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Effects of energy-restricted high-protein, low-fat compared with standard-protein, low-fat diets: a meta-analysis of randomized controlled trials[1–3]

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ABSTRACT

Background: It is currently unclear whether altering the carbohydrate-to-protein ratio of low-fat, energy-restricted diets augments weight loss and cardiometabolic risk markers.

Objective: The objective was to conduct a systematic review and meta-analysis of studies that compared energy-restricted, isocaloric, high-protein, low-fat (HP) diets with standard-protein, low-fat (SP) diets on weight loss, body composition, resting energy expenditure (REE), satiety and appetite, and cardiometabolic risk factors.

Design: Systematic searches were conducted by using MEDLINE, EMBASE, PubMed, and the Cochrane Central Register of Controlled Trials to identify weight-loss trials that compared isocalorically prescribed diets matched for fat intake but that differed in protein and carbohydrate intakes in participants aged ≥18 y. Twenty-four trials that included 1063 individuals satisfied the inclusion criteria.

Results: Mean (±SD) diet duration was 12.1 ± 9.3 wk. Compared with an SP diet, an HP diet produced more favorable changes in weighted mean differences for reductions in body weight (−0.79 kg; 95% CI: −1.50, −0.08 kg), fat mass (FM; −0.87 kg; 95% CI: −1.26, −0.48 kg), and triglycerides (−0.23 mmol/L; 95% CI: −0.33, −0.12 mmol/L) and mitigation of reductions in fat-free mass (FFM; 0.43 kg; 95% CI: 0.09, 0.78 kg) and REE (595.5 kJ/d; 95% CI: 67.0, 1124.1 kJ/d). Changes in fasting plasma glucose, fasting insulin, blood pressure, and total, LDL, and HDL cholesterol were similar across dietary treatments ($P \geq 0.20$). Greater satiety with HP was reported in 3 of 5 studies.

Conclusion: Compared with an energy-restricted SP diet, an isocalorically prescribed HP diet provides modest benefits for reductions in body weight, FM, and triglycerides and for mitigating reductions in FFM and REE. *Am J Clin Nutr* doi: 10.3945/ajcn.112.044321.

INTRODUCTION

For overweight and obese patients, energy-restricted diets can induce substantial weight loss and improve a number of cardiometabolic risk factors (1). Traditionally, energy-restricted diets for obesity treatment are commonly prescribed with a macronutrient percentage energy contribution of ∼10–20% from protein, 45–65% from carbohydrate, and <35% from fat (2). However, in recent years, there has been substantial focus on the macronutrient profile of a diet as an important consideration that may potentiate weight loss, long-term weight maintenance, and cardiometabolic risk (2).

Reductions in fat-free mass (FFM)[4] during diet-induced weight loss typically account for ∼20% (1.2 of every 6 kg) of total weight loss (3). FFM, and specifically its skeletal muscle component, plays an important role in the regulation of resting energy expenditure (REE) (4) and protein metabolism (5) and is the body's primary site of glucose uptake (6). A growing body of evidence suggests that compared with a conventional low-fat (<30% of total energy), standard-protein (SP) diet [12–18% of energy (7)], a low-fat, high-protein (HP) diet [25–35% of energy (7)] may increase body fat mass (FM) loss (3, 8, 9) and attenuate reductions in FFM (3, 10, 11) and REE (12, 13). A number of studies have also shown that an HP diet may increase satiety (9, 10) and improve an array of cardiovascular disease risk factors, including glucose homeostasis (9, 12) and the blood lipid profile (8, 9, 14–16). However, these effects are not consistently reported in all studies. Variability in study design factors, including sample size, duration, population, and macronutrient composition, may contribute to the variability in response between studies.

Previous meta-analyses and large well-controlled dietary studies have evaluated the effects of ad libitum weight-loss diets with varying amounts of protein (17–22). The cardiometabolic benefits derived from ad libitum diets are primarily influenced by factors that affect the quantity of food/energy consumed. Conversely, there is currently no definitive study or comprehensive systematic review or meta-analysis that evaluates whether there is any metabolic advantage obtained by modifying the

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[4] Abbreviations used: FFM, fat-free mass; FM, fat mass; HP, high-protein, low-fat; REE, resting energy expenditure; SP, standard-protein (higher carbohydrate), low-fat; WMD, weighted mean difference.

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carbohydrate-to-protein ratio of low-fat diets in structured, controlled, energy-matched studies. This has somewhat limited the understanding of the effects of HP diets on weight loss and related outcomes. Therefore, the aim of this study was to conduct a systematic review and meta-analysis of studies to compare the effects of energy-restricted HP diets with those of isocalorically prescribed SP diets on weight loss, body composition, REE, and cardiometabolic risk markers.

METHODS

Search strategy

Searches for English-language studies published between 1947 and 12 May 2011 were conducted by using MEDLINE (http://www.nlm.nih.gov/bsd/pmresources.html), EMBASE (http://www.embase.com/), PubMed (http://www.ncbi.nlm.nih.gov/pubmed), and the Cochrane Central Register of Controlled Trials (http://www.thecochranelibrary.com) databases (**Table 1**) to identify all randomized controlled trials that compared an HP diet with an SP diet. Reference lists of identified publications were searched for citations of additional relevant articles.

Selection criteria

To be included in the meta-analysis, studies had to include a completers analysis of HP and SP weight-loss diets that were not ad libitum and that were matched (within 1250 kJ/d) for a specified amount of restricted caloric intake. Other inclusion criteria were matching of SP and HP diets for fat intake (≤10% difference in energy contribution from fat between diets), prescription of fat intake at ≤30% of total energy, diet duration of ≥4 wk, and participant age of ≥18 y. There were no restrictions on sex, body weight, or BMI.

Studies were excluded if they had comparative diet groups in which one or both were high in fat (>30% for prescribed fat intake or >35% for the achieved fat intake) or if they had either a prescribed or achieved difference between comparison diets of >10% for fat intake, <10% for protein intake, or ≥1250 kJ/d for energy intake. Other exclusion criteria were as follows: a concurrent structured exercise program, diets that prescribed very low energy intakes (<4184 kJ/d), a nonparallel study design (eg, crossover), studies that reported only an intention-to-treat analysis, studies with participants who were pregnant or breastfeeding, or studies with participants who were receiving concurrent weight-loss medication or who had undergone a surgical procedure that affects weight loss.

To avoid selection bias, 2 investigators (TPW and LJM) independently assessed trial eligibility, with any disagreement resolved by consensus with a third investigator (GDB).

TABLE 1
Literature search terms[1]

MeSH terms
Search 1: weight loss/
Search 2: caloric restriction/
Search 3: (energy restrict* or diet* restrict*).mp. (mp = protocol supplementary concept, rare disease supplementary concept, title, original title, abstract, name of substance word, subject heading word, unique identifier)
Search 4: macronutrient*.mp.
Search 5: dietary proteins/
Search 6: dietary carbohydrates/
Search 7: 1 or 2 or 3
Search 8: 4 or 5 or 6
Search 9: 7 and 8
Search 10: limit 9 to (English language and humans and clinical trial, all)

[1] The search strategy identified in this table was designed specifically for MEDLINE (http://www.nlm.nih.gov/bsd/pmresources.html); equivalent subject headings were used for EMBASE (http://www.embase.com/), PubMed (http://www.ncbi.nlm.nih.gov/pubmed), and the Cochrane Central Register of Controlled Trials (http://www.thecochranelibrary.com). MeSH, Medical Subject Headings.

Outcomes

The primary outcomes were body weight and body composition (FM and FFM, assessed by either laboratory or field techniques including dual-energy X-ray absorptiometry, bioelectrical impedance analysis, and air-displacement plethysmography). The secondary outcomes were blood lipid profile (total cholesterol, LDL cholesterol, HDL cholesterol, and triglycerides), blood pressure, fasting plasma glucose, fasting insulin, satiety/appetite, and REE. Demographic characteristics of the study population (age, body weight, sex, and chronic disease) and details of the study protocol and methodology were also extracted from all included studies. The consumed relative daily protein content of treatment groups was calculated for all studies on the basis of the mean quantity of protein per kilogram of mean baseline body weight. In studies in which dietary composition was provided in absolute quantities of macronutrients, macronutrients as a percentage of total energy intake and/or total energy intake were calculated on the basis of the following energy densities per gram: protein and carbohydrate, 16.736 kJ; fat, 37.656 kJ; and alcohol, 29.288 kJ.

Data abstraction

One reviewer (TPW) extracted the data from all articles, whereas the second (LJM) independently extracted data from 5 of the studies identified through random selection to test the reliability of the abstraction process. The intrastudy data abstraction reliability was 98.7% based on dividing the number of variables that were coded the same by both investigators by the total number of variables abstracted. Discrepancies were resolved by consensus.

Original trial investigators were contacted by e-mail with a request for the provision of additional information and data where required. For studies with multiple treatment arms, treatments that did not meet the inclusion criteria were excluded from the analysis. Data were collected, when possible, only for the pre– and post–energy-restriction periods. However, in some studies, included data for outcomes were available only after a combined period of energy restriction and subsequent energy balance (11, 23, 24), and these data were subsequently analyzed.

Critical appraisal

Studies were evaluated for risk of selection, performance, and detection bias on the basis of a modified Cochrane risk of bias assessment (**Table 2**) (25). Qualitative dietary prescription and

TABLE 2
Risk of bias and methodologic quality of dietary intervention[1]

	Selection bias		Performance bias		Detection bias	Dietary methods				
First author, year (reference)	Randomization	Concealed allocation	Patients blinded	Intervention provider blinded	Outcome assessor blinded	Prescription	Compliance	Objective biomarker for protein intake	Body-composition analysis technique	Additional study notes
Baba, 1999 (12)	Unclear	Unclear	No (high risk)	No (high risk)	Unclear	7-d rotating menu; standardized recipes and menus; food items catered to each subject for entire study; weekly nutrition counseling	Uneaten portion or deviation recorded daily		BIA	
Belobrajdic, 2010 (27)	Unclear	Unclear	No (high risk)	No (high risk)	Unclear	60% of food items supplied; biweekly individual visits with a dietitian	Daily food checklists; pre-/poststudy food-frequency questionnaire		DXA	
Campbell, 2010 (study 1) (28)	Unclear	Unclear	No (high risk)	No (high risk)	Unclear	Participants counseled to follow 7-d menus; specified quantities and brand-specific foods		Differential poststudy blood urea nitrogen	DXA	Study 2: achieved protein levels <10% difference
Das, 2007 (29)	Unclear	Unclear	No (high risk)	No (high risk)	Yes (low risk)	First 6 mo: all food provided; second 6 mo: individual menus, recipes, portion sizes, and food lists developed by dietitian; scales provided; grocery store tour and cooking classes provided	Leftovers and additional foods reported on datasheet; leftover foods returned and weighed		ADP	
Evangelista, 2003 (30)	Unclear	Unclear	No (high risk)	No (high risk)	Unclear	Dietitian visits at weeks 1, 2, 4, 8, and 12; provision of resources (food lists, serving sizes) and tools (weight chart, checklists, and diaries) by dietitians	3-d food diaries reviewed during dietitian visits		DXA	SD for change in LDL cholesterol excluded

(Continued)

TABLE 2 (*Continued*)

	Selection bias		Performance bias		Detection bias	Dietary methods				
First author, year (reference)	Randomization	Concealed allocation	Patients blinded	Intervention provider blinded	Outcome assessor blinded	Prescription	Compliance	Objective biomarker for protein intake	Body-composition analysis technique	Additional study notes
Farnsworth, 2003 (11)	Unclear	Unclear	No (high risk)	No (high risk)	Unclear	60% of food items supplied; biweekly individual visits with a dietitian; group training in use of scales and completing food checklists	Daily food checklists; pre-/poststudy food-frequency questionnaire	Time × diet effect for change in urinary urea:creatinine ratio	DXA	Data available only for pre and post combined weight-loss and weight-maintenance phase
Flechtner-Mors, 2010 (phase 1) (31)	Unclear	Unclear	No (high risk)	Unclear	Unclear	Meal replacements were provided for the study duration; participants advised and educated by dietitian weekly (first 4 wk) and monthly thereafter individually and in groups	3-d food records conducted every 3 mo and reviewed by dietitians	Differential poststudy blood urea nitrogen	BIA	
Johnston, 2004 (32)	Unclear	Unclear	No (high risk)	No (high risk)	Unclear	14-d rotating menu devised for each diet plan; all meals prepared by staff in metabolic kitchens—lunch consumed on site, breakfast, dinner, and weekend meals were take-away	Participants asked to report incidences of eating nonprescribed foods	Differential poststudy blood urea nitrogen	BIA	
Kasim-Karakas, 2009 (33)	Unclear	Unclear	Yes (low risk)	Yes (low risk)	Unclear	7-d food records collected at baseline and monthly during study; uniform dietary guidelines offered to participants; separate protein- or carbohydrate-based daily supplements were provided			BIA	Article does not state whether error values are SD or SEM (inferred as SEM)

(Continued)

TABLE 2 (*Continued*)

	Selection bias		Performance bias		Detection bias	Dietary methods				
First author, year (reference)	Randomization	Concealed allocation	Patients blinded	Intervention provider blinded	Outcome assessor blinded	Prescription	Compliance	Objective biomarker for protein intake	Body-composition analysis technique	Additional study notes
Kleiner, 2006 (34)	Unclear	Unclear	No (high risk)	No (high risk)	Unclear	All meals on 2-wk cycle prepared in metabolic kitchen; lunches served to participants; all other meals and weekend meals were provided as take-away; participants were asked to consume only foods and beverages provided to them			DXA	Baseline FFM values reported in article are incorrect (FFM > body weight), no precise energy intake data are reported
Krauss, 2006 (35)	Unclear	Unclear	No (high risk)	No (high risk)	Unclear	Frozen take-away meals provided for lunch and dinner; participants prepared their own breakfast and snacks according to 6-d rotating menus	Daily checklists of consumed foods		BIA	54% CHO vs 39% CHO groups used; study had a eucaloric run-in phase—all changes are given from the end of the eucaloric run-in to the end of the active weight-loss phase (weeks 4–13)
Labayan, 2003 (36)	Unclear	Unclear	No (high risk)	No (high risk)	Unclear	Biweekly nutrition counseling			ADP	FM values for HP and SP are mixed-up in the article; assumed correct values are reported in this data set
Lasker, 2008 (37)	Unclear	Unclear	No (high risk)	No (high risk)	Unclear	Menus, food substitutions, portion sizes, meal plans, and procedures for filling out food checklists were provided; electronic scales provided; 1-h weekly group meetings with dietitian	3-d weighted food record documented each week		DXA	

(Continued)

TABLE 2 (*Continued*)

	Selection bias		Performance bias		Detection bias	Dietary methods				
First author, year (reference)	Randomization	Concealed allocation	Patients blinded	Intervention provider blinded	Outcome assessor blinded	Prescription	Compliance	Objective biomarker for protein intake	Body-composition analysis technique	Additional study notes
Layman, 2003 (9)	Unclear	Unclear	No (high risk)	No (high risk)	Unclear	All food provided for first 4 wk of study; 2-wk rotating menu plan for remaining 6 wk	3-d weighed food records kept by participants; food records checked for reliability by staff who reweighed food during first 4-wk period	Diet effect for urinary urea	DXA	
Layman, 2005 (38)	Unclear	Unclear	No (high risk)	No (high risk)	Unclear	Provided with menus and scales; food substitutions, portion sizes, meal plans, and procedures for filling out food checklists were provided; 1-h weekly group meetings with dietitian	3-d food records collected weekly		DXA	Only the nonexercise groups were used in analysis
Layman, 2009 (weight-loss phase) (39)	Unclear	Unclear	No (high risk)	No (high risk)	Unclear	Provided with menus and scales; food substitutions, portion sizes, meal plans, and procedures for filling out food checklists were provided; 1-h weekly group meetings with dietitian	3-d food records collected weekly	Diet effect for urinary urea	DXA	
Leidy, 2007 (10)	Unclear	Unclear	No (high risk)	No (high risk)	Unclear	7-d menus with specified quantities of foods; shopping lists and dietary counseling provided; some key foods provided	Daily food checklists; extra foods recorded on food logs	Time × diet effect for change in blood urea nitrogen	DXA	Week 1 dietary intake used for dietary data

(*Continued*)

TABLE 2 (*Continued*)

	Selection bias		Performance bias		Detection bias	Dietary methods				
First author, year (reference)	Randomization	Concealed allocation	Patients blinded	Intervention provider blinded	Outcome assessor blinded	Prescription	Compliance	Objective biomarker for protein intake	Body-composition analysis technique	Additional study notes
Luscombe, 2003 (23)	Unclear	Unclear	No (high risk)	No (high risk)	Unclear	Biweekly individual dietitian visits; 60% of key foods provided	3-d weighed food records collected every 2 wk	Diet effect for change in urine urea:creatinine ratio	DXA	Data available only for pre and post combined weight-loss and weight-maintenance phase
Noakes, 2005 (8)	Unclear	Unclear	No (high risk)	No (high risk)	Unclear	Food scales provided; biweekly individual dietitian visits; monthly food preparation at-home sessions; 60% of key foods supplied	Daily food checklists; 3-d weighed food records collected each month	Diet effect for change in urine urea:creatinine ratio	DXA	End glucose SEM values reported in the article have been confirmed to actually be SDs
Parker, 2002 (24)	Unclear	Unclear	No (high risk)	No (high risk)	Unclear	60% of key foods supplied; biweekly individual dietitian visits; group session for use of scales and food checklist completion instructions	Daily food checklists; 3-d weighed food records collected biweekly	Diet effect for change in urine urea: creatinine ratio	DXA	Lipids and glucose data are week 0 and week 8 data (weight-loss phase only); weight and body-composition data are week 0 and week 12 data (weight-loss plus -maintenance phase); Table 3 weight reported as SE but confirmed to be SD
Stamets, 2004 (40)	Yes (low risk)	Yes (low risk)	No (high risk)	No (high risk)	Unclear	Initial individual meeting with dietitian	Daily food monitoring submitted and discussed with a dietitian weekly		None	Dietary energy intake was not reported
Torbay, 2002 (normoinsulinemic) (41)	Unclear	Unclear	No (high risk)	No (high risk)	Unclear	7-d rotating menu; standardized recipes and menus; food items catered to each subject for entire study; weekly nutrition counseling	Uneaten portion or deviation recorded daily		BIA	Hyperinsulinemic data are a replication of the Baba et al (12) data

(*Continued*)

TABLE 2 (*Continued*)

	Selection bias		Performance bias		Detection bias	Dietary methods				
First author, year (reference)	Randomization	Concealed allocation	Patients blinded	Intervention provider blinded	Outcome assessor blinded	Prescription	Compliance	Objective biomarker for protein intake	Body-composition analysis technique	Additional study notes
Treyzon, 2008 (42)	Yes (low risk)	Yes (low risk)	Yes (low risk)	No (high risk)	Unclear	Meal replacements plus treatment-specific protein or carbohydrate supplements provided; individual meetings with dietitian at weeks 2, 4, and 8; individualized menu plans			BIA	Article states that 100 commenced and 15 withdrew (HP, 6; SP, 9)—numbers do not add up because 87 was listed in baseline table with sex split
Wycherley, 2010 (43)	Unclear	Unclear	No (high risk)	No (high risk)	Unclear	Biweekly dietitian visits; 50% of key foods provided	Daily semiquantitative food checklists; 7-d weighed food records collected every 2 wk	Diet effect for change in urine urea:creatinine ratio	DXA	

[1] ADP, air-displacement plethysmography; BIA, bioelectrical impedance analysis; CHO, carbohydrate; DXA, dual-energy X-ray absorptiometry; FFM, fat-free mass; FM, fat mass; HP, high-protein, low-fat diet; SP, standard-protein, low-fat diet.

compliance information were documented for all studies (dietary prescription/instruction/counseling methods, provision of foods/meals, dietary intake reporting methods, objective dietary assessment measures).

Statistical analysis

Statistical analysis was conducted by using Review Manager (RevMan, version 5.1.7; The Nordic Cochrane Centre, The Cochrane Collaboration, 2011). Data are reported as means ± SDs or as weighted mean difference (WMD) and 95% CIs. For all group comparisons significance was set at $P < 0.05$. Treatment effects were pooled, and the WMD was calculated for all outcome variables in the HP and SP groups. Heterogeneity between studies was examined by chi-square tests for significance, with $P < 0.1$ considered to be significant, and measured inconsistency (I^2) statistics with a measurement >50% taken to indicate substantial heterogeneity (25). A random-effects model was used to analyze outcomes with heterogeneity, and a fixed-effects model was used if no statistical heterogeneity was evident [Mantel-Haenszel methods (26)]. Subgroup analysis was performed to examine the effect of dietary intervention duration. Studies were classified as either of shorter duration (<12 wk) or of longer duration (≥12 wk).

RESULTS

Studies

Searches identified 1284 potential articles of which 1150 were excluded on the basis of title and abstract and 110 were excluded on the basis of full text assessment (**Figure 1**). After combining multiple reports of the same study participants, a total of 24 separate articles contained intervention groups that met the inclusion criteria (8–12, 23, 24, 27–43). The studies included 520 and 543 individuals who consumed HP and SP diets, respectively (**Table 3**).

Additional data were requested for outcomes in 19 studies (11 different corresponding authors). Eight of the contacted authors

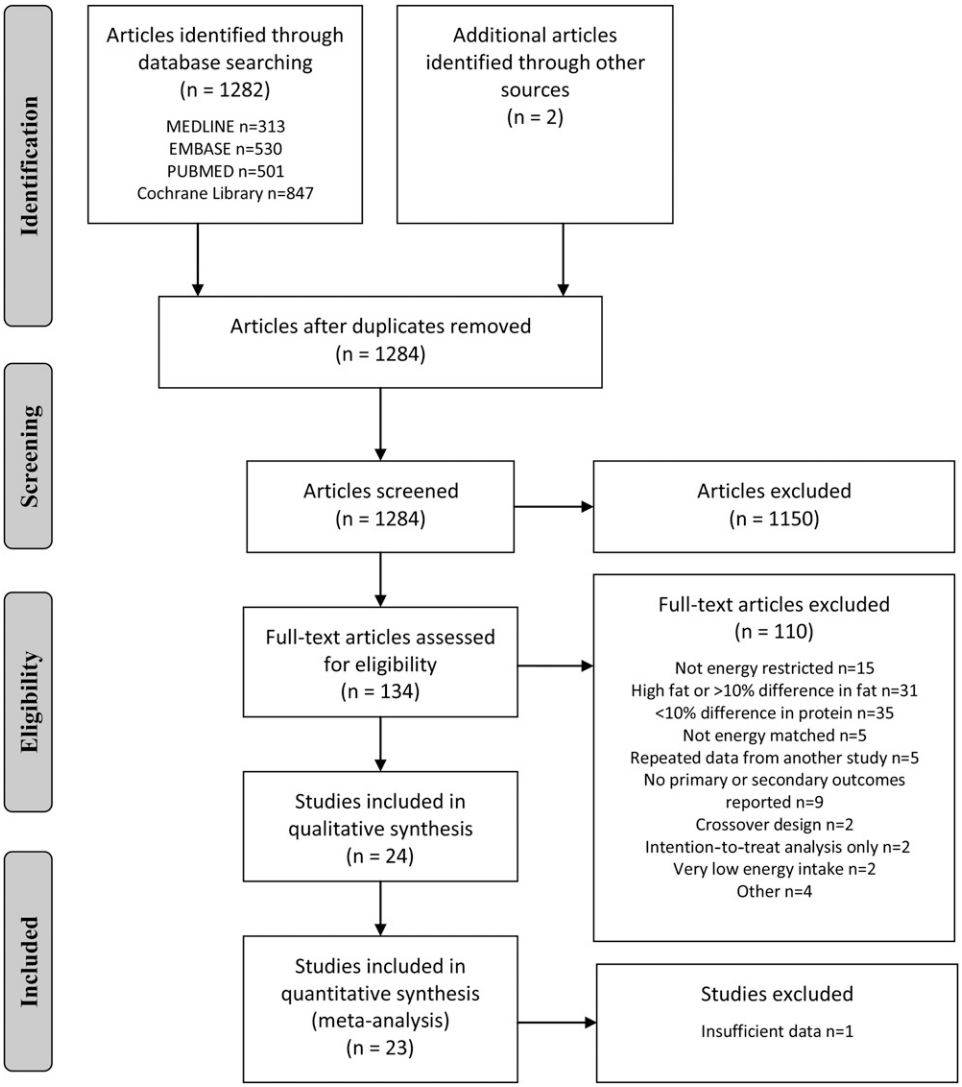

FIGURE 1. PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flowchart. MEDLINE, http://www.nlm.nih.gov/bsd/pmresources.html; EMBASE, http://www.embase.com/; PubMed, http://www.ncbi.nlm.nih.gov/pubmed; Cochrane Library, http://www.thecochranelibrary.com.

TABLE 3
Study participants[1]

First author, year (reference)	Population	Diet	Commenced			Completed				
			n	Men	Women	*n*	Men	Women	Baseline weight	Age
									kg	*y*
Baba, 1999 (12)	Hyperinsulinemic	HP	7	7	0	7	7	0	113.2 ± 18.0[2]	20.6 ± 1.5
		SP	6	6	0	6	6	0	105.5 ± 11.5	24.7 ± 8.0
Belobrajdic, 2010 (27)	Overweight and obese	HP	61	61	0	34	34	0	103 ± 14.6	50.9 ± 8.7
		SP	62	62	0	42	42	0	101 ± 14.3	50.9 ± 8.6
Campbell, 2010 (study 1) (28)	Postmenopausal women	HP	27	0	27	13	0	13	82.5 ± 15.1	51 ± 7
		SP	27	0	27	15	0	15	80.0 ± 11.2	60 ± 12
Das, 2007 (29)	Overweight	HP	17	4	13	14	—	—	78.0 ± 9.3	35 ± 6
		SP	17	4	13	15	—	—	78.5 ± 12.3	34 ± 5
Evangelista, 2003 (30)	Heart failure patients	HP	5	4	1	5	4	1	110.8 ± 11.7	56.4 ± 6.6
		SP	5	4	1	5	4	1	99.5 ± 8.0	58.6 ± 13
Farnsworth, 2003 (women) (11)	Hyperinsulinemic	HP	66	0	—	21	0	21	89.5 ± 9.6	50.6 ± 12.4
		SP		0	—	22	0	22	88.3 ± 10.3	50.6 ± 9.9
Farnsworth, 2003 (men) (11)		HP		—	0	7	7	0	107.4 ± 15.4	51.9 ± 8.7
		SP		—	0	7	7	0	109.4 ± 13.8	48.6 ± 8.5
Flechtner-Mors, 2010 (phase 1) (31)	Metabolic syndrome	HP	55	12	43	49	11	38	~100.2 ± 16.5	~49.3 ± 12.3
		SP	55	10	45	53	10	43	~100.5 ± 16.6	~50.2 ± 13
Johnston, 2004 (32)	Overweight and obese	HP	10	1	9	9	1	8	82.1 ± 26.7	40.1 ± 10.8
		SP	10	1	9	7	1	6	78.2 ± 19.6	36.4 ± 11.1
Kasim-Karakas, 2009 (33)	Polycystic ovary syndrome	HP	14	0	14	11	0	11	106.6 ± 18.9	~28
		SP	16	0	16	13	0	13	95.3 ± 19.8	
Kleiner, 2006 (34)	Hyperinsulinemic	HP	10	3	7	9	2	7	94.5 ± 10.8	35.2 ± 14.7
		SP	10	3	7	7	2	5	107.1 ± 20.6	34.6 ± 9.5
Krauss, 2006 (35)	Overweight	HP	56	56	0	42	42	0	92.7 ± 9.1	51.5 ± 11.6
		SP	57	57	0	49	49	0	91.6 ± 9.0	50.3 ± 9.8
Labayan, 2003 (36)	Obese	HP	6	0	6	6	0	6	—	42.2 ± 16.2
		SP	5	0	5	5	0	5	—	41.4 ± 9.6
Lasker, 2008 (37)	Overweight and obese	HP	32	—	—	25	19	31	96.6 ± 19.5	47.2 ± 7.1
		SP	33	—	—	25			94.3 ± 10.5	
Layman, 2003 (9)	Overweight	HP	12	0	12	12	0	12	84.8 ± 12.6	50.1 ± 5.4
		SP	12	0	12	12	0	12	85.7 ± 9.6	
Layman, 2005 (38)	Overweight	HP	12	0	12	12	0	12	91.1 ± 17.7	47.0 ± 5.9
		SP	12	0	12	12	0	12	93.7 ± 12.1	45.2 ± 4.9
Layman, 2009 (weight-loss phase) (39)	Obese	HP	64	28	36	52	—	—	~91.7 ± 16.0	~45.2 ± 9.6
		SP	66	31	35	51	—	—	~93.8 ± 13.0	~46.0 ± 8.1
Leidy, 2007 (10)	Overweight and obese	HP	54	0	54	21	0	21	83.4 ± 10.1	46 ± 9
		SP		0		25	0	25	82.6 ± 17	53 ± 15
Luscombe, 2003 (23)	Hyperinsulinemic	HP	17	4	13	17	4	13	~94.3 ± 15.7	55 ± 8
		SP	19	6	13	19	6	13	~93.7 ± 16.1	53 ± 9
Noakes, 2005 (8)	Obese	HP	58	0	58	52	0	52	87 ± 12	50 ± 10
		SP	61	0	61	48	0	48	86 ± 12	49 ± 9
Parker, 2002 (24)	Type 2 diabetes	HP	31	13	18	26	9	17	97.7 ± 17.4	~60.3
		SP	33	11	22	28	10	18	91.4 ± 18.2	~62.1
Stamets, 2004 (40)	Polycystic ovary syndrome	HP	17	0	17	13	0	13	104.6 ± 14.6	29 ± 4
		SP	18	0	18	13	0	13	104.0 ± 13.7	26 ± 4
Torbay, 2002 (normoinsulinemic) (41)	Obese	HP	7	7	0	7	7	0	112.7 ± 13.8	20–40[3]
		SP	7	7	0	7	7	0	108.7 ± 11.4	20–40
Treyzon, 2008 (42)	Obese	HP	50	—	—	44	8	36	93.5 ± 14.0	48.9 ± 11.8
		SP	50	—	—	41	15	26	92.7 ± 15.9	49.7 ± 9.1
Wycherley, 2010 (43)	Type 2 diabetes	HP	21	13	8	12	7	5	102.7 ± 15.4	56.3 ± 7.6
		SP	19	8	11	16	8	8	97 ± 10.6	58 ± 6.8

[1] CHO, carbohydrate; HP, high-protein, low-fat diet; SP, standard-protein, low-fat diet.
[2] Mean ± SD (all such values).
[3] Range (all such values).

(responsible for a total of 14 studies) responded to the e-mail request, and 6 authors provided additional data for a total of 8 studies. One study (29) did not report error range data for the change values for any of the assessed outcomes and could not be included in the meta-analysis for any of the outcomes.

Methodologic quality

The risk of selection bias was unclear because of unspecified methods of randomization/diet allocation for all but 3 studies that were identified as low risk (40, 42) (Table 2). Only one study identified that the outcome assessors were blinded to treatment

TABLE 4
Study diet characteristics[1]

First author, year (reference)	Duration	Diet	Baseline diet					Prescribed diet					Achieved diet				
			Energy	Protein		CHO	Fat	Energy	Protein		CHO	Fat	Energy	Protein		CHO	Fat
	wk		*kJ/d*	g · kg^{-1} · d^{-1}	%	%	%	*kJ/d*	g · kg^{-1} · d^{-1}	%	%	%	*kJ/d*	g · kg^{-1} · d^{-1}	%	%	%
Baba, 1999 (12)	4	HP	—	—	—	—	—	7495	1.78	45	25	30	—	—	—	—	—
		SP	—	—	—	—	—	7377	0.50	12	58	30	—	—	—	—	—
Belobrajdic, 2010 (27)	12	HP	—	—	—	—	—	~7000	1.5	—	—	—	7151 ± 789[2]	1.37	33	37	28
		SP	—	—	—	—	—	~7000	—	—	—	—	7113 ± 617	0.88	21	51	26
Campbell, 2010 (study 1) (28)	12	HP	9347	0.91	17	49	35	6209	1.4	30	45	25	6343 ± 934	1.38	30	45	26
		SP	7560	1.12	17	44	37	4422	0.6	18	57	25	5937 ± 754	0.78	17	58	25
Das, 2007 (29)	52	HP	—	—	—	—	—	7950	1.80	30	40	30	10,255	—	—	—	—
		SP	—	—	—	—	—	8200	1.24	20	60	20	9799	—	—	—	—
Evangelista, 2003 (30)	12	HP	—	—	—	—	—	5021–6276[3]	—	30	40	30	—	—	—	—	—
		SP	—	—	—	—	—	5021–6276	—	15	55	30	—	—	—	—	—
Farnsworth, 2003 (women) (11)		HP	—	—	—	—	—		~1.26	30	40	30		~1.14	27	44	27
	12 (hypocaloric)	SP	—	—	—	—	—	HP: 6300	~0.66	15	55	30	HP: 6300 ± 529	~0.70	16	57	27
Farnsworth, 2003 (men) (11)	4 (eucaloric)	HP	—	—	—	—	—	SP: 6500	~1.05	30	40	30	SP: 6500 ± 539	~0.95	27	44	27
		SP	—	—	—	—	—		~0.53	15	55	30		~0.57	16	57	27
Flechtner-Mors, 2010 (phase 1) (31)	12	HP	7138	0.77	18	46.7	35.2	2092 deficit	1.34	30	40	30	5539 ± 1386	1.15	34.9	35	30
		SP	6812	0.69	17	48.2	34.6	2092 deficit	0.8	15	55	30	5263 ± 1319	0.55	17.5	51	31
Johnston, 2004 (32)	6	HP	—	—	—	—	—	7080	1.63	32	40	28	—	—	—	—	—
		SP	—	—	—	—	—	7080	0.82	15	66	21	—	—	—	—	—
Kasim-Karakas, 2009 (33)	8	HP	9075	0.78	20.7	49.8	33.8	1883 deficit	—	—	—	—	5770 ± 1027	1.07	33.7	40	26
		SP	7958	0.80	17.0	51.3	29.4	1883 deficit	—	—	—	—	5657 ± 1478	0.61	16.6	57	26
Kleiner, 2006 (34)	8	HP	—	—	—	—	—	5021–8368	—	32	41	27	—	—	—	—	—
		SP	—	—	—	—	—	5021–8368	—	14	59	27	—	—	—	—	—
Krauss, 2006 (35)	1 (control) 3 (eucaloric) 5 (hypocaloric) 4 (eucaloric)	HP	—	—	—	—	—	~4184 deficit	—	29	39	31	—	—	—	—	—
		SP	—	—	—	—	—	~4184 deficit	—	16	54	30	—	—	—	—	—
Labayan, 2003 (36)	10	HP	—	—	—	—	—	2092 deficit	—	30	40	30	—	—	—	—	—
		SP	—	—	—	—	—	2092 deficit	—	15	55	30	—	—	—	—	—
Lasker, 2008 (37)	16	HP	9952	0.98	15.9	49.0	34.2	7900 (men)	1.6	30	40	30	6607 ± 1175	1.27	31	39	32
		SP	9147	0.93	16.0	48.5	33.6	7100 (women)	0.8	15	55	30	5875 ± 1955	0.71	19	61	25
Layman, 2003 (9)	10	HP	8196	0.88	15.3	50.2	34.5	7100	1.6	~30	~40	<30	6987 ± 682	1.47	30	41	29
		SP						7100	0.8	~15	~55	<30	6941 ± 579	0.79	16	58	26
Layman, 2005 (38)	16	HP	8888	0.87	14.9	49.4	35.9	7100	1.6	~30	~40	<30	6062 ± 405	1.6	30	39	32
		SP	8479	0.88	16.2	48.6	35.2	7100	0.8	~15	~55	<30	5377 ± 620	0.8	18	61	24
Layman, 2009 (weight-loss phase) (39)	16	HP	10060	~1.06	16.2	48.9	35.0	7940 (men)	1.6	30	40	30	6730 ± 1659	~1.15	29	40	33
		SP	8780	~0.89	15.9	50.2	32.9	7100 (women)	0.8	15	55	30	6200 ± 1713	~0.69	19	59	26
Leidy, 2007 (10)	12	HP	—	—	—	—	—	3138 deficit	1.4	30	45	25	6527 ± 1150	1.40	30	45	26
		SP	—	—	—	—	—	3138 deficit	0.8	18	57	25	6402 ± 837	0.82	18	57	25
Luscombe, 2003 (23)	12 (hypocaloric) 4 (eucaloric)	HP	—	—	—	—	—	~30% deficit	~1.17	30	40	30	6358 ± 586	1.10	27	45	27
		SP	—	—	—	—	—	~30% deficit	~0.64	15	55	30	6663 ± 820	0.67	16	57	27

(Continued)

TABLE 4 (*Continued*)

First author, year (reference)	Duration	Baseline diet						Prescribed diet						Achieved diet					
		Diet	Energy	Protein				Energy	Protein					Energy	Protein				
				g · kg^{-1} · d^{-1}	%	CHO	Fat		g · kg^{-1} · d^{-1}	%	CHO	Fat			g · kg^{-1} · d^{-1}	%	CHO	Fat
Noakes, 2005 (8)	12	HP	—	—	—	—	—	5600	1.30	34	46	20	5310 ± 400		1.13	31	44	22
		SP	—	—	—	—	—	5600	0.66	17	64	20	5219 ± 539		0.65	18	61	20
Parker, 2002 (24)	8 (hypocaloric)	HP	—	—	—	—	—	6694	1.23	30	40	30	6640 ± 768		1.14	28	42	28
	4 (eucaloric)	SP	—	—	—	—	—	6694	0.66	15	60	25	6456 ± 974		0.68	16	55	26
Stamets, 2004 (40)	4	HP	—	—	—	—	—	4184 deficit	—	30	40	30	—		—	—	—	—
		SP	—	—	—	—	—	4184 deficit	—	15	55	30	—		—	—	—	—
Torbay, 2002 (normoinsulinemic) (41)	4	HP	—	—	—	—	—	7668 (80% of REE)	1.83	45	25	30	—		—	—	—	—
		SP	—	—	—	—	—	8094 (80% of REE)	0.53	12	58	30	—		—	—	—	—
Treyzon, 2008 (42)	12	HP	—	—	—	—	—	2092 deficit	—	30	40	30	—		—	—	—	—
		SP	—	—	—	—	—	2092 deficit	—	15	55	30	—		—	—	—	—
Wycherley, 2010 (43)	16	HP	—	—	—	—	—	6619	1.26	33	43	22	6321 ± 763		1.18	32	47	23
		SP	—	—	—	—	—	6421	0.75	19	53	26	6278 ± 648		0.73	19	54	18

[1] CHO, carbohydrate; HP, high-protein, low-fat diet; REE, resting energy expenditure; SP, standard-protein, low-fat diet.
[2] Mean ± SD (all such values).
[3] Range (all such values).

(29) and was classified as low risk for detection bias; the remaining studies did not specify whether outcome assessor blinding occurred. Participants in 2 studies (33, 42) and intervention providers in one study (33) were blinded to dietary treatment through the use of unidentifiable dietary supplements that were rich in either protein or carbohydrate rather than the use of whole dietary patterns with different food types. For dietary prescription and compliance, 22 studies reported prescribed dietary macronutrient composition, 14 studies reported values for achieved dietary macronutrient composition, 12 studies reported both prescribed and achieved dietary macronutrient composition, 11 studies confirmed dietary compliance to protein intake with a biochemical urea measure, 17 studies provided some or all foods to participants, and 20 studies required participants to complete food checklists, diaries, or nonprescribed food records.

Whole-group analysis

Study diet characteristics are provided in **Table 4**. The mean (±SD) duration of the weight-loss phase of the dietary protocol was 12.1 ± 9.3 wk (range: 4–52 wk). For studies that reported achieved dietary intakes, the mean total energy intakes for HP and SP diets were 6593 ± 1130 kJ (range: 5310–10,255 kJ) and 6379 ± 1110 kJ (range: 5219–9799 kJ), respectively (Table 4). The mean relative protein contents of the achieved diets were 1.25 ± 0.17 g · kg^{-1} · d^{-1} (range: 1.07–1.60 g · kg^{-1} · d^{-1}) and 0.72 ± 0.09 g · kg^{-1} · d^{-1} (range: 0.55–0.88 g · kg^{-1} · d^{-1}) for HP and SP diets, respectively. The mean dietary macronutrient composition of the diets was as follows: protein [HP: 30.5 ± 2.4% (range: 27.0–34.9%); SP: 17.5 ± 1.5% (range: 16.0–21%)], carbohydrate [HP: 41.6 ± 3.5% (range: 35.0–47.0%); SP: 56.9 ± 3.3% (range: 51.0–61.0%)], and fat [HP: 27.8 ± 3.2% (range: 22.0–33.0%); SP: 25.1 ± 3.1% (range: 18.0–31.0%)] (Table 4). Five studies measured satiety/appetite outcomes (9, 10, 29, 32, 34). Although the methodologies were inconsistent, which precluded this outcome from the meta-analysis, 3 of the 5 studies (9, 10, 32) reported greater satiety with an HP diet.

On meta-analysis, compared with an SP diet, an HP diet produced greater reductions in weight (**Figure 2**), FM (**Figure 3**), and triglycerides (**Figure 4**) and lesser reduction in FFM loss (**Figure 5**). There was no difference between diets for changes in total cholesterol, LDL cholesterol, HDL cholesterol, systolic blood pressure, diastolic blood pressure, fasting insulin, or fasting glucose (**Table 5**).

Only 4 studies that examined REE were included in the analysis (12, 32, 42, 44). There was significantly less reduction in REE with an HP diet (**Figure 6**). Significant statistical heterogeneity was present for analysis of body weight, FFM, total cholesterol, LDL cholesterol, HDL cholesterol, REE, and glucose, and random-effects analyses were conducted on these outcomes.

Subgroup analysis

The comparison between studies of longer (≥12 wk) and shorter (<12 wk) duration showed no significant differences for any outcome variable ($P \geq 0.12$; Figures 2–6, Table 5). When the WMD of outcomes for studies of either shorter or longer duration was analyzed separately, the greater weight loss produced with

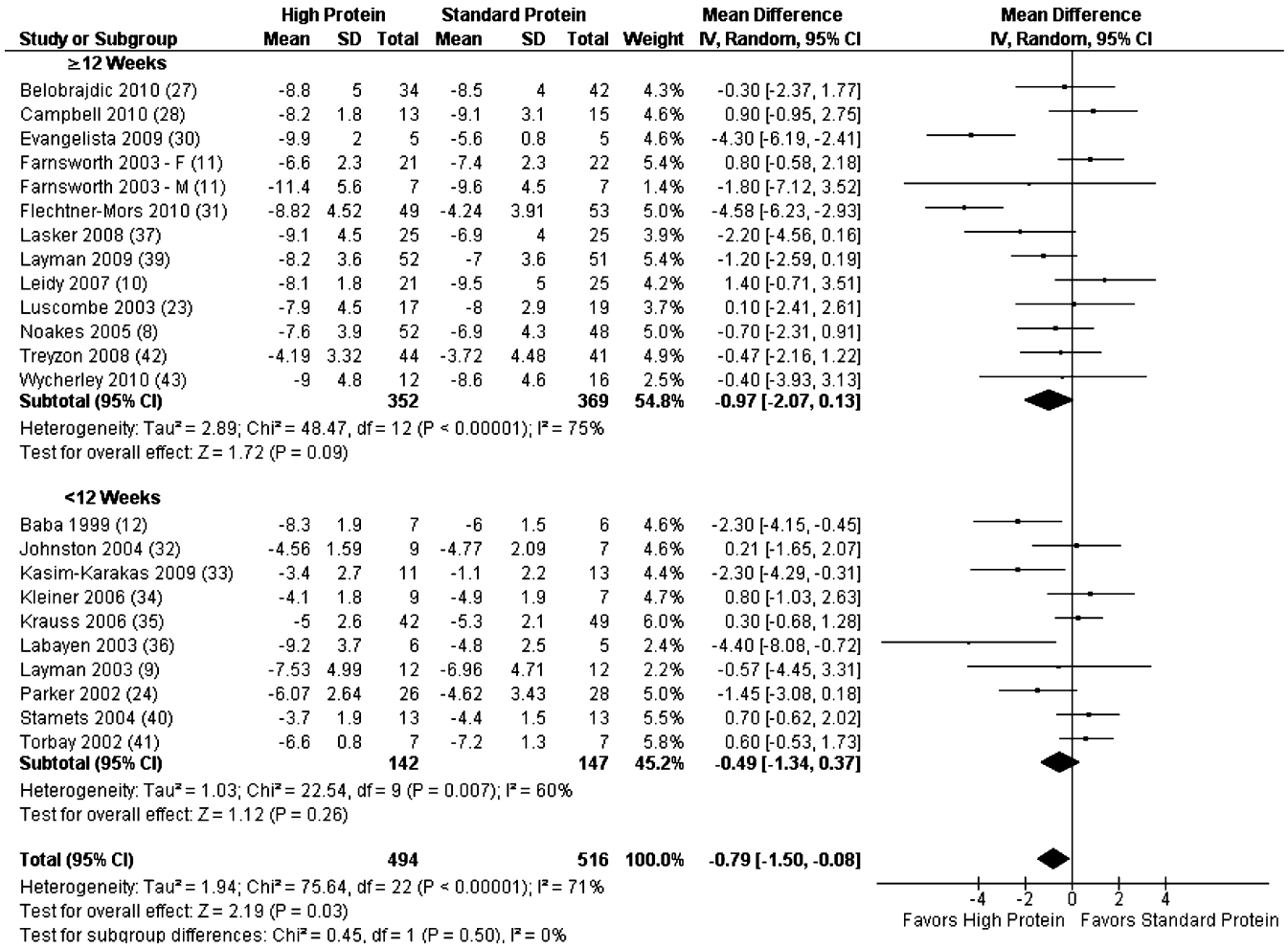

FIGURE 2. Meta-analysis for changes in body weight (kg) in randomized controlled trials that compared high-protein, low-fat diets with isocalorically prescribed standard-protein, low-fat, energy-restricted diets. IV, inverse variance.

the HP diet in the full group analysis was no longer significant in either subgroup. However, studies of either duration still showed a beneficial effect of the HP diet on reducing FM and triglycerides. For FFM a significant favorable effect of HP was evident only in the analysis of the studies of longer duration. There was a trend ($P = 0.05$) for a favorable effect of a greater reduction in fasting glucose with the SP diet for studies of longer duration.

DISCUSSION

In the first, to our knowledge, systematic review and meta-analysis on this topic, this study showed that compared with an SP diet, consuming an isocalorically prescribed HP diet provides a beneficial effect on weight loss, body composition (increasing FM loss and mitigating the reduction in FFM), REE, and triglycerides.

The preservation of FFM with the HP diet supports the finding of a meta-regression by Krieger et al (3), who reported that the degree of FFM retention during energy-restricted weight loss tended to increase with each successive quartile of dietary protein intake ($\leq$0.70, $>$0.70 to $\leq$1.05, $>$1.05 to $\leq$1.20, and $>$1.20 g $\cdot$ kg^{-1} $\cdot$ d^{-1}) and that protein intakes $>$1.05 g $\cdot$ kg^{-1} $\cdot$ d^{-1} may improve FFM retention. However, unlike the current study, by design the meta-regression did not provide direct meta-analysis comparisons of HP and SP diets.

Because energy-matched diets were compared, the relatively small difference in weight loss observed between diets was not surprising. Nevertheless, a significant 0.79-kg greater weight loss produced with the HP diet was still evident. Although the effect size is relatively modest, a greater weight loss of this magnitude may still represent clinical relevance on a population level. The diabetes prevention program showed that 1 kg of weight loss is associated with a 16% risk reduction in the development of diabetes (45). The mechanism for this greater weight loss with the HP diet compared with the SP diet under reported isocaloric conditions is unclear but may in part be a result of the greater preservation of FFM and REE (4). Because REE, which is strongly correlated with FFM, accounts for the majority ($\sim$60–70%) of daily energy expenditure (4, 46), it is possible that maintenance of higher REE via greater preservation of FFM with the HP diet induced a greater net energy deficit over time, which promoted greater FM and weight loss (5). Alternatively, the thermic effect of protein is greater compared with an equivalent energy intake of fat or carbohydrate (47, 48), which may also have contributed to the small, but significant, greater weight

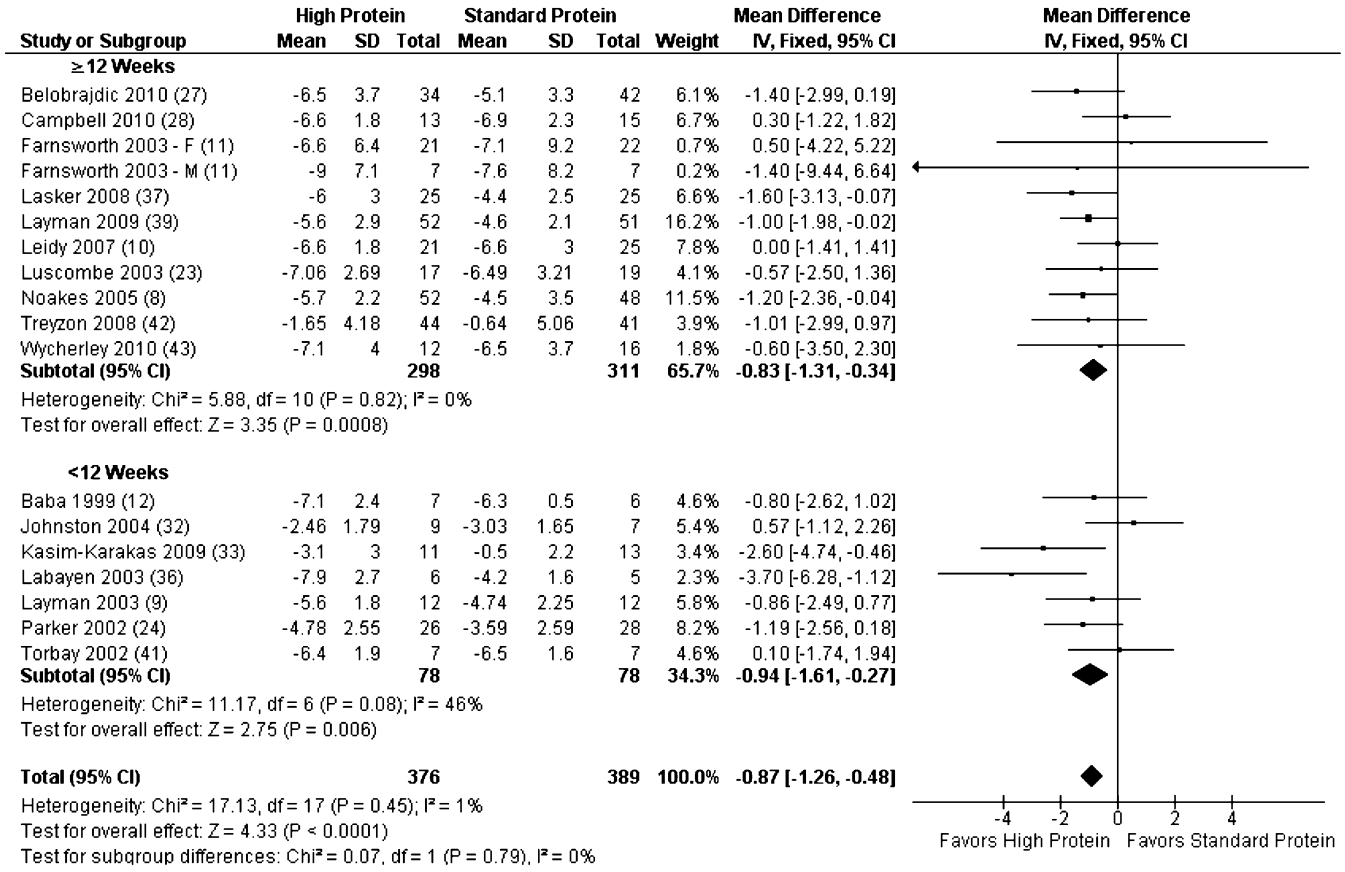

FIGURE 3. Meta-analysis for changes in fat mass (kg) in randomized controlled trials that compared high-protein, low-fat diets with isocalorically prescribed standard-protein, low-fat, energy-restricted diets. IV, inverse variance.

and FM loss. Alternatively, the possibility that the differences in weight and FM losses between the HP and SP diets may have occurred because of differences in energy intake that are beyond the sensitivity of food record analysis cannot be entirely dismissed (49). It has been postulated that because an HP diet is further removed than an SP diet from a usual dietary intake it may have more limited food choices that are easier to catalog and report with accuracy (50). Dietary protein also exerts greater satiety compared with carbohydrate or fat and consuming higher protein meals throughout the day prolongs greater satiety compared with consuming standard-protein meals (51). Consequently, within a prescribed energy-restricted diet, individuals who consume an SP compared with an HP diet may be more likely to consume additional calories from foods and from serving sizes extraneous to dietary prescription (48), which may or may not be recorded in dietary records (52).

The observed 595.5-kJ/d lesser reduction in REE with the HP diet could translate to ~1 kg of FM loss over an 8-wk period if maintained (53). However, the REE WMD is derived from only 4 studies with a relatively short mean weight-loss duration of 6 wk, and caution should be taken when interpreting this finding. The estimated difference in REE between the diets on the basis of a tissue contribution to the REE model by Heymsfield et al (54) was considerably lower (~24 kJ/d), with the assumption that the greater reduction in FFM observed in an SP diet was derived from skeletal muscle. Whether between-diet differences in the REE response to weight loss translates to any effect on long-term weight control remains a topic for future research. Preliminary evidence from a meta-review by Astrup et al (55) suggests that a low REE is likely to contribute to weight regain in formerly obese patients.

A homogeneous greater reduction in triglycerides with an HP diet was observed across studies. This supports a previous view that triglyceride reduction is the most consistently observed effect on blood lipids after consumption of an HP diet, which is primarily influenced by dietary carbohydrate reduction (56). Triglycerides are an independent risk factor for cardiovascular disease (57–59), but whether triglyceride reductions translate to reduced cardiovascular disease risk remains unclear (60).

No differences were observed between the HP and SP diets for changes in fasting glucose. However, data interpretation is limited because the majority of studies (10 of 12) included in the glucose analysis were conducted in nondiabetic individuals (24, 43). Furthermore, although FFM (skeletal muscle) is the primary site of glucose uptake (6), a direct relation between the quantity of skeletal muscle and glucose tolerance or insulin sensitivity does not follow (61). Effects of diet composition, particularly HP diets, during energy-reduced conditions on blood glucose control in patients with type 2 diabetes should be a focus of further exploration.

Subgroup analysis showed no significant differences between studies of shorter and longer duration for any outcome. This suggests that the observed benefits of an HP diet on weight loss, FM loss, FFM loss mitigation, and triglyceride reduction occur

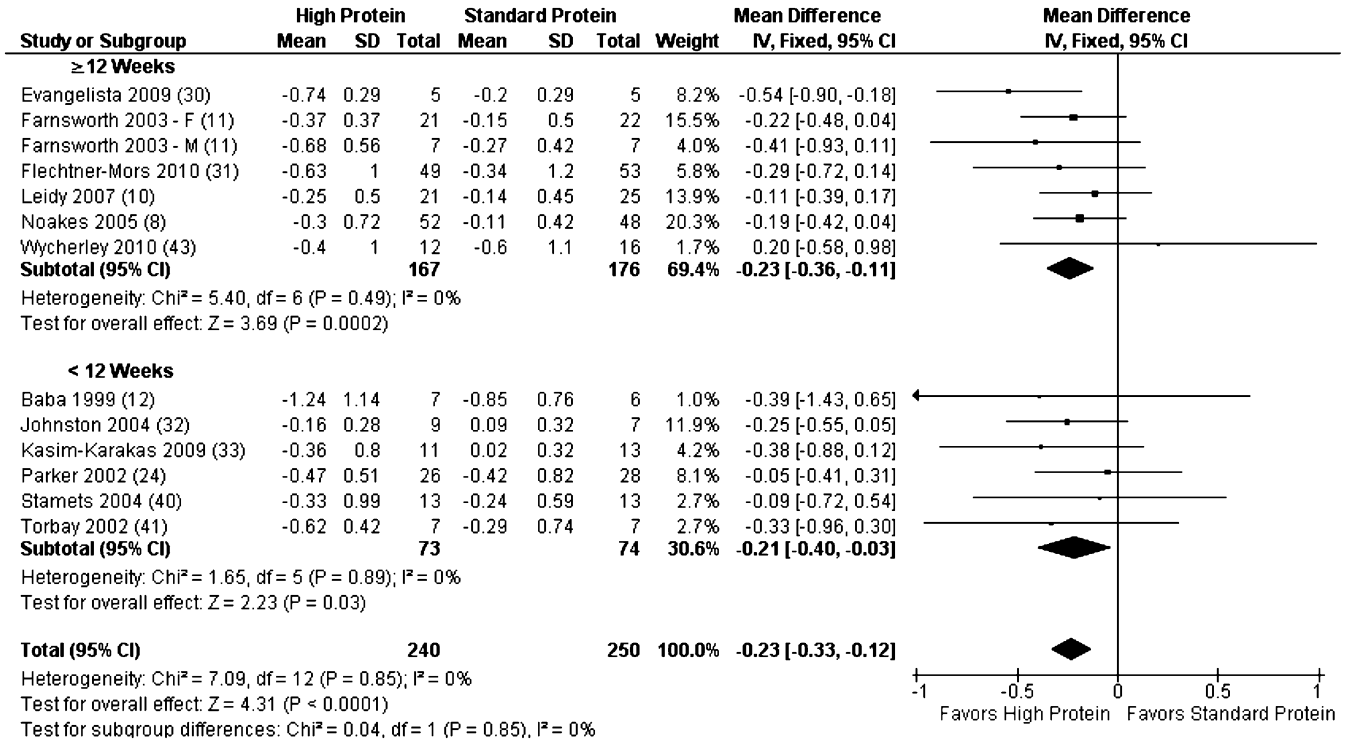

FIGURE 4. Meta-analysis for changes in triglycerides (mmol/L) in randomized controlled trials that compared high-protein, low-fat diets with isocalorically prescribed standard-protein, low-fat, energy-restricted diets. IV, inverse variance.

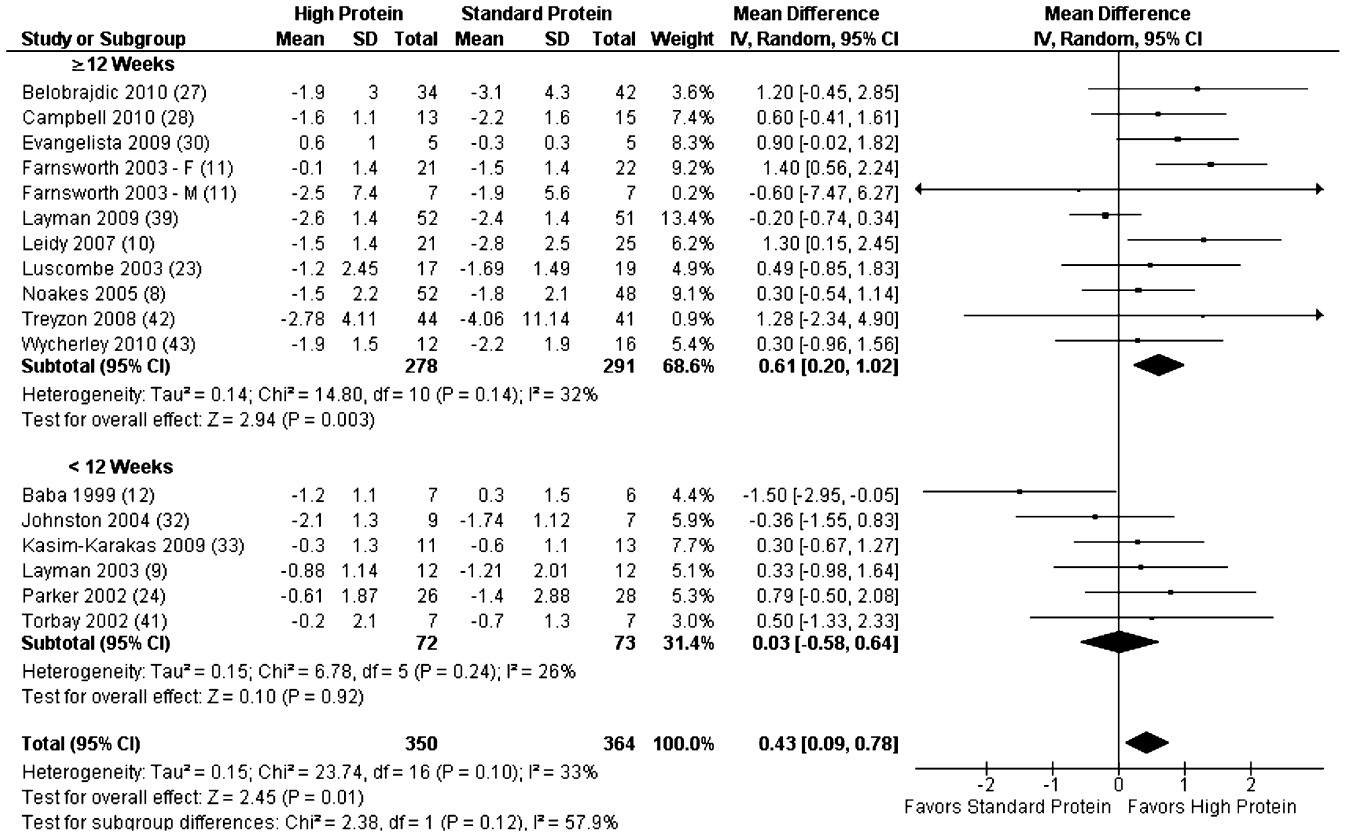

FIGURE 5. Meta-analysis for changes in fat-free mass (kg) in randomized controlled trials that compared high-protein, low-fat diets with isocalorically prescribed standard-protein, low-fat, energy-restricted diets. IV, inverse variance.

TABLE 5
Meta-analysis for changes in total cholesterol, LDL cholesterol, HDL cholesterol, systolic blood pressure, diastolic blood pressure, fasting glucose, and fasting insulin in randomized controlled trials that compared HP diets with isocalorically prescribed SP diets[1]

	No. of studies	Group numbers (HP/SP)	*P* value[2]	I^2	Weighted mean difference[3]	95% CI	*P* value: Overall effect	*P* value: Subgroup differences[4]
		n		%				
Total cholesterol (mmol/L)	15	351/365	<0.01	52	−0.09	−0.23, 0.05	0.20	0.95
LDL cholesterol (mmol/L)	11	261/269	<0.01	58	0.05	−0.10, 0.21	0.52	0.46
HDL cholesterol (mmol/L)	13	282/299	<0.001	92	0.00	−0.08, 0.09	0.97	0.23
Systolic blood pressure (mm Hg)	5	106/124	0.82	0	−2.09	−5.01, 0.83	0.16	0.41
Diastolic blood pressure (mm Hg)	5	106/124	0.55	0	−0.72	−2.67, 1.23	0.47	0.48
Fasting glucose (mmol/L)	12	281/299	0.04	46	0.08	−0.06, 0.22	0.28	0.13
Fasting insulin (mU/L)	11	248/262	0.21	24	−0.73	−1.84, 0.38	0.20	0.37

[1] HP, high-protein, low-fat; SP, standard-protein, low-fat.
[2] Derived by chi-square analysis.
[3] A negative weighted mean difference value refers to a greater effect with the HP diets. A positive weighted mean difference value refers to a greater effect with the SP diets.
[4] Subgroups were studies of shorter duration (<12 wk) or of longer duration (≥12 wk).

independently of the duration of caloric restriction (≥4 wk). However, there is a lack of tightly controlled long-term (≥12 mo) studies. The only study of long duration (52 wk) that met the inclusion criteria for this review (29) did not provide error range data for any of the change variables investigated and could not be included in the meta-analysis. Consequently, the long-term efficacy of a HP diet remains largely unknown. This is of particular importance given the potential for an HP diet to be associated with greater long-term weight maintenance and warrants future investigation.

The achievement of high levels of dietary adherence within the studies is an important consideration. Only 11 of the 24 studies measured and reported significant diet effects on urea as an objective marker of dietary protein intake. However, the routine use of comprehensive dietary delivery strategies, summarized in Table 2 (eg, food provision and regular dietary counseling), indicates that the studies included in this analysis were capable of evaluating the efficacy of the dietary patterns being studied. The possibility of a performance bias existing as a result of nonblinding of participants and intervention providers in the majority of studies cannot be dismissed. However, this is considered an unavoidable limitation of dietary intervention studies of this nature, given the interactive nature of the intervention and the use of commercially available whole foods in the dietary prescription. The inability to acquire missing data from all eligible studies is also a limitation, but is not unexpected, with the 42% success rate being consistent with the meta-analysis process (62). In this analysis, there was a small but significant difference in mean fat intake between the HP and SP diets (~5.5 g/d). Although it is unlikely that the higher fat intake in the HP diet contributed to the differential anthropometric and metabolic results observed given the directional effects, this influence cannot be entirely dismissed. To reduce heterogeneity and to evaluate the efficacy of modifying the dietary protein-to-carbohydrate ratio, only studies with ≥10% protein differential between the HP and SP diet groups were included in this analysis. Nevertheless, a 5–10% difference in protein intake may represent a more typically achieved protein differential that may still provide many of the advantages observed in the current

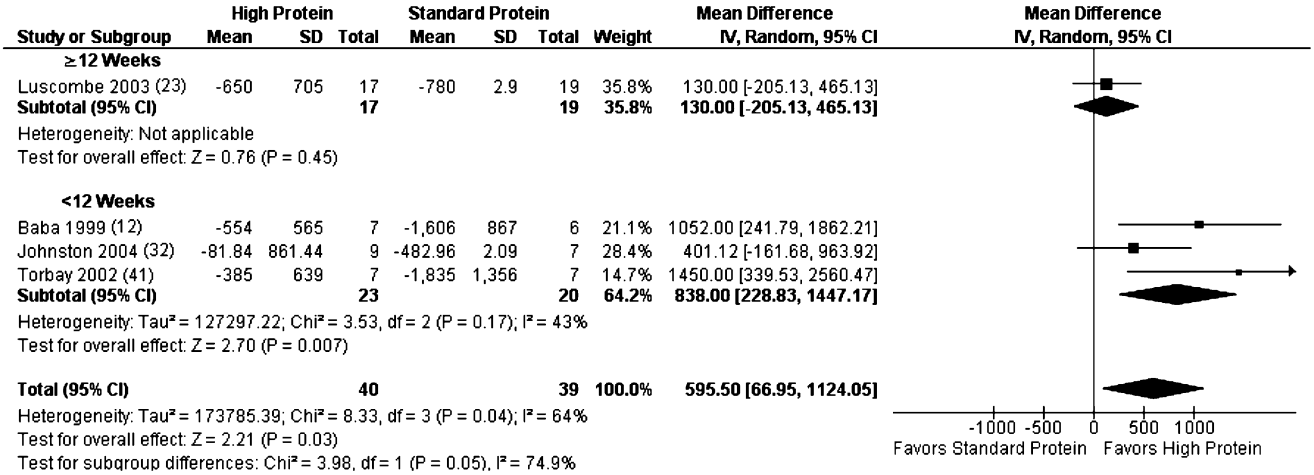

FIGURE 6. Meta-analysis for changes in resting energy expenditure (kJ/d) in randomized controlled trials that compared high-protein, low-fat diets with isocalorically prescribed standard-protein, low-fat, energy-restricted diets. IV, inverse variance.

analysis. Further research is required to evaluate the dose-response benefits achievable with smaller modification of dietary protein content.

Within a diet there are a number of factors that can affect the anabolic response to consumed protein and may therefore affect the FFM response to weight loss. These include the following: the absolute per meal dose of protein (63), the number of meals/protein ingestions throughout the day (the daily distribution of protein) (64), and the type of protein being ingested (65). There is a need for further research to investigate the contribution of these factors to the FFM response to weight loss.

Furthermore, older individuals experience age-related declines in skeletal muscle (sarcopenia) and may be more adversely affected by diet-induced reductions in FFM than their younger counterparts (66). In addition, older individuals may have an altered anabolic response to dietary protein (67), and further research is required to determine whether this population group experiences similar responses to an energy-restricted HP diet on FFM/REE to those observed in this analysis.

In summary, the results of this systematic review and meta-analysis show that compared with an energy-restricted SP diet, an isocalorically prescribed HP diet provides modest benefits for reductions in body weight, FM, and triglycerides and for mitigating reductions in FFM and REE. The long-term effects of HP diets on weight status and cardiometabolic risk remain largely unknown.

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The authors' responsibilities were as follows—TPW, LJM, PMC, MN, and GDB: designed the research; TPW and LJM: conducted the research; TPW: analyzed the data and had primary responsibility for the final content; and TPW, LJM, and GDB: wrote the manuscript. All authors read and approved the final manuscript. All funding sources supporting the work and all institutions or corporate affiliations of the authors are acknowledged, and the authors certify that they had no commercial associations (eg, consultancies, stock ownership, equity interest, patent-licensing arrangements) that might pose a conflict of interest in connection with the submitted article.

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