

## CORRESPONDENCE



## Comparison of Weight-Loss Diets

**TO THE EDITOR:** Sacks et al. (Feb. 26 issue)<sup>1</sup> compare weight-loss diets that vary in macronutrient content, with a targeted maximal difference in the proportion of calories derived from carbohydrates, fat, and protein of 30, 20, and 10 percentage points, respectively. The realized macronutrient differences were substantially smaller than the planned targets, and at 2 years, weight loss was similar in pairwise comparisons of intakes at the high and low extremes of each macronutrient. Neither the targeted nor the actual intakes of carbohydrates or fat in any of the diets would classify them as being substantially low in these macronutrients. Unfortunately, the diets were portrayed this way in the media.<sup>2</sup> Given the small differences in reported macronutrient intake and the even smaller differences in biomarker-predicted intakes, one may conclude that small differences in dietary macronutrient content do not affect weight loss. However, the question of whether larger differences in macronutrients preferentially promote weight loss remains unanswered by this study.

Christy L. Boling, M.D.

Durham Veterans Affairs Medical Center  
Durham, NC 27705  
christy.boling@duke.edu

Eric C. Westman, M.D., M.H.S.

Duke University Medical Center  
Durham, NC 27710

William S. Yancy, M.D., M.H.S.

Durham Veterans Affairs Medical Center  
Durham, NC 27705

1. Sacks FM, Bray GA, Carey VJ, et al. Comparison of weight-loss diets with different compositions of fat, protein, and carbohydrates. *N Engl J Med* 2009;360:859-73.

2. Parker-Pope T. Study zeroes in on calories, not diet, for loss. *New York Times*. February 25, 2009.

**THE AUTHORS REPLY:** Boling and colleagues raise a valid point. We did not test very-low-carbohydrate intake because we had a concern — based

on previous studies — that participants would not be able to sustain such a low intake beyond the initial 2 to 4 months, even with continual instruction and assistance from the research staff of dietitians and behavioral psychologists. For example, Foster et al. found that after 3 months there was no difference in levels of urinary ketones between participants who were assigned to the Atkins diet, which starts with an intake of 20 g or less of carbohydrates per day and increases to an intake of 50 g or less per day (approximately 10% of the daily requirement of kilocalories), and participants who were assigned to conventional diets.<sup>1</sup> Foster and colleagues opined that long-term adherence may be difficult, and other studies support this view, showing that adherence to carbohydrate goals deteriorates within 2 to 3 months and that intake increases to 37% at 6 months<sup>2</sup> and to approximately 34 to 40% at 12 months.<sup>3-5</sup> The Atkins approach may work well for some persons, but the data from randomized trials provide support for the view that low-carbohydrate diets,

### THIS WEEK'S LETTERS

- 2247 Comparison of Weight-Loss Diets
- 2248 IDH1 and IDH2 Mutations in Gliomas
- 2249 Cytochrome P-450 Polymorphisms and Response to Clopidogrel
- 2251 Geographic Atrophy in Age-Related Macular Degeneration and TLR3
- 2256 Weight Loss for Urinary Incontinence in Overweight and Obese Women
- 2257 Preemption and Malpractice Liability
- 2259 Nickel Allergy in Danish Women before and after Nickel Regulation

whether extreme or moderate, do not consistently result in more weight loss than other approaches. Moreover, our findings confirm that despite best efforts, studies that compare diets for weight loss have not shown large differences in dietary macronutrient composition.

Frank M. Sacks, M.D.

Harvard School of Public Health  
Boston, MA 02115  
fsacks@hsph.harvard.edu

George A. Bray, M.D.

Pennington Biomedical Research Center  
Baton Rouge, LA 70808

Catherine Loria, Ph.D.

National Heart, Lung, and Blood Institute  
Bethesda, MD 20892

1. Foster GD, Wyatt HR, Hill JO, et al. A randomized trial of a low-carbohydrate diet for obesity. *N Engl J Med* 2003;348:2082-90.
2. Samaha FF, Iqbal N, Seshadri P, et al. A low-carbohydrate as compared with a low-fat diet in severe obesity. *N Engl J Med* 2003; 348:2074-81.
3. Dansinger ML, Gleason JA, Griffith JL, Selker JP, Schaefer EJ. Comparison of the Atkins, Ornish, Weight Watchers, and Zone diets for weight loss and heart disease risk reduction: a randomized trial. *JAMA* 2005;293:43-53.
4. Gardner CD, Kiazand A, Alhassan S, et al. Comparison of the Atkins, Zone, Ornish, and LEARN diets for change in weight and related risk factors among overweight premenopausal women. *JAMA* 2007;297:969-77. [Erratum, *JAMA* 2007;298:178.]
5. Shai I, Schwarzfuchs D, Henkin Y, et al. Weight loss with a low-carbohydrate, Mediterranean, or low-fat diet. *N Engl J Med* 2008;359:229-41.

## IDH1 and IDH2 Mutations in Gliomas

**TO THE EDITOR:** Yan et al. (Feb. 19 issue)<sup>1</sup> found that mutations of genes encoding isocitrate dehydrogenases (*IDH1* and *IDH2*), as compared with no mutations, are associated with younger age and better prognosis in adults with gliomas. Their study and other, similar studies<sup>2-4</sup> prompted us to search for mutations at codon 132 of *IDH1* in children and adolescents with gliomas. In our series, 155 of 404 adults (38%) and 4 of 73 children (5%) with nonpilocytic gliomas had *IDH1* mutations ( $P < 0.001$ ). We did not find *IDH2* mutations in tumors in children. We also found that *IDH1* mutations in adults were significantly associated with a lower tumor grade, increased overall survival, and younger age. Children with tumors bearing *IDH1* mutations were older than children with mutation-negative tumors (median age, 16 years vs. 7 years;  $P = 0.002$ ). No association with survival was observed in children.

Our results and other studies in children<sup>5</sup> suggest that pediatric and adult gliomas differ biologically, although adolescents may have gliomas resembling those in adults.

Emilie De Carli, M.D.

Institut Gustave Roussy  
94805 Villejuif, France  
emilie.decarli@igr.fr

Xiaowei Wang, M.D.

Hôpital de la Pitié-Salpêtrière  
75013 Paris, France

Stéphanie Puget, M.D.

Université Paris Descartes  
75015 Paris, France

1. Yan H, Parsons DW, Jin G, et al. *IDH1* and *IDH2* mutations in gliomas. *N Engl J Med* 2009;360:765-73.

2. Parsons DW, Jones S, Zhang X, et al. An integrated genomic analysis of human glioblastoma multiforme. *Science* 2008;321:1807-12.
3. Watanabe T, Nobusawa S, Kleihues P, Ohgaki H. *IDH1* mutations are early events in the development of astrocytomas and oligodendrogliomas. *Am J Pathol* 2009;174:1149-53.
4. Bleeker FE, Lamba S, Leenstra S, et al. *IDH1* mutations at residue p.R132 occur frequently in high-grade gliomas but not in other solid tumors. *Hum Mutat* 2009;30:7-11.
5. Faury D, Nantel A, Dunn SE, et al. Molecular profiling identifies prognostic subgroups of pediatric glioblastoma and shows increased YB-1 expression in tumors. *J Clin Oncol* 2007;25:1196-208.

**TO THE EDITOR:** Yan et al. report that gliomas with *IDH1* mutations have distinctive genetic characteristics (particularly frequent codeletion of 1p and 19q) and are associated with a better outcome than gliomas without these mutations. We studied the gene-expression profile of 100 gliomas (21 World Health Organization [WHO] grade II, 24 grade III, and 55 grade IV gliomas), with the use of Affymetrix U133 plus 2.0 microarrays; 40 gliomas had *IDH1* mutations at codon 132, and 60 did not have such mutations. We found that the association between *IDH1* mutations and a good prognosis was related to the proneural gene-expression profile. After hierarchical clustering with the use of the gene-expression signature reported by Phillips et al.,<sup>1</sup> 36 of 40 mutated tumors (90%) were classified as proneural as compared with only 8 of 60 nonmutated tumors (13%). Conversely, 36 of 44 proneural tumors (82%) had mutated *IDH1*, as compared with only 4 of 56 proliferative and mesenchymal tumors (according to the categories described by Phillips et al.) (7%) ( $P < 10^{-14}$  according to the chi-square test). Thus,