Weight Loss with a Low-Carbohydrate, Mediterranean, or Low-Fat Diet

To the Editor: How do Shai et al. (July 17 issue) explain why the subjects in their study regained weight between month 6 and month 24, despite a reported reduction of 300 to 600 calories per day? Contributing possibilities may include the notion that a food-frequency questionnaire cannot precisely determine energy or macronutrient intake but, rather, ascertains general dietary patterns. Certain populations may underreport intake and have a decreased metabolic rate. The authors did not measure body composition, which is critical for documenting weight-loss components.

In addition, the titles of the diets that are described in the article are misleading. Labeling the “low-carbohydrate” diet as such is questionable, since 40 to 42% of calories were from carbohydrates from month 6 to month 24, and data regarding ketosis support this view. Participants in the low-fat and Mediterranean-diet groups consumed between 30% and 33% of calories from fat and did not increase fiber consumption, highlighting the importance of diet quality. Furthermore, the authors should have provided baseline values and P values for within-group changes from baseline (see Table 2 of the article).

Contrary to the authors’ assertion, it is not surprising that the effects on many biomarkers were minimal, since the dietary changes were minimal. The absence of biologically significant weight loss (2 to 4% after 2 years) highlights the fact that energy restriction and weight loss in themselves may minimally affect metabolic outcomes and that lifestyle changes must incorporate physical activity to optimize the reduction in the risk of chronic disease.4,5

Christian K. Roberts, Ph.D.
R. James Barnard, Ph.D.
Daniel M. Croymans, B.S.
University of California, Los Angeles
Los Angeles, CA 90095-1606
croberts@ucla.edu


To the Editor: Shai and colleagues found that a low-fat diet was less effective than either a Medi-
terranian diet or a low-carbohydrate diet in achieving weight loss. However, the “low-fat” group was actually not instructed to follow a low-fat diet, because the diet composition (i.e., calories from fat) did not change during the intervention. So, in reality, since the members of this group consumed the same diet as they did habitually, it should have been called the control group. Weight loss is known to occur as a consequence of reducing the proportion of calories from fat, so the design of the study was not really fair to the low-fat diet. Moreover, the dropout rate was 15% in the Mediterranean group, 22% in the low-carbohydrate group, and only 10% in the low-fat group (P=0.04). In a study involving Danish subjects, my colleagues and I also observed that there was a significantly higher dropout rate among participants on a Mediterranean diet (28%) than among those on a (real) low-fat diet (16%), after both 6 months and 18 months. Retention is an end point that deserves comment.

Arne Astrup, M.D.
University of Copenhagen
1958 Frederiksberg, Denmark
ast@life.ku.dk

Dr. Astrup reports receiving consulting fees from Weight Watchers and Global Dairy Platform and reports that his department at the University of Copenhagen has received research funding from many food companies. No other potential conflict of interest relevant to this letter was reported.


TO THE EDITOR: Shai et al. report that either a Mediterranean diet or a low-carbohydrate diet was an effective alternative to a low-fat diet in terms of weight loss. Absolute values for the energy intake before and after the intervention are not given for any of the groups. However, the data provided in the article suggest that the weight loss in the low-carbohydrate group may have been simply a hypocaloric effect, even though the authors state that the energy intake in this group was not restricted. Thus, if the daily intake of carbohydrates was no more than 120 g (equal to 500 kcal), as stated in the Methods section, and if the fraction of the energy intake provided by carbohydrates was around 40%, as stated in Table 2, then the total daily energy intake in the low-carbohydrate group must have been no more than approximately 1250 kcal, which is significantly less than the daily intake targeted for the two other groups.

Kirsten Moller, M.D., Ph.D.
Rikke Krogh-Madsen, M.D., Ph.D.
University Hospital Rigshospitalet
DK-2100 Copenhagen, Denmark
kirsten.moller@dadlnet.dk

Dr. Moller reports receiving lecture fees from Merck, Schering-Plough, and Gilead Sciences. Dr. Moller also reports receiving lecture fees from the Harry Walker speaker’s bureau and consulting fees from PepsiCo, Mars, and Safeway. No other potential conflict of interest relevant to this letter was reported.


TO THE EDITOR: Shai et al. report very low attrition rates among study participants, and this is surely a good point, given the 2-year length of the study. The authors properly recognize that this finding is probably due to a closely monitored intervention, but they do not report anything about the costs of their face-to-face, dietitian-based approach. As noted by Glasgow and Emmons, among factors that impede the translation of research into widespread practice, important obstacles are the high cost and large time demands on both staff and participants. Even if the authors’ strategies for maintaining adherence could be applied outside the workplace, we are not as optimistic as they are, considering the low cost-effectiveness that usually characterizes face-to-face approaches targeting eating habits.

Gian Mauro Manzoni, Psy.D.
Gianluca Castelnuovo, Ph.D.
Enrico Molinari, Ph.D.
Istituto Auxologico Italiano
28824 Piancavallo, Italy
gm.manzoni@auxologico.it


THE AUTHORS REPLY: Roberts and colleagues correctly note that a food-frequency questionnaire cannot precisely assess exact caloric intake. In our study, we used identical nutritional values for each of the 137 questionnaire items, irrespective of the specific dietary intervention. For example, “vegetable soups” were not specially analyzed within the low-fat group as “no fat added” or in the low-carbohydrate group as “creamed” or “no starch added.” Thus, although the questionnaire data revealed three distinct dietary regimens throughout the intervention, these data might have underestimated the true differences among the groups. Correlations between data from food-frequency questionnaires and those from 24-hour dietary recalls, which were used in a subgroup of participants, were more than 0.8 for most nutrients.

In response to the letters from Astrup and Moller and Krogh-Madsen: the diet-recall data confirm that the total caloric deficit was similar among the groups and that the low-fat group maintained a relatively low intake of fat (Table 1). Obviously, with a substantial total caloric deficit, the absolute consumption of fiber was decreased; however, the decrease in the low-fat group was half of that in the low-carbohydrate group.

We agree with Roberts et al. on the importance of physical activity, but our study specifically focused on diet composition. Roberts et al. are incorrect in characterizing the weight loss as biologically not meaningful, since it yielded clinically important changes in risk factors. Intriguingly, the weight reduction achieved among the

<table>
<thead>
<tr>
<th>Variable</th>
<th>Low-Fat Diet</th>
<th>Mediterranean Diet</th>
<th>Low-Carbohydrate Diet</th>
</tr>
</thead>
<tbody>
<tr>
<td>Energy (kcal)</td>
<td>1347±239</td>
<td>1356±258</td>
<td>1281±380</td>
</tr>
<tr>
<td>Fat</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Total (g)</td>
<td>38.7±13.9</td>
<td>48.8±19.8</td>
<td>58.8±25.7†</td>
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<tr>
<td>% of energy</td>
<td>25.9±8.0</td>
<td>31.7±9.1†</td>
<td>40.5±10.0‡</td>
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<tr>
<td>Protein</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Total (g)</td>
<td>94.2±24.4</td>
<td>83.2±22.5</td>
<td>105.9±36.0</td>
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<tr>
<td>% of energy</td>
<td>28.3±6.1</td>
<td>25.2±8.0</td>
<td>32.9±7.6†</td>
</tr>
<tr>
<td>Carbohydrates</td>
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<td></td>
</tr>
<tr>
<td>Total (g)</td>
<td>135.8±44.1</td>
<td>152.9±0.3</td>
<td>87.4±37.5‡</td>
</tr>
<tr>
<td>% of energy</td>
<td>48.2±0.7</td>
<td>45.0±11.7</td>
<td>28.3±11.7‡</td>
</tr>
<tr>
<td>Dietary cholesterol (mg)</td>
<td>174±82</td>
<td>181±93</td>
<td>358±162‡</td>
</tr>
</tbody>
</table>

* Plus–minus values are means ±SD. During the first 6 months of the study, 24-hour dietary recalls were obtained from 27 participants on the low-fat diet, 22 on the Mediterranean diet, and 18 on the low-carbohydrate diet; the results were analyzed with the use of the Israeli nutritional database.† P<0.05 for the comparison with the low-fat diet.
‡ P<0.001 for the comparison with the low-fat diet.
moderately obese subjects in our study was identical to that reported in a recent meta-analysis on long-term pharmacotherapy for obesity. In response to Ornish’s letter: the low-carbohydrate diet was based on Atkins’s book, although we encouraged the study participants to consume a variety of protein and fat sources to maintain successful long-term adherence. We specifically reported on retention in detail and noted that adherence was higher in this trial than in any other trial of a similar length that we know of. The setting and methods we used to maximize adherence rates permitted a robust test of the three dietary strategies, as assessed by weight loss and established measurements of lipids, glycemic control, and hepatic and inflammatory biomarkers. As noted by Manzoni and colleagues, we did not assess cost-effectiveness. However, we believe that cost-effective interventions can be implemented in the workplace, with the use of group meetings and by working with food-service providers.

Several readers have informed us that our online Supplementary Appendix was incomplete. We have updated the appendix to provide more complete information.

Iris Shai, R.D., Ph.D.
Ben-Gurion University
Beer-Sheva 84105, Israel
irish@bgu.ac.il

Yaakov Henkin, M.D.
Soroka University Medical Center
Beer-Sheva 84101, Israel

Meir J. Stampfer, M.D., Dr.P.H.
Harvard Medical School
Boston, MA 02115

TO THE EDITOR: In a randomized study of the effect of tibolone on fracture rates among postmenopausal women between the ages of 60 and 85 years, Cummings et al. (Aug. 14 issue) report that tibolone significantly reduced the risk of invasive breast cancer. The authors also report that this finding contradicted the results of the observational Million Women Study, which showed that the use of tibolone for up to 5 years was associated with an increased risk of breast cancer. In analyses combining clinical-trial and observational-study cohorts, the Women’s Health Initiative (WHI) showed that a decreased risk of breast cancer was associated with estrogen therapy only if estrogen was given several years after menopause and not when it was begun soon thereafter.

Since women in nontrial settings usually begin such hormonal therapy shortly after the onset of menopause, the gap time after menopause provides a potential effect modifier, suggesting caution in extrapolating findings to women closer to menopause. In the WHI randomized trial, estrogen plus progestin increased the risk of breast cancer that was diagnosed at an advanced stage, suggesting diagnostic delay with fewer cancers in the hormone group through the first 3 years of follow-up. The current tibolone trial was reported after a median of 34 months and without information on tumor stage. Although tibolone does not increase breast density, as does combined hormone therapy, could diagnostic delay account for some of the breast-cancer findings?

Rowan T. Chlebowski, M.D., Ph.D.
LABioMed
Torrance, CA 90502
rchlebowsk@gmail.com

Ross Prentice, Ph.D.
Fred Hutchinson Cancer Research Center
Seattle, WA 98109

Dr. Chlebowski reports receiving consulting fees from AstraZeneca, Novartis, Eli Lilly, and Wyeth and grant support from Eli Lilly, Organon, and Amgen. No other potential conflict of interest relevant to this letter was reported.

