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COMMENT & RESPONSE

Low-Fat vs Low-Carbohydrate Diets and Weight Loss

To the Editor In the Diet Intervention Examining The Factors Interacting with Treatment Success (DIETFITS) randomized clinical trial, the investigators concluded that there was no significant difference in weight change between a healthy low-fat diet vs a healthy low-carbohydrate diet.[1] At baseline, both groups consumed a comparable percentage of daily calories from fat: 34.8% for the low-fat group and 36.0% for the low-carbohydrate group. At the conclusion of the 12-month study period, the percentage of daily calories from fat was 28.7% in the low-fat group and 44.6% in the low-carbohydrate group. Although the percentage of daily calories from fat was reduced from 34.8% to 28.7% in the low-fat group, a diet composed of 28.7% of the daily calories from fat is a high-fat diet.

In the Lifestyle Heart Trial,[2] participants with angiographically documented coronary artery disease were randomized to an experimental group or a control group. The experimental group was asked to eat a low-fat vegetarian diet, quit smoking, practice stress management techniques, and engage in moderate physical exercise for 12 months. The percentage of daily calories from fat decreased from 31.5% to 6.8%, and the average weight decreased from 91.1 to 81.0 kg. In the control group receiving usual care, the percentage of daily calories from fat changed minimally from 30.1% to 29.5%, and the average weight increased from 80.4 to 81.8 kg.

The DIETSFITS randomized clinical trial compared a high-fat diet with a very high-fat diet; therefore, it is not surprising that both groups showed comparable weight loss results. Is it possible that comparing a low-carbohydrate diet vs a low-fat diet in which less than 10% of the daily calories are from fat would have yielded different results?

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1. Gardner CD, Trepanowski JF, Del Gobbo LC, et al. Effect of low-fat vs low-carbohydrate diet on 12-month weight loss in overweight adults and the association with genotype pattern or insulin secretion: the DIETFITS randomized clinical trial [published corrections appear in *JAMA*. 2018;319(13):1386 and *JAMA*. 2018;319(16):1728]. *JAMA*. 2018;319(7):667-679. doi:10.1001/jama.2018.0245

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To the Editor In a 12-month, behavior modification diet intervention study, Dr Gardner and colleagues[1] compared the effects of a healthy low-fat diet with a healthy low-carbohydrate diet on weight loss among 609 overweight adults. The authors did not find a significant difference in weight loss between the 2 diet intervention groups, in line with results from several previous studies.[2] Different from traditional diet intervention trials, 1 of the primary aims of the DIETFITS study was to test diet × genotype pattern interactions on weight loss in response to the diet intervention. The authors did not observe significant diet × genotype pattern interactions and concluded that there was no significant difference in genotype pattern associated with the dietary effects on weight loss.

Even though the rationale to test diet × genotype pattern interaction on weight loss in response to interventions was sound, the strategy in the selection and analysis of the genetic variations was not. The participants were grouped into low-fat–responsive genotype and low-carbohydrate–responsive genotype groups according to single-nucleotide polymorphisms (SNPs) of 3 genes (*PPARG*, *ADRB2*, and *FABP2*). These genes are biological candidates relevant to fat and carbohydrate metabolism; however, there is no prior biological evidence supporting the hypothesis that these genetic variations may modify the dietary effects on weight loss.

During the past decade, genome-wide association studies have identified common variations associated with various obesity traits, which can be used to search for genetic variations affecting weight loss in diet interventions. The ultimate achievement of identifying new genetic factors interacting with diets will mainly rely on genome-wide analysis with replications.

The study enrolled participants with relatively good ethnic and racial diversity. Genetic variations may differ in various ethnic and racial groups and therefore introduce the hazard of spurious associations.[3] In addition, successful replication has been widely accepted as a requirement in establishing genetic associations, whereas no replication was reported in the DIETFITS study. Emerging data are encouraging that findings from studies of diet × genotype pattern interaction in clinical trials may be reproducible.[4,5]

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In Reply Dr Rahman questions whether the DIETFITS healthy low-fat diet can be considered a low-fat diet with a mean reported 12-month intake of 28.7% energy from fat. A similar question could be raised regarding the healthy low-carbohydrate diet, with a mean reported 12-month intake of 29.8% energy from carbohydrates. The approach of defining and communicating to study participants "how low is low?" was very intentional.[1]

Briefly, every participant was instructed to achieve a fat or carbohydrate intake level concordant with their assignment that was as "low as they could go, while also being a level perceived as realistic to potentially maintain for the rest of their lives." The objective was to avoid studying unrealistically extreme diets that could not or would not be maintained long-term. We specifically instructed participants to consider these as "eating plans" rather than "diets" for that reason. Initially, both groups were instructed to strive to achieve a restriction of fat or nonfiber carbohydrate intake to 20 g/d within the first 8 weeks of the study so as to anchor the 2 approaches at relatively extreme levels. Next, they were instructed to titrate their intake to realistic longer-term levels that were maximally differentiated between the 2 diet groups.

Some participants in both groups achieved restrictions far greater than average. In future secondary analyses, we plan to examine and contrast subsets of participants from both groups who achieved the lowest levels of fat and carbohydrate intake; by definition those findings will be less generalizable.

Dr Qi and colleagues commented on the 3 SNPs used for the multilocus genotype patterns: low-fat genotype, low-carbohydrate genotype, and neither genotype. They suggest there was no prior biological evidence supporting a hypothesis for these specific genetic variations and a lack of replication. In response, preliminary results using these same 3 SNPs and multilocus genotype patterns were presented during an oral session at the American Heart Association annual meeting of the joint Epidemiology and Prevention/Nutrition, Physical Activity, and Metabolism councils in March 2010, in San Francisco, California, but have not been published.

The positive predictive findings involved a post hoc analysis of diet × genotype pattern interactions using data from the A TO Z study.[2] The DIETFITS study was designed to be a replication study of those preliminary findings, as described in the main article, supplemental materials, protocol, and original National Institute of Diabetes and Digestive and Kidney Diseases grant application. The preliminary 2010 findings were not replicated in DIETFITS.

A second comment involved the ethnic/racial demographics. The original study was designed to test for genetic effect modification in white adults only with a sample size of 400. As explained in the supplemental materials, subsequent to receiving funding, additional funds were obtained that allowed for an increase in total sample size to 609 (approximately two-thirds of the sample being white adults and one-third of the sample being nonwhite adults). The test for genetic effect modification was performed for white adults only as well as for the full study sample with similar null findings. Regardless, we are in complete agreement with our colleagues that diet × genotype pattern interactions for weight loss are still plausible for other genetic variations not tested in the DIETFITS study.

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Importance of Intelligence and Emotional Intelligence for Physicians

To the Editor In a Viewpoint, Dr Emanuel and Ms Gudbranson[1] outlined the need to consider applicant abilities beyond surrogate measures of IQ when selecting medical school applicants. Although the authors highlighted emotional intelligence (EQ) as an alternative to IQ, other predictors of success in medicine should be considered as well.

As alluded to by the authors, there is not a binary choice between IQ and EQ. A wide range of other intelligences, some of which may strongly predict medical school success, have been explored.[2] Formulaic intelligence, the ability to extrapolate from known or intuited formulas to novel problems triggered by overcoming adversity, may be a strong predictor of success both academically and personally, whereas grit, or resilience, is a better predictor of academic success in adolescents than IQ.[2] A minimum level of academically oriented intelligence, whether judged as formulaic intelligence, grit, or IQ, is needed—along with high EQ—for effective medical practice.

Data from a systematic review highlighted the correlation between EQ and medical education core competencies,[3] whereas another review suggested that EQ education in medical school may be of value but that further study is warranted before its "wholesale adoption in any curriculum."[4]

The role of specialty self-selection should also be considered because different skill sets may be of value for radiologists and geriatricians. Moreover, finding applicants with a high degree of creativity who possess at least a minimum level of EQ is valuable if medical schools are to train the next generation of leading physician scientists. Embracing diversity in the medical student body, including diversity of EQ and IQ levels within limits, may be of substantial value.

If medical school recruiting practices are to change, it is important to heed the authors' call for change while also following the same principles of evidence-based medicine used when deciding on therapeutic interventions. A similar suggestion to deemphasize IQ at the expense of EQ was proposed in the veterinary literature more than a decade ago, and those authors called for further study to better elucidate the value of EQ.[5] Rigorous systematic reviews, public engagement, and further research may be helpful to better identify ideal characteristics beyond IQ for the next generation in medicine.

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To the Editor Dr Emanuel and Ms Gudbranson suggested that medical school admissions committees should explicitly assess EQ and deemphasize IQ.[1] Ideally, the anticipated outcome would be an increased number of students who have the potential to become effective, compassionate physicians able to collaborate, communicate, and integrate care for their patients. However, EQ is a measure of ability that can improve with formal training. EQ training has been shown to be a critical component of leadership development, although the optimal type and timing of training in a person's education or career has yet to be determined.[2] Some groups suggest that medical professionalism and leadership education should be modeled around EQ competencies.[3] Additionally, Cabello et al found that the total ability EQ score changes with age, increasing from adolescence to middle life before trending downward.[4] If EQ scores become the main criteria for admission, age could become an influential factor in who is admitted. Because of its growth potential and inherent plasticity, EQ may not be a reliable factor to consider during admissions decisions in the absence of documented prior training.

EQ can predict success in interpersonal performance in medical school but does not predict success in academic courses.[5] Undoubtedly, interpersonal skills such as communication and sensitivity are essential in health care. However, to use interpersonal skills as physicians, students must first complete the rigorous academic requirements of medical school. Therefore, medical schools must continue their dependence on cognitive ability to predict a student's intellectual performance.

Because IQ is invariant and EQ can be improved through training, overemphasis on EQ in the admissions process may result in accepting medical students who will not become the most competent physicians. Rather, identifying those students who will be the most receptive and responsive to