# A High-Carbohydrate, High-Fiber, Low-Fat Diet Results in Weight Loss among Adults at High Risk of Type 2 Diabetes

Allison C Sylvetsky,<sup>1,2,5</sup> Sharon L Edelstein,<sup>3,4</sup> Geoffrey Walford,<sup>6</sup> Edward J Boyko,<sup>7,8</sup> Edward S Horton,<sup>9</sup> Uzoma N Ibebuogu,<sup>10</sup> William C Knowler,<sup>11</sup> Maria G Montez,<sup>12</sup> Marinella Temprosa,<sup>3,4</sup> Mary Hoskin,<sup>11</sup> Kristina I Rother,<sup>5</sup> and Linda M Delahanty,<sup>6</sup> for the Diabetes Prevention Program Research Group

<sup>1</sup>Department of Exercise and Nutrition Sciences, <sup>2</sup>Sumner M. Redstone Global Center for Prevention and Wellness, <sup>3</sup>Biostatistics Center, and <sup>4</sup>Department of Epidemiology and Biostatistics Milken Institute School of Public Health, George Washington University, Washington, DC; <sup>5</sup>Section on Pediatric Diabetes and Metabolism, National Institute of Diabetes and Digestive and Kidney Diseases, NIH, Bethesda, MD; <sup>6</sup>Department of Medicine, Massachusetts General Hospital and Harvard Medical School, Boston, MA; <sup>7</sup>General Medicine Service, VA Puget Sound, Seattle, WA; <sup>8</sup>Department of Medicine, University of Washington, Seattle, WA; <sup>9</sup>Joslin Diabetes Center, Harvard Medical School, Boston, MA; <sup>10</sup>Department of Medicine, University of Tennessee Health Sciences Center, Memphis, TN; <sup>11</sup>Diabetes Epidemiology and Clinical Research Section, National Institute of Diabetes and Digestive and Kidney Diseases, NIH, Phoenix, AZ; and <sup>12</sup>Department of Medicine, University of Texas Health Science Center at San Antonio, San Antonio, TX

#### Abstract

**Background:** Weight loss is a key factor in reducing diabetes risk. The Diabetes Prevention Program (DPP) is a completed clinical trial that randomly assigned individuals at high risk of diabetes to a placebo (PLBO), metformin (MET), or intensive lifestyle intervention (ILS) group, which included physical activity (PA) and reduced dietary fat intake.

**Objective:** We aimed to evaluate the associations between diet and weight at baseline and to identify specific dietary factors that predicted weight loss among DPP participants.

**Methods:** Diet was assessed by a food frequency questionnaire. The associations between intakes of macronutrients and various food groups and body weight among DPP participants at baseline were assessed by linear regression, adjusted for race/ethnicity, age, sex, calorie intake, and PA. Models that predicted weight loss at year 1 were adjusted for baseline weight, change in calorie intake, and change in PA and stratified by treatment allocation (MET, ILS, and PLBO). All results are presented as estimates ± SEs.

**Results:** A total of 3234 participants were enrolled in the DPP; 2924 had completed dietary data (67.5% women; mean age: 50.6  $\pm$  10.7 y). Adjusted for calorie intake, baseline weight was negatively associated with carbohydrate intake (-1.14  $\pm$  0.18 kg body weight/100 kcal carbohydrate, *P* < 0.0001) and, specifically, dietary fiber (-1.26  $\pm$  0.28 kg/5 g fiber, *P* < 0.0001). Baseline weight was positively associated with total fat (1.25  $\pm$  0.21 kg/100 kcal, *P* < 0.0001), saturated fat (1.96  $\pm$  0.46 kg/100 kcal, *P* < 0.0001), and protein (0.21  $\pm$  0.05 kg/100 kcal, *P* < 0.0001). For all groups, weight loss after 1 y was associated with increases in carbohydrate intake, specifically dietary fiber, and decreases in total fat and saturated fat intake. **Conclusions:** Higher carbohydrate consumption among DPP participants, specifically high-fiber carbohydrates, and lower total and saturated fat intake best predicted weight loss when adjusted for changes in calorie intake. Our results support the benefits of a high-carbohydrate, high-fiber, low-fat diet in the context of overall calorie reduction leading to weight loss, which may prevent diabetes in high-risk individuals. This trial was registered at clinicaltrials.gov as NCT00004992. *J Nutr* 2017;147:2060–6.

Keywords: diabetes, diet, weight, macronutrient, carbohydrate

## Introduction

Poor diet, lack of physical activity (PA), and obesity are generally accepted risk factors for the development of type 2 diabetes. It is therefore recommended that individuals at risk of type 2 diabetes achieve moderate weight loss through intensive lifestyle modification focused on modifying diet and increasing PA (1). In the Diabetes Prevention Program (DPP), a completed clinical trial beginning in 1996, individuals at high risk of diabetes at

baseline were assigned to a metformin (MET) 850 mg twice daily group, a troglitazone (discontinued in 1998 due to hepatic toxicity) group, a placebo (PLBO) group, or an intensive lifestyle intervention (ILS) group. Individuals in the ILS treatment arm were instructed to reduce their calorie and fat intake, aiming for <25% of total calories from fat and to achieve  $\geq$ 150 min of PA/wk (2). After a mean follow-up of 2.8 y, diabetes risk was

© 2017 American Society for Nutrition. Manuscript received April 10, 2017. Initial review completed May 12, 2017. Revision accepted August 31, 2017. First published online September 27, 2017; doi: https://doi.org/10.3945/jn.117.252395. 58% lower in individuals randomly assigned to the ILS group than those in the PLBO group (2).

Although the low-fat diet was the gold standard weight loss approach at the start of the DPP in 1996, the optimal dietary macronutrient composition for promoting weight loss and reducing diabetes risk is still controversial (3, 4). Because low-fat diets often contain a proportionally higher content of carbohydrates, the primary nutrient that influences postprandial blood glucose concentrations and insulin secretion, their role in diabetes prevention and management is still debated (5). However, the results from the majority of clinical trials suggest that any diet that effectively reduces calorie intake for a sustained period is similarly effective for weight loss (6-8). Several large, prospective cohort studies have reported no association between total carbohydrate intake and diabetes risk (9, 10), whereas some have demonstrated a positive association (11) and others an inverse association (12). Given these mixed findings, it is possible that the types and quality of the carbohydrates consumed and, specifically, their dietary fiber content (13, 14) play an important role in determining the effectiveness of a low-fat, high-carbohydrate diet for weight loss and diabetes prevention (10).

Previous analyses of DPP data demonstrated that weight loss, achieved through reduced calorie intake and increased PA, was the main driver of reduced diabetes risk in the ILS group (15). These findings further emphasize the importance of determining which specific dietary changes are associated with the greatest weight loss in individuals at high risk of diabetes.

Abbreviations used: DPP, Diabetes Prevention Program; ILS, intensive lifestyle intervention; MET, metformin; PA, physical activity; PLBO, placebo.

The primary purpose of our study was to investigate the associations between dietary intake and weight in the DPP cohort at baseline and to evaluate the dietary changes that predicted the most successful weight loss among DPP participants. We evaluated changes over time separately by treatment group because those in the ILS group had an intervention focused on reducing fat. Therefore, the proportionately higher carbohydrate intake and lower fat intake for ILS participants could simply reflect better adherence to the prescribed intervention, whereas the MET group was taking a medication known to influence weight (16). Individuals randomly assigned to troglitazone were not included in these analyses because this treatment arm was discontinued in 1998 due to hepatic toxicity.

## Methods

*DPP.* The DPP was a multicenter, randomized controlled clinical trial, which enrolled adults at higher risk of type 2 diabetes. Enrollment occurred between 1996 and 1999 (2). The study was specifically designed to determine whether lifestyle intervention or treatment with metformin prevents or delays the development of type 2 diabetes. The design and methods of the DPP have been described in detail elsewhere (2), and the study protocol is publicly available (17). Eligible DPP participants were  $\geq 25$  y of age, had a BMI (in kg/m<sup>2</sup>)  $\geq 24$  ( $\geq 22$  for Asian Americans), and had elevated fasting plasma glucose concentrations (95–125 mg/dL or 5.3–6.9 mmol/L) and impaired glucose-tolerance (140–199 mg/dL or 7.8–11.0 mmol/L) during an oral-glucose-tolerance test.

Details of the ILS, MET, and PLBO groups have been described previously (2). Briefly, participants assigned to the ILS group were encouraged to achieve and maintain  $\geq$ 7% weight loss (based on their initial body weight) and were counseled to follow a reduced-calorie, lowfat diet and to engage in  $\geq$ 150 min of moderate-intensity PA/wk. Those assigned to the ILS group received a detailed and individualized 16lesson curriculum focused on diet, exercise, and behavior change that included extensive support from coaches. Participants assigned to the MET group were instructed to consume 850 mg of metformin twice daily. Participants assigned to MET and PLBO groups also received written instructions with standard lifestyle recommendations along with a brief individual session focused on healthy lifestyle once annually. Those assigned to the PLBO group were to take placebo capsules twice daily. The DPP trial was registered at clinicaltrials.gov as NCT00004992.

Measures. Dietary data were collected at baseline and year 1 with the use of a modified version of the Insulin Resistance Atherosclerosis Study's (IRAS) FFQ (18), which contains 117 items and asks about foods consumed over the past year. Six food groups were then determined based on the 1992 USDA Food Pyramid (19) (grains, vegetables, fruits, dairy, meats, and fats) and were further subcategorized into an additional 27 food groups by the DPP Nutrition Coding Center at the University of South Carolina (e.g., high-fiber, low-fat grains, citrus fruit and fruit juice, eggs, lean meat, cruciferous vegetables, etc.). Regular and diet soft drinks were also analyzed separately because they were not included in either the pyramid food groups or the additional food groups and have been proposed to influence weight and diabetes risk (20-22). Alcohol was excluded from the current analysis because associations of alcohol use with weight change and diabetes risk in the DPP have been previously described (23). Calories from alcohol, however, were included in the estimates of total calories. Self-reported PA was assessed through the use of the Modifiable Activity Questionnaire and was summed for all activities performed and expressed as the mean metabolic equivalent for task-hours per week over the previous year (2).

Quantities of each food group were analyzed as servings per day, whereas intake of macronutrients (e.g., carbohydrates, fats, and protein) was assessed in both grams and as percentage of total daily calories (% kcal). One-year changes in dietary intake and weight were calculated

During the Diabetes Prevention Program (DPP) and Diabetes Prevention Program Outcomes Study (DPPOS), the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) of the NIH provided funding to the clinical centers and the Coordinating Center for the design and conduct of the study, and collection, management, analysis, and interpretation of the data (U01 DK048489). The Southwestern American Indian Centers were supported directly by the NIDDK, including its Intramural Research Program, and the Indian Health Service. The General Clinical Research Center Program, National Center for Research Resources, and the Department of Veterans Affairs supported data collection at many of the clinical centers. Funding was also provided by the National Institute of Child Health and Human Development, the National Institute on Aging, the National Eye Institute, the National Heart Lung and Blood Institute, the National Cancer Institute, the Office of Research on Women's Health, the National Institute on Minority Health and Health Disparities, the CDC, and the American Diabetes Association. Bristol-Myers Squibb and Parke-Davis provided additional funding and material support during the DPP, Lipha (Merck-Sante) provided medication and LifeScan Inc. donated materials during the DPP and DPPOS. This research was also supported, in part, by the intramural research program of the NIDDK. LifeScan Inc., Health O Meter, Hoechst Marion Roussel, Inc., Merck-Medco Managed Care, Inc., Merck and Co., Nike Sports Marketing, Slim Fast Foods Co., and Quaker Oats Co. donated materials, equipment, or medicines for concomitant conditions. McKesson BioServices Corp., Matthews Media Group, Inc., and the Henry M. Jackson Foundation provided support services under subcontract with the Coordinating Center at the George Washington University Biostatistics Center.

Author disclosures: ACS, SLE, GW, EJB, ESH, UNI, WCK, MGM, MT, MH, KIR, and LMD, no conflicts of interest.

The sponsor of this study (NIDDK) was represented on the Steering Committee and played a part in study design, how the study was done, and publication. The funding agency was not represented on the writing group, although all members of the Steering Committee had input into the report's contents. All authors in the writing group had access to all data. The opinions expressed are those of the investigators and do not necessarily reflect the views of the funding agencies. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Supplemental Table 1 and the Supplemental Appendix are available from the "Online Supporting Material" link in the online posting of the article and from the same link in the online table of contents at http://jn.nutrition.org.

Address correspondence to ACS, c/o Diabetes Prenetion Program Coordinating Center (e-mail: dppmail@bsc.gwu.edu).

as year 1 intake minus the baseline value so that increases were reported as positive numbers.

*Analysis.* Analyses included study participants in the PLBO, MET, and ILS groups. The associations between diet, baseline weight, and weight change (from baseline to year 1) were assessed by linear regression. Baseline models were adjusted for race/ethnicity, age, sex, total calorie intake, and PA. Change models were further adjusted for baseline weight and changes in calorie intake and physical activity and were stratified by treatment arm. Although this analysis was exploratory and post hoc, a more conservative *P* value of 0.01 was considered statistically significant to reduce the likelihood of type 1 error, given the multiple tests and variables in this analysis and our large sample size. SAS version 9.3 was used for all analyses (SAS Institute).

## **Results**

Baseline dietary data were available for 98.2% of participants (3175 of 3234 total participants), and 90.4% had dietary data available at year 1. The characteristics of DPP participants have been described elsewhere (2); there were no baseline differences in body weight, biochemical measures, sociodemographic factors, or dietary intake between treatment groups. The baseline dietary intakes of the combined sample (all 3 treatment groups) and stratified by treatment group are shown in **Supplemental Table 1**.

Baseline associations of weight with food and nutrient intake. As shown in Table 1, baseline weight was inversely associated with carbohydrate intake (in means  $\pm$  SEs;  $-1.14 \pm 0.18$  kg/100 kcal, P < 0.0001;  $-0.32 \pm 0.04$  kg/% total calories from carbohydrate, P < 0.0001) and, specifically, dietary fiber intake ( $-1.26 \pm 0.28$  kg/5 g dietary fiber, P < 0.0001) at baseline. Within specific food groups and after adjustment for total calorie intake at baseline (Table 1), weight was also inversely associated with total fruit, noncitrus fruit and fruit juice, and dark green and bright yellow vegetables. Baseline weight also tended to be inversely associated with intake of low-fat dairy and low-fat, high-fiber grains, but these associations were not statistically significant (P < 0.01 was used as a cutoff). Body weight at baseline was also positively associated with intake of both regular (P < 0.0085) and diet (P < 0.0001) soft drinks.

Baseline weight was positively associated with total fat intake  $(1.25 \pm 0.28 \text{ kg}/100 \text{ kcal}, P < 0.0001; 0.40 \pm 0.05 \text{ kg}/\%$  total calories from fat, P < 0.0001, and protein intake  $(0.21 \pm 0.52 \text{ kg}/100 \text{ kcal}, P < 0.0001; 0.37 \pm 0.12 \text{ kg}/\%$  total calories from protein, P = 0.0021). Within specific food groups high in fat or protein and after adjustment for total calorie intake (Table 1), baseline weight was positively associated with the meat and legumes groups of the food pyramid  $(1.78 \pm 0.36 \text{ kg/serving}, P < 0.0001)$ , specifically fried fish, eggs, high-fat meat, fried chicken, and poultry, whereas baseline weight was inversely associated with nuts and seeds and dried beans. Baseline weight was also positively associated with intake of fats, oils, and sweets  $(0.57 \pm 0.18 \text{ kg/serving}, P = 0.0018)$ .

Changes in food and nutrient intake predictive of weight loss: PLBO group. As shown in Table 2, weight loss at year 1 was positively associated with increasing protein intake, both as absolute intake adjusted for total calories and as a percentage of total calorie intake  $(-0.30 \pm 0.10 \text{ kg}/40 \text{ kcal}, P = 0.0052;$  $-0.23 \pm 0.05 \text{ kg}/\%$  total calories from protein, P < 0.0001) in the PLBO group. Weight loss also tended to be associated with increases in carbohydrate intake (both as absolute grams adjusted

	Estimate $\pm$ SE <sup>2,3</sup>	Р
Nutrient		
Carbohydrates, per 100 kcal	$-1.1 \pm 0.2$	< 0.0001
Carbohydrates, % calories	$-0.3 \pm 0.0$	< 0.0001
Fat, per 100 kcal	$1.3 \pm 0.3$	< 0.0001
Fat, % calories	$0.4 \pm 0.1$	< 0.0001
Protein, per 100 kcal	$0.2 \pm 0.5$	< 0.0001
Protein, % calories	$0.4 \pm 0.1$	0.0021
Dietary fiber, per 5 g	$-1.3 \pm 0.3$	< 0.0001
Saturated fat, % calories	$0.8 \pm 0.1$	< 0.0001
Saturated fat, per 100 kcal	$2.0 \pm 0.5$	< 0.0001
Food group, <sup>4</sup> servings/d		
Fruit	$-0.4 \pm 0.2$	0.0059
Citrus fruit and juice	$-0.8 \pm 0.5$	0.086
Noncitrus fruit and juice	$-0.5 \pm 0.2$	0.0088
Vegetables	$-0.3 \pm 0.2$	0.22
Tomatoes <sup>5</sup>	$-1.4 \pm 0.7$	0.045
Dark green or bright yellow	$-3.2 \pm 0.7$	< 0.0001
Cruciferous vegetables	$1.3 \pm 1.0$	0.19
Other vegetables <sup>6</sup>	$0.4 \pm 0.4$	0.31
Grains	$0.1 \pm 0.3$	0.62
High-fiber, low-fat grains	$-1.1 \pm 0.5$	0.02
Low-fiber, high-fat grains	$0.3 \pm 0.7$	0.68
Low-fiber, low-fat grains	$0.6 \pm 0.3$	0.046
Dairy	$-0.6 \pm 0.3$	0.018
Low-fat dairy	$-0.6 \pm 0.3$	0.035
High-fat dairy	$-0.4 \pm 0.4$	0.34
Meat and legumes	1.8 ± 0.4	< 0.0001
Fried fish	$10.6 \pm 3.6$	0.0033
High omega-3 fatty acid fish	1.3 ± 2.0	0.51
Low-fat fish (other fish, shellfish)	2.7 ± 1.9	0.17
Eggs	$4.9 \pm 1.3$	0.0001
Dried beans	$-4.0 \pm 1.0$	< 0.0001
Nuts and seeds	$-3.6 \pm 1.2$	0.002
High-fat meat	$3.0 \pm 0.5$	< 0.0001
Lower-fat meat (game or fat removed)	3.4 ± 1.1	0.0024
Fried chicken	8.7 ± 2.5	0.0004
Other (nonfried) poultry	$2.2 \pm 0.8$	0.0036
Fats, oils, and sweets	0.6 ± 0.2	0.0018
Sweets and desserts	$0.4 \pm 0.2$	0.088
Regular soft drinks	$0.9 \pm 0.3$	0.0085
Diet soft drinks	1.6 ± 0.2	< 0.0001

 $^1$  Values are  $\beta$  coefficients and indicate the mean differences in kilograms of body weight at baseline  $\pm$  SE. DPP, Diabetes Prevention Program.

<sup>2</sup> Adjusted for age, sex, race/ethnicity, total calories, physical activity, and weight. Models of percentage of calories from carbohydrates, fat, and protein are not adjusted for calories.

<sup>3</sup> Estimates reflect kilograms of body weight per specified unit of each nutrient and per serving of each food group.

<sup>4</sup> Servings were defined by the DPP Nutrition Coding Center as medium-sized portions for a given age range.

<sup>5</sup> Food items combined to generate the vegetable subcategory tomatoes included spaghetti with sauce, pizza, and tacos.

<sup>6</sup> Food items combined to generate the vegetable subcategory "other vegetables" included French fries.

for total calories and as a percentage of total calorie intake: -0.07  $\pm$  0.04 kg body weight/40 kcal carbohydrates, *P* = 0.072; -0.05  $\pm$  0.02 kg/% total calories from carbohydrates, *P* = 0.01), but this association did not reach statistical significance (*P* < 0.01). However, weight loss was strongly predicted by increases in **TABLE 2** Associations of changes in nutrients and food groups with body weight (kilogram per specified unit of each nutrient) from baseline to year 1 among DPP participants randomly assigned to placebo, intensive lifestyle intervention, or metformin<sup>1</sup>

	Placebo ( <i>n</i> = 978)		Lifestyle (n	Lifestyle ( $n = 967$ )		Metformin ( $n = 979$ )	
	Estimate $\pm$ SE	Р	Estimate $\pm$ SE	Р	Estimate $\pm$ SE	Р	
Nutrient							
Carbohydrates, per 40 kcal	$-0.1 \pm 0.0$	0.072	$-0.2 \pm 0.1$	< 0.0001	$-0.1 \pm 0.0$	0.17	
Carbohydrates, % calories	$-0.1 \pm 0.0$	0.010	$-0.2 \pm 0.0$	< 0.0001	$-0.0 \pm 0.0$	0.063	
Dietary fiber, per 5 g	$-0.6 \pm 0.2$	0.0001	$-1.5 \pm 0.2$	< 0.0001	$-0.5 \pm 0.2$	0.0007	
Fat, per 45 kcal	$0.2 \pm 0.1$	0.0024	$0.3 \pm 0.1$	< 0.0001	$0.1 \pm 0.1$	0.30	
Fat, % calories	$0.1 \pm 0.0$	< 0.0001	$0.2 \pm 0.0$	< 0.0001	$0.0$ $\pm$ $0.0$	0.16	
Saturated fat, per 45 kcal	$0.3 \pm 0.1$	0.0054	$0.8 \pm 0.2$	< 0.0001	$0.3 \pm 0.1$	0.0099	
Saturated fat, % calories	$0.2 \pm 0.1$	< 0.0001	$0.6 \pm 0.1$	< 0.0001	$0.2 \pm 0.1$	0.0002	
Protein, per 40 kcal	$-0.3 \pm 0.1$	0.0052	$-0.3 \pm 0.1$	0.071	$-0.1 \pm 0.1$	0.47	
Protein, % calories	$-0.2 \pm 0.1$	< 0.0001	$-0.1 \pm 0.1$	0.15	$-0.1 \pm 0.1$	0.18	
Food group, <sup>2,3</sup> servings/d							
Fruit	$-0.2 \pm 0.1$	0.019	$-0.4 \pm 0.1$	0.0017	$-0.3 \pm 0.1$	0.0024	
Citrus fruit and juice	$-0.4 \pm 0.3$	0.103	$-0.6 \pm 0.3$	0.061	$-0.4 \pm 0.2$	0.11	
Noncitrus fruit and juice	$-0.2 \pm 0.1$	0.042	$-0.4 \pm 0.1$	0.0032	$-0.3 \pm 0.0$	0.0043	
Vegetables	$-0.4 \pm 0.1$	0.0022	$-0.5 \pm 0.2$	0.0005	$-0.2 \pm 0.1$	0.13	
Tomatoes <sup>4</sup>	$-0.4 \pm 0.3$	0.18	$-1.4 \pm 0.4$	0.0016	$0.2 \pm 0.3$	0.51	
Dark green or bright yellow vegetables	$-0.5 \pm 0.4$	0.16	$-1.7 \pm 0.4$	0.0002	$-0.3 \pm 0.3$	0.30	
Cruciferous vegetables	$-1.6 \pm 0.5$	0.0062	$-0.6 \pm 0.7$	0.40	$-1.1 \pm 0.5$	0.015	
Other vegetables <sup>5</sup>	$-0.4 \pm 0.2$	0.021	$-0.4 \pm 0.3$	0.12	$-0.3 \pm 0.2$	0.17	
Grains	$-0.1 \pm 0.1$	0.63	$-0.2 \pm 0.2$	0.22	$-0.1 \pm 0.1$	0.41	
High-fiber, low-fat grains	$-0.6 \pm 0.2$	0.0057	$-0.6 \pm 0.3$	0.05	$-0.6 \pm 0.2$	0.0050	
Low-fiber, high-fat grains	$0.0$ $\pm$ $0.3$	0.89	$1.0 \pm 0.4$	0.03	$-0.0 \pm 0.3$	0.94	
Low-fiber, low-fat grains	$0.2 \pm 0.2$	0.24	$-0.2 \pm 0.2$	0.25	$0.1 \pm 0.2$	0.38	
Other vegetables <sup>5</sup>	$-0.4 \pm 0.2$	0.021	$-0.4 \pm 0.3$	0.12	$-0.3 \pm 0.2$	0.17	
Dairy	$-0.2 \pm 0.1$	0.071	$0.3 \pm 0.2$	0.15	$-0.0 \pm 0.1$	0.77	
Low-fat dairy	$-0.2 \pm 0.1$	0.14	$-0.3 \pm 0.2$	0.16	$-0.2 \pm 0.1$	0.09	
High-fat dairy	$0.1 \pm 0.2$	0.69	$1.2 \pm 0.3$	< 0.0001	$0.4 \pm 0.2$	0.08	
Meat, eggs, and legumes	$-0.2 \pm 0.2$	0.32	$-0.4 \pm 0.2$	0.14	$-0.1 \pm 0.2$	0.78	
Fried fish	1.0 ± 1.6	0.55	$3.4 \pm 2.5$	0.17	0.5 ± 1.7	0.80	
High omega-3 fatty acid fish	$0.4 \pm 1.0$	0.72	0.6 ± 1.2	0.65	$0.6\pm0.8$	0.45	
Low-fat fish (other fish, shellfish)	$-1.2 \pm 0.9$	0.23	$-1.9 \pm 1.2$	0.095	$-1.8 \pm 1.0$	0.08	
Eggs	$-0.1 \pm 0.5$	0.80	$1.3 \pm 0.9$	0.15	$0.0\pm0.7$	0.97	
Dried beans	$-0.3 \pm 0.5$	0.53	$-2.4 \pm 0.7$	0.0002	$-0.0 \pm 0.5$	0.95	
Nuts and seeds	$0.0$ $\pm$ $0.5$	0.99	$1.0 \pm 0.8$	0.18	$-0.8 \pm 0.5$	0.07	
High-fat meat	$-0.0 \pm 0.3$	0.92	$0.4 \pm 0.4$	0.37	$0.1 \pm 0.3$	0.84	
Lower-fat meat (game or fat removed)	$0.2 \pm 0.5$	0.67	$0.1 \pm 0.7$	0.84	$1.1 \pm 0.5$	0.03	
Fried chicken	0.5 ± 1.2	0.66	2.0 ± 2.3	0.40	$-1.2 \pm 1.0$	0.23	
Other (nonfried) poultry	$-0.4 \pm 0.3$	0.31	$-1.7 \pm 0.5$	0.0013	$-0.1 \pm 0.3$	0.80	
Fats, oils, and sweets	$0.3 \pm 0.1$	0.0011	$0.6 \pm 0.1$	< 0.0001	$0.2 \pm 0.1$	0.026	
Sweets and desserts	$0.4 \pm 0.1$	0.0041	$0.3 \pm 0.2$	0.059	$0.4 \pm 0.1$	0.0025	
Regular soft drinks	$0.2 \pm 0.2$	0.24	$0.4 \pm 0.3$	0.10	$0.4 \pm 0.2$	0.04	
Diet soft drinks	$-0.1 \pm 0.1$	0.28	$-0.8 \pm 0.2$	0.0001	$0.2 \pm 0.2$	0.15	

<sup>1</sup> Adjusted for age, sex, race/ethnicity, baseline weight, baseline calories, change in calories, baseline physical activity, and change in physical activity. DPP, Diabetes Prevention Program.

<sup>2</sup> Servings were defined by the DPP Nutrition Coding Center as medium-sized portions for a given age range.

<sup>3</sup> Effect estimates are β-coefficients and reflect the mean change in kilograms of body weight per serving of each food group.

<sup>4</sup> Food items combined to generate the vegetable subcategory "tomatoes" included spaghetti with sauce, pizza, and tacos.

<sup>5</sup> Food items combined to generate the vegetable subcategory "other vegetables" included French fries.

dietary fiber intake  $(-0.60 \pm 0.15 \text{ kg} \text{ body weight/5 g} \text{ increase}$ in dietary fiber, P = 0.0001) and, particularly, increases in servings of vegetables per day, specifically cruciferous vegetables and high-fiber, low-fat grains (Table 2). No associations were observed between weight loss and changes in the intake of regular or diet soft drinks when adjusted for total calorie intake.

After adjustment for baseline and change in calorie intake, weight loss was strongly associated with decreases in total fat  $(0.15 \pm 0.05 \text{ kg} \text{ body weight}/45 \text{ kcal of fat, } P = 0.0024; 0.11 \pm 0.02 \text{ kg}/\%$  total calories from fat, P < 0.0001) and saturated fat intake  $(0.30 \pm 0.10 \text{ kg} \text{ body weight}/45 \text{ kcal saturated fat, } P = 0.0054; 0.23 \pm 0.05 \text{ kg}/\%$  total calories from saturated fat, P < 0.0001), both as absolute grams adjusted for total calories and as a percentage of total calorie intake (Table 2), and, specifically, decreasing intake of fats, oils, and sweets (Table 2). A weight change at year 1 was not associated with changes in total consumption of meats and legumes (e.g., poultry, eggs, fish, etc.).

Changes in food and nutrient intake predictive of weight loss: ILS group. In the ILS group, in which participants were prescribed a low-fat, high-carbohydrate diet, trends similar to the PLBO group were observed, but tended to be of greater magnitude. Weight loss at year 1 was strongly and significantly associated with increases in carbohydrate intake ( $-0.22 \pm 0.05 \text{ kg}/40 \text{ kcal}$ , P < 0.0001;  $-0.19 \pm 0.03 \text{ kg}/\%$  total calories from carbohydrate, P < 0.0001). As in the PLBO group, weight loss was positively associated with increased dietary fiber intake ( $-1.45 \pm 0.20 \text{ kg}/5 \text{ g}$ , P < 0.0001), independent of changes in calorie intake. In particular, weight loss was positively associated with increases of fruit, specifically noncitrus fruit and fruit juice, and vegetables, specifically tomatoes and dark green and bright yellow vegetables (Table 2).

In the ILS group, weight loss was associated with decreases in total fat ( $0.34 \pm 0.06$  kg/45 kcal, P < 0.0001;  $0.23 \pm 0.03$  kg/% total calories from fat, P < 0.0001) and saturated fat intake ( $0.75 \pm 0.15$  kg/45 kcal, P < 0.0001;  $0.55 \pm 0.07$  kg/% total calories from saturated fat, P < 0.0001), specifically decreases in servings of fats, oils, sweets, and high-fat dairy (Table 2). Weight change at year 1 was not associated with changes in total protein intake, although weight loss was positively associated with increases in the intake of low-fat poultry and dried beans (Table 2). In contrast with the PLBO group, weight loss was associated with consumption of diet soft drinks ( $-0.77 \pm 0.19$  kg/serving, P < 0.0001) in the ILS group.

Changes in food and nutrient intake predictive of weight loss: MET group. In the MET group, weight loss at year 1 was not associated with increases in carbohydrate intake (Table 2). However, consistent with the PLBO and ILS groups, weight loss was positively associated with increases in dietary fiber intake  $(-0.54 \pm 0.15 \text{ kg/5 g}$  dietary fiber, P = 0.0007), specifically increases in the consumption of total fruit, noncitrus fruit and fruit juice, and high-fiber, low-fat grains (Table 2). Weight loss was also positively associated with decreases in the intake of saturated fat  $(0.28 \pm 0.10 \text{ kg/5 g}, P = 0.0099; 0.20 \pm 0.05 \text{ kg/\%}$ total calories from saturated fat, P = 0.0002), specifically sweets and desserts. In contrast with the other treatment groups, weight change was not associated with changes in total fat intake in those assigned to the MET group.

## Discussion

Lower body weight at baseline was associated with higher carbohydrate intake (both as absolute intake and as a percentage of total calories) for all participants combined. As expected, increasing carbohydrates, in the context of overall calorie reduction, from DPP baseline to year 1 was strongly associated with weight loss in the ILS group, which was likely due to the low-fat, high-carbohydrate diet that ILS participants adopted. However, in the PLBO group, weight loss was also moderately associated with increases in carbohydrate intake as a percentage of total calories during the first year of DPP. For MET participants, weight change was not associated with a change in carbohydrate intake, which was possibly due to diet-independent effects of the medication on weight loss.

Weight loss was strongly associated with increases in dietary fiber in all 3 groups, and this association remained significant after adjustment for changes in calorie intake. This finding suggests that higher consumption of carbohydrates, specifically those high in fiber, may in fact be beneficial for weight control, in the context of a diet focusing on reducing total fat and calorie intake. Baseline weight was positively associated with total fat and saturated fat intake and consumption of high-fat food groups, such as fats, oils, sweets, poultry, and meat, and weight loss was predicted by decreasing total and saturated fat intakes in all DPP participants regardless of treatment allocation. Weight loss was also associated with an increased percentage of calories from protein in the PLBO group, but not in the ILS or MET groups.

The observation that increases in carbohydrate consumption and lowering fat intake (in the context of energy restriction) predicted weight loss for individuals randomly assigned to the ILS group is not surprising because reducing fat was a primary goal of the dietary intervention. It is noteworthy, however, that a similar trend was also observed in the PLBO group, which was comprised of individuals who did not undergo an intensive dietary intervention. Although lowering fat intake is often thought to promote weight loss through lowering energy density of the diet (24), these analyses adjusted for baseline weight and changes in calorie intake, suggesting that energy-independent mechanisms (e.g., changes in the gut microbiota, satietyenhancing effects of dietary fiber, etc.) may also be important contributors.

These findings are consistent with those of other studies reporting that higher carbohydrate intake (when adjusted for total calories) is associated with a lower risk of overweight and obesity. The beneficial effects of diets that lower calorie intake and contain proportionally higher carbohydrates, specifically those diets emphasizing low-glycemic index carbohydrates that are high in dietary fiber, have been reported in several randomized controlled weight loss trials (25). Similar findings have also been reported in overweight and obese adults randomly assigned to 1 of 3 isocaloric diets varying in carbohydrate content and glycemic index for 6 mo (26).

In contrast, several studies have shown greater weight loss on high-protein, low-carbohydrate diets compared with an isocaloric low-fat, high-carbohydrate control (27). However, some studies, including a systematic review, do not report any differences in weight loss after several isoenergetic diets varying in macronutrient composition (28, 29). Given these inconsistent findings, it is critical to consider the types of foods that are being consumed because different foods within a given food group (e.g., grains) or nutrient category (e.g., carbohydrates) likely have divergent effects on weight and health (30–32).

The observation that increasing carbohydrate intake, specifically increasing fruit, vegetable, and fiber intake, in the context of overall calorie reduction predicts weight loss, independent of total calorie intake, may be explained by several related mechanisms. First, soluble fibers in fruits and vegetables delay the rate of gastric emptying, increasing satiety and slowing intestinal glucose absorption and postprandial insulin secretion (33). In addition, nondigestible polysaccharides delivered as dietary fiber stimulate the production of SCFAs in the distal colon, which may alter energy metabolism and improve the metabolic function of skeletal muscle and adipose tissue (34). SCFAs are also thought to potentially increase energy expenditure, perhaps due to increased thermogenesis (35). However, whether increased production of SCFAs is beneficial for weight control remains unknown (34).

Another emerging mechanism that may explain our findings involves the potential prebiotic effects of dietary fiber and other biologically active compounds present in fruits and vegetables (36). Many constituents of plant-based foods, including inulin, have been suggested to work as prebiotics, which stimulate the growth of beneficial bacterial populations in the gut. Evidence from animal and human studies suggests that the composition and function of the gut microbiota play critical roles in energy homeostasis and the development of obesity (37), which may also explain the observed benefits of high-fiber carbohydrates, independent of total calorie intake. Furthermore, many of the high-carbohydrate foods associated with weight loss are very low in energy density, which may augment satiety, consistent with the concept of "volumetrics" for weight control (38, 39).

Interestingly, higher consumption of diet soda was associated with a higher weight at baseline; however, increases in diet soda intake from baseline to year 1 predicted weight loss in the ILS group, but not in the PLBO or MET groups. Because the role of diet soda in weight and health is highly controversial (21, 40), these findings suggest that replacing sugar-sweetened beverages with diet soda may serve as a useful tool for lowering calorie intake, specifically in individuals cognitively engaged in lowering calorie intake (41). However, simply consuming diet soda without intentionally modifying other aspects of the overall diet is unlikely to be effective in achieving calorie reduction and weight loss (42).

The limitations of the present study are the use of an FFQ, which requires participants to recall their intake over a 1-y period, and the self-reported dietary data collection, which likely led to underreporting of energy intake. However, the IRAS instrument has been validated in a multiethnic population and allows for reporting of additional food and beverage items not listed on the questionnaire. Our analysis is also limited by the assessment of dietary intake only at baseline and year 1, given that the mean follow-up in DPP was almost 3 y, and the absence of a direct comparison with a high-fat, reduced-calorie diet. Despite these limitations, DPP involved a large, diverse sample of individuals at high risk of diabetes and had very low attrition over the follow-up period. Our analysis is also novel because prior analyses of DPP dietary intake data have been primarily descriptive (43) or have assessed only nutrients rather than foods and food groups (15). The current investigation also extends on the prior report of Mayer-Davis et al. (44) in evaluating subcategories (e.g., high-fiber, low-fat grains and low-fiber, low-fat grains) of pyramid food groups (e.g., grains, fruits, and vegetables).

Taken together, our findings suggest that, in the context of overall calorie reduction, a dietary shift toward greater carbohydrate and lower fat intake, specifically increasing the intake of dietary fiber, fruits, and vegetables, promotes weight loss in individuals at high risk of developing type 2 diabetes. Therefore, emphasis on increasing carbohydrate- and fiber-rich fruits, vegetables, and whole grains while reducing total calorie intake may provide a unique opportunity for achieving longer-term weight loss and maintenance (43). Given the widespread public perception that carbohydrates are detrimental in increasing diabetes risk and the increasing prominence of low-carbohydrate diets for weight loss (45), the current findings are critical to the development of evidence-based recommendations for optimal dietary approaches to prevent diabetes.

#### Acknowledgments

A complete list of centers, investigators, and staff can be found in the **Supplemental Appendix**. The authors' responsibilities were as follows—ACS, SLE, and KIR: designed the research; SLE: performed the statistical analyses; ACS, LMD, and SLE: interpreted the data; ACS: wrote the first draft of the manuscript and had primary responsibility for the final content; SLE: analyzed the data; ACS, SLE, MT, WCK, KIR, and LMD: wrote the paper; GW, EJB, ESH, UNI, MGM, and MH: reviewed the manuscript and contributed to the discussion; and all authors: were involved in editing the manuscript and read and approved the final manuscript.

## References

- American Diabetes Association, Bantle JP, Wylie-Rosett J, Albright AL, Apovian CM, Clark NG, Franz MJ, Hoogwerf BJ, Lichtenstein AH, Mayer-Davis E, Mooradian AD, et al. Nutrition recommendations and interventions for diabetes: a position statement of the American Diabetes Association. Diabetes Care 2008;31:S61–78.
- Knowler WC, Barrett-Connor E, Fowler SE, Hamman RF, Lachin JM, Walker EA, Nathan DM; Diabetes Prevention Program Research Group. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. N Engl J Med 2002;346:393–403.
- van Dam RM, Rimm EB, Willett WC, Stampfer MJ, Hu FB. Dietary patterns and risk for type 2 diabetes mellitus in U.S. men. Ann Intern Med 2002;136:201–9.
- 4. Maki KC, Phillips AK. Dietary substitutions for refined carbohydrate that show promise for reducing risk of type 2 diabetes in men and women. J Nutr 2015;145:159S-63S.
- Sheard NF, Clark NG, Brand-Miller JC, Franz MJ, Pi-Sunyer FX, Mayer-Davis E, Kulkarni K, Geil P. Dietary carbohydrate (amount and type) in the prevention and management of diabetes: a statement by the american diabetes association. Diabetes Care 2004;27: 2266–71.
- Sacks FM, Bray GA, Carey VJ, Smith SR, Ryan DH, Anton SD, McManus K, Champagne CM, Bishop LM, Laranjo N, et al. Comparison of weight-loss diets with different compositions of fat, protein, and carbohydrates. N Engl J Med 2009;360:859–73.
- Kennedy ET, Bowman SA, Spence JT, Freedman M, King J. Popular diets: correlation to health, nutrition, and obesity. J Am Diet Assoc 2001;101:411–20.
- Foreyt JP, Salas-Salvado J, Caballero B, Bullo M, Gifford KD, Bautista I, Serra-Majem L. Weight-reducing diets: are there any differences? Nutr Rev 2009;67:S99–101.
- Schulze MB, Schulz M, Heidemann C, Schienkiewitz A, Hoffmann K, Boeing H. Carbohydrate intake and incidence of type 2 diabetes in the European Prospective Investigation into Cancer and Nutrition (EPIC)-Potsdam Study. Br J Nutr 2008;99:1107–16.
- AlEssa HB, Bhupathiraju SN, Malik VS, Wedick NM, Campos H, Rosner B, Willett WC, Hu FB. Carbohydrate quality and quantity and risk of type 2 diabetes in US women. Am J Clin Nutr 2015;102:1543–53.
- Alhazmi A, Stojanovski E, McEvoy M, Garg ML. Macronutrient intakes and development of type 2 diabetes: a systematic review and metaanalysis of cohort studies. J Am Coll Nutr 2012;31:243–58.
- Hodge AM, English DR, O'Dea K, Giles GG. Glycemic index and dietary fiber and the risk of type 2 diabetes. Diabetes Care 2004;27:2701–6.
- Meyer KA, Kushi LH, Jacobs DR Jr., Slavin J, Sellers TA, Folsom AR. Carbohydrates, dietary fiber, and incident type 2 diabetes in older women. Am J Clin Nutr 2000;71:921–30.
- Montonen J, Knekt P, Jarvinen R, Aromaa A, Reunanen A. Whole-grain and fiber intake and the incidence of type 2 diabetes. Am J Clin Nutr 2003;77:622–9.
- Hamman RF, Wing RR, Edelstein SL, Lachin JM, Bray GA, Delahanty L, Hoskin M, Kriska AM, Mayer-Davis EJ, Pi-Sunyer X, et al. Effect of weight loss with lifestyle intervention on risk of diabetes. Diabetes Care 2006;29:2102–7.
- Desilets AR, Dhakal-Karki S, Dunican KC. Role of metformin for weight management in patients without type 2 diabetes. Ann Pharmacother 2008;42:817–26.
- Diabetes Prevention Program Research Group. Protocol for the Diabetes Prevention Program (DPP) [Internet]. 2001 [cited 2017 Jun 1]. Available from: https://dppos.bsc.gwu.edu/documents/1124073/1127212/ DPPPROTOCOL.PDF/807eddd1-d9bf-497d-89f0-5de15fc43d79.
- Wagenknecht LE, Mayer EJ, Rewers M, Haffner S, Selby J, Borok GM, Henkin L, Howard G, Savage PJ, Saad MF, et al. The insulin resistance atherosclerosis study (IRAS) objectives, design, and recruitment results. Ann Epidemiol 1995;5:464–72.
- USDA Center for Nutrition Policy and Promotion. The food guide pyramid [Internet]. [cited 2017 Jun 1]. Available from: https://www. cnpp.usda.gov/sites/default/files/archived\_projects/FGPPamphlet.pdf.

- Malik VS, Pan A, Willett WC, Hu FB. Sugar-sweetened beverages and weight gain in children and adults: a systematic review and metaanalysis. Am J Clin Nutr 2013;98:1084–102.
- Fowler SP, Williams K, Resendez RG, Hunt KJ, Hazuda HP, Stern MP. Fueling the obesity epidemic? Artificially sweetened beverage use and long-term weight gain. Obesity (Silver Spring) 2008;16: 1894–900.
- 22. O'Connor L, Imamura F, Lentjes M, Khaw K, Wareham N, Forouhi N. Prospective associations and population impact of sweet beverage intake and type 2 diabetes, and effects of substitutions with alternative beverages. Diabetologia 2015;58:1474–83.
- 23. Crandall JP, Polsky S, Howard AA, Perreault L, Bray GA, Barrett-Connor E, Brown-Friday J, Whittington T, Foo S, Ma Y, et al.; Diabetes Prevention Program Research Group. Alcohol consumption and diabetes risk in the Diabetes Prevention Program. Am J Clin Nutr 2009;90:595–601.
- Bray GA, Siri-Tarino PW. The role of macronutrient content in the diet for weight management. Endocrinol Metab Clin North Am 2016; 45:581–604.
- 25. Santiago S, Zazpe I, Bes-Rastrollo M, Sanchez-Tainta A, Sayon-Orea C, de la Fuente-Arrillaga C, Benito S, Martinez JA, Martinez-Gonzalez MA. Carbohydrate quality, weight change and incident obesity in a Mediterranean cohort: the SUN Project. Eur J Clin Nutr 2015;69:297–302.
- 26. Juanola-Falgarona M, Salas-Salvado J, Ibarrola-Jurado N, Rabassa-Soler A, Diaz-Lopez A, Guasch-Ferre M, Hernandez-Alonso P, Balanza R, Bullo M. Effect of the glycemic index of the diet on weight loss, modulation of satiety, inflammation, and other metabolic risk factors: a randomized controlled trial. Am J Clin Nutr 2014;100:27–35.
- 27. Te Morenga LA, Levers MT, Williams SM, Brown RC, Mann J. Comparison of high protein and high fiber weight-loss diets in women with risk factors for the metabolic syndrome: a randomized trial. Nutr J 2011;10:40.
- Naude CE, Schoonees A, Senekal M, Young T, Garner P, Volmink J. Low carbohydrate versus isoenergetic balanced diets for reducing weight and cardiovascular risk: a systematic review and meta-analysis. PLoS One 2014;9:e100652.
- Noakes M, Keogh JB, Foster PR, Clifton PM. Effect of an energyrestricted, high-protein, low-fat diet relative to a conventional highcarbohydrate, low-fat diet on weight loss, body composition, nutritional status, and markers of cardiovascular health in obese women. Am J Clin Nutr 2005;81:1298–306.
- van Dam RM, Seidell JC. Carbohydrate intake and obesity. Eur J Clin Nutr 2007;61:S75–99.

- Wylie-Rosett J, Segal-Isaacson CJ, Segal-Isaacson A. Carbohydrates and increases in obesity: does the type of carbohydrate make a difference? Obes Res 2004;12:124S–9S.
- 32. Slyper AH. The influence of carbohydrate quality on cardiovascular disease, the metabolic syndrome, type 2 diabetes, and obesity an overview. J Pediatr Endocrinol Metab 2013;26:617–29.
- 33. Konings E, Schoffelen PF, Stegen J, Blaak EE. Effect of polydextrose and soluble maize fibre on energy metabolism, metabolic profile and appetite control in overweight men and women. Br J Nutr 2014;111:111–21.
- Canfora EE, Jocken JW, Blaak EE. Short-chain fatty acids in control of body weight and insulin sensitivity. Nat Rev Endocrinol 2015;11:577–91.
- Hu J, Lin S, Zheng B, Cheung PC. Short-chain fatty acids in control of energy metabolism. Crit Rev Food Sci Nutr 2016 27:1–7.
- Landete JM. Updated knowledge about polyphenols: functions, bioavailability, metabolism, and health. Crit Rev Food Sci Nutr 2012;52: 936–48. Retraction in: Crit Rev Food Sci Nutr 2015;55:1792.
- Sanz Y, Santacruz A, Gauffin P. Gut microbiota in obesity and metabolic disorders. Proc Nutr Soc 2010;69:434–41.
- Rolls BJ, Castellanos VH, Halford JC, Kilara A, Panyam D, Pelkman CL, Smith GP, Thorwart ML. Volume of food consumed affects satiety in men. Am J Clin Nutr 1998;67:1170–7.
- 39. Rolls BJ, Meengs JS, Roe LS. Variations in cereal volume affect the amount selected and eaten for breakfast. J Acad Nutr Diet 2014;114:1411–6.
- Swithers SE. Artificial sweeteners produce the counterintuitive effect of inducing metabolic derangements. Trends Endocrinol Metab 2013;24: 431–41.
- Peters JC, Beck J. Low Calorie Sweetener (LCS) use and energy balance. Physiol Behav 2016;164:524–8.
- Sylvetsky AC, Blau JE, Rother KI. Understanding the metabolic and health effects of low-calorie sweeteners: methodological considerations and implications for future research. Rev Endocr Metab Disord 2016 17:187–94.
- 43. Jaacks LM, Ma Y, Davis N, Delahanty LM, Mayer-Davis EJ, Franks PW, Brown-Friday J, Isonaga M, Kriska AM, Venditti EM, et al. Long-term changes in dietary and food intake behaviour in the Diabetes Prevention Program Outcomes Study. Diabet Med 2014;31:1631–42.
- 44. Mayer-Davis EJ, Sparks KC, Hirst K, Costacou T, Lovejoy JC, Regensteiner JG, Hoskin MA, Kriska AM, Bray GA; Diabetes Prevention Program Research Group. Dietary intake in the diabetes prevention program cohort: baseline and 1-year post randomization. Ann Epidemiol 2004;14:763–72.
- 45. Malik VS, Hu FB. Popular weight-loss diets: from evidence to practice. Nat Clin Pract Cardiovasc Med 2007;4:34–41.