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Original Research

Effects of Whey Protein and Resistance Exercise on Body Composition: A Meta-Analysis of Randomized Controlled Trials

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Key words: whey protein, body composition, meta-analysis, randomized controlled trials, exercise

Objectives: The objective of the present meta-analysis was to examine the effect of whey protein (WP), with or without resistance exercise, on body weight and body composition in randomized controlled trials (RCTs) conducted in generally healthy adult study populations.

Methods: A comprehensive literature search was conducted to identify RCTs that investigated WP (concentrate, isolate, or hydrolystate) and body weight, body mass index (BMI), body fat, lean body mass (LBM), fat-free mass (FFM), and waist circumference. Random effects meta-analyses were conducted to generate weighted group mean differences (WGMD) for between-group comparisons (WP vs other protein sources or carbohydrates) and within-WP group comparisons (i.e., differences from baseline to trial end). Studies were classified into 2 distinct groups—WP as a supplement without dietary modification (WPS) and WP as a replacement for other sources of calories (WPR)—and were meta-analyzed separately. Subgroup analyses included examining the effect of resistance exercise and type of WP on the relationship between WP and body composition.

Results: Fourteen RCTs were included, with a total of 626 adult study completers. Five studies examined the effects of WPR and the remaining 9 studies examined the effects of WPS. Body weight (WGMD: −4.20 kg, 95% confidence interval [CI], −7.67, −0.73) and body fat (WGMD: −3.74 kg, 95% CI, −5.98, −1.50) were significantly decreased from baseline in the WPR within-group analyses. In the between-group analyses, the effects of WP were more favorable when compared with carbohydrates than protein sources other than whey, although findings did not reach statistical significance. Results from the subgroup analyses indicated a statistically significant increase in LBM (WGMD: 2.24 kg, 95% CI, 0.66, 3.81) among studies that included a resistance exercise component along with WP provision.

Conclusion: The current body of literature supports the use of WP, either as a supplement combined with resistance exercise or as part of a weight loss or weight maintenance diet, to improve body composition parameters.

INTRODUCTION

Accumulating evidence indicates that diet composition affects weight loss and weight maintenance [1–3] and may affect the decline in energy expenditure that accompanies weight loss [4]. Findings from 2 recent meta-analyses of randomized controlled trials (RCTs) favor a relatively higher protein and lower carbohydrate diet for weight loss [2,3]. Furthermore, comparatively higher protein diets appear beneficial for reducing fat mass as well as preserving lean body mass and resting energy expenditure [3]. Although foods and nutrients are not consumed in isolation and the effect of any one dietary component should be considered in context of overall dietary patterns, some individual food groups or other dietary constituents have received considerable attention for their potentially favorable influence on satiety, energy balance, body weight, and body composition [5–8]. Dairy products are one such food group [8]; however, findings from RCTs examining dairy products and body composition have been mixed. These inconsistent findings may be attributable to the heterogeneous nature of the dairy food group. Individual dairy foods contain variable levels of nutrients and other components; thus, considering dairy products as one single exposure is challenged by this heterogeneity. Examining specific constituents of dairy products may be important because it could

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explain why dairy products as a whole have been inconsistently associated with body composition outcomes [8]. Whey protein (WP) is one such component that is only present in high quantities in certain dairy products. Specifically, WP is a by-product of cheese production, one of two intact proteins found in milk, and a highly digestible complete protein that contains all essential amino acids [9].

Consumption of WP has been shown to suppress appetite and increase satiety more than other proteins, including casein, soy, and egg albumin [10–12]. Whey protein also possesses functional properties that promote fat mass reduction and lean mass preservation, including increased fat oxidation [7,13]. Prior research shows that WP is more effective in stimulating protein synthesis in older adults compared to casein. This finding has clear implications for counteracting age-related sarcopenia (i.e., degenerative loss of muscle mass) [9,14]. Whey protein is digested and absorbed rapidly in comparison to other protein sources [15], leading to elevated blood levels of amino acids. This state of hyperaminoacidemia stimulates an increase in muscle protein synthesis and a slight suppression of muscle protein breakdown postresistance exercise [16]. An additional mechanism by which WP stimulates protein synthesis is its relatively higher content of the branched-chain amino acid leucine [9]. Furthermore, factors yet to be fully elucidated are likely involved; for example, a recent trial [17] reported that 25 g of WP postresistance exercise was superior to a lower dose of WP (6.25 g) plus either additional leucine or a mixture of essential amino acids (without leucine) at sustaining rates of exercise-induced muscle protein synthesis. Another important quality of WP is its high net protein utilization. The net protein utilization rate for WP is 92% compared to rates of 86%, 78%, and 72% for nonfat milk solids, casein, and soy, respectively [9].

Although a number of individual RCTs have been conducted to examine the effects of WP on body weight and composition, to the best of our knowledge, no study has integrated and quantitatively summarized results from past studies. Therefore, the objective of the present meta-analysis was to examine the effect of WP, with or without resistance exercise, on body weight and body composition in RCTs conducted in generally healthy adult study populations.

METHODS

A systematic review was conducted to evaluate the effect of WP on body weight and composition among free-living adult populations. Established guidelines for systematic reviews described in the scientific literature were followed [18–21]. Literature searches of PubMed through November 2012 (with no lower date limit) identified English-language articles in human populations eligible for review. The primary search string included terms specific to WP and outcomes related to body weight and composition (i.e., body mass, body mass index, body weight, lean body mass, lean body tissue, fat-free mass, lean mass, waist circumference, waist to hip, body habitus, weight loss, weight gain, weight change, and body fat). All abstracts were reviewed and relevant full-text articles were obtained. Supplementary literature searches included examining the reference lists of all relevant studies, pertinent review articles, meta-analyses, and the Cochrane Library Database to identify articles not identified in the initial PubMed search.

Inclusion and Exclusion Criteria

Inclusion criteria for this systematic review were as follows: the trial was randomized and controlled using a placebo or other supplement; participants were at least 18 years of age; whey protein isolate, concentrate, or hydrolysate (herein labeled WP) was used rather than a multicomponent supplement or whey-containing food such as milk; data on total calories consumed pre- and postintervention and total calories from the whey protein or control supplements were available; the intervention was a minimum of 4 weeks; the only difference between the experimental and control arms was the dietary supplement; and at least one of the aforementioned body weight or composition outcomes was examined. Studies that included participants with a recent history of protein supplementation at baseline screening were excluded. Pre- and postintervention group means and SDs for outcomes of interest had to be available from either the published study or through contact with the authors. There were no restrictions on the number of subjects evaluated in each study. If studies reported results from multiple time points, the means and SDs from the last time point were retained to avoid data duplication.

Data Extraction and Quality Assessment

The following qualitative and quantitative information was extracted from each included study: authors, publication year, geographic location, baseline population characteristics, intervention and control regimens, study duration, blinding, per group sample size, type and dose of WP and control supplements, complete nutrient profile of supplements, study compliance, diet assessment, resistance exercise protocol, outcome assessment, and group means and SDs for body weight and composition outcomes. Whether the trial examined the effect of WP provided as a supplement to the diet without dietary modification (WPS) or as a partial or full meal replacement (WPR) was documented. Methodological information regarding the potential impact of bias was critically examined. Two reviewers ascertained individual study information independently as part of our quality control process.

Statistical Analysis

A meta-analysis was performed by random effects modeling with Comprehensive Meta-Analysis Software version 2 (Biostat, Englewood, NJ). Studies were classified into 2 distinct groups (WPS or WPR) and meta-analyzed separately. Whey protein was considered the experimental arm in this meta-analysis. All other arms, such as carbohydrates or other types of proteins, were considered control arms. WPS and WPR studies were examined separately because the WP in the WPS studies contributed up to an additional 500 kcal per day, in which case weight loss would not be expected. In addition, the RCT had to provide isocaloric experimental and control diets to be classified as a WPS.

Two or more studies by outcome were required to generate weighted group mean differences (WGMDs), 95% confidence intervals (CIs), and corresponding p values for heterogeneity. The same outcomes measured on different scales were converted to the same unit [22]. For the purpose of this meta-analysis, one label was selected and used consistently in the text and tables for each body composition measure.

The primary meta-analyses generated within-WP group and between group (e.g., WP vs other protein sources or carbohydrates) weighted mean differences. Secondary analyses included subgroup meta-analyses to examine the effect of resistance exercise and the type of WP (concentrate vs isolate) on the relationship between WP and body weight and body composition outcomes. The one study that used WP hydrolysate [23] and the one that used a combination of WP concentrate and isolate [24] were not included in the subgroup analysis of WP type. These secondary subgroup analyses also were performed to identify potential sources of heterogeneity. Sensitivity analyses were conducted by evaluating the impact of adding or removing studies based on different study characteristics. The presence of publication bias was evaluated by examining a funnel plot measuring the standard error as a function of effect size, as well as performing Egger's regression method and the Duval and Tweedie imputation method [25].

RESULTS

Literature Search Results

A flow diagram of the search strategy is shown in Fig. 1. The original search yielded 493 English-language articles, of which 455 were deemed irrelevant after title and/or abstract review. The remaining 38 articles underwent full-text review, from which 24 were excluded for the following reasons: no relevant end points ($n = 4$); required data could not be obtained from the publication and corresponding authors, all of whom were contacted ($n = 6$); WP was not one of the study arms ($n = 11$); the study was not randomized ($n = 1$); the trial duration was less than 1 month ($n = 1$); or the study included participants who were taking protein supplements before the start of the trial ($n = 1$). A review of reference lists from the 14 identified studies and relevant reviews and meta-analyses yielded 33 additional articles. Twenty of these were duplicate studies from the original search and the remaining 13 were deemed irrelevant following a review of the abstracts. Therefore, a total of 14 studies [23,24,26–37] were included in the meta-analysis.

Study Characteristics

Descriptive study characteristics are shown in Table 1. All included studies had parallel designs, although crossover design was not an exclusion criterion. A total of 626 study completers were included in this meta-analysis; individual study completer sample size ranged from 12 to 114 participants. There were wide ranges in study duration (6–52 weeks), age (18–72 years), and descriptive population characteristics. Notable differences in population characteristics included male recreational body builders in 2 studies [28,29] and menopausal women in one study [35]. Seven studies included only overweight or obese participants [23,24,31–36], of which one study population was also hyperlipidemic [32]. Six studies included only men [23,26,28–30,32], 2 evaluated only women [27,35], and the remaining 6 were mixed [24,31,33,34,36,37]. The control arm in 13 studies consisted of a supplement or meal replacement that was isocaloric to the WP arm. One exception was the control arm of Gatorade in the study by Eliot et al. (300 fewer kilocalories per week than the WP arm) [30]. In the remaining studies, the content of the control supplements included carbohydrates (glucose or maltodextrin) [24,26,29,32–37], other proteins (casein and soy protein) [23,24,27,28,32–34], and/or skim milk powder [31].

The presence, type, frequency, and intensity of resistance exercise differed considerably across studies. All but 2 of the WPS studies [27,34] included a resistance exercise component in both the intervention and control arms, effectively controlling for the effects of resistance exercise on body composition outcomes. In contrast, only one [23] of the 5 WPR studies [23,24,31,33,35] included resistance exercise as part of the intervention. Frequency and intensity of the exercise component varied substantially. One regimen consisted of 3 consecutive days of supervised weight training that targeted different muscle groups, followed by a rest day [26], and a different program was 2 or 3 days per week of low-to-moderate-intensity walking combined with flexibility training [35].

Dose, distribution, and timing of WP and control supplementation or meal replacement varied largely. The lowest dose of WP was 0.23 g/kg BW ($\sim$35 g) for 3 days per week [30] compared to the highest dose of 1.2 g/kg BW ($\sim$80–88 g) for 7 days per week [23]. The distribution of recommended WP consumption in the WPR studies was similar (half in the morning and half in the afternoon or evening), although participants consumed only one dose in replacement of a meal for the second half of the year-long study by Keogh and Clifton [31]. Three WPS studies [28,29,32] recommended WP consumption in multiple doses throughout the day, with one dose immediately following resistance exercise. In contrast, Burke et al. [26] recommended WP consumption 4 times per day but did not specify

Table 1. Characteristics of Studies Included in the Meta-Analysis[1]

			Age (y)	Sex	Sample Size (Completers)	Duration	Intervention and Control Regimen		
First Author, Year [ref]	Country	Descriptive Population Characteristics	Range or Mean + SD	M/F	*n*	wk	WP Group[2]	Control Group(s)	Outcomes Assessed[3]
Studies with WP as a replacement for other sources of calories in the diet (WPR)									
Claessens,[4] 2009 [24]	The Netherlands	Overweight or obese but otherwise healthy adults	30–60	11/19	48	12	2 × 25 g/d (∼0.52 g/kg/d)	2 × 25 g casein/d (∼0.52 g/kg/d) 2 × 25 g/d CHO (∼0.52 g/kg/d)	BW, body fat, FFM, WC
Demling, 2000 [23]	United States	Overweight police officers	28–40	38/0	38	12	70–75 g/d (∼0.73 g/kg/d) + RE + hypocaloric diet[5]	70–75 g casein/d (∼0.73 g/kg/d) + RE + hypocaloric diet[5]	BW, body fat, LBM
Keogh, 2008 [31]	Australia	Overweight or obese but otherwise healthy adults	20–70	21/51	72	52	2 × 33 g (∼0.68 g/kg/d for wk 1–26); 1 × 33 g (∼0.34 g/kg/d for wk 27–52)[6]	2 × 33 g protein from skim milk powder (∼0.68 g/kg/d for wk 1–26); 1 × 33 g (∼0.34 g/kg/d for wk 27–52)[6]	BW, body fat, LBM
Mojtahedi, 2011 [35]	United States	Overweight or obese, relatively inactive women; menopausal for >5 y but otherwise healthy	65 + 4 (WP);65 + 5 (control)	0/26	26	24	2 × 22.5 g (∼0.52 g/kg/d) + prescribed diet + aerobic/flexibility exercise[7,8]	2 × 25 g CHO (∼0.58 g/kg/d) + prescribed diet + aerobic/flexibility exercise	BMI, BW, LBM

Pal, 2010 [33]	Australia	Overweight or obese but otherwise healthy adults	18–65	10/60	70	12	2 × 27 g/d (~0.63 g/kg/d)	2 × 27 g CHO/d (~0.63 g/kg/d) 2 × 27 g casein/d (~0.63 g/kg/d)	BMI, BW, LBM, body fat, WC, waist-to-hip
Studies with WP as a supplement to the diet, without dietary modification (WPS)									
Baer, 2011 [34]	United States	Overweight or obese but otherwise healthy adults	49 + 9 (WP);53 + 9 (soy);51 + 9 (CHO)	32/39	73	23	2 × 28 g/d (~0.60 g/kg/d)	2 × 28 g CHO/d (~0.60 g/kg/d)2 × 28 g soy protein/d (~0.60 g/kg/d)	LBM, body fat
Burke, 2001 [26]	Canada	Healthy active adults with >3 y RE experience	18–36	15/0	15	6	1.2 g/kg/d in 4 equal servings + RE	1.2 g CHO/kg/d in 4 equal servings + RE	LBM, body fat
Cribb, 2006 [28]	Australia	Recreational body builders	27 + 7 (WP);26 + 5 (control)	13/0	13	10	1.35 g/kg/d + RE	1.35g casein/kg/d + RE	LBM, body fat
Cribb, 2007 [29]	Australia	Recreational body builders	24 + 5 (WP);24 + 7 (control)	12/0	12	11	1.35 g/kg/d + RE	1.5g CHO/kg/d + RE	LBM, body fat
Denysschen, 2009 [32]	United States	Overweight, hyperlipidemic, and generally sedentary adults	21–50	28/0	28	12	1 × 27 g/d (~0.3 g/kg/d) + RE	1 × 25 g CHO/d (0.28 g/kg/d) + RE 1 × 26 g soy protein/d (~0.29 g/kg/d) + RE	Body fat, FFM, waist-to-hip
Eliot, 2008 [30]	United States	NR	48–72	21/0	21	14	0.23 g/kg + 480 mL Gatorade after each RE session (3 times/wk)	1 × 480 mL Gatorade after each RE session (3 times/wk)	Body fat, FFM

(Continued on next page)

Table 1. Characteristics of Studies Included in the Meta-Analysis[1] *(Continued)*

			Age (y)	Sex	Sample Size (Completers)	Duration	Intervention and Control Regimen		
Moeller, 2003 [27]	United States	Generally healthy, perimenopausal women (BMI between 20 and 31)	41–61	0/69	69	24	2 × 20 g/d (∼0.6 g/kg/d)	2 × 20 g isoflavone-rich soy protein/d (∼0.6 g/kg/d) 2 × 20 g isoflavone-poor soy protein/d (∼0.6 g/kg/d)	Body fat, LBM
Weinheimer, 2012 [36]	United States	Overweight or obese but otherwise healthy adults; engaged in <2 h of exercise/wk	35–66	46/68	114	36	2 × 30 g/d (∼0.68 g/kg/d) + RE	2 × 30 g CHO (∼0.68 g/kg/d) + RE	Body fat, LBM
Weisgarber, 2012 [37]	Canada	Healthy adults who were not engaged in structured resistance exercise	25 + 2 (WP);24 + 4 (control)	9/8	17	8	0.3 g/kg throughout day × 4 d/wk + RE	0.3 g CHO/kg throughout day × 4 d/wk + RE	Body fat, LBM

WP = whey protein, BW = body weight, FFM = fat-free mass, WC = waist circumference, CHO = carbohydrate, RE = resistance exercise, LBM = lean body mass, BMI = body mass index (kg/m^2), NR = not reported.

[1]All studies had a parallel design.

[2]Because some studies provided an absolute supplement amount regardless of weight and others provided grams per kilogram of BW, we generated estimates of the grams per kilogram of BW based on the average baseline weight of participants in all groups in a study to allow for comparisons across studies.

[3]Change in BW was only included as an outcome in this meta-analysis if whey protein was used as a replacement for other calories in the diet.

[4]A 5- to 6-week hypocaloric diet (500 kcal) preceded the 12-week WPR weight maintenance portion of study that was included in this meta-analysis.

[5]Hypocaloric diet was 80% of estimated needs.

[6]All participants were instructed to restrict energy intake.

[7]Whey supplement was isocaloric to control supplement.

[8]Prescribed diet by registered dietitian was a reduction in food intake by 500 kcal/d; supplement provided 200 kcal.

[9]Supplement consumption was distributed before, during, and after RE.

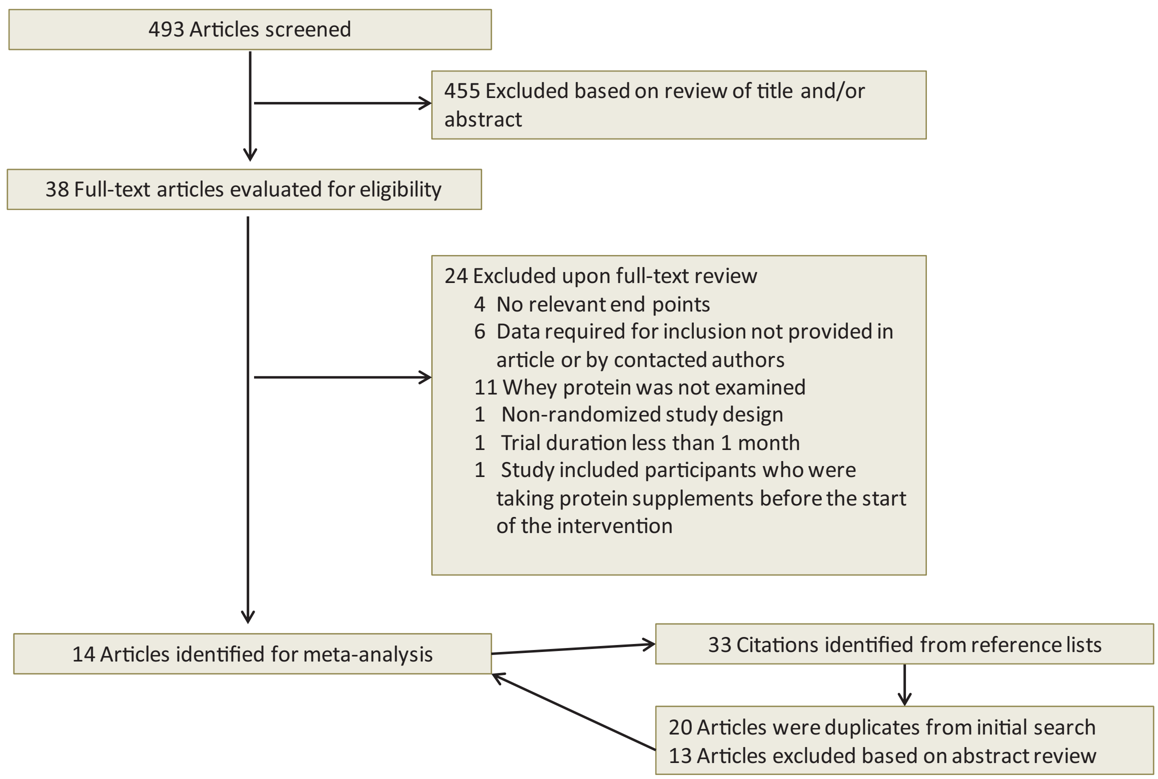


Fig. 1. Study selection process.

timing, and Eliot et al. [30] instructed participants to consume the supplement only on training days immediately upon exercise completion. Because there were no exercise components in the studies by Moeller et al. [27] and Baer et al. [34], participants were asked to consume the supplement twice daily. Weinhermer et al. [36] instructed participants to consume one supplement with breakfast and one with lunch, whereas participants in the study by Weisgarber et al. [37] consumed part of the supplement before the start of resistance exercise and the remaining supplement throughout, and immediately following, the exercise session.

Results from Between-Group Meta-Analyses

Results from the between-group meta-analyses are shown in Table 2. Whey protein as a dietary replacement (WPR) compared with a carbohydrate control produced consistent, yet nonstatistically significant, beneficial effects on body fat, body weight, waist circumference, and body mass index (BMI) but not lean body mass (LBM). Weighted group mean decreases in body fat (−0.60; 95% CI, −4.08, 2.88), LBM (−0.66; 95% CI, −2.91, 1.59), body weight (−1.85; 95% CI, −6.73, 3.02), waist circumference (−0.92; 95% CI, −4.86, 3.03), and BMI (−0.67; 95% CI, −2.85, 1.51) were greater in the WPR group compared to carbohydrate controls. Weighted group mean decreases in body fat, body weight, and waist circumference were slightly greater in the other protein source group (soy and casein) vs the WPR group. Although statistical heterogeneity was nonsignificant in the WPR models, these analyses were based on only 2 or 3 studies, thereby limiting our power to detect heterogeneity and our ability to conduct comprehensive subgroup analyses.

Whey protein as a supplement to the diet without dietary modification (WPS) had nonsignificant modest beneficial effects on body fat and LBM. There were no significant effects on body weight. Compared to carbohydrate controls, the weighted group mean decrease in body fat in the WPS group was 0.21 kg (95% CI, −2.16, 1.75) and the weighted group mean increase in LBM was 0.28 kg (95% CI, −2.79, 3.35). Similarly, compared to other protein sources, a weighted group mean decrease in body fat of 0.14 kg (95% CI, −2.05, 1.76) and a weighted group mean increase in LBM of 0.37 kg (95% CI, −1.47, 2.21) in the WPS group were observed. Statistically significant heterogeneity was not detected in the WPS studies.

Results from Within-Group Meta-Analyses

In addition to the variation in the utilization of WP (i.e., either as a meal replacement or as a supplement without dietary modification), studies also varied in the type of comparison group. Thus, the concern of dissimilar comparison groups was alleviated by conducting within-WP group comparisons (Figs. 2–4). Of the 9 trials that evaluated the effects of WP as a supplement

Table 2. Results Summary for Between-Group Meta-Analyses: Weighted Group Mean Differences[1]

	No. of Studies	Weighted Group Mean Difference (95% CI)	*p* Heterogeneity
Studies with WP as a replacement for other sources of calories in the diet (WPR, $n = 5$)			
Body fat (kg)			
WP vs carbohydrates	2	−0.60 (−4.08, 2.88)	0.462
WP vs other protein sources	3	2.78 (0.22, 5.35)	0.241
LBM (kg)			
WP vs carbohydrates	2	−0.66 (−2.91, 1.59)	0.778
Body weight (kg)[2]			
WP vs carbohydrates	3	−1.85 (−6.73, 3.02)	0.871
WP vs other protein sources	3	0.10 (−4.41, 4.62)	0.997
Waist circumference (cm)			
WP vs carbohydrates	2	−0.92 (−4.86, 3.03)	0.686
WP vs other protein sources	2	0.47 (−4.19, 5.14)	0.985
BMI (kg/m^2)[2]			
WP vs carbohydrates	2	−0.67 (−2.85, 1.51)	0.590
Studies with WP as a supplement to the diet, without dietary modification (WPS, $n = 9$)[3]			
Body fat (kg)			
WP vs carbohydrates	6	−0.21 (−2.16, 1.75)	0.969
WP vs other protein sources[4]	4	−0.14 (−2.05, 1.76)	0.909
LBM (kg)			
WP vs carbohydrates	5	0.28 (−2.79, 3.35)	0.995
WP vs other protein sources[4]	3	0.37 (−1.47, 2.21)	0.544

CI = confidence interval, WP = whey protein, LBM = lean body mass, BMI = body mass index.

[1]Results are shown if more than one study in each respective between-group comparison examined an outcome.

[2]Body weight and BMI were considered relevant outcomes only for studies examining WP as a replacement for other sources of calories because the objective in studies with WP as a supplement, without dietary modification, was for improved body composition measures rather than loss of body weight.

[3]No studies in the WPS group examined waist circumference, although one study examined waist-to-hip measurements.

[4]One WPS study [38] had 2 comparison groups, isoflavone-poor soy and isoflavone-rich soy; the results from the isoflavone-poor soy comparison are included in the summary effects in this table. Including the isoflavone-rich soy comparison, in place of the isoflavone-poor soy, resulted in similar summary effects (data not shown).

without dietary modification and body fat, 6 reported a decrease [26,28,32,34,36,37], one found no difference [30], and 2 reported increases [27,29] from baseline to trial end (Fig. 2). The weighted group mean decrease in body fat in the WPS group was 0.54 kg (95% CI, −1.74, 0.66), with no evidence of statistical heterogeneity. In the WPR group, body fat decreased significantly by 3.74 kg (95% CI, −5.98, −1.50), although statistical heterogeneity was detected (p heterogeneity $= 0.023$). This heterogeneity was driven by the study by Pal et al. [33], as determined in a sensitivity analysis. Subgroup analyses that combined WPR and WPS studies to allow for sufficient studies in each group evaluated the effect of WP on body fat while stratifying by resistance exercise (yes vs no per study protocol) and by WP type (concentrate vs isolate). These analyses revealed no statistically significant findings (data not shown).

Fig. 3 shows the results from the within-group analyses of LBM from baseline to trial end. A modest, nonsignificant 0.83 kg (95% CI, −0.36, 2.03) weighted mean group increase in LBM was observed among the 7 studies that evaluated the effects of WP as a supplement on LBM. In contrast, a small decrease in LBM was found among the 4 studies that examined WP as a replacement for other sources of calories in the diet (WGMD: −0.11 kg, 95% CI, −2.86, 2.64), although statistical heterogeneity was present. When the study by Mojtahedi et al. [35], which was unique in that it included a population comprised entirely of postmenopausal women, was removed in a sensitivity analysis, LBM increased by 1.20 kg (95% CI, −1.22, 3.63) and homogeneity increased (p heterogeneity $= 0.251$). A statistically significant increase in LBM (WGMD: 2.24 kg, 95% CI, 0.66, 3.81) was observed among studies that included a resistance exercise component along with WP provision. No statistically significant differences between WP concentrate and isolate were observed for LBM.

Fig. 4 illustrates results from the within-group analyses of change in body weight among the 5 WPR studies and the nine WPS studies. Body weight decreased, on average, by 4.20 kg (95% CI, −7.67, −0.73) from baseline to trial end in the WPR studies. Removal of the study by Mojtahedi et al. [35] modified the overall effect slightly (WGMD: −3.51 kg, 95% CI, −7.73, 0.72). There were no significant effects of WPS on body weight. In the subgroup analyses, a nonsignificant reduction in body weight was observed in studies without resistance exercise (WGMD: −2.66 kg, 95% CI, −6.16, 0.84), whereas no effect was apparent in studies with resistance exercise (WGMD: −0.02 kg, 95% CI, −1.42, 1.37). Similar differences were observed in the subgroup analyses by WP type (WGMD for WP isolate: −2.23 kg, 95% CI, −6.49, 2.03; WGMD for WP concentrate: −0.16, 95% CI, −1.67, 1.35). These findings were largely influenced by Keogh and Clifton's [31] and Mojtahedi et al.'s [35] studies, both of which evaluated WP isolate and did

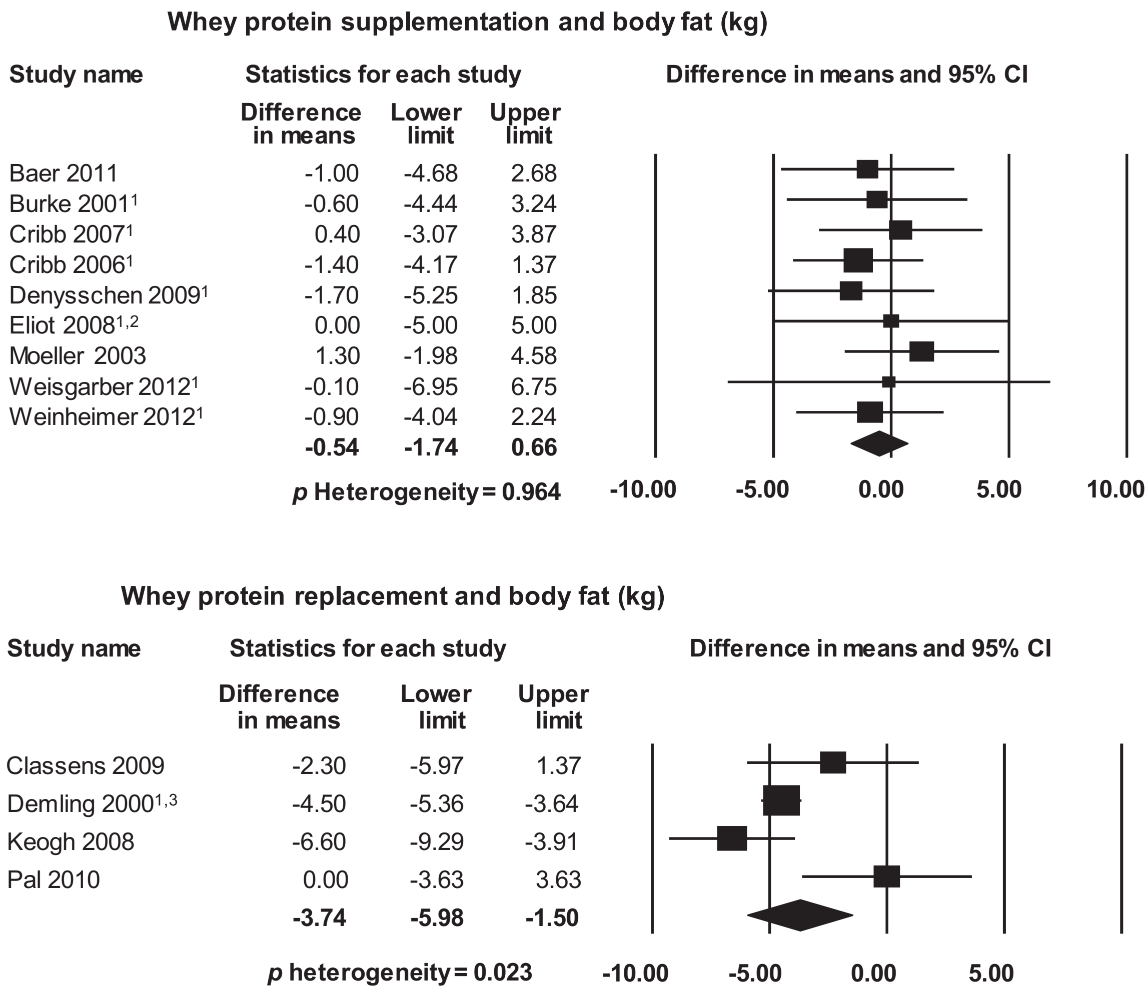


Fig. 2. Within-group weighted mean differences in body fat (kg) for whey protein as a supplement without dietary modification (WPS) and whey protein as a replacement for other calories (WPR). [1]Intervention included resistance exercise. [2]Intervention included Gatorade. [3]Intervention included a hypocaloric diet.

not incorporate resistance exercise. Waist circumference also decreased from baseline to trial end in the WPR group (WGMD: −0.86 cm; 95% CI, −3.76, 2.04), but this finding did not reach statistical significance and was based on only two trials [24,33]. Although potential publication bias was examined, it is difficult to comprehensively determine its potential impact given the limited number of studies in each group (5 in the WPR studies and 9 in WPS studies). With this limitation in mind, no consistent influence of publication bias in the meta-analysis models was observed.

DISCUSSION

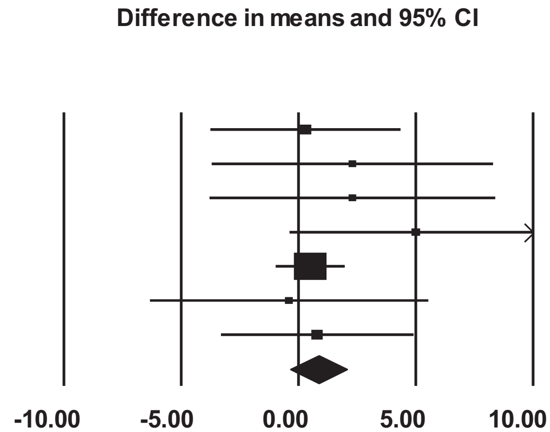
The currently available evidence from RCTs supports a modest beneficial effect of WP on body weight and composition. This benefit is observed with WP provided either as a supplement combined with resistance exercise or as part of a weight loss or weight maintenance diet. Statistically significant decreases in body weight and body fat were observed when WP was provided as a dietary replacement, indicating the possible importance of utilizing WP as part of a meal replacement program. Generally consistent decreases in body weight, BMI, body fat, and waist circumference were observed when WP as a dietary replacement was compared to carbohydrates, although the opposite trend was observed when WP was compared with non-WP sources. However, there was an insufficient number of studies to perform subgroup analyses comparing WP with specific non-WP protein sources.

Assessing potential sources of heterogeneity across studies provides important insight into the impact of differences in study characteristics on results. The models herein appeared to be statistically homogeneous, with most p values for heterogeneity in the between-group analyses well above 0.10 (commonly considered the standard demarcation for heterogeneity in meta-analyses). Nevertheless, it is difficult to fully assess and

Whey protein supplementation and lean body mass (kg)

Study name	Difference in means	Lower limit	Upper limit
Baer 2011	0.30	-3.77	4.37
Burke 2001[1]	2.30	-3.71	8.31
Cribb 2007[1]	2.30	-3.80	8.40
Cribb 2006[1]	5.00	-0.40	10.40
Moeller 2003	0.50	-0.98	1.98
Weisgarber 2012[1]	-0.40	-6.35	5.55
Weinheimer 2012[1]	0.80	-3.32	4.92
	0.83	**-0.36**	**2.03**

p **Heterogeneity = 0.787**



Whey protein replacement and lean body mass (kg)

Study name	Difference in means	Lower limit	Upper limit
Demling 2000[1,2]	2.50	0.41	4.59
Keogh 2008	-1.80	-6.84	3.24
Mojtahedi 2011[2,3]	-1.90	-3.47	-0.33
Pal 2010	0.30	-4.31	4.91
	-0.11	**-2.86**	**2.64**

p **heterogeneity = 0.010**

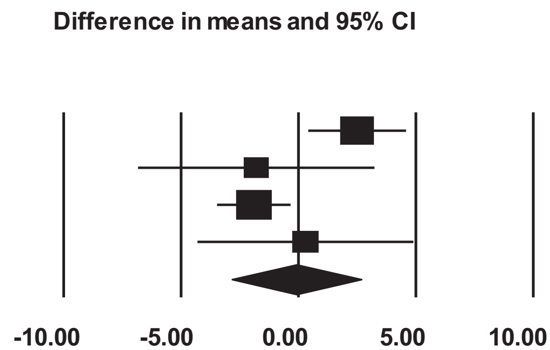


Fig. 3. Within-group weighted mean differences in lean body mass (kg) for whey protein as a supplement without dietary modification (WPS) and whey protein as a replacement for other calories (WPR). [1]Intervention included resistance exercise. [2]Intervention included a hypocaloric diet. [3]Intervention included aerobic and flexibility exercise.

identify the potential sources of between-study variation given few studies in each analytical model. Furthermore, it is essential in a meta-analysis to perform numerous subgroup and sensitivity analyses even in the absence of statistical heterogeneity. There were numerous potential sources of heterogeneity across the 14 studies in this systematic review, although the dearth of data for potentially relevant subgroup stratifications limited comprehensive evaluations. One stratification was selected *a priori* based on a key distinction in the intervention regimen; 5 studies used WP as a replacement for other sources of calories in the diet (WPR) [23,24,31,33,35] and 9 studies used WP to supplement the diet without other dietary modifications (WPS) [26–30,32,34,36,37].

Several other differences across studies deserve mention and should be taken into consideration in the design of future interventions. Only one [23] of the WPR studies included a resistance exercise component, whereas 7 [26,28–30,32,36,37] of the WPS studies included this component. Among studies with resistance exercise, the type, frequency, intensity, and duration varied considerably. All of these factors can impact body composition outcomes regardless of protein supplementation [38]. A recent review of the literature concluded that a resistance exercise protocol should be a minimum of 10 to 12 weeks (with 3–5 sessions per week) if the goal is to improve muscle hypertrophy and strength [38]. In the present meta-analysis, study duration was at least 10 weeks in all but 2 studies [26,37]. Weisbarger et al. [37] found no significant effect of resistance exercise plus WP on body fat percentage and LBM in an 8-week trial, whereas Burke et al. [26] reported a significant increase in LBM but no change in body fat percentage in a 6-week trial. Overall, a statistically significant increase in LBM was observed among studies that included a resistance exercise component along with WP provision, indicating that the benefits of WP on LBM are stronger as part of resistance exercise regimen.

One reason for the positive effect on LBM in the study by Burke et al. [26] despite the short study duration may be due to another potential source of heterogeneity: different doses of WP. Participants in the trial conducted by Burke et al. [26] received 1.2 g of WP per kilogram of body weight, a markedly higher dose than the ones provided in several other studies in this meta-analysis. For example, Weisbarger et al. [37] and

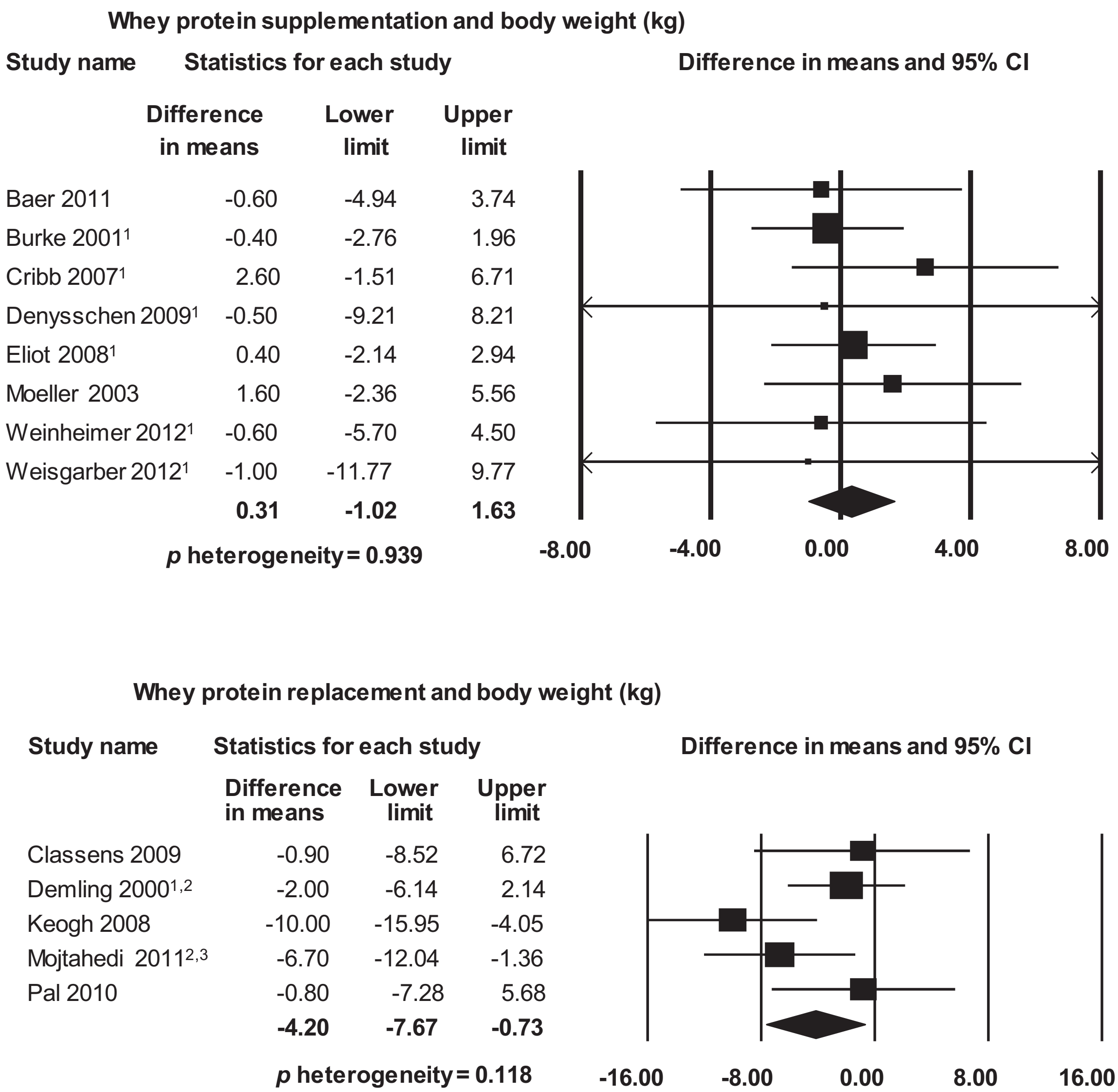


Fig. 4. Within-group weighted mean differences in lean body mass (kg) for whey protein as a supplement without dietary modification (WPS) and whey protein as a replacement for other calories (WPR). [1]Intervention included resistance exercise. [2]Intervention included a hypocaloric diet. [3]Intervention included aerobic and flexibility exercise.

Denysschen et al. [32] each provided approximately 0.3 g of WP per kilogram of body weight, and Eliot et al. [30] provided only 0.23 g of WP per kilogram of body weight 3 times per week. Timing and distribution of WP consumption also varied across studies. A recent review of the literature [38] concluded that timing of protein supplementation is important. Supplementation with protein that contains all essential amino acids immediately following resistance exercise promotes a positive net protein balance, increases in LBM, and decreases in body fat.

There were also considerable differences in study population characteristics, including age, sex, baseline health status, and history of physical activity. For example, the same dose of protein supplementation in combination with resistance exercise may be less effective in increasing LBM and reducing body fat among older compared to younger adults [39]. Past studies have shown that older adults experience a loss of muscle mass and LBM with long-term consumption of the recommended dietary allowance for protein (0.8 g per kilogram of body weight per day), even when combined with resistance exercise [39]. Therefore, protein supplementation may help reduce the rate of muscle loss rather than promote gains. Studies with older adults may have diluted the overall summary effects when combined with younger study populations. Because most studies had large age ranges and did not provide results stratified by age, stratification by age was not possible in our meta-analysis. Future studies designed to investigate differences by age and other important strata, such as baseline health status, will be valuable in furthering our understanding of the impact of WP on body composition.

Whey protein has a number of functional properties that could positively affect body composition. Consumption of WP has been shown to suppress appetite and increase satiety more than other proteins, including casein, soy, and egg albumin [10–12]. Although longer-term effects have not been studied in human populations, evidence from animal studies suggests a long-term effect of WP on appetite suppression and food intake reduction [13]. Whey protein is digested and absorbed rapidly, leading to a state of hyperaminoacidemia [15]. This state stimulates an increase in muscle protein synthesis and a small suppression of resistance exercise-associated muscle protein breakdown [16,40]. Moreover, WP has a relatively higher content of the branched-chain amino acid leucine, which plays an integral role in muscle protein synthesis [41,42]. Findings from animal studies have shed light on additional mechanisms that may underlie beneficial effects of WP, including improved metabolic rate and increased fat oxidation [13].

CONCLUSION

Overall, the currently available evidence from RCTs supports the use of WP to improve body composition parameters. The beneficial effects of WP on body composition are likely most pronounced when consumed in concert with resistance exercise and an overall healthy diet that compensates for the additional calories from supplementation. A significant contribution to the literature would be longer-term RCTs with WP supplementation, calorie compensation, and resistance exercise. In addition, future studies designed to examine the effects of WP by relevant demographic characteristics and uncover the optimal dosage, trial duration, and type and frequency of resistance exercise are warranted.

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