusion is false and based on a common misunderstanding.

Matthan et al. confuse the terms "glycemic response" (a variable characteristic of an individual) and "glycemic index" (a property of a food that is assessed with the use of human subjects). They state in the Introduction that "The objective of the present study was to determine the intraindividual and interindividual variability in *glycemic response* to a single food challenge and potential methodological and biological factors that could mediate responses among healthy adults" (our italics). However, the results and conclusions do not refer to glycemic responses, but rather to GI. The distinction between "glycemic response" and "GI" is more than a matter of semantics: GI is widely recognized to have clinical (2–4) and public health (5) significance and it would be irresponsible to discard this evidence for inadequate reasons. People have glycemic responses; foods have GI values. The former is well known to vary substantially due to intra- and interindividual variations in carbohydrate metabolism; the latter is reliable and reproducible with the use of standardized methodology.

Matthan et al. (1) reported that the mean ± SD GI of Pepperidge Farm Original White Bread was 62.4 ± 15.3, and they consider this amount of variation to be substantial enough to show that GI should not be used to guide food choices because of the potential to misclassify foods as low (GI $\leq$55), medium (56–69), or high (GI $\geq$70) GI. However, this interpretation is incorrect. The GI of a food is the mean in $n = 10$ subjects (5). Thus, with an SD = 15.3, the SEM for $n = 10$ subjects would be 4.8 and the 95% margin of error, by using the t-distribution, would be 10.9. This margin of error, 10.9, is much smaller than the difference between low- and high-GI categories (i.e., 70–55 = 15), and there would be a chance of $<$1% of misclassifying a high-GI food as low GI. The margin of error is ±17% of the mean, which is less than the ±20% difference that is legally allowed between the measured macronutrient or fiber content of foods and the values on the Nutrition Facts table (6), and thus is within the range accepted by regulatory authorities for labeling macronutrients. Furthermore, the GI values of common foods vary across a range from 35 to 90, implying that there are highly significant differences in GI between common foods. Therefore, contrary to the authors' contention, the variability in GI values they observed is sufficiently small to support the utility of GI for distinguishing between high- and low-GI foods.

Furthermore, it is illogical to reject GI as an approach to guiding food choices on the basis of high intraindividual variations in glycemic responses. On this basis, therefore, we should also discard glucose-tolerance testing for the diagnosis of diabetes and carbohydrate counting in the management of type 1 diabetes. The purpose of the GI is not to indicate what an individual's glycemic response will be on any one eating occasion but rather to indicate which carbohydrate-containing foods will produce, on average, relatively different responses. The utility of GI in this respect has been shown by studies showing that GI is a significant determinant of the mean glycemic response elicited by a range of test meals of varying nutritional composition tested in a group of subjects (7) and a significant determinant of individual glycemic responses elicited by self-selected breakfast meals in a large number of subjects (8).

Matthan et al. (1) indicate that subject glycated hemoglobin explained 16% of the interindividual variability in mean GI without indicating if this correlation was significant nor whether there were any outliers driving the relation. This finding conflicts with the results of other studies that showed a similar ranking of foods according to mean GI among individuals with glycated hemoglobin values varying from normal to poorly controlled diabetes (9, 10).

One of the major objectives of the study by Matthan et al. (1) was to investigate methodologic factors that could influence the results; they found that the mean GI value depended on the length of time that blood was sampled and the method of calculating the AUC, that intraindividual variation tended to become smaller as the number of reference tests increased, and that increasing the number of subjects from 10 to 63 had little or no effect on the mean or SD value. All of these findings support current GI methodology, which dictates that GI must be determined by using a standardized protocol: a defined method for calculating AUC, a defined blood sampling schedule, at least 2 tests of the reference food, and with the use of at least $n = 10$ subjects.

In summary, Matthan et al. confirm the well-established observation that individual glycemic responses vary substantially. However, their results do not impeach the validity of GI, nor do they undermine evidence from clinical trials and observational research that show important public health benefits of reducing GI.

TMSW and his wife receive payment as officers and part owners of Glycemic Index Laboratories, Inc. (GI Laboratories) a contract research organization. However, neither they, nor GI Laboratories, have any financial interest in any intellectual property developed as a result of research done at GI Laboratories and have no equity in companies that produce or sell food products. LSAA has co-organized an International Summit on Glycemic Index, Glycemic Load, and Glycemic Respone (2013) and received honoraria from the Nutrition Foundation of Italy (NFI, Milan) and from Lega Italiana per la Lotta Contro i Tumori (LILT-Catania). JCB-M is the co-author of books about the GI and is president of a not-for-profit food endorsement program related to the GI (www.gisymbol.com). She manages a GI testing service at the University of Sydney (SUGiRS). She has no equity in companies that produce or sell food products. ED is the co-author of books pertaining to the GI. She is a founding member,

[1] A Supplemental Appendix is available from the "Online Supporting Material" link in the online posting of the article and from the same link in the online table of contents at http://ajcn.nutrition.org.

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co-owner, and research manager of the GI Foundation of South Africa (GIFSA), which conducts GI testing, and also conducts a food endorsement program, as approved by the Department of Health (Republic of South Africa). She and her partner both receive salaries from the GI Foundation SA but have no equity in companies that produce or market foodstuffs. GL holds shares in Independent Nutrition Logic, UK, a company that works with a wide range of food companies, academics, health professionals, and governmental organizations, some of which seek information and advice about the GI. DSL received royalties for books on obesity and nutrition, including a popular diet book advocating a carbohydrate-modified diet. He has advocated for lowering consumption of processed carbohydrates in scholarly articles, professional society meetings, testimony to the government, and in the media. JLS has received research support and served on the scientific advisory board and/or received travel support and/or honoraria from multiple food companies and marketing boards (details in the **Supplemental Appendix**). His wife is an employee of Unilever.

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Reply to TMS Wolever et al.

Dear Editor:

Wolever et al. criticize terminology but do not question the conclusions of our work (1), that the use of the recommended approach to determine the glycemic index (GI) value for a simple food, white bread, results in highly variable individual responses, such that among a group of 63 healthy individuals, the GI value for white bread ranged from 35 to 103. Although this resulted in a mean GI value of 64, classifying it as a medium-GI food, it is important to note that only for 23 volunteers did the GI value for white bread fall within the medium-GI range (56–69). For the remaining 40 volunteers (63% of our study population), blood glucose responses to the carbohydrate in white bread were between GI values of 35 and 55 ($n = 22$) or 70 and 103 ($n = 18$) for the blood glucose response to pure glucose, thus classifying white bread as a low-GI food or high-GI food, respectively. On the basis of these data we concluded that labeling foods with a single GI value was not useful, and for some individuals could be misleading. This substantial variation in GI value observed in our study is consistent with that reported by previous researchers (2–6).

Nonetheless, Wolever et al. continue to attempt to justify the inclusion of GI values on food labels on the basis that the "margin of error is $\pm$17% of the mean; less than the $\pm$20% difference which is legally allowed between the measured macronutrient or fiber content of foods and the values on the Nutrition Facts Table…." For our volunteers who under the most rigorous and standardized testing conditions had a postprandial hypo- or hyperglycemic response to white bread, is it ethical to recommend that they depend on published GI values for other foods that are based on an $n = 10$ and hope that it applies equally to them?

Our data also challenge the accepted dogma, that "GI values represent the inherent property of the food and not the metabolic response of an individual to the food." The significant contribution of baseline glycated hemoglobin concentrations and insulin index (both $P < 0.0001$) to the variability in GI value determinations clearly shows that longer-term glycemic control and insulin response, even in normoglycemic individuals, affect GI values.

Finally, as a point of clarification, their statement, "GI is widely recognized to have clinical (2–4) and public health (5) significance" is an overstatement of the current status of GI on clinical outcomes and as a component of dietary guidance. Findings of randomized controlled clinical trials are mixed, with the most recent trial (7) concluding that