Glycemic index in overweight development: distinguishing limited evidence from limits in evidence

Dear Sir:

Evidence for the role of the dietary glycemic index (GI) or glycemic load (GL) in the primary prevention of overweight and obesity remains scarce. We therefore read with interest the recent article by Mendez et al (1) in which they report the relation of dietary GI and GL, and associated dietary patterns, to body mass index (BMI) in a Mediterranean population. However, conclusions from their findings may be severely hampered by a number of methodologic flaws, in addition to limitations due to the cross-sectional nature of their analysis.

First, for any meaningful conclusions to be drawn, the estimates of the GI and GL need to be reasonably valid. Mendez et al report that their food-frequency questionnaire (FFQ) was validated; however, their validation study was conducted in a sample of 44 young (mean age: 31 y) healthy individuals (2), who were clearly not representative of the middle-aged (age range: 35–74 y) population included in the present study. In the validation of their FFQ against a 3-d unweighed food record, they found correlation coefficients of 0.31 for total carbohydrate and 0.33 for dietary fiber, both of which clearly fall in the range of values that indicate a poor agreement between the methods (3, 4). Thus, considerable errors in measuring carbohydrate intake and in assigning appropriate GI values to FFQ items might have resulted in a low validity of estimated dietary GI and GL. Unfortunately, the authors do not report such data from their study.

Second, the authors use a new, innovative statistical approach, the reduced rank regression (RRR) method, to derive dietary patterns associated with GI and GL. However, some potential limitations in their application of RRR need to be addressed. This method builds on the incorporation of a priori knowledge on diet-disease associations by making use of a set of intermediate response variables lying on the pathway between diet and the outcome—eg, specific biomarkers or nutrients—to extract dietary patterns (5). Thereby, the RRR approach attempts to convert the knowledge on several response-disease associations into a meaningful dietary pattern, which can ultimately provide guidance for the implementation of dietary guidelines. However, the approach chosen by Mendez et al to derive dietary patterns on the basis of responses that do not or only weakly correlate with the disease is rather counterintuitive. Furthermore, because GI and GL are computed on the basis of observed food intake, evaluating food patterns with respect to BMI is highly dependent on the preceding analysis of GI or GL and BMI. Thus, results for these food patterns should be replicated in independent data sets. Finally, if only one disease-related response is chosen, as in the analysis of Mendez et al (ie, GI or GL), the advantages of RRR no longer hold. In fact, in this case, RRR is similar to a simple multivariable regression of the association between food groups and GI or GL.

A third concern is that the authors fail to use subgroup-specific tertiles for their analyses and end up testing model coefficients of strangely selected groups against each other (eg, it is surprising that mean GLs were similar for men in tertiles 2 and 3). Mendez et al further argue that it may be relevant to present estimates for the association between GI or GL and BMI both with and without energy adjustments. Unfortunately, they do not appear to base their “tertiles” on residuals when presenting energy-adjusted associations (6). Overall, it must be suspected that the correct use of energy-adjusted residuals and subgroup-specific tertiles would have resulted in comparison of completely different subgroups.

Finally, it remains questionable whether cross-sectional data derived from a population in which underreporting of energy and fat intake is clearly related to the degree of overweight allow any meaningful conclusion to be drawn. In the study by Mendez et al, up to 58% of the participants in a subgroup were classified as energy underreporters, and the degree of underreporting was strongly related to GL. Admittedly, cross-sectional studies can provide indications for possible nutrient-disease relations, which then require more detailed analyses in prospective observational studies or randomized controlled trials. However, given that other studies have already indicated a potential role of the dietary GI or GL in overweight development, we believe that new meaningful insights can now only be expected from prospective studies or randomized controlled trials. Conversely, further cross-sectional analyses—especially if conducted in populations with a high percentage of potential underreporters—are not only of limited value but may in fact be mistakenly interpreted as a new piece of scientific evidence.

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Reply to AE Buyken et al

Dear Sir:

Buyken et al suggest that our analysis on dietary glycemic quality and body mass index (BMI) in Spanish adults (1) is of limited interest and value because of a number of methodologic issues. However, as noted in their first sentence, evidence on the role of dietary glycemic index (GI) or glycemic load (GL) in the “primary prevention of obesity remains scarce”: relatively few articles on these measures of diet quality have focused on obesity as the outcome (1). Buyken et al also imply that our findings of largely negative associations between dietary GI and BMI, and null associations with dietary GL, are likely due to methodologic problems. However, as described both in our article and in an earlier review (2), despite the prevailing hypothesis that high GI diets may increase risk of obesity, the majority of earlier epidemiologic studies have reported similar null or inverse associations between GI or GL and measures of obesity. Given that the evidence remains controversial and inconclusive, publications from studies conducted in diverse populations and food cultures—including findings that may not support the prevailing hypothesis—seem to be warranted to better understand the issue.

A primary aim was to provide insights on the food patterns underlying high dietary GI and GL in order to assess whether these patterns may help to explain our results. Given this aim, our main purpose in applying the reduced rank regression (RRR) technique was to simultaneously examine the food patterns underlying high dietary GI and GL—the latter being analogous to “intermediate response variables lying on the pathway between diet and the outcome”—in a manner similar to previous studies (3). Indeed, the RRR analysis illustrated important disparities in the food groups associated with elevated GI compared with GL, with intakes of fruit, vegetables, and legumes positively associated with GL but negatively associated with GI. These disparities were consistent with the discrepant associations observed for GI compared with GL.

Another important aim was to evaluate a second issue raised by Buyken et al: how dietary data quality may influence findings on GI or GL in relation to BMI. Therefore, as in a previous study (4), we examined how the presence of underreporters affected associations and unexpectedly found that, in our data, positive associations between GL and BMI were observed only among underreporters. Overall, the proportion of underreporters in our study (19.7%) was comparable to other studies (5, 6), although the proportion was higher among subjects in the lowest tertiles of GI or GL (the “subgroups” referred to by Buyken et al).

As in all observational studies on diet and health, particularly when food-frequency questionnaires are used, validation of dietary data are a challenge, and this study is no exception. Correlations for carbohydrate and fiber intakes with food records were modest. Energy-adjusted correlations were somewhat stronger than those cited (r = 0.40 for carbohydrate and 0.39 for dietary fiber); the Pearson correlation coefficient for energy-adjusted dietary GI, not previously reported, was 0.42 (95% CI: 0.25, 0.56), which is comparable to other studies (7). More importantly, however, as shown in the Bland-Altman plot (Figure 1), there was no evidence that dietary glycemic quality estimates were biased (P value for linear trend not significant). Measurement error may explain the null findings between BMI and dietary GI but seems less likely to explain the negative associations observed with GL after energy adjustment.

Buyken et al raise several concerns about the analysis strategy, including the use of GI and GL tertiles based on the entire sample, rather than defined separately for the plausible and underreporter subgroups. We used overall instead of subgroup-specific tertiles to make the interpretation of associations with these tertile groupings comparable across all models. Nonetheless, substituting subgroup-specific tertiles did not meaningfully change the results (Table 1): associations between BMI and dietary GI and GL remained null or negative after energy adjustment. Similarly, as expected, using the residual approach to obtain energy-adjusted GI and GL values yielded very similar results to the previously reported models adjusting separately for energy intakes (Table 1). Because use of the residual method yields different tertile groups than those obtained by using unadjusted GI or GL, this approach was not used initially as it would not have allowed us to examine the effect of additionally adjusting for energy in a series of comparable models. The apparent

FIGURE 1. Bland Altman plot assessing the agreement between the food-frequency questionnaire (FFQ) and dietary recalls (24h-R) for glycemic load adjusted for energy intake.