

# High-Protein and Low-Glycemic Diets Improve Weight Maintenance Among Overweight Adults

Reviewed by Michael Pignone, MD, MPH

## STUDY

Larsen TM, Dalskov SM, van Baak M, Jebb SA, Papadaki A, Pfeiffer AF, Martinez JA, Handjieva-Darlenska T, Kunešová M, Pihlsgård M, Stender S, Holst C, Saris WH, Astrup A; Diet, Obesity, and Genes (Diogenes) Project: Diets with high or low protein content and glycemic index for weight-loss maintenance. *N Engl J Med* 363:2102–2113, 2010

## SUMMARY

**Design.** A randomized trial with factorial design.

**Subjects.** European adults with an initial BMI of 27–45 kg/m<sup>2</sup> and at least one child at home who successfully completed an initial low-calorie diet “run-in” period were eligible for the trial. A total of 773 adults with a mean age of 41 years and mean BMI of 34 kg/m<sup>2</sup> were enrolled and randomized from eight participating centers. Exclusion criteria included current diabetes, uncontrolled hypertension or hyperlipidemia, and history of heart disease.

**Methods.** Participants were randomized using a 2×2 factorial design to one of five diet groups: low protein/low glycemic index, low protein/high glycemic index, high protein/low glycemic index, high protein/high glycemic index, or a control diet (country-specific and moderate in protein). All diets had moderate fat content (25–30% of calories) and did not have a specific calorie restriction.

Dietary counseling was provided every other week for 6 weeks and

then monthly through the end of the trial. Two of the eight centers provided all foods from a study “food shop,” while participants from the other six centers were given instruction and counseling only.

The main outcome of interest was change in weight over 26 weeks based on intention-to-treat analysis using a mixed linear model. Missing data were modeled under the assumption that those dropping out had similar patterns of effect as those remaining in the trial throughout.

**Results.** During the 26-week trial, 225 of 773 participants (29%) dropped out, with a greater dropout rate among participants assigned to the low-protein/high-glycemic index group. All groups except the high-protein/low-glycemic index group gained some amount of weight. However, groups assigned to high-protein or low-glycemic index diets had less weight gain (difference of 0.93 and 0.95 kg, respectively) than those assigned to low-protein and/or high-glycemic index diets. The combination of high protein and low glycemic index did not appear to have more than additive effects.

The investigators noted that participants did not report differences in subjective appetite sensations, but these data were not presented quantitatively. There did not appear to be any clear indications of adverse effects from specific diets. Benefits were larger for the high-protein diet at the centers with “food shops”

compared to centers with instruction only. Benefits with low-glycemic index diets were larger in the instructional centers compared to the “food shop” centers.

**Conclusion.** A high-protein and low-glycemic index, calorically unrestricted, moderate-fat diet was more successful than diets with moderate or low protein content and/or a high glycemic index in maintaining weight loss among adults who had successfully completed a very-low-calorie initial weight loss.

## COMMENTARY

The optimal diet (or diets) for weight loss, weight maintenance, and overall health remains a controversial topic in research and in practice for patients with diabetes and those at risk of developing it. In this trial, European investigators examined different diets for weight maintenance among study participants who had successfully lost weight on a calorie-restricted initial diet. They compared five different diets that were all moderate in fat content (25–30% of calories) and calorically unrestricted and found that lower-glycemic index and higher-protein diets were more effective than higher-glycemic index and lower-protein diets for weight maintenance.

Conducting trials comparing different dietary approaches can be challenging because it is often difficult for subjects to maintain adherence to their assigned diet. Despite the highly selected population and intensive intervention

in this trial, 29% of participants dropped out during the 26-week period of observation.

To address this issue, the investigators performed intention-to-treat analyses, assuming those who dropped out (and thus had missing data) were similar to those who continued throughout. In a sensitivity analysis, they also tested an assumption that those who dropped out gained 1 kg per month, with similar results in terms of the differences in weight observed for the effects of differing protein and glycemic index dietary content as the main analyses. These findings increase our confidence that the observed benefits of high-protein and low-glycemic index diets are likely to be real.

It is also notable that the observed findings were achieved even though the actual difference in the proportion of calories from protein between the high- and low-protein diets was only 5 percentage points (compared to the original target of 12 percentage points) and the difference in glycemic index between the low and high groups was only 5 units (compared to the original target of 15 units).

There has been considerable recent interest in low-glycemic index (LGI) diets for prevention and treatment of diabetes, as well as for weight loss in general. A meta-analysis of several small, randomized trials suggests that LGI diets can improve A1C and reduce hypoglycemic events for patients with diabetes<sup>1</sup> and produce more weight loss than control diets and similar or greater weight loss than low-fat, calorie-restricted diets.<sup>2</sup>

Similarly, there has been greater recognition of the potential adverse effects of higher-carbohydrate diets on diabetes outcomes.<sup>3</sup> Limited evidence suggests that carbohydrate restriction may improve diabetes-related outcomes, but its effect on weight and overall health compared to other diets remains controversial, and further research is needed.<sup>4</sup> In this trial, both increasing the protein content of the diet at the expense of carbohydrates and improving the quality of the carbohydrates through reductions in glycemic index seemed to be effective for weight maintenance.

These findings must be considered in the context of a highly selected population that received

intensive counseling. Whether similar benefits would be seen in unselected patients with typical comorbidity profiles (including the presence of diabetes) and with less intensive support is unclear and should be the subject of additional research.

## REFERENCES

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<sup>3</sup>Kodama S, Saito K, Tanaka S, Maki M, Yachi Y, Sato M, Sugawara A, Totsuka K, Shimano H, Ohashi Y, Yamada N, Sone H: Influence of fat and carbohydrate proportions on the metabolic profile in patients with type 2 diabetes: a meta-analysis. *Diabetes Care* 32:959–965, 2009

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