



## Applied nutritional investigation

## Impact of weight loss and maintenance with ad libitum diets varying in protein and glycemic index content on metabolic syndrome

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## ABSTRACT

**Objectives:** We investigated the effects of weight loss and maintenance with diets that varied with regard to protein content and glycemic index (GI) on metabolic syndrome (MetSyn) status.

**Methods:** Secondary analyses were performed within the Diet, Obesity and Genes (DiOGenes) study (2006–2008), a randomized controlled dietary intervention. Nine hundred and thirty-eight overweight and obese adults from eight European countries entered an 8-wk low-calorie-diet period. Seven hundred and seventy-three adults who lost at least 8% of their body weights were randomized to one of five ad libitum diets for 6 mo: 1) low-protein (LP)/low-GI (LGI); 2) LP/high-GI (HGI); 3) high-protein (HP)/LGI; 4) HP/HGI; and 5) control diet. MetSyn prevalence and a standardized MetSyn score were assessed at baseline, after the low-calorie diet, and after the intervention.

**Results:** Weight loss among participants while on the low-calorie diet significantly reduced MetSyn prevalence (33.9% versus 15.9%;  $P < 0.001$ ) and MetSyn score (−1.48 versus −4.45;  $P < 0.001$ ). During weight maintenance, significant changes in MetSyn score were observed between the groups, with the highest increase detected in the LP/HGI group ( $P = 0.039$ , partial  $\eta^2 = 0.023$ ). Protein, GI, and their interaction did not have isolated effects on study outcomes.

**Conclusions:** Neither protein nor GI affected MetSyn status in this sample of European overweight and obese adults. However, a diet with a combination of an increased protein-to-carbohydrate ratio with low-GI foods had beneficial effects on MetSyn factors.

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All authors revised the manuscript, and A.P. had primary responsibility for the final content. All authors read and approved the final manuscript.

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## Introduction

Metabolic syndrome (MetSyn)—a clustering of abnormalities characterized by central adiposity, elevated blood pressure, impaired glucose tolerance, and dyslipidemia [1]—has been associated with an increased risk of cardiovascular disease [2,3]. Weight and dietary management can decrease mortality among patients with MetSyn [4], whereas weight loss has been shown to favorably affect all MetSyn components [5,6] and prevalence [7]. Nevertheless, it is unclear which dietary macronutrient composition is the most beneficial for successful MetSyn management. High-protein diets have been found to promote weight loss [8], to reduce abdominal obesity [9,10] and triglyceride levels [11], and to improve glucose and blood lipid concentrations [12] as compared with low-protein (LP), high-carbohydrate diets [13,14]. Carbohydrate-restricted diets with either high-protein or high-monounsaturated-fat content have been shown to reduce body weight and to improve insulin sensitivity and other MetSyn components [15], often independently of weight loss [16]. Low glycemic index (GI) diets have also been associated with low MetSyn prevalence [17,18], and they were shown to result in weight loss [19] and to improve glucose and blood lipid levels in intervention studies [20]. However, large-scale interventions examining the effect of dietary protein and GI on MetSyn status (in contrast with individual MetSyn components) are lacking.

The Diet, Obesity and Genes (DiOGenes) study is a European project that focused on dietary means of preventing weight (re) gain after weight loss [21,22]. The 6-mo randomized controlled dietary intervention was performed in eight European centers and assessed the effects of ad libitum diets that varied with regard to dietary protein and GI content on weight maintenance and obesity-related risk factors after a low-calorie-diet (LCD) period. A recent publication has reported the effects of the DiOGenes weight-loss and weight-maintenance periods on individual cardiovascular risk markers [23]. The aim of the present study was to explore the effect of the DiOGenes intervention on MetSyn status as assessed by MetSyn prevalence and a standardized MetSyn score.

## Materials and methods

### Participants

Details of the DiOGenes study design, procedures, and protocols have been published elsewhere [21–25]. Volunteer families from eight European cities (Maastricht, The Netherlands; Copenhagen, Denmark; Cambridge, United Kingdom; Heraklion, Greece; Potsdam, Germany; Pamplona, Spain; Sofia, Bulgaria; and Prague, Czech Republic) were invited to participate from November 2005 through April 2007. Eligible families were generally healthy, with at least one parent who was overweight (i.e., with a body mass index [BMI] of  $\geq 27$  kg/m<sup>2</sup> and  $\leq 45$  kg/m<sup>2</sup>) and between the ages of 18 and 65 y and with at least one child between the ages of 5 and 18 y [21]. Participants were excluded if they reported using medications or suffering from conditions related to the study's outcome, such as medication or diseases that influence weight regulation (e.g., untreated hypothyroidism or hyperthyroidism) and obesity-related cardiovascular risk factors (e.g., heart disease, hypertension, diabetes mellitus, hypertriglyceridemia, hypercholesterolemia). Informed consent was obtained from participants, and the study was approved by the medical ethical committees in each city.

### Study design and procedures

Eligible overweight and obese adults underwent clinical examinations to obtain baseline measurements; anthropometric measures and blood pressure were assessed, blood samples were collected, and a 3-d weighed dietary record was provided. Participants subsequently began an 8-wk LCD period with the aim of obtaining a minimum weight loss of 8% of the original body weight. Those who achieved the target weight loss underwent a second clinical examination to

obtain their “post-LCD” measurements. At the end of this clinical examination, families with at least one overweight or obese parent who achieved the target weight loss were randomized with the use of a simple block randomization procedure with stratification [21,22] to follow one of five energy ad libitum diets for 6 mo. Participants then underwent a final clinical examination at week 26 to obtain their “post-intervention” measurements.

### Low-calorie-diet period

The 8-wk LCD period involved the daily consumption of meal-replacement products that provided 800 kcal of nutrition (Modifast®, Nutrition et Santé, France), with an additional allowance of 400 g of vegetables. Participants were thus provided with 3.4 to 4.2 MJ/d (800–1000 kcal/d) [21,26].

### Dietary instruction period

On the day that the families were randomized, trained dietitians gave detailed instructions regarding the ad libitum moderate-fat (i.e., 25–30% of energy) diets, which differed in protein content and GI. The diets were differentiated as follows: a low-protein (LP)/low-GI (LGI) diet; a LP/high-GI (HGI) diet; a high-protein (HP)/LGI diet; a HP/HGI diet; and a control diet (national dietary guidelines, with medium protein content and no specific instructions regarding GI) [22]. The target was for protein content to comprise 10 to 15% of energy intake in the LP groups and 23 to 28% in the HP groups for a difference between the groups of 12% of energy; the aim with regard to GI was to achieve a 15-point difference between the HGI and LGI groups [22,24]. During the 6-mo intervention, participants were advised to maintain their weight, but further weight loss was also allowed [22].

### Dietary assessment

All participants were asked to complete a 3-d weighed dietary record at baseline and at weeks 4 and 26 of the dietary intervention. Participants were provided with weighing scales and instructed to record their food and liquid intake for 3 consecutive days (i.e., 2 weekdays and 1 weekend d) [21,22].

### Anthropometric/blood pressure measurements

To ensure standardization across the participating centers, standard operating procedures were produced for the measurement of body weight and height, BMI, waist circumference, and arterial blood pressure. The same measurement device was used in each center on every occasion that a measurement was provided. Participants fasted for 12 h before their clinical examinations [21].

### Blood parameters

Blood was collected in serum-separating Vacutainers for blood glucose and lipid assessment. After centrifugation (15 min at  $2500 \times g$ , at 22°C for gel tubes), serum was stored at  $-80^\circ\text{C}$  at each center until it was sent for analysis at a central laboratory (Department of Clinical Biochemistry, Gentofte University Hospital, Denmark). The labeling, storage, packing, and shipping of samples were performed in accordance with identical procedures. The fasting serum glucose level was analyzed via colorimetric assays (Ortho-Clinical Diagnostics, Johnson & Johnson, Birkerød, Denmark).

Fasting serum high-density lipoprotein cholesterol and triglyceride levels were measured with the use of routine enzymatic assays (Roche Diagnostics, Hvidovre, Denmark) in a COBAS Integra-400 analyzer (Roche Diagnostics Limited, Rotkreuz, Switzerland).

### Metabolic syndrome definition and score

MetSyn was defined as the presence of three or more of the following factors: an impaired fasting blood glucose level ( $\geq 6.10$  mmol/L); elevated blood pressure ( $\geq 130/\geq 85$  mm Hg); abdominal obesity (waist circumference of  $>102$  cm for men and  $>88$  cm for women); hypertriglyceridemia ( $\geq 1.7$  mmol/L); and a low high-density lipoprotein cholesterol level ( $<1.03$  mmol/L for men and  $<1.30$  mmol/L for women) [1].

A continuous MetSyn score was used to assess MetSyn status by standardizing the individual MetSyn components. By subtracting a participant's individual value for each component from the adult treatment panel (ATP)-III criteria, dividing by the sample's standard deviation, and then summing the individual standardized component scores, a continuous and standardized MetSyn score was calculated [27,28].

### Statistical analyses

All analyses were performed with the use of the Statistical Package for the Social Sciences (IBM SPSS Statistics for Windows, Version 20.0; IBM Corporation,

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