Effects of variation in protein and carbohydrate intake on body mass and composition during energy restriction: a meta-regression[1–3]

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ABSTRACT

Background: It is unclear whether low-carbohydrate, high-protein, weight-loss diets benefit body mass and composition beyond energy restriction alone.

Objective: The objective was to use meta-regression to determine the effects of variations in protein and carbohydrate intakes on body mass and composition during energy restriction.

Design: English-language studies with a dietary intervention of ≥4200 kJ/d (1000 kcal/d), with a duration of ≥4 wk, and conducted in subjects aged ≥19 y were considered eligible for inclusion. A self-reported intake in conjunction with a biological marker of macronutrient intake was required as a minimum level of dietary control. A total of 87 studies comprising 165 intervention groups met the inclusion criteria.

Results: After control for energy intake, diets consisting of ≤35–41.4% energy from carbohydrate were associated with a 1.74 kg greater loss of body mass, a 0.69 kg greater loss of fat-free mass, a 1.29% greater loss in percentage body fat, and a 2.05 kg greater loss of fat mass than were diets with a higher percentage of energy from carbohydrate. In studies that were conducted for >12 wk, these differences increased to 6.56 kg, 1.74 kg, 3.55%, and 5.57 kg, respectively. Protein intakes of >1.05 g/kg were associated with 0.60 kg additional fat-free mass retention compared with diets with protein intakes ≤1.05 g/kg. In studies conducted for >12 wk, this difference increased to 1.21 kg. No significant effects of protein intake on loss of either body mass or fat mass were observed.

Conclusion: Low-carbohydrate, high-protein diets favorably affect body mass and composition independent of energy intake, which in part supports the proposed metabolic advantage of these diets. *Am J Clin Nutr* 2006;83:260–74.

KEY WORDS Meta-analysis, body composition, high-protein diet, low-carbohydrate diet, weight loss

INTRODUCTION

Low-carbohydrate diets have become popular in recent years and contain less carbohydrate than that found in the Acceptable Macronutrient Distribution Range of 45–65% of energy (1). Samaha et al (2) reported that a low-carbohydrate diet resulted in greater weight loss than did a low-fat diet over a period of 6 mo; however, this was confounded by a greater, but not significant, reduction in energy intake in the low-carbohydrate group. In other studies, low-carbohydrate diets have resulted in greater weight loss than have low-fat diets, despite similar energy intakes between groups (3–5). However, this was not observed in all studies (6). Thus, whether a reduction in carbohydrate intake offers any benefit beyond energy restriction alone is unclear.

Low-carbohydrate diets typically contain more protein than the Recommended Dietary Allowance (RDA) of 0.8 g protein/kg body mass (7). The protein RDA is established by using data from subjects in energy balance (7). Because energy restriction can decrease nitrogen balance (8), the RDA may not be optimal for fat-free mass (FFM) retention during energy restriction. The effects of replacing carbohydrate with protein during energy restriction have been the focus of some recent investigations (9–12), but results have been inconsistent, with some studies showing an increased fat loss or FFM preservation in women but not men (9–11) and one study showing no effect (12).

These inconsistencies may relate to either differences in the study designs or small trials with low statistical power. Thus, it may be advantageous to combine the results of dietary intervention trials with meta-regression and to use study-level and group-level characteristics to predict changes in body mass and composition. Bravata et al (13) performed a meta-analysis of 94 dietary intervention trials and observed that carbohydrate content was not associated with the degree of weight loss ($P = 0.90$). However, they did not present data on body composition. It is also possible that they did not detect an effect of carbohydrate intake because of the high heterogeneity between the studies. In support for this possibility, they reported a near-trend ($P = 0.10$) of carbohydrate intake on weight loss when only a subset of homogeneous trials was examined. They excluded highly controlled interventions in which subjects were confined to a hospital or research center. Because self-reported energy intake is unreliable (14), a meta-regression of more highly controlled dietary interventions is needed. The purpose of this meta-regression was to determine the effects of variations in protein and carbohydrate intake on body mass and body composition measurements during energy restriction.

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TABLE 1
Results of literature search

Description	No. of articles
PubMed keyword searches	
Search 1: *body* AND *composition* AND *diet* LIMIT English, human	3396
Search 2: *body* AND *composition* AND *diet* LIMIT 1 January 2003–19 July 2004[1]	672
Search 3: *diet* AND *body* AND *weight* NOT *cancer* LIMIT All adult: ≥19 y, English, randomized controlled trial, human	1412
Search 4: *diet* AND *body* AND *weight* LIMIT 1 January 1950–1 January 1970[2]	1467
Search 5: *diet* AND *weight* LIMIT OLDMEDLINE (for Pre-1966)	302
Search 6: *diet* AND *weight* AND (*loss* OR *reduction* OR *reduce*) NOT *cancer* NOT *HIV* NOT *AIDS* NOT *body* LIMIT All adult: ≥19 y, English, randomized controlled trial, human, MEDLINE	275
Search 7: *diet* AND *weight* AND (*loss* OR *reduction* OR *reduce*) NOT *cancer* NOT *HIV* NOT *AIDS* NOT *body* LIMIT All adult: ≥19 y, English, clinical trial, human, MEDLINE	381
Search 8: *diet* AND (*weight* OR "*body composition*" OR "*body mass*") NOT (*cancer* OR *HIV* OR *AIDS*) LIMIT All adult: ≥19 y, English, human, 20 July 2004–18 September 2005[3]	880
Cochrane Central Register of Controlled Trials keyword searches	
Search 1: *diet* AND *body* AND (*composition* OR *weight*) LIMIT Ovid full text	48
Search 2: *diet* AND *body* AND (*composition* OR *weight*) LIMIT embase	279
Search 3: *diet* AND *body* AND (*composition* OR *weight*) LIMIT MEDLINE	1737
CINAHL keyword searches	
Search 1: MM "*Obesity-Diet Therapy*"	88
Search 2: MM "*Diet, reducing*" LIMIT Research	170
SPORT Discus keyword searches	
Search 1: *diet* AND *body* AND (*composition* OR *weight*) LIMIT Journal-Article, English	641
Relevant articles identified via bibliography searches	30
Total relevant articles (excluding duplicates)	771
Exclusion criteria[4]	
Inadequate dietary control	325
Insufficient reported data for abstraction	101
Use of drug or supplement that affected weight loss	13
No energy deficit or weight loss	38
Postpartum females	1
Energy intake <4200 kJ/d (1000 kcal/d)	166
Duration <4 wk	49
Hypokinesia	1
Total articles excluded from analysis	694
Total articles included (excluding duplicates)	87

[1] When search 1 was limited to studies conducted in humans and published in English, some relevant articles from 2004 were not present in the results; therefore, a search of 2003–2004 was completed without these limits.
[2] Some older relevant studies were not classified under the randomized controlled trial classification, therefore, this search was performed to identify older studies that may not have been identified in search 3.
[3] An additional search through 2005 was completed when the initial revisions of this article were completed.
[4] Several articles met >1 exclusion criterion.

SUBJECTS AND METHODS

Study selection

Searches for English language studies that were published between 1 January 1950 and 18 September 2005 were performed in PubMed, the Cochrane Central Register of Controlled Trials, the Cumulative Index of the Nursing and Allied Health Literature, and SportDiscus (**Table 1**). Relevant studies published before 1950 were identified via bibliography searches of the retrieved articles. Studies involving a dietary intervention, subjects aged ≥19 y, and pre- and postdietary measurements of body mass or body composition constituted the initial criteria for eligibility. Sufficient data to determine energy intake, baseline body mass, macronutrient composition, and the mean change of the outcome measures were also required. The exclusion criteria are shown in Table 1. Studies were selected to meet a minimum level of dietary control. When dietary intake was self-reported, a biological marker measurement (ie, urinary or serum ketones, urinary nitrogen excretion, blood urea nitrogen, or plasma fatty acids) was required as an objective measure of compliance. In the absence of a biological marker, the investigators had to supply ≥60% of the subjects' energy intake as a requirement for eligibility in the meta-regression. Studies in which the authors reported that subjects were not in full compliance with the dietary intervention were excluded. All studies were performed in accordance with ethical guidelines.

Data abstraction

Data were tabulated onto a spreadsheet with the use of MICROSOFT EXCEL (Microsoft Corp, Redmond, WA). Treatment arms that did not meet the inclusion criteria were excluded from the analysis. For crossover designs, separate rows were coded for each intervention. Periods of energy balance or insufficient dietary control were excluded.

Variables abstracted from each study were the following: study design, *n*, age, sex, baseline body mass (kg), quality of dietary control (moderate or high), duration of treatment (wk), exercise intervention (yes or no), method to measure body composition (field or laboratory), protein intake (percentage of energy, total g, and g/kg body mass), carbohydrate intake (percentage of energy and total g), fat intake (percentage of energy and total g), total energy intake (kJ), body mass change (kg), fat-free mass change (kg), percentage change in body fat (BF), and percentage change in fat mass (FM). The study design, age, sex, baseline body mass, quality of dietary control, duration of treatment, exercise intervention, method to measure body composition, percentage energy from carbohydrate (categorized into quartiles), and protein intake (g/kg body mass; categorized into quartiles) were included as predictors in the statistical models. If means (±SEMs) were not reported, the values were calculated from the individual subject data (when available). Data from subjects who did not meet the inclusion criteria were not included in the calculations. In some studies, there were multiple treatment arms, but the mean age was only provided for the entire study participant population. In those cases, the mean age for the entire participant population was included.

A dietary control quality classification was assigned to each group. The control was classified as moderate when the dietary control consisted of food records and a biological marker. The control was also classified as moderate when only part of the subjects' energy intake was supplied to them. The control was classified as high when all subjects' energy intake was supplied. The mean duration of the study was used when the duration of diet varied. The method of measuring body composition was classified as either a laboratory measure (ie, dual-energy X-ray absorptiometry, air densitometry, or hydrodensitometry) or a field measure (ie, skinfold thicknesses, bioelectric impedance analysis, or total-body electrical conductivity) (15). Carbohydrate intake (percentage energy) and protein intake (g/kg body mass) were classified into quartiles. Additional analyses were carried out with carbohydrate intake separated into low (1st quartile) and high (quartiles 2–4) intakes and protein intake separated into low (less than or equal to the median) and high (more than the median) intakes.

An independent investigator recoded 10 randomly selected studies to test the reliability of the abstraction process. Per case agreement was determined by dividing the variables coded the same by the total number of variables. A mean agreement of 0.96 was reached, which indicated that the abstraction process was reliable.

Missing values

In many studies, there was insufficient data to abstract all variables. When a value was missing for a dependent variable, the intervention group was excluded from the analysis for that outcome. Missing values for covariates were calculated from available data when possible. Any remaining missing covariates and within-group variances were replaced by using multiple imputation (16). Ten imputed data sets were created and analyzed for each outcome, and the results were combined for statistical inferences.

Statistical analyses

The variance within each intervention group was calculated as the squared SEM of the difference between pre- and postdiet outcomes. If the SEM of the difference was not reported, the SEM of the difference was calculated by using the *P* value or CI (when available). Otherwise, an upper bound on the SEM was calculated by using the following formula (17):

$$\mathrm{SEM} = \sqrt{[(s_1^2/n) + (s_2^2/n)]} \qquad (1)$$

where s_1 and s_2 are the SD for the pre- and posttest means, respectively. Where the posttest SD was not reported, the pretest SD was used in its place.

Meta-analyses were performed with hierarchical linear mixed models, which modeled the variation between studies as a random effect, the variation between treatment groups as a random effect nested within studies, and group-level predictors as fixed effects (18). The within-group variances were assumed known. Model variables were estimated by the method of maximum likelihood. Denominator dfs for statistical tests and CIs were calculated according to Berkey et al (19) For each outcome, an intercept-only model was created. Models were constructed for the change in body mass, FFM, percentage BF, and FM. For each outcome variable, a full model was created with all predictors thought to influence that outcome (study design, age, sex, baseline body mass, quality of dietary control, duration of treatment, exercise intervention, method to measure body composition, energy intake, percentage of energy from carbohydrate intake, and protein intake in g/kg). Models were reduced by removing predictors one at a time, starting with the most insignificant predictor (20). The final model represented the reduced model with the lowest Bayesian Information Criterion (21) that was not significantly different ($P > 0.05$) from the full model when compared with a likelihood ratio test. Protein intake and carbohydrate intake were not removed during the model reduction process. Adjustment for post hoc multiple comparisons between carbohydrate and protein quartiles were performed with a Hochberg correction (22). Histograms of residuals were examined to identify major departures from normality; no significant departures from normality were found. Publication bias was assessed via a funnel plot regression method described by Macaskill et al (23)

To identify the presence of highly influential studies that may have biased the analysis, a sensitivity analysis was carried out for each model by removing one study at a time and then examining the predictors of interest and the variance components. Studies were identified as influential if their removal resulted in a change of >1 SE in any of the coefficients of interest. All analyses were performed with S-PLUS version 7.0 (Insightful, Seattle, WA). Effects were considered significant at $P \leq 0.05$. Data are reported as means (±SEMs) and 95% CIs.

RESULTS

Body mass change

The analysis of changes in the subjects' body mass comprised 165 treatment groups from 87 studies (**Table 2**). The mean change in body mass between these studies was −5.99 kg (CI: −6.71, −5.26 kg). The Bayesian Information Criterion decreased from 735.0 in the full model to 726.9 in the reduced model. The reduced model was not significantly different from the full model ($P = 0.31$).

Predictors in the reduced models are shown in **Table 3**. Diets with carbohydrate intake in the lowest quartile (≤35% energy) were associated with a 1.6–1.7 kg greater body-mass loss than were diets with carbohydrate intake in the highest 3 quartiles.

TABLE 2
Studies included in the analysis

Reference	Age[1]	Sex	Duration	Carbo-hydrate	Carbo-hydrate	Protein (g/kg)	Energy intake	Change[2] Body mass	Fat-free mass	Percentage body fat	Fat mass
	y		*wk*	*%*	*g/d*	*g/kg*	*kJ*	*kg*	*kg*	*%*	*kg*
Alford et al, 1990 (24)											
n = 11	38.8 ± 5.8	F	10	45	135	0.81	5040	−5.6 ± 2.5	0.0	−4.1 ± 2.2	−5.6
n = 12	40.5 ± 5.9	F	10	25	75	1.21	5040	−6.4 ± 2.2	−0.6	−4.5 ± 1.9	−5.9
n = 12	38.6 ± 4.6	F	10	75	225	0.62	5040	−4.8 ± 1.9	−0.5	−2.8 ± 2.0	−4.3
Archer et al, 2003 (25)											
n = 31	36.5 ± 9.6	M	6.5	58.3	443	1.36	12 760	−2.2 ± 3.4	NA	NA	NA
n = 32	39.1 ± 12.5	M	6.5	44.7	333	1.27	12 499	−2.1 ± 3.9	NA	NA	NA
Baba et al, 1999 (26)											
n = 6	NA	M	4	58	256	0.5	7405	−6.0 ± 0.6	0.3 ± 0.4	NA	−6.3 ± 0.2
n = 7	NA	M	4	25	112	1.78	7523	−8.3 ± 0.7	−1.0 ± 0.3	NA	−7.1 ± 0.9
Bowen et al, 2004 (27)											
n = 25	47.0 ± 10.0	M, F	12	38.8	142	1.09	5821	−9.0 ± 0.6	NA	NA	NA
n = 25	47.0 ± 10.0	M, F	12	37.6	140	1.12	5936	−9.3 ± 0.7	NA	NA	NA
Bray et al, 2002 (28)											
n = 14	37.0 ± 9.8	M	12	52	370	1.07	11 956	−3.7 ± 0.5	−0.4 ± 0.3	−2.3	−3.3 ± 0.7
n = 14	36.1 ± 9.6	M	12	58.4	426	1.15	12 256	−2.5 ± 0.6	−0.9 ± 0.3	−2.6	−3.3 ± 0.7
Brehm et al, 2003 (3)											
n = 20	43.1 ± 8.6	F	24	53.5	166	0.6	5233	−3.9 ± 1.0	−0.7 ± 1.6	−1.0	−2.0 ± 0.8
n = 22	44.2 ± 6.8	F	24	22.5	69	0.83	5162	−8.5 ± 1.0	−2.0 ± 1.8	−2.3	−4.8 ± 0.7
Brehm et al, 2005 (4)											
n = 20	44.8 ± 10.7	F	16	19.5	69	1.01	5902	−9.8 ± 0.7	−3.3 ± 0.9	−2.7	−6.2 ± 1.6
Brown et al, 1946 (29)											
n = 7	19.7 ± 1.1	F	14.7	51.9	149	0.97	4801	−11.1 ± 1.3	NA	NA	NA
Buskirk et al, 1963 (30)[3]											
n = 2	20.0 ± 1.4	M, F	4	45	348	0.62	12 978	−5.5 ± 1.1	0.5 ± 2.1	−2.3 ± 1.6	−6.0 ± 3.2
			4	45	348	0.64	12 978	−2.2 ± 0.2	−3.6 ± 1.6	1.7 ± 0.9	1.4 ± 1.3
			4	49	129	0.6	4410	−8.3 ± 0.9	−3.9 ± 1.5	−0.5 ± 0.9	−4.4 ± 0.5
			4	49	129	0.64	4410	−8.7 ± 1.2	−1.9 ± 2.0	−2.2 ± 1.8	−6.8 ± 3.2
Coleman et al, 2005 (31)											
n = 13	39.2 ± 3.7	F	12	15	58	1.09	6447	−7.0 ± 4.8	NA	NA	NA
Colette et al, 2003 (32)											
n = 15	45.0 ± 15.5	M, F	8	52.4	187	0.81	6000	−6.7 ± 1.3	−1.8 ± 0.9	−2.8	−4.8 ± 1.0
n = 17	51.0 ± 12.4	M, F	8	40.3	173	0.88	7200	−6.8 ± 1.4	−2.9 ± 0.7	−1.8	−4.0 ± 0.8
Doi et al, 2001 (33)											
n = 8	34.0 ± 7.4	M	12	47.6	228	1.07	8043	−4.1 ± 2.2	−2.0 ± 1.1	−1.7 ± 0.9	−2.1 ± 1.1
n = 9	33.1 ± 6.9	M	12	47.4	226	1.1	8007	−4.2 ± 2.2	−1.8 ± 1.0	−2.1 ± 1.1	−2.5 ± 1.3
Farnsworth et al, 2003 (11)											
n = 7	48.6 ± 8.5	M	12	57.3	222	0.56	6500	−9.6 ± 1.7	−1.9 ± 2.1	−4.3	−7.6 ± 3.1
n = 7	51.9 ± 8.7	M	12	44.4	167	0.95	6300	−11.4 ± 2.1	−2.5 ± 2.8	−5.2	−9.0 ± 2.7
n = 21	50.6 ± 9.8	F	12	57.3	222	0.69	6500	−7.4 ± 0.5	−1.5 ± 0.3	−4.4	−7.1 ± 2.0
n = 21	50.6 ± 12.4	F	12	44.4	167	1.15	6300	−6.6 ± 0.5	−0.1 ± 0.3	−4.1	−6.6 ± 1.4
Finkelstein et al, 1971 (34)[4]											
n = 4	21.0 ± 0.5	F	4.29	46.4	197	1.62	7140	−2.1 ± 0.5	NA	NA	NA
			4.29	44	154	1.54	5880	−3.5 ± 0.5	NA	NA	NA
n = 4	21.0 ± 0.5	F	4.29	46.4	197	1.5	7140	−2.6 ± 0.9	NA	NA	NA
			4.29	44	154	1.43	5880	−3.5 ± 0.7	NA	NA	NA
Gannon et al, 2004 (35)											
n = 8	63.3 ± 11	M	5	55	388	1.07	11 865	−1.8 ± 6.4	NA	NA	NA
n = 8	63.3 ± 11	M	5	20	142	2.14	11 865	−1.8 ± 6.1	NA	NA	NA
Gerhard et al, 2004 (36)											
n = 11	50.4 ± 4.8	M, F	6	64.7	435	0.95	11 294	−1.5 ± 0.4	NA	NA	NA
n = 11	50.4 ± 4.8	M, F	6	45.1	327	1.08	12184	−0.5 ± 0.3	NA	NA	NA
Geliebter et al, 1997 (37)											
n = 20	35.0 ± 6.0	M, F	8	41.4	133	1.28	5375	−7.8 ± 0.9	−1.1 ± 0.5	−3.7	−6.7 ± 0.6
n = 22	36.0 ± 8.0	M, F	8	41.4	133	1.32	5375	−9.5 ± 0.7	−2.7 ± 0.5	−3.2	−6.8 ± 0.6
n = 23	36.0 ± 7.0	M, F	8	41.4	133	1.34	5375	−9.6 ± 0.9	−2.3 ± 0.5	−3.9	−7.2 ± 0.6
Golay et al, 1996 (38)											
n = 21	45.0 ± 18.0	M, F	6	45	115	0.72	4296	−7.5 ± 0.5	−0.5	−4.2	−7.0 ± 2.0
n = 22	41.0 ± 9.0	M, F	6	15	37	0.74	4214	−8.9 ± 0.6	0.1	−5.2	−9.0 ± 2.5
Golay et al, 2000 (39)											
n = 26	44.0 ± 17.8	M, F	6	47	123	0.68	4500	−6.2 ± 0.6	−1.4	NA	−4.8 ± 0.3
n = 28	43.1 ± 15.3	M, F	6	42	114	0.68	4600	−7.5 ± 0.4	−1.3	NA	−6.2 ± 0.4
Hanssen, 1936 (40)											
n = 19	(18–55)	M, F	9.55	25	112	0.67	7770	−8.3 ± 0.6	NA	NA	NA
Hays et al, 2004 (41)											
n = 11	67.5 ± 7.3	M, F	14	62.8	353	1.21	9450	−3.2 ± 1.2	−0.5	−2.2 ± 1.2	−2.7
n = 11	64.8 ± 6.6	M, F	14	62.5	377	1.39	10 135	−4.8 ± 0.9	−0.2	−3.5 ± 0.7	−4.6

(*Continued*)

TABLE 2 (*Continued*)

Reference	Age[1]	Sex	Duration	Carbohydrate	Carbohydrate	Protein (g/kg)	Energy intake	Change[2]: Body mass	Change[2]: Fat-free mass	Change[2]: Percentage body fat	Change[2]: Fat mass
	y		*wk*	*%*	*g/d*	*g/kg*	*kJ*	*kg*	*kg*	*%*	*kg*
Heilbronn et al, 2002 (42)											
n = 21	57.5 ± 9.6	M, F	8	60.8	218	0.8	6031	−4.8 ± 3.9	NA	NA	NA
n = 24	56.0 ± 9.4	M, F	8	58.9	212	0.84	6056	−4.4 ± 4.7	NA	NA	NA
Hoeger et al, 1998 (43)											
n = 67	41.9 ± 9.7	M, F	4	65.2	236	0.76	6064	−2.8 ± 3.4	−0.7 ± 1.9	−1.2 ± 1.1	−2.1 ± 1.9
Jenkins et al, 2003 (44)											
n = 12	60.0 ± 9.9	M, F	4	58.8	119	1.54	10 172	−0.9 ± 0.3	NA	NA	NA
n = 13	60.0 ± 9.9	M, F	4	56.6	121	1.62	10 189	−1.0 ± 0.4	NA	NA	NA
Johnston et al, 2004 (45)											
n = 9	40.1 ± 10.8	M, F	6	40	170	1.63	7080	−4.7 ± 0.6	−1.9	−1.3	−2.8 ± 0.9
n = 7	36.4 ± 11.1	M, F	6	65.9	280	0.82	7080	−4.6 ± 0.9	−1.6	−1.8	−3.1 ± 1.0
Keim et al, 1990 (46)											
n = 5	27.0 ± 6.7	F	12	55	187	0.7	5208	−13.1 ± 0.7	−4.2 ± 3.0	−5.0 ± 2.2	−8.4 ± 2.6
Keim et al, 1997 (47)[5]											
n = 10	29.4 ± 5.4	F	6	59.7	293	1.12	8000	−3.9 ± 0.2	−1.3 ± 0.1	−1.8 ± 0.2	−2.6
			6	59.7	292	1.14	8000	−3.3 ± 0.3	−0.3 ± 0.2	−2.5 ± 0.3	−3.0
Keim et al, 1998 (48)											
n = 12	31.0 ± 3.5	F	12	60	286	1.08	8000	−7.0 ± 0.5	−0.9	−4.7	−6.2 ± 0.4
Kinsell et al, 1964 (49)											
n = 2	35.0 ± 14.1	M, F	4	61	183	0.71	5040	−6.1 ± 3.1	NA	NA	NA
Kriketos et al, 2001 (50)											
n = 16	47.0 ± 8.2	M, F	10	50	178	0.7	5985	−7.8 ± 3.3	−1.8 ± 0.6	−3.2 ± 2.2	−6.0 ± 1.9
n = 17	47.0 ± 8.2	M, F	10	50	177	0.67	5930	−9.8 ± 4.1	−2.8 ± 0.6	−3.6 ± 2.3	−7.0 ± 2.3
n = 19	47.0 ± 8.2	M, F	10	50	174	0.64	5834	−9.9 ± 4.7	−3.1 ± 0.4	−3.2 ± 2.0	−6.8 ± 2.2
Kush et al, 1986 (51)											
n = 5	27.0 ± 2.0	M	6	45	136	0.43	5060	−13.6 ± 1.7	NA	NA	NA
Landry et al, 2003 (52)											
n = 18	34.0 ± 12.0	M	7	46	351	1.4	13 000	−1.7 ± 0.7	NA	NA	NA
n = 19	34.0 ± 10.0	M	7	60	434	1.37	12 000	−2.5 ± 0.6	NA	NA	NA
Larosa et al, 1980 (53)											
n = 10	39.0 ± 9.5	F	8	2.9	8.5	1	4898	−6.9 ± 1.5	NA	NA	NA
n = 14	39.0 ± 9.5	M	8	1.2	5.1	1.23	6955	−6.4 ± 1.0	NA	NA	NA
Layman et al, 2003 (9)											
n = 12	50.1 ± 5.4	F	10	41	171	1.47	6987	−7.5 ± 1.4	−0.9 ± 0.3	−2.7	−5.6 ± 0.5
n = 12	50.1 ± 5.4	F	10	57.6	239	0.79	6941	−7.0 ± 1.4	−1.2 ± 0.6	−2.0	−4.7 ± 0.7
Leidy et al, 2004 (54)											
n = 10	20.3 ± 1.6	F	12	55	276	1.25	8442	−3.2 ± 0.8	−0.6 ± 0.7	−2.9 ± 1.2	−2.6 ± 0.7
Liu et al, 1985 (55)											
n = 10	54.0 ± 9.5	M, F	4	40	168	0.92	7048	−6.5 ± 0.6	NA	NA	NA
n = 10	57.0 ± 9.5	M, F	4	40	178	0.95	7459	−6.4 ± 0.5	NA	NA	NA
Low et al, 1996 (56)											
n = 8	51.0 ± 14.1	M, F	6	70	312	0.79	7350	−8.3 ± 0.9	NA	NA	NA
n = 9	55.0 ± 9.0	M, F	6	10	39	0.83	6703	−7.3 ± 0.9	NA	NA	NA
Luscombe et al, 2002 (57)											
n = 11	64.2 ± 10.9	M, F	8	55.3	219	0.7	6649	−4.3 ± 0.7	NA	NA	NA
n = 15	62.1 ± 8.5	M, F	8	42.1	167	1.18	6657	−4.9 ± 0.4	NA	NA	NA
Luscombe et al, 2003 (12)											
n = 17	55.0 ± 8.2	M, F	12	44.6	211	1.1	6358	−7.9 ± 1.1	NA	NA	NA
n = 19	53.0 ± 8.7	M, F	12	57.4	228	0.66	6663	−8.0 ± 0.7	NA	NA	NA
Luscombe-Marsh et al, 2005 (58)											
n = 13	50.0 ± 10.8	M	12	35	123	0.61	5972	−11.2 ± 1.7	−3.8 ± 1.1	−2.4	−5.9 ± 1.1
n = 17	48.0 ± 12.4	F	12	35	123	0.76	5972	−7.9 ± 1.3	−3.1 ± 0.5	−1.3	−4.8 ± 1.2
n = 12	50.0 ± 10.4	M	12	35	126	1.30	6164	−10.5 ± 1.7	−3.9 ± 0.9	−2.8	−5.6 ± 1.2
n = 15	53.0 ± 7.7	F	12	35	126	1.44	6164	−7.8 ± 0.8	−2.2 ± 0.5	−0.8	−4.3 ± 0.8
McCarron et al, 1997 (59)											
n = 109	54.0 ± 11.0	M	10	62	287	0.93	7765	−4.5 ± 0.3	NA	NA	NA
n = 163	54.0 ± 11.0	F	10	61	217	0.92	6031	−4.8 ± 0.2	NA	NA	NA
Meckling et al, 2002 (60)											
n = 20	34.4 ± 11.4	F	8	20.8	71	1.06	5736	−5.0 ± 1.1	−1.0 ± 0.6	−2.4 ± 0.9	−4.0 ± 0.9
Meckling et al, 2004 (61)											
n = 15	41.2 (27–61)	M, F	10	15.4	59	1.11	6421	−7.0 ± 4.0	−1.9 ± 1.1	−2.5 ± 1.4	−4.1 ± 2.3
Miyashita et al, 2004 (62)											
n = 11	52.4 ± 13.0	M, F	4	39	98	0.86	4200	−9.0 ± 1.1	0.0 ± 7.5	−3.0 ± 0.8	−9.0
n = 11	52.4 ± 13.0	M, F	4	62	155	0.92	4200	−7.0 ± 1.1	0.0 ± 6.8	−3.0 ± 1.1	−7.0
Moriguti et al, 2000 (63)											
n = 11	25.7 ± 3.2	M, F	6	50.8	242	1.17	8009	−3.1 ± 0.3	−1.4 ± 0.3	−1.8	−1.8 ± 0.4
n = 12	25.8 ± 3.6	M, F	6	51.1	303	1.12	9954	−4.3 ± 0.3	−1.5 ± 0.4	−2.1	−2.8 ± 0.4
n = 18	68.4 ± 3.3	M, F	6	46.1	181	1.14	6577	−4.8 ± 0.2	−1.6 ± 0.2	−2.0	−3.2 ± 0.2
Moulin et al, 1998 (64)											
n = 15	53.9 ± 9.4	M, F	4	59	244	0.65	6939	−1.2 ± 0.7	NA	NA	NA

(*Continued*)

TABLE 2 (*Continued*)

Reference	Age[1]	Sex	Duration	Carbo-hydrate	Carbo-hydrate	Protein (g/kg)	Energy intake	Change[2] Body mass	Fat-free mass	Percentage body fat	Fat mass
	y		*wk*	*%*	*g/d*	*g/kg*	*kJ*	*kg*	*kg*	*%*	*kg*
Nicholson et al, 1999 (65)											
n = 4	62.5 ± 5.8	M, F	12	51	195	0.71	6409	−3.8 ± 16	NA	NA	NA
n = 7	48.0 ± 7.0	M, F	12	75	264	0.51	5918	−7.2 ± 7.4	NA	NA	NA
Nieman et al, 1990 (66)											
n = 10	38.0 ± 6.3	F	5	49.1	272	0.8	9202	−5.6 ± 0.2	−0.6 ± 3.2	−3.6 ± 1.8	−4.9 ± 2.9
n = 11	37.1 ± 4.0	F	5	50.8	256	0.81	8308	−5.5 ± 0.6	−0.4 ± 1.6	−4.0 ± 1.8	−5.1 ± 2.8
Noakes et al, 2000 (67)											
n = 18	46.0 ± 8.5	M, F	12	52.1	199	0.79	6400	−8.2 ± 0.7	NA	NA	NA
n = 22	46.0 ± 9.4	M, F	12	71.6	281	0.85	6600	−7.9 ± 0.9	NA	NA	NA
n = 24	45.0 ± 9.8	M, F	12	48.5	185	0.89	6400	−9.5 ± 0.6	NA	NA	NA
Noakes et al, 2005 (68)											
n = 52	50.0 ± 10.0	F	12	44.2	140	1.14	5310	−7.6 ± 0.4	−1.5 ± 0.3	−2.6	−5.7 ± 0.6
n = 48	49.0 ± 9.0	F	12	60.8	189	0.64	5219	−6.9 ± 0.5	−1.8 ± 0.3	−1.4	−4.5 ± 0.5
Parker et al, 2002 (10)											
n = 9	63.4 ± 5.1	M	8	42.1	167	1.04	6665	−4.7 ± 8.2	−1.5	−1.5	−3.2 ± 5.6
n = 10	64.2 ± 12	M	8	54.8	211	0.63	6481	−5.8 ± 7.6	−1.4	−2.5	−4.4 ± 5.7
n = 17	58.7 ± 9.1	F	8	42.1	167	1.2	6665	−6.0 ± 5.2	−0.7	−2.9	−5.3 ± 3.6
n = 18	60.9 ± 9.8	F	8	54.8	211	0.73	6481	−4.2 ± 5.8	−1.3	−1.2	−2.9 ± 4.5
Pereira et al, 2004 (69)											
n = 17	32.6 ± 4.3	M, F	9.9	65	244	0.69	6300	−9.5 ± 0.3	−2.7	−3.8	−6.8
n = 22	28.8 ± 6.3	M, F	9.3	43	161	1.11	6300	−9.6 ± 0.3	−2.7	−3.9	−6.9
Piers et al, 2003 (70)											
n = 8	36.5 ± 6.3	M	4	43.2	306	0.95	11 897	−1.6 ± 0.4	−0.1 ± 0.3	−1.1 ± 0.3	−1.7 ± 0.3
Prewitt et al, 1991 (71)											
n = 6	34.8 ± 5.9	F	20	59.4	324	1.15	9160	−2.1 ± 8.5	1.6 ± 0.7	−3.5 ± 0.6	−4.1 ± 0.6
n = 12	28.5 ± 12.1	F	20	59.4	285	1.53	8047	−1.9 ± 4.1	0.8 ± 0.8	−2.3 ± 0.9	−1.7 ± 0.7
Raben et al, 1995 (72)											
n = 6	23.3 ± 1.7	F	11	57.4	362	1.33	10 600	−1.4 ± 0.6	0.3 ± 0.1	−2.0	−1.7 ± 0.5
n = 18	24.1 ± 2.1	M	11	58.9	501	1.7	14 300	−1.2 ± 0.5	0.2 ± 0.3	−1.3	−1.5 ± 0.3
Raben et al, 2002 (73)											
n = 20	37.1 ± 9.8	M, F	10	44	225	0.98	8685	−1.0 ± 0.4	−0.7 ± 0.2	0.1	−0.3 ± 0.4
Roy et al, 2002 (74)											
n = 5	25.8 ± 2.0	F	4	43.1	218	1.05	8478	−1.8 ± 0.5	−1.0 ± 2.8	0.4 ± 6.8	−0.1 ± 11.0
n = 5	24.6 ± 2.9	F	10	49.1	222	1.21	7602	−3.1 ± 0.4	−0.1 ± 2.8	−2.6 ± 3.8	−2.4 ± 2.1
Rumpler et al, 1991 (75)											
n = 4	43.0 ± 7.9	M	4	46	177	0.57	6465	−5.2 ± 1.2	−1.3 ± 1.9	−2.5 ± 1.3	−3.9 ± 1.0
n = 4	34.5 ± 6.8	M	4	66	263	0.57	6684	−5.0 ± 1.2	−0.9 ± 0.7	−3.0 ± 1.3	−4.1 ± 1.0
Saltzman et al, 2001 (76)											
n = 21	44.1 ± 21.3	M, F	6	50.2	234	1.05	7833	−4.0 ± 0.2	−1.3	−2.0	−2.7 ± 0.4
n = 22	45.1 ± 22.7	M, F	6	50.3	229	1.05	7645	−3.9 ± 0.3	−1.4	−1.8	−2.5 ± 0.3
Saltzman et al, 2001B (77)											
n = 20	45.0 ± 21.5	M, F	6	48.8	236	1.19	8114	−4.4 ± 0.3	−1.4 ± 0.2	−2.4	−3.0 ± 0.3
n = 21	44.1 ± 22.5	M, F	6	49	229	1.17	7867	−4.4 ± 0.4	−1.7 ± 0.3	−1.9	−2.6 ± 0.3
Saris et al, 2000 (78)											
n = 76	41.0 ± 9.0	M, F	24	55.5	344	1.06	10 400	−0.9 ± 0.4	0.3 ± 0.3	−1.1	−1.3 ± 0.4
n = 83	38.0 ± 9.0	M, F	24	51.8	290	1.12	9300	−1.8 ± 0.4	0.0 ± 0.3	−1.3	−1.8 ± 0.4
Scott et al, 1992 (79)											
n = 17	37.0 ± 5.0	F	8	60	152	0.64	4204	−6.5 ± 2.7	−1.6 ± 1.7	−3.6	−5.2 ± 1.8
n = 19	38.0 ± 6.0	F	8	40	104	0.64	4196	−7.4 ± 2.5	−1.3 ± 1.4	−4.3	−5.9 ± 1.5
Sharman et al, 2004 (80)											
n = 15	33.2 ± 11.3	M	6	8	36	1.19	7770	−6.1 ± 0.8	NA	NA	NA
Skov et al, 1999 (81)											
n = 25	39.4 ± 10.0	M, F	26	59.2	384	0.89	10 900	−5.0 ± 0.7	−0.7	−3.1	−4.3 ± 0.6
n = 25	39.8 ± 9.5	M, F	26	46.4	247	1.49	8950	−8.7 ± 0.7	−1.1	−6.1	−7.6 ± 0.7
Surwit et al, 1997 (82)											
n = 20	40.6 ± 8.2	F	6	73.3	199	0.52	4552	−7.0 ± 4.0	−2.4	−1.2 ± 1.1	−4.5
n = 22	40.3 ± 7.3	F	6	70.9	204	0.58	4841	−7.4 ± 4.1	−2.4	−1.6 ± 1.0	−5.0
Velthuis-te Wierik et al, 1994 (83)											
n = 8	43.0 ± 5.0	M	10	51	349	1.31	11 500	−2.7 ± 0.7	−0.3 ± 0.3	−2.1 ± 0.7	−2.3 ± 0.7
n = 16	43.0 ± 4.0	M	10	47	257	1.17	9200	−7.4 ± 0.7	−0.7 ± 0.4	−6.9 ± 0.4	−6.8 ± 0.5
Volek et al, 2002 (84)											
n = 12	36.7 ± 11.6	M	6	8	46	2.22	9770	−2.2 ± 0.5	1.1 ± 0.3	−3.6 ± 2.3	−3.3 ± 0.6
Volek et al, 2003 (85)											
n = 10	26.3 ± 6.1	F	4	10	43	2.14	7500	−1.2 ± 0.3	NA	NA	NA
Volek et al, 2004 (86)											
n = 13	34.0 ± 8.6	F	4	9.1	29	1.15	5410	−3.0 ± 0.4	NA	NA	NA
Wadden et al, 1998 (87)											
n = 25	45.0 ± 9.6	F	9	43.9	110	0.76	4214	−7.0 ± 0.5	NA	NA	NA
Walker et al, 1999 (88)[5]											
n = 21	58.0 ± 7.0	F	12	51.6	190	1.22	6200	−1.6 ± 0.4	−0.6	−0.6	−1.0 ± 0.4
			12	43.4	163	1.08	6300	−0.9 ± 0.4	−0.5	−0.1	−0.4 ± 0.3

(*Continued*)

TABLE 2 (*Continued*)

Reference	Age[1]	Sex	Duration	Carbohydrate	Carbohydrate	Protein (g/kg)	Energy intake	Change[2] Body mass	Fat-free mass	Percentage body fat	Fat mass
	y		*wk*	*%*	*g/d*	*g/kg*	*kJ*	*kg*	*kg*	*%*	*kg*
Wang et al, 2005 (89)											
$n = 39$	54.2 ± 3.1	M	8	65	422	1.51	10 907	−1.1 ± 0.3	NA	NA	NA
Weigle et al, 2003 (90)											
$n = 18$	45.3 ± 13.6	M,F	12	65	318	1.31	8219	−3.8 ± 1.0	−0.1	−3.4 ± 0.9	−3.7 ± 1.0
Weigle et al, 2005 (91)											
$n = 19$	41.0 ± 11.0	M,F	12	50.2	251	2.06	8400	−4.9 ± 0.5	−1.2	−3.2 ± 1.5	−3.7 ± 0.4
Wien et al, 2003 (92)											
$n = 32$	53.0 ± 2.0	M,F	24	32	81	0.65	4250	−19.5 ± 1.3	−5.1 ± 1.0	−6.5	−14.1 ± 1.5
$n = 33$	57.0 ± 2.0	M,F	24	53	135	0.65	4263	−12.1 ± 1.3	−2.5 ± 0.9	−4.1	−9.1 ± 1.5
Wolever et al, 1992 (93)[5]											
$n = 6$	63.0 ± 9.8	M,F	6	57	198	0.77	5830	−2.5 ± 3.7	NA	NA	NA
			6	57	197	0.79	5830	−1.8 ± 4.3	NA	NA	NA
Yancy et al, 2004 (5)											
$n = 45$	45.3 ± 9.5	M,F	24	8	30	1.00	6140	−12.0 ± 0.9	−3.3 ± 0.3	−5.8 ± 0.5	−9.4 ± 0.7
Young et al, 1952 (94)											
$n = 7$	19.9 ± 0.9	F	8.5	22.9	80	1.22	5880	−7.7 ± 1.0	NA	NA	NA
Young et al, 1953 (95)											
$n = 5$	22.4 ± 5.1	F	10	22.9	80	1.15	5880	−9.0 ± 1.0	NA	NA	NA
Young et al, 1957 (96)											
$n = 8$	22.0 ± 1.8	M	8.29	23	104	1.28	7560	−10.3 ± 0.8	NA	NA	NA
Young et al, 1958 (97)											
$n = 7$	21.7 ± 1.6	M	8.86	23.1	104	1.27	7560	−13.8 ± 0.3	NA	NA	NA
Young et al, 1960 (98)[6]											
$n = 4$	19.9 ± 0.9	F	4	37.5	225	1.06	10 080	−1.2 ± 0.1	NA	NA	NA
$n = 7$	20.1 ± 0.9	F	10.57	22.9	80	1.17	5880	−9.3 ± 1.4	NA	NA	NA
Young et al, 1960B (99)											
$n = 5$	21.0 ± 2.5	F	8.43	22.9	80	1.26	5880	−7.8 ± 0.6	NA	NA	NA
Young et al, 1965 (100)											
$n = 3$	20.7 ± 2.1	F	12	22.9	80	1.27	5880	−6.6 ± 0.8	−0.8 ± 0.7	−5.1 ± 0.4	−5.8 ± 0.4
$n = 4$	22.5 ± 1.3	M	12	23.1	104	1.28	7560	−13.8 ± 1.9	−2.9 ± 1.2	−9.3 ± 1.2	−11.0 ± 1.4
Young et al, 1971 (101)											
$n = 2$	23.3 ± 1.8	M	9	23.1	104	1.17	7560	−11.2 ± 2.7	−2.8 ± 0.9	−6.2 ± 0.5	−8.4 ± 1.8
$n = 3$	23.3 ± 1.8	M	9	13.3	60	1.2	7560	−12.3 ± 0.6	−2.0 ± 0.8	−7.9 ± 0.4	−10.2 ± 0.3
$n = 3$	23.3 ± 1.8	M	9	6.7	30	1.13	7560	−14.0 ± 1.6	−0.8 ± 0.2	−10.7 ± 0.6	−14.9 ± 0.2
Young et al, 1971B (102)[7]											
$n = 3$	22.2 ± 1.3	M	4–5	23.1	104	1.07	7560	−4.8 ± 0.9	NA	NA	−4.1 ± 0.4
$n = 3$	22.2 ± 1.3	M	4–5	23.1	104	1.13	7560	−4.9 ± 0.8	NA	NA	−6.9 ± 0.6
$n = 4$	22.2 ± 1.3	M	4–5	23.1	104	1.07	7560	−6.5 ± 1.0	NA	NA	−7.2 ± 0.7
$n = 4$	22.2 ± 1.3	M	4–5	23.1	104	1.07	7560	−6.5 ± 0.6	NA	NA	−10.0 ± 1.4
$n = 4$	22.2 ± 1.3	M	4–5	23.1	104	1.14	7560	−5.7 ± 0.4	NA	NA	−4.4 ± 0.4
$n = 4$	22.2 ± 1.3	M	4–5	23.1	104	1.13	7560	−5.7 ± 0.9	NA	NA	−6.8 ± 1.3
Zimmerman et al, 1984 (103)											
$n = 5$	36.8 ± 8.5	M	7	35	88	0.85	4200	−10.2 ± 1.4	NA	NA	NA
$n = 7$	34.5 ± 6.9	F	7	35	88	1.15	4200	−7.6 ± 1.4	NA	NA	NA

[1] Values are $\bar{x}$ ± SD; age range is given in parentheses if SD was not reported.
[2] Values are $\bar{x}$ or $\bar{x}$ ± SEM. NA, not available.
[3] Crossover design; subjects underwent 4 different exercise and diet combinations.
[4] Sequential treatment design; 2 groups of subjects received one diet followed by a second diet.
[5] Crossover design; each group received 2 different treatments.
[6] Four subjects in the first group represent a subset of the 7 subjects in the second group. These 4 subjects lost weight during a prereducing phase.
[7] Crossover design; each subject received 2 different treatments. There were 6 total treatments in the study; each group represents a different mix of subjects because they did not all cross over to the same treatment.

When carbohydrate intake was categorized as low (≤35% energy) or high (>35% energy), the significant effect in the low-carbohydrate intake group remained ($\bar{x}$: 1.74 kg; CI: 0.96, 2.51 kg). In studies conducted for ≤12 wk, this estimate decreased to 1.25 kg (CI: 0.45, 2.04 kg). In studies conducted for >12 wk, low-carbohydrate diets were associated with a 6.56 kg greater body-mass loss than were high-carbohydrate diets (CI: 3.78, 9.34 kg). No significant effects of protein were observed. A sensitivity analysis did not uncover any influential studies, and there was no evidence of a publication bias ($P = 0.48$).

Fat-free mass change

The analysis of changes in FFM included 102 treatment groups from 51 studies (Table 3). The mean change was −1.20 kg (CI: −1.51, −0.87 kg). The reduced model was not significantly different from the full model ($P = 0.83$).

Predictors in the reduced models are shown in **Table 4**. The amount of FFM retained tended to increase with each successive quartile of protein intake, with a significant difference existing between the upper 2 quartiles (>1.05 g/kg) and the first quartile

TABLE 3
Final reduced models for body mass[1]

Reduced models	Coefficient	95% CI	*P*
Protein and carbohydrate intake quartiles[2]			
Intercept[3]	−4.36 ± 1.47	(−7.26, −1.46)	0.004
Age (y)	0.04 ± 0.01	(0.01, 0.06)	0.004
Body mass (kg)	−0.10 ± 0.01	(−0.13, −0.07)	<0.0001
Study duration (wk)	−0.23 ± 0.04	(−0.31, −0.14)	<0.0001
Energy intake (kJ)	0.0008 ± 0.0001	(0.0007, 0.001)	<0.0001
Protein intake			
≤0.77 g/kg	0		
≤1.07 g/kg	−0.36 ± 0.41	(−2.45, 1.73)[4]	0.73[5]
≤1.21 g/kg	−0.13 ± 0.40	(−0.89, 0.63)[4]	0.73[5]
>1.21 g/kg	−0.34 ± 0.46	(−1.25, 0.57)[4]	0.46[5]
Carbohydrate intake			
≤35.0%	0		
≤46.4%	1.59 ± 0.44	(0.76, 2.41)[4]	0.0002[5]
≤57.0%	1.66 ± 0.44	(0.80, 2.52)[4]	0.0002[5]
>57.0%	1.74 ± 0.45	(0.84, 2.66)[4]	0.0002[5]
Quality of diet control			
High	0		
Moderate	2.38 ± 0.51	(1.37, 3.39)	<0.0001
Study design			
Parallel or single treatment	0		
Crossover	2.32 ± 0.69	(0.95, 3.70)	0.001
Protein (low compared with high) and carbohydrate (low compared with high) intakes[6]			
Intercept[3]	−2.92 ± 1.25	(−5.38, −0.46)	0.02
Protein intake			
≤1.07 g/kg	0.06 ± 0.23	(−0.39, 0.52)	0.79
>1.07 g/kg	0		
Carbohydrate intake			
≤35.0%	−1.74 ± 0.39	(−2.51, −0.96)	<0.0001
>35.0%	0		
Protein intake (low compared with high), carbohydrate intake (low compared with high), and study duration (≤12 wk)[7]			
Intercept[3]	−0.92 ± 1.33	(−3.55, 1.70)	0.49
Protein intake			
≤1.07 g/kg	−0.08 ± 0.24	(−0.55, 0.38)	0.74
>1.07 g/kg	0		
Carbohydrate intake			
≤35.0%	−1.25 ± 0.40	(−2.04, −0.45)	0.002
>35.0%	0		
Protein intake (low compared with high), carbohydrate intake (low compared with high), and study duration (>12 wk)[8]			
Intercept[3]	−5.43 ± 4.94	(−18.12, 7.27)	0.32
Age (y)	0.11 ± 0.04	(0.008, 0.21)	0.04
Body mass (kg)	−0.15 ± 0.05	(−0.29, −0.01)	0.04
Energy intake (kJ)	0.0007 ± 0.0002	(0.0002, 0.001)	0.02
Protein intake			
≤1.07 g/kg	0.79 ± 0.62	(−0.82, 2.39)	0.26
>1.07 g/kg	0		
Carbohydrate intake			
≤35.0%	−6.56 ± 1.08	(−9.33, −3.78)	0.002
>35.0%	0		
Quality of diet control			
High	0		
Moderate	5.96 ± 0.65	(4.28, 7.63)	0.0003

[1] Negative values of coefficients indicate larger decreases in body mass. Positive values indicate smaller decreases in body mass. Coefficients of 0 represent the default categories in the model. Coefficients for other categories within the same variable represent the difference from the default category.

[2] Bayesian Information Criterion = 726.9.

[3] Intercept of the line produced by hierarchical linear regression.

[4] Hochberg-adjusted CI.

[5] Hochberg-adjusted *P* value.

[6] Bayesian Information criterion = 708.1. Estimates, CIs, and *P* values for age, body mass, study duration, energy intake, quality, and study design were similar to the quartile-based model and are not shown.

[7] Estimates, CIs, and *P* values for age, body mass, study duration, energy intake, quality, and study design were similar to the quartile-based model and are not shown. The interaction between duration of study and protein and carbohydrate intakes was significant.

[8] Study design was not included in this model because all studies were of the same design. The interaction between duration of study and protein and carbohydrate intakes was significant.

TABLE 4
Final reduced models for fat-free mass[1]

Reduced model	Coefficient	95% CI	P
Protein and carbohydrate intake quartiles[2]			
Intercept[3]	−3.51 ± 0.45	(−4.41, −2.62)	<0.0001
Energy intake (kJ)	0.0002 ± 0.0001	(0.0000, 0.0003)	0.02
Protein intake			
≤0.70 g/kg	0		
≤1.05 g/kg	0.31 ± 0.41	(−0.48, 1.09)[4]	0.44[5]
≤1.20 g/kg	0.78 ± 0.35	(0.02, 1.54)[4]	0.04[5]
>1.20 g/kg	0.96 ± 0.36	(0.16, 1.77)[4]	0.02[5]
Carbohydrate intake			
≤41.4%	0		
≤49.0%	0.65 ± 0.34	(−0.03, 1.33)[4]	0.06[5]
≤56.9%	0.62 ± 0.34	(−0.03, 1.28)[4]	0.06[5]
>56.9%	0.98 ± 0.33	(0.25, 1.70)[4]	0.009[5]
Protein (low compared with high) and carbohydrate (low compared with high) intakes[6]			
Intercept[3]	−2.08 ± 0.51	(−3.09, −1.06)	0.0001
Protein intake			
≤1.05 g/kg	−0.60 ± 0.22	(−1.05, −0.16)	0.44
>1.05 g/kg	0		
Carbohydrate intake			
≤41.4%	−0.69 ± 0.27	(−1.22, −0.16)	0.01
>41.4%	0		
Protein intake (low compared with high), carbohydrate intake (low compared with high), and study duration (≤12 wk)[7]			
Intercept[3]	−2.09 ± 0.52	(−3.11, −1.06)	0.0001
Protein intake			
≤1.05 g/kg	−0.34 ± 0.24	(−0.82, 0.14)	0.16
>1.05 g/kg	0		
Carbohydrate intake			
≤41.4%	−0.31 ± 0.29	(−0.90, 0.27)	0.29
>41.4%	0		
Protein intake (low compared with high), carbohydrate intake (low compared with high), and study duration (>12 wk)[7]			
Intercept[3]	−1.64 ± 1.31	(−4.73, 1.45)	0.25
Protein intake			
≤1.05 g/kg	−1.21 ± 0.30	(−1.93, −0.49)	0.005
>1.05 g/kg	0		
Carbohydrate intake			
≤41.4%	−1.74 ± 0.73	(−3.47, −0.005)	0.05
>41.4%	0		

[1] Negative values of coefficients indicate larger decreases in fat-free mass. Positive values indicate smaller decreases in fat-free mass. Coefficients of 0 represent the default categories in the model. Coefficients for other categories within the same variable represent the difference from the default category.
[2] Bayesian Information Criterion = 341.8.
[3] Intercept of the line produced by hierarchical linear regression.
[4] Hochberg-adjusted CI.
[5] Hochberg adjusted P value.
[6] Bayesian Information Criterion = 326.0. Estimates, CIs, and P value for energy intake were similar to the quartile-based model and are not shown.
[7] Estimates, CIs, and P value for energy intake were similar to the quartile-based model and are not shown. The interaction between duration of study and protein and carbohydrate intakes was significant.

(≤0.70 g/kg). Specifically, the third quartile (>1.05 and ≤1.20 g/kg) was associated with 0.78 kg additional FFM retention (CI: 0.02, 1.54 kg) and the fourth quartile (>1.20 g/kg) was associated with 0.96 kg additional FFM retention (CI: 0.16, 1.77 kg). When protein intake was categorized as high (>1.05 g/kg) or low (≤1.05 g/kg), a significant effect remained, although the amount of FFM retained in the high-protein intake group decreased to 0.60 kg (CI: 0.16, 1.05 kg). In studies conducted for ≤12 wk, the additional FFM retained by the high-protein intake group decreased to 0.34 kg and was no longer significant (CI: −0.14, 0.82 kg). In studies conducted for >12 wk, high-protein diets were associated with an additional 1.21 kg FFM retention (CI: 0.49, 1.93 kg).

Compared with carbohydrate intake in the lowest quartile (≤41.4% of energy), the carbohydrate intake in the highest quartile (>56.9% of energy) was associated with 0.98 kg greater FFM retention (CI: 0.25, 1.70 kg). Carbohydrate intake in the second (>41.4%, ≤46.4%) and third (>46.4%, ≤56.9%) quartiles tended to be associated with 0.62–0.65 kg more FFM retention (P = 0.06). When carbohydrate intake was classified as either

TABLE 5
Final reduced models for percentage body fat[1]

Reduced model	Coefficient	95% CI	*P* value
Protein and carbohydrate intake quartiles[2]			
Intercept[3]	−4.86 ± 0.72	(−6.29, −3.42)	<0.0001
Sex			
F	0		
M	−1.89 ± 0.49	(−2.87, −0.91)	0.0002
M, F	−0.15 ± 0.44	(−1.04, 0.73)	0.74
Study duration (wk)	−0.13 ± 0.03	(−0.20, −0.07)	0.0001
Energy intake (kJ)	0.0004 ± 0.0001	(0.0002, 0.0006)	0.0002
Protein intake			
≤0.73 g/kg	0		
≤1.06 g/kg	−0.56 ± 0.53	(−1.55, 0.43)[4]	0.26[5]
≤1.20 g/kg	−1.32 ± 0.54	(−2.53, −0.11)[4]	0.03[5]
>1.20 g/kg	−0.59 ± 0.56	(−1.64, 0.46)[4]	0.26[5]
Carbohydrate intake			
≤41.4%	0		
≤49.0%	1.37 ± 0.54	(0.37, 2.38)[4]	0.008[5]
≤56.9%	1.48 ± 0.55	(0.40, 2.57)[4]	0.008[5]
>56.9%	1.32 ± 0.51	(0.35, 2.28)[4]	0.008[5]
Quality of diet control			
Moderate	2.53 ± 0.46	(1.61, 3.44)	<0.0001
High	0		
Protein (low compared with high) and carbohydrate (low compared with high) intakes[6]			
Intercept[3]	−4.35 ± 0.83	(−6.00, −2.69)	<0.0001
Protein intake			
≤1.06 g/kg	0.64 ± 0.37	(−0.09, 1.38)	0.09
>1.06 g/kg	0		
Carbohydrate intake			
≤41.4%	−1.29 ± 0.42	(−0.46, −2.12)	0.003
>41.4%	0		

[1] Negative values of coefficients indicate larger decreases in percentage body fat. Positive values indicate smaller decreases in percentage body fat. Coefficients of 0 represent the default categories in the model. Coefficients for other categories within the same variable represent the difference from the default category.

[2] Bayesian Information Criterion = 415.6.

[3] Intercept of the line produced by hierarchical linear regression.

[4] Hochberg-adjusted CI.

[5] Hochberg-adjusted *P* value.

[6] Bayesian Information Criterion = 402.4. Estimates, CIs, and *P* values for sex, study duration, energy intake, and quality were similar to the quartile-based model and are not shown.

low (≤41.4%) or high (>41.4%), low-carbohydrate diets were associated with a greater loss of FFM (0.69 kg; CI: −0.16, −1.22 kg) than were high-carbohydrate diets. In studies conducted for ≤12 wk, the magnitude of this effect decreased to 0.31 kg (CI: −0.90, 0.27 kg) and was no longer significant. In studies conducted for >12 wk, low-carbohydrate diets were associated with a greater loss of FFM (1.74 kg; CI: 0.01, 3.47 kg) than were high-carbohydrate diets. A sensitivity analysis did not uncover any influential studies and there was no evidence of a publication bias ($P = 0.10$).

Percentage changes in body fat

The analysis of percentage changes in BF was composed of 98 treatment groups from 49 studies (Table 3). The mean change was −3.00% (CI: −3.53%, −2.46%). The reduced model was not significantly different from the full model ($P = 0.75$).

Predictors in the reduced model are shown in **Table 5**. Protein intake in the third quartile (>1.06 g/kg and ≤1.20 g/kg) was associated with a greater loss of percentage BF (1.32%; CI: 0.11%, 2.53%) than was the first quartile (≤0.73 g/kg). When protein intake was classified as high (>1.06 g/kg) or low (≤1.06 g/kg), there was a trend ($P = 0.09$) toward a 0.64% (CI: −0.09%, 1.38%) greater loss of percentage BF with the higher protein intake. In studies conducted for ≤12 wk, the loss in percentage BF in the high-protein group compared with the low-protein group decreased to 0.45% and the trend no longer existed ($P = 0.38$; CI: −0.56%, 1.46%). In studies conducted for >12 wk, the loss in percentage BF increased to 0.96% in the high-protein group compared to the low-protein group, but the difference was not significant ($P = 0.21$; CI: −0.76%, 2.67%).

Diets with a carbohydrate intake in the lowest quartile (≤41.4% energy) were associated with a 1.32–1.48% greater decrease in percentage BF than were diets with carbohydrate intake in the highest 3 quartiles. When carbohydrate intake was categorized as low (≤41.4% energy) or high (>41.4% energy), the significantly greater decrease in percentage BF in the low-carbohydrate intake group remained (1.29%; CI: 0.46%, 2.12%). In studies conducted for ≤12 wk, the greater loss in percentage BF in the lowest carbohydrate intake quartile tended toward significance (1.00%; CI: −0.06%, 2.06%; $P = 0.06$). In studies conducted for >12 wk, low-carbohydrate diets were associated with a greater decrease in percentage BF (3.55%; CI: 1.62%, 5.49%) than were high-carbohydrate diets. A sensitivity analysis did not uncover any influential studies and there was no evidence of publication bias ($P = 0.27$).

Fat mass changes

The analysis of changes in FM included 108 treatment groups from 52 studies (Table 3). The mean change was −4.71 kg (CI: −5.41, −4.00 kg). The reduced model was not significantly different from the full model ($P = 0.48$).

Predictors in the reduced model are shown in **Table 6**. Protein intake in the third quartile (>1.06 and ≤1.18 g/kg) was associated with a greater loss of FM (1.68 kg; CI: 0.01, 3.35 kg) than was the first quartile of protein intake (≤0.73 g/kg). When protein intake was classified as high (>1.06 g/kg) or low (≤1.06 g/kg), there was no significant effect of protein intake on FM loss ($P = 0.19$).

Diets with carbohydrate intake in the lowest quartile (≤40% of energy) were associated with a 1.79–2.32 kg greater loss of FM than were diets with carbohydrate intake in the highest 3 quartiles. When carbohydrate intake was categorized as low (≤40% of energy) or high (>40% of energy), low-carbohydrate diets were associated with a greater loss of FM (2.05 kg; CI: 1.05, 3.05 kg) than were high-carbohydrate diets. In studies conducted for ≤12 wk, the loss of FM observed with the low-carbohydrate diets decreased to 1.86 kg (CI: 0.73, 2.99 kg). In studies conducted for >12 wk, low-carbohydrate diets were associated with a greater FM loss (5.57 kg; CI: 2.47, 8.67 kg) than were high-carbohydrate diets. A sensitivity analysis did not uncover any influential studies. A funnel plot regression uncovered a significant positive relation between sample size and study weight [$\bar{x}$ (±SEM) slope: 0.10 ± 0.03; $P = 0.001$].

DISCUSSION

The purpose of this meta-analysis was to determine whether low-carbohydrate, high-protein diets have effects on body composition independent of energy intake. By including carbohydrate and protein intake as predictors in multilevel regression models, one can determine the independent contributions of these variables to the variation in body mass and composition changes across a large number of studies while simultaneously adjusting for the differences in energy intake and other covariates between the studies and treatment groups.

Protein intake was a significant predictor of FFM retention. A daily protein intake of >1.05 g/kg ($\bar{x}$ intake in the high-protein studies: 1.27 g/kg) was associated with a greater FFM retention than was a protein intake closer to the RDA ($\bar{x}$ intake: 0.74 g/kg). The magnitude of this effect increased when studies of >3 mo duration were analyzed. Thus, the protein RDA may not be optimal for FFM retention during energy restriction, particularly during prolonged periods of dieting. Energy restriction can decrease nitrogen balance (8) and thus decrease the amount of protein and FFM retained by the body. An increase in protein intake would increase nitrogen balance and thus increase the amount of FFM retained.

When protein intake was categorized as quartiles, loss of both percentage BF and FM were greater when protein intake was in the third rather than the first quartile. However, no significant differences were observed between the fourth and the first quartile. The significant effect of the third quartile may be due to chance. When protein intake was categorized into low and high intakes, it was not a significant predictor of changes in FM. A trend for protein intake to predict changes in percentage BF existed, however. This may relate to the positive effect of protein on FFM retention, which would increase the change in percentage BF for a given change in FM.

Compared with higher carbohydrate intakes, low-carbohydrate diets (≤35–41.4% energy) increased the loss of body mass, BF, and percentage BF, even after control for energy intake as a covariate in the regression analyses. The mean total carbohydrate intake in the low-carbohydrate studies ranged from 79–97 g, depending on the analysis. Typically, a carbohydrate intake of <100 g will cause ketosis (1). These results support the apparent metabolic advantage of low-carbohydrate, ketogenic diets (104). The additional body mass change is not likely due to water loss, because the duration of the diet periods (6–24 wk) was too protracted (5, 75, 92) and estimations of total body water tend to be similar between low-carbohydrate and low-fat diets after 2 wk (5). The similar results of the analyses on body mass and BF also supports the concept that the effect on body mass of low-carbohydrate diets is an effect on FM rather than on body water. Feinman and Fine (104) argued that low-carbohydrate diets increase the demands on protein and amino acid turnover for gluconeogenesis. Because this process has a high energy cost, it would increase the energy deficit for a given energy intake, thereby supporting the theory of a metabolic advantage of low-carbohydrate diets. In contrast, Buchholz and Schoeller (105) averaged the results of 10 studies and reported no effect of low-carbohydrate diets on 24-h energy expenditure. However, none of the studies they cited involved ketogenic diets, and most of the studies were conducted with subjects in energy balance. A hypocaloric, ketogenic diet would be expected to increase the demand for gluconeogenesis because of the low energy and carbohydrate availability. In contrast to this hypothesis, Brehm et al (4) reported no differences in total energy expenditure when a low-carbohydrate diet was compared with a low-fat diet. However, total energy expenditure was estimated rather than directly measured with the use of a whole-body calorimeter or doubly labeled water. Future research should focus on the effects of low-carbohydrate diets on energy expenditure with the use of these measurement tools.

Alternatively, the higher loss in BF observed with low-carbohydrate diets than that observed with low-fat diets may relate to changes in insulin concentrations, because less insulin promotes free-fatty acid mobilization from BF storage (106). Volek et al (75) reported a significant positive correlation between decreases in insulin concentration and reductions in FM ($R^2 = 0.67$) and percentage BF ($R^2 = 0.70$) when subjects were placed on a diet of 8% energy from carbohydrate (46 g/d) for 6 wk. The additional fat loss may also be related to the excretion of ketones in the urine and breath; however, this would only account for a maximum of ≈420 kJ/d (107), which would only amount to ≈1 kg of additional BF loss over a 3-mo dieting period. This is only one-half of the greater loss of FM observed with the low-carbohydrate diets the current analysis.

It is also possible that subjects on low-fat diets systematically underreport energy intake compared with subjects on low-carbohydrate diets. In support for this hypothesis, Brehm et al (4) observed that actual weight loss closely matched the predicted

TABLE 6
Final reduced models for fat mass[1]

Reduced model	Coefficient	95% CI	P
Protein and carbohydrate intake quartiles[2]			
Intercept[3]	−3.23 ± 2.10	(−7.40, 0.94)	0.13
Body mass (kg)	−0.07 ± 0.02	(−0.11, −0.04)	0.0002
Study duration (wk)	−0.10 ± 0.04	(−0.18, −0.02)	0.02
Energy intake (kJ)	0.0006 ± 0.0001	(0.0004, 0.0008)	<0.0001
Protein intake			
≤0.73 g/kg	0		
≤1.06 g/kg	−0.74 ± 0.69	(−2.16, 0.68)[4]	0.31[5]
≤1.18 g/kg	−1.68 ± 0.73	(−3.35, −0.01)[4]	0.05[5]
>1.18 g/kg	−0.74 ± 0.76	(−2.16, 0.68)[4]	0.31[5]
Carbohydrate intake			
≤40.0%	0		
≤47.5%	2.00 ± 0.59	(0.84, 3.17)[4]	0.001[5]
≤55.1%	2.32 ± 0.62	(1.07, 3.57)[4]	0.0004[5]
>55.1%	1.79 ± 0.66	(0.56, 3.02)[4]	0.005[5]
Quality of diet control			
Moderate	2.62 ± 0.58	(1.47, 3.78)	<0.0001
High	0		
Study design			
Parallel or single treatment	0		
Crossover	2.58 ± 0.79	(1.01, 4.14)	0.002
Protein (low compared with high) and carbohydrate (low compared with high) intakes[6]			
Intercept[3]	−2.11 ± 1.65	(−5.39, 1.16)	0.20
Protein intake			
≤1.06 g/kg	0.59 ± 0.45	(−0.31, 1.49)	0.19
>1.06 g/kg	0		
Carbohydrate intake			
≤40.0%	−2.05 ± 0.51	(−3.05, −1.05)	0.0001
>40.0%	0		
Protein intake (low compared with high), carbohydrate intake (low compared with high), and study duration (≤12 wk)[7]			
Intercept[3]	0.16 ± 2.16	(−4.15, 4.46)	0.94
Protein intake			
≤1.06 g/kg	0.42 ± 0.54	(−0.66, 1.50)	0.44
>1.06 g/kg	0		
Carbohydrate intake			
≤40.0%	−1.86 ± 0.57	(−2.99, −0.73)	0.002
>40.0%	0		
Protein intake (low compared with high), carbohydrate intake (low compared with high), and study duration (>12 wk)[8]			
Intercept[3]	11.78 ± 4.64	(23.71, 66.15)	0.05
Body mass (kg)	−0.14 ± 0.05	(−0.26, −0.02)	0.03
Study duration (wk)	−0.23 ± 0.16	(−0.64, 0.19)	0.22
Protein intake			
≤1.06 g/kg	1.34 ± 1.17	(−1.66, 4.34)	0.30
>1.06 g/kg	0		
Carbohydrate intake			
≤40.0%	−5.57 ± 1.21	(−8.67, −2.47)	0.006
>40.0%	0		
Quality of diet control			
Moderate	3.79 ± 0.95	(1.34, 6.25)	0.01
High	0		

[1] Negative values of coefficients indicate larger decreases in fat mass. Positive values indicate smaller decreases in fat mass. Coefficients of 0 represent the default categories in the model. Coefficients for other categories within the same variable represent the difference from the default category.

[2] Bayesian Information Criterion = 491.1.

[3] Intercept of the line produced by hirarchical linear regression.

[4] Hochberg-adjusted CI.

[5] Hochberg-adjusted P value.

[6] Bayesian Information Criterion = 479.4. Estimates, CIs, and P values for body mass, energy intake, study duration, quality, and study design were similar to the quartile-based model and are not shown.

[7] Estimates, CIs, and P values for body mass, energy intake, study duration, quality, and study design were similar to the quartile-based model and are not shown. The interaction between duration of study and protein and carbohydrate intake was significant.

[8] Energy intake was not a significant predictor in this model and was removed, decreasing the Bayesian Information Criterion from 68.2 to 66.1. The models were not significantly different ($P = 0.60$). The interaction between duration of study and protein and carbohydrate intake was significant.

weight loss in the low-carbohydrate group, but actual weight loss was less than the predicted weight loss in the low-fat group. In the current analysis, high quality studies (ie, those in which food was prepared for the subjects) resulted in greater weight and FM loss than did lower quality studies (ie, those that generally involved self-reported measurements in conjunction with a biological marker of macronutrient intake). However, the effects of carbohydrate intake were independent of study quality, which indicates that carbohydrate intake had an effect whether the subjects self-reported food intake or consumed food that was prepared for them. Thus, our analyses do not support the idea of a systematic bias in the reporting of energy intake.

Low-carbohydrate diets were associated with a greater FFM loss than were low-fat diets. The additional FFM loss may reflect an additional loss of body water, because body water is a component of FFM and ketosis may cause water excretion (108). The additional FFM loss may also be caused by lower insulin concentrations, because insulin inhibits proteolysis (109).

Sensitivity analyses indicated that the results were quite robust to the removal of individual studies. Thus, no studies had a large effect on the estimates produced by the regression models. Also, with the exception of FM, there was no evidence of a publication bias. The slope of the funnel plot regression for FM was quite low (0.10), which indicated a weak relation between sample size and weight. This relation was in a positive direction, which indicated that larger population studies had a greater effect on the analysis than did smaller studies. This is expected, because larger sample sizes tend to reduce the variation in within-treatment groups. Thus, the significant slope observed for FM likely does not represent a publication bias.

In conclusion, low-carbohydrate diets may increase the loss of body mass, FFM, FM, and percentage BF during weight reduction compared with traditional diets. The RDA for protein may be insufficient for optimal FFM retention during weight loss; high protein intakes (>1.05 g/kg) may improve FFM retention.

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