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EFFECT OF PROTEIN SOURCE DURING WEIGHT LOSS ON BODY COMPOSITION, CARDIOMETABOLIC RISK AND PHYSICAL PERFORMANCE IN ABDOMINALLY OBESE, OLDER ADULTS: A PILOT FEEDING STUDY

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Abstract

Objectives—The purpose of this pilot study was to begin to examine the effect of dietary protein source (soy protein versus non-soy protein) during weight loss on body composition, and cardiometabolic and functional decline risk factors in older, abdominally obese adults.

Design—Two-arm, single-blind, randomized, controlled trial.

Setting—Wake Forest School of Medicine, Winston-Salem NC 27157, USA.

Participants—25 older (68.4±5.5 years, 88% female), abdominally obese (BMI: 35.1±4.3 kg/m^2; WC: 101.4±13.1 cm) men and women were randomized to participate in the study.

Intervention—A 12-week weight loss intervention, with participants randomized to consume soy protein-based meal replacements (S; n=12) or non-soy protein-based meal replacements (NS; n=12), in addition to prepared meals, and all participants targeted to receive an individualized caloric deficit of 500 kcal/day.

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Competing Interests: The funding sources had no role in the conduct of the study or in the collection, analysis, and interpretation of the data. None of the authors had any conflicts of interest to report.

Ethical Standards: Experiments performed as a part of this study comply with the current laws United States.

Measurements—Body weight and composition (assessed via DXA and CT), conventional biomarkers of cardiometabolic risk, and physical performance measures were assessed pre- and post-intervention. Additional endpoints of feasibility (accrual, participation, retention, compliance, and safety) are reported.

Results—A total of 24 participants (87% female) completed the study (96% retention) and lost an average of 7.8±3.0 kg over the 12-week period, with no difference seen between groups (p=0.83). Although nearly all measures of global and regional body composition were significantly reduced following the 12-week intervention, differences were not observed between groups. Among cardiometabolic risk factors and physical performance measures, only diastolic blood pressure was significantly lower in the NS group compared to the S group (66.7±2.7 mmHg vs 73.5±2.7 mmHg, respectively; p=0.04). Interestingly, in groups combined, despite significant reductions in body weight and lean mass, no significant changes in 400-meter walk time (+5.3±43.4 s), short physical performance battery score (+0.1±1.0), grip strength (−0.3±3.2 kg), or relative knee extensor strength (−0.0±0.0 N/m/cm^3 thigh muscle volume) were observed.

Conclusions—Data presented here suggest that a 12-week weight loss intervention, which incorporates S and NS meal replacement products, is associated with clinically significant weight loss and improvements in several parameters of cardiometabolic risk and unchanged physical function and strength. Results do not differ by protein source and suggest that soy protein is at least as good as other protein sources for weight loss during low-calorie dietary interventions in older adults.

Keywords

Weight loss; soy; older adults; obesity; meal replacement

Introduction

Aging is associated with increased adiposity and altered fat distribution (1), including increased ectopic fat stores -such as visceral, hepatic, and intermuscular fat - which are independently associated with increased risk of cardiometabolic (2, 3) and physical (4, 5) dysfunction. Weight loss in older adults is effective in reducing global and ectopic fat stores (6, 7), and frequently results in immediate improvement in many health consequences of obesity. Despite its benefits, however, intentional weight loss is not routinely recommended for obese, older adults, due in part to the perceived risk of functional impairment associated with loss of fat-free mass (8). In theory, weight loss therapies for older adults that target fat compartments while preserving fat-free mass should provide maximal cardiometabolic benefit, while minimizing loss of physical function.

Dietary composition during weight loss may differentially affect body composition and associated health risk. Diets rich in soyfoods, for instance, have been extensively studied for their cardioprotective benefit (9–11), and recent data suggest that one mechanism underlying this well-known association is a preferential reduction in body fat (12). Animal models of obesity demonstrate that soy consumption, during a hypocaloric diet, promotes greater weight and fat mass loss – including ectopic fat depots - when compared to a non-soy control (13–18). Additionally, promising clinical trial data suggest that in middle-aged

overweight and obese adults, adherence to a soy-based low-calorie diet results in significantly greater fat mass loss compared to a calorie-matched control diet (19, 20), yet importantly, preserves fat-free mass (20). In agreement with the latter finding, recent observational data suggest higher protein intake from vegetables sources (including soy) is associated with reduced muscle loss in older Chinese adults over a four-year period, while no association was found between animal protein intake and subsequent decline in muscle mass (21). Intriguingly, soy supplementation in the absence of caloric restriction has also been shown to reduce abdominal fat area in postmenopausal women when compared to women receiving an isocaloric casein placebo (22, 23). Collectively, these data suggest that consumption of soyfoods may reduce global and ectopic fat stores while preserving fat-free mass; although, the effect of a soy-based diet on body composition and associated cardiometabolic and physical performance measures has not been assessed. The purpose of this pilot study was to begin to examine the effect of dietary protein source (soy protein versus non-soy protein) during weight loss on body composition, and cardiometabolic and functional decline risk factors in older, abdominally obese adults.

Materials and Methods

Study Design Overview

The Soy IsofLavones and ViscERal fat loss (SILVER) pilot study was a 12-week, 2-arm, randomized, single-blind, controlled trial comparing the effects of a soy protein-based meal replacement weight loss intervention (S) to a non-soy (i.e. whey and egg proteins; NS) control. The dietary intervention included a highly structured, individualized program of caloric restriction, which consisted of a combination of meal replacement products and prepared meals, and targeted a total caloric deficit of 500 kcals/d for each participant. Although the degree of caloric restriction was similar for all participants, protein source used in the meal replacement products differed by group. All participants involved in the study provided written informed consent, according to the Wake Forest School of Medicine (WFSM) Institutional Review Board, and a data safety and monitoring board routinely evaluated the execution of the study protocol and adverse events.

Participant Recruitment and Eligibility

Recruitment strategies included newspaper advertisements and direct mailings. Eligibility criteria identified 25 otherwise healthy, older, abdominally obese, community dwelling men and women for participation, utilizing the following inclusion criteria: (1) age 60–79 years; (2) BMI ≥ 27 kg/m^2 and (3) waist circumference ≥ 102 and 88 cm for men and women, respectively; (4) willingness to consume prepared meals and meal replacement products as a part of the dietary intervention; and (5) no contraindications for participation in a weight loss program. Exclusions included: (1) weight loss or gain (±5%) in the past 6 months; (2) body mass > 136 kg (DXA limit); (3) regular smoker (> 1 cigarette/day within the past year); (4) history of alcohol or substance abuse/dependence within the past 2 years; (5) insulin-dependent or uncontrolled diabetes (FPG ≥ 126 mg/dL); (6) abnormal kidney (creatinine > 2.0 mg/dL) or (7) liver (self-reported hepatitis, AST, ALT, total bilirubin-greater than twice the upper limit of normal; albumin < 2.0 g/dL) function; (8) past or current ischemic heart disease (unstable angina; MI, PCI or cardiac surgery < 3 month ago;

uncontrolled blood pressure (> 160/90 mmHg), pulmonary disease (>mild or recent exacerbations), thyroid disease, or known significant hematological disease (including HBG < 11); (9) active known cancer requiring treatment in past year, except non-melanoma skin cancers, or life expectancy < 2 years; and (10) regular use of any medications that could influence study variables (growth/steroid hormones, including estrogen replacements, thiazolidinediones, statins, regular anti-inflammatory medications, blood thinners, or weight loss medications).

Dietary Intervention

Blocked randomization was used to assign each participant to one of two intervention groups within each gender stratum. Individual calorie goals were developed by a registered dietitian (RD), utilizing baseline resting metabolic rate (measured by indirect calorimetry using the Medical Graphics Ultima Series metabolic cart and Breeze Suite software v6.4.1) and assignment of an activity factor based on participant self-reported physical activity. Caloric estimates were then reduced by 500 kcals/d to promote approximately 0.45 kg/week weight loss for 12 weeks (for safety, no woman was provided with less than 1100 kcals/d and no man less than 1300 kcals/d). The intervention length was selected based on our prior success in providing a controlled diet for this length of time, while allowing for a long enough caloric restriction intervention period to elicit significant reduction in visceral fat stores (24). Once caloric goals were determined, all meals were prepared in the WFSM metabolic kitchen.

Throughout the course of the 12-week intervention, participants were provided with daily lunch (320 kcals) and dinner (330 kcals). Meals were prepared according to each participant's choices from a repeating 14-day menu designed by the RD. The macronutrient content of all prepared meals was 25–30% fat, 15–20% non-soy protein, and 50–60% carbohydrate. "Fat add-ons" (e.g. margarine pat, peanuts, salad dressing containing 45 kcals/each) were provided as necessary to achieve individual caloric goals. If necessary, and in consultation with the RD, participants purchased and prepared an additional breakfast meal and/or snacks from a provided menu plan to reach their daily caloric goal. No restriction was placed on non-caloric beverage consumption, and participants were allotted two "free days" per month during which they were not provided food, but they were given guidelines for diet intake at their study-prescribed energy level.

In addition to the two meals provided by the metabolic kitchen, participants were asked to consume four Medifast® meal replacement products per day. These meal replacements, donated by Medifast, Inc. (Owings Mills, MD), were among those commercially available at the time of the study (e.g., shakes, bars, smoothies, soups, breakfast and dessert items). Each meal replacement product contained approximately 90–110 kcals, 11–15 g protein, 10–15 g carbohydrates, and 0–3.5 g fat. Approximately two-thirds (36 products) of the meal replacement products were soy protein-based (i.e., 7–9 g soy protein of the 11–15 g total protein, containing 1.5–3.0 milligrams isoflavones/g soy protein), with the remaining one-third (15 products) of meal replacement products produced using whey and egg proteins. Consumption of four soy protein-based meal replacements/day provided at least 44 g soy protein and 60–135 mg isoflavones/d, which was specifically designed to meet the amount

of soy protein recommended in the FDA health claim for lipid lowering (10), as well as what is typically consumed in Asian populations (25, 26).

All participants received a minimum of 1100 kcals/d based on study-provided lunches (320 kcals), dinners (330 kcals), Medifast® meal replacement products (360–440 kcals), and fat add-ons (45 kcals/each). Participants were asked to (a) eat only the food/meal replacements that were given to them or that were approved from the breakfast/snack menu, (b) pick up their food 2–3 times/week, and (c) keep a log of all foods/meal replacements consumed. Protocol compliance was defined as the proportion of meal replacements taken according to protocol. Additional measures of compliance included body weight and post-intervention fasting serum isoflavone levels (quantified using isotope dilution tandem liquid chromatography mass spectrometry according to previously published methods (27)).

Outcome Measures

Self-reported demographic information (age, gender, and ethnicity) was captured at baseline and participants were queried weekly about potential adverse events. Body weight and composition, cardiometabolic risk factors and measures of physical performance were measured at baseline and after the 12-week intervention by trained research interventionists at WFSM.

Body Weight, Anthropometrics, and Composition—Height and weight were measured with shoes and outer garments removed on a wall mounted stadiometer and calibrated digital scale. Waist (minimal circumference) and hip (maximal gluteal protuberance) were measured in triplicate. Whole body fat mass and lean mass were determined by a certified technician using Dual Energy X-ray Absorptiometry (DXA, Hologic Delphi QDR) technology.

Fat accumulation in specific depots was measured using a computed tomography (CT) scanner (LightSpeed PlusTM, General Electric Medical Systems, Milwaukee) and quantified as adipose tissue volume using the Advantage Windows 4.2 Volume Viewer (GE Healthcare, Waukesha, WI) by the same technician. CT scan parameters were set at 120 kV and 350 mA. Abdominal visceral and subcutaneous fat volumes were measured using approximately 60 slices taken within 15 mm centered at the L4–L5 level. Liver attenuation (HU) was measured as the average density of 3 regions (1 cm^2 each), selected from the parenchyma of the right lobe of the liver 15 mm from the top. Lastly, approximately 50 scans were obtained covering the entire femur from the hip through the knee joint to obtain thigh intermuscular fat and muscle volume estimates.

Cardiometabolic Risk Factors—Blood pressure was measured in the right arm, using a digital sphygmomanometer, with the participant in a seated position (feet flat on the floor and legs uncrossed) after having rested quietly for five minutes. Appropriate cuff size was used and systolic and diastolic blood pressures were defined as the average of two repeated measures.

Blood samples were collected in EDTA-treated evacuated tubes by venipuncture in the early morning after a 12-hour fast. All blood was collected, processed, and analyzed for total

cholesterol, low density lipoprotein (LDL) cholesterol, high density lipoprotein (HDL) cholesterol, triglycerides, glucose, serum insulin, and high sensitivity CRP (hsCRP) using standardized procedures in a certified laboratory.

Physical Performance Assessments—Lower-extremity physical function was assessed by administering the Short Physical Performance Battery (SPPB) as well as a fast 400-meter (m) walk test. The SPPB consists of a 4-meter walk (m/s), repeated chair stands (sec), and three hierarchical standing balance tests (score, 0–4) (28). Each of the three performance measures is assigned a categorical score ranging from 0 to 4, with 4 indicating the highest level of performance and 0 the inability to complete the test. A summary score ranging from 0 (worst performers) to 12 (best performers) was calculated by adding walking speed, chair stands, and balance scores. Walking endurance over 400 meters was also measured (29). The 400–m walk was assessed on a 20-m course, and participants were instructed to walk as fast as they could (without running) with time-to-complete recorded. The 400-m walk test was terminated if the participant reported chest pain, tightness or pressure, significant shortness of breath or difficulty breathing, or feeling faint, lightheaded or dizzy.

Maximal knee extensor strength was measured over two trials (four efforts per trial) using an isokinetic dynamometer (Biodex; Shirley, NY) at a speed of 60° per second, with the participant sitting and the hips and knee flexed at 90°. All testing was performed on the right leg unless contraindicated, and the average of the middle two efforts of both trials was expressed in Newton-meters (Nm). Grip strength (kg) was measured to the nearest 2 kilograms, twice in each hand using an isometric Hydraulic Hand Dynamometer (Jamar, Bolingbrook, IL). The average value from the stronger hand was used and matching hands were used through time.

Statistical Analysis

Descriptive statistics (mean±SD or n, %) were calculated by intervention group and overall at baseline. Means and standard deviations were calculated for each measure of body composition, cardiometabolic risk, and physical function by intervention group and time point. Intervention compliance measures (body composition changes and isoflavone biomarkers) were assessed using two-sample t-tests for normally distributed outcomes and Wilcoxon rank sum tests for all others. Analysis of covariance was used to determine the overall intervention effect at 12-weeks on individual outcome measures, with results presented as means ± standard errors (SE), after adjustment for the baseline outcome measure. Model residuals were examined to ensure a normal distribution assumption was appropriate, and when the fit was deemed inappropriate by the Kolmogorov-Smirnov statistic ($p<0.05$), a Wilcoxon rank sum test was used instead. There were no differences in statistical significance of variables ($p<0.05$) using ANCOVA versus the nonparametric test. Unadjusted associations among 12-week serum isoflavone levels and change in all outcome variables were determined using Spearman correlation coefficients. Lastly, paired t-tests were performed to determine whether weight loss, regardless of intervention group, altered outcome measures from baseline, and Spearman correlations between 12-week changes in body weight and composition and measures of physical function were performed. SAS

software (version 9.3, SAS Institute Inc, Cary, NC) was used for all analyses, with a Type I error rate of 0.05 for overall group comparisons and associations.

Results

Study Recruitment and Retention

Study recruitment occurred over 18-months (March 11, 2011 – September 9, 2012). A total of 147 men and women were initially screened by telephone (accrual rate of phone screenings = 1.99/week) and of those, 34 were further screened in the clinic (accrual rate of screening visits = 0.46/week). Ineligible participants who were screened in clinic included 4 whose fasting plasma glucose>126 mg/dl, 2 who could not tolerate the meal replacements, and 1 whose BMI was < 27 kg/m^2 (eligible n=27). Two eligible participants did not consent to the protocol (acceptance rate = 93%) yielding a total of 25 men and women who met all study criteria and were randomly assigned to S or NS intervention groups (accrual rate of randomized participants = 0.34/week). The participation rate for all screening visits (eligible per phone screening) was 73.5% (25/34) and a 24 men and women completed the study and returned for follow-up testing (96% retention).

Baseline Participant Characteristics

Demographics and physical characteristics at baseline in the 24 individuals who completed the study are seen in Table 1. Briefly, participants were 68.0±5.5 years of age with an average BMI of 36.0±6.0 kg/m^2 and total body fat percentage of 45.2±10.1%. Eighty-eight percent of participants were women, 63% were of Caucasian descent, and target goal blood pressure, lipids, and glucose values were observed at baseline (with the exception of total cholesterol, which was slightly elevated above 200 mg/dL). Similarly, performance on baseline physical function tests was also reflective of a healthy/well-functioning sample. Excluded potential participants (n=3) were all female, and were similar in age to the study sample.

Compliance and Safety

Process measures of compliance are presented in Table 2. Overall, SILVER participants lost an average of 7.8±3.0 kg over the 12-week period, with no difference seen between groups (p=0.83). Self-reported compliance to the dietary protocol was excellent (97.5±3.3% and 92.9±9.3% in the soy and non-soy group, respectively), with only one participant (NS group) reporting less than 80% compliance. Serum isoflavone levels confirmed self-reported consumption of meal replacements in the soy group, as the concentration of genistein, daidzein, and glycitein were markedly higher in the soy versus the non-soy group post-intervention (all $p<0.05$). Importantly, although three adverse events (cellulitis, colon polyp detection, and medicinal smell in urine) and one serious adverse event (hospitalization for removal of colon polyp) were reported during the study, none were identified as being related to the study protocol.

Intervention-Related Changes in Body Composition, Cardiometabolic Risk, and Physical Performance

Randomization effects on body weight and composition at 12 weeks, adjusted for baseline outcome measure, are presented in Table 3. No significant intervention effect for any measure of body weight or composition was observed, although the NS group presented with a slightly lower thigh intermuscular fat volume compared to S post-intervention (45.3±1.4 cm^3 versus 49.1±1.4 cm^3; p=0.07). In both groups combined, all measures of body weight and composition were significantly reduced following the 12-week intervention (all p<0.01), with the exception of thigh intermuscular fat volume (−0.66±5.77; p=0.58). Total body fat and lean mass were reduced by 5.3±2.4 kg and 2.5±1.9 kg, respectively, yielding a 2% decrease in the relative amount of total body fat mass and 2% increase in the relative amount of total body lean mass.

Table 4 shows the randomization effect on cardiometabolic risk factors and physical function and strength at 12 weeks, adjusted for the baseline outcome measure. A significant intervention effect was only observed for diastolic blood pressure, with the NS group presenting with lower 12-week values than the S group (66.7±2.7 mmHg versus 73.5±2.7 mmHg; p=0.04). Both intervention groups saw reductions in several, but not all, markers of cardiometabolic risk. Specifically, systolic blood pressure (Δ: −9.4±45.6 mmHg), total cholesterol (Δ:−24.6±20.6 mg/dL), LDL cholesterol (Δ:−14.0±20.0 mg/dL), triglycercides (Δ: −36.9±43.2 mg/dL), and insulin (Δ: −4.4±6.0 μIU/mL) were all improved post intervention, while diastolic blood pressure, HDL cholesterol, glucose, and hsCRP remained unchanged from baseline (all p>0.05).

No intervention effect was observed for any physical performance measure (Table 4). In groups combined, despite significant changes in body weight and composition, 400-meter walk time (+5.3±43.4 s), SPPB battery score (+0.1±1.0), or grip strength (−0.3±3.2 kg) were unchanged (all p>0.05). Knee extensor strength was significantly reduced in both groups over the 12-week period (−5.0±9.4 N/m; p=0.04); however, once divided by thigh muscle volume (to yield relative knee extensor strength), this association was attenuated to non-significance (−0.00±0.02 N/m/cm3 thigh muscle volume; p=0.41). Interestingly, changes in physical performance did not correlate with changes in fat or lean mass and no associations were seen between post-intervention serum isoflavones and change in measures of body composition, cardiometabolic risk or physical performance (data not shown).

Discussion

Results of this pilot study suggest that administration of a highly structured weight loss intervention consisting of prepared meals and meal replacement products offered to abdominally obese, older adults is feasible and has a beneficial impact on important health outcomes. Both intervention groups achieved an average of 8% weight loss in 12-weeks, resulting in a favorable shift in body composition (e.g. larger loss of fat than lean mass) and significant improvements in many risk factors for cardiovascular disease. Notably, despite some loss in lean mass, measures of physical performance were unchanged. Results from this small pilot study do not suggest a differential effect of protein source during weight loss on body composition, and cardiometabolic and functional decline risk factors; however, it is

important to emphasize that the purpose of this work was to generate preliminary effect sizes, not test for statistical significance. Our findings do suggests that soy protein is at least as good as other protein sources for weight loss during low-calorie diet interventions, and findings do not refute the general recommendation for inclusion of soy protein into a “heart-healthy” diet (10).

Although a body of in vitro, animal, and epidemiologic data provide provocative evidence for the ability of isoflavone containing soy protein to increase weight and/or fat loss when compared to an isocaloric control (30), due to the wide range of publications and significant heterogeneity in study designs, we limit our discussion to comparisons of randomized controlled trials (RCTs) of weight loss in humans, comparing soy to control diets, and assessing changes in body weight and composition. Overall, when compared to a “standard diet”, diets containing soy protein based meal replacements products are associated with enhanced weight (31, 32) and fat loss (19, 20, 32) in most, but not all (33), studies. However, when a soy-based meal replacement dietary intervention is compared to a non-soy meal replacement intervention, studies generally show similar reductions in body weight (34–37). Although we were underpowered to detect significant differences between intervention groups, effect size estimates presented here are in line with prior work. Results also concur with data showing weight loss programs utilizing meal replacements in place of one or two daily meals are associated with a high degree of dietary compliance and weight loss success (38, 39).

While not designed to induce weight loss, three RCTs of isoflavone containing soy protein supplementation are worth discussing in some detail, as they report on changes in total (40) and regional measures of adiposity (22, 23). In the first study, 180 post-menopausal Chinese women were randomly assigned to receive 15 grams of soy or milk protein, with or without 100 mg of isoflavones per day for six months. Consumption of soy protein plus isoflavones resulted in greater reductions in total body weight and fat mass when compared to milk protein groups post intervention (40). Two smaller studies measured changes in CT-derived measures of adiposity with isoflavone containing soy protein compared to a casein control, under weight-stable conditions (22, 23). In the first study, 15 postmenopausal women were randomized to consume an isoflavone containing soy protein shake (n=9; 20 g protein, 160 mg isoflavones) or a casein protein shake (n=6; 20 g protein) for 12 weeks as a part of their usual diet (23). Interestingly, although weight did not change between groups, total and subcutaneous abdominal fat significantly decreased in the soy group and increased in the non-soy group. A follow-up to this study (using the same dietary supplement protocol) reported similar findings, with no change in total body weight, yet significant reduction in total abdominal and subcutaneous fat in the soy compared to the casein control group (22). As an extension of this work, results presented here represent the first RCT of weight loss including soy and non-soy protein control groups to assess changes in CT-derived regional adiposity. Although a differential intervention effect was not observed, both groups experienced marked reductions in abdominal, liver, and thigh fat depots and it may be that the impressive magnitude of weight loss experienced by SILVER participants trumped any effect of dietary protein source on change in regional adiposity.

An interesting observation in the present study, of relevance to the controversy surrounding the promotion of intentional weight loss in older adults, is the finding that caloric restriction alone (i.e. without exercise) resulting in significant reductions in body weight, fat and lean mass, did not adversely affect measures of physical function and relative strength in this population. Although physical inactivity is associated with decreased muscle mass and function (41, 42), and several studies demonstrate significant health benefits associated with dietary-induced weight loss and exercise in overweight and obese, older adults, data presented here add to a limited body of research indicating that significant weight loss produced by caloric restriction without exercise, does not adversely affect physical function (43–46). If confirmed, findings may influence current weight management recommendations for overweight and obese older adults (47), as many are unable (or unwilling) to perform regular exercise. Further, the lack of any association between change in body weight and composition and change in measures of physical function and strength in this study also add to literature suggesting that factors other than absolute muscle mass (such as strength, quality (48), and inflammation (49)) are stronger predictors of functional status in older adults.

This study has several strengths. The weight loss intervention involved a highly structured feeding study, and participant adherence to the dietary protocol was excellent, with biomarker and weight data corroborating self-reported dietary compliance. Additionally, this study utilized highly sophisticated imaging technology, including DXA and CT, to assess changes in body composition. This study, however, is not without limitations. This was an exploratory pilot trial with a small sample size and only 12 weeks of follow-up. Therefore, external validity of our findings is low, and we cannot extrapolate beyond 12 weeks to evaluate the long-term effects of the intervention protocol on study outcomes. Our study design approach also ignores the importance of satiety in cuing food intake. Limited data do support satiating properties of soy foods (50), which may explain the improvement in weight and fat loss when induced as part of an ad libitum diet observed in some studies. Although our intervention groups were designed to assess differences in protein source during weight loss, they cannot address other dietary differences, and it is entirely possible that intake of different types or amounts of soy foods may yield different effects on health outcomes. Lastly, other potential benefits of using soy (or plant based) protein during weight loss in older adults may exist, including preservation of bone mass (51) and achievement of optimal acid-base balance (52), which this study did not assess. Future studies may consider comparing diets of differing protein source during free-living weight loss conditions, utilize different types or amounts of protein during weight loss, and/or include additional health-related outcomes measures of relevance to a geriatric population undergoing intentional weight loss.

In conclusion, there is increasing interest in optimizing weight loss strategies in overweight and obese older adults to promote cardioprotective benefit while preserving physical function. Data presented here suggest that a 12-week weight loss intervention, which incorporates soy and non-soy meal replacement products, is associated with clinically significant weight loss and improvements in several parameters of cardiometabolic risk and unchanged physical function and strength. Results did not differ by protein source and

suggest that soy protein is at least as good as other protein sources for weight loss during low-calorie diet interventions.

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Table 1

Baseline characteristics of SILVER study sample by intervention group and overall

Baseline Participant Characteristics	Soy (n=12)	Non-Soy (n=12)	Overall (n=24)
Age (years)	67.4 ± 4.5	69.5 ± 6.3	68.4 ± 5.5
Female, n (%)	11 (91.7)	10 (83.3)	21 (87.5)
White, n (%)	7 (58.3)	8 (66.7)	15 (62.5)
Weight (kg)	95.4 ± 9.6	97.9 ± 18.5	96.6 ± 14.5
Body Composition Measures			
BMI (kg/m^2)	35.1 ± 4.3	37.0 ± 7.4	36.0 ± 6.0
Waist circumference (cm)	100.3 ± 8.0	102.4 ± 17.0	101.4 ± 13.1
Hip circumference (cm)	116.0 ± 9.4	123.8 ± 17.2	119.9 ± 14.1
Total body fat mass (kg)	44.3 ± 7.9	46.2 ± 12.4	45.2 ± 10.1
Total body lean mass (kg)	51.5 ± 6.5	52.3 ± 10.9	51.9 ± 8.7
Percent body fat mass (%)	46.4 ± 5.6	46.7 ± 6.8	46.5 ± 6.1
Percent body lean mass (%)	54.2 ± 5.6	53.4 ± 6.8	53.8 ± 6.0
Total abdominal fat volume (cm^3)	660.8 ± 158.7	726.6 ± 187.5	693.7 ± 173.2
Subcutaneous abdominal fat volume (cm^3)	405.1 ± 93.7	483.3 ± 169.3	444.2 ± 139.7
Visceral abdominal fat volume (cm^3)	239.2 ± 88.5	221.2 ± 80.0	230.2 ± 83.0
Liver fat attenuation (HU)	54.9 ± 5.3	49.4 ± 10.6	52.1 ± 8.7
Thigh intermuscular fat volume (cm^3)	48.4 ± 18.5	47.4 ± 17.4	47.9 ± 17.6
Thigh muscle volume (cm^3)	636.8 ± 94.8	635.1 ± 125.2	635.9 ± 108.6
Cardiometabolic Risk Factors			
Systolic blood pressure (mmHg)	134.0 ± 18.7	138.1 ± 11.8	136.0 ± 15.4
Diastolic blood pressure (mmHg)	73.1 ± 10.7	72.1 ± 3.8	72.6 ± 7.9
Total cholesterol (mg/dL)	215.8 ± 39.2	213.8 ± 35.8	214.8 ± 36.7
LDL cholesterol (mg/dL)	134.2 ± 32.2	128.4 ± 28.6	131.3 ± 29.9
HDL cholesterol (mg/dL)	57.3 ± 10.7	53.6 ± 15.2	55.4 ± 13.0
Triglycerides (mg/dL)	121.7 ± 50.3	159.2 ± 68.0	140.4 ± 61.6
Glucose (mg/dL)	95.9 ± 12.0	98.0 ± 7.0	97.0 ± 9.7
Insulin (μIU/mL)	14.2 ± 9.8	14.9 ± 10.1	14.6 ± 9.7
hsCRP (mg/L)	2.2 ± 1.5	4.3 ± 4.1	3.2 ± 3.2
Physical Performance Measures			
SPPB (score, 1–12)	11.3 ± 0.8	10.8 ± 1.2	11.1 ± 1.0
400-meter walk time (s)	292.1 ± 23.5	328.9 ± 72.1	310.5 ± 55.8
Grip strength (kg)	29.0 ± 9.3	30.1 ± 9.0	29.5 ± 9.0
Knee extensor strength (N/m)	116.1 ± 32.3	104.4 ± 23.1	110.8 ± 28.4

Table 2

Unadjusted measures of compliance to the dietary protocol by intervention group

Study Compliance Measures	Soy (n=12)		Non-Soy (n=12)		p-value
	Mean ± SD 12-Weeks	Mean ± SD Δ From Baseline	12-Weeks	Δ From Baseline	
Weight (kg)	88.2 ± 9.4	−7.2 ± 1.8	89.5 ± 17.9	−8.4 ± 3.7	0.83
Self-reported compliance * (%)	97.5 ± 3.3	—	92.9 ± 9.3	—	0.13
Serum Isoflavone Levels (nM)					
Genistein	445.8 ± 653.9	366.8 ± 515.9	8.9 ± 10.0	−33.5 ± 73.0	<0.01**
Daidzein	254.9 ± 323.8	187.4 ± 278.6	8.9 ± 13.9	−12.6 ± 33.6	<0.01**
Glycitein	10.2 ± 9.8	4.5 ± 7.1	3.9 ± 1.7	−0.7 ± 3.1	0.02**
Equol	81.2 ± 66.3	62.3 ± 81.1	2.4 ± 4.7	−4.0 ± 13.6	<0.01**

* Self-reported compliance is defined as the proportion of meal replacements taken according to protocol. All statistical comparisons based on independent t-tests or nonparametric Wilcoxon signed rank tests, indicated by **.

Table 3

Randomization effects on body weight and composition at 12 weeks, adjusted for baseline outcome measure

Body Weight and Composition	Soy (n=12) Mean ± SE	Non-Soy (n=12) Mean ± SE	p-value
Weight (kg)	89.4 ± 0.8	88.3 ± 0.8	0.35
BMI (kg/m^2)	33.4 ± 0.3	32.9 ± 0.3	0.31
Waist circumference (cm)	93.5 ± 1.2	96.4 ± 1.2	0.11
Hip circumference (cm)	113.5 ± 1.3	113.7 ± 1.3	0.92
DXA-acquired measures			
Total body fat mass (kg)	40.4 ± 0.7	39.5 ± 0.7	0.42
Total body lean mass (kg)	49.5 ± 0.5	49.2 ± 0.5	0.68
Percent body fat mass (%)	44.8 ± 0.6	44.2 ± 0.7	0.55
Percent body lean mass (%)	55.6 ± 0.6	55.8 ± 0.6	0.86
CT-acquired measures			
Total abdominal fat volume (cm^3)	585.4 ± 18.7	569.6 ± 18.7	0.55**
Subcutaneous abdominal fat volume (cm^3)	382.3 ± 13.5	376.6 ± 13.5	0.78
Visceral abdominal fat volume (cm^3)	183.8 ± 9.3	176.7 ± 9.3	0.60
Liver fat attenuation (HU)	58.5 ± 1.9	56.4 ± 1.9	0.45
Thigh intermuscular fat volume (cm^3)	49.1 ± 1.4	45.3 ± 1.4	0.07
Thigh muscle volume (cm^3)	610.2 ± 8.0	623.4 ± 8.0	0.26

All statistical comparisons based on either a parametric ANCOVA adjusted for baseline values of the outcome or the nonparametric Wilcoxon rank sum test, denoted by **.

Table 4

Randomization effects on measures of cardiometabolic risk and physical function and strength at 12 weeks, adjusted for baseline outcome measure

Cardiometabolic and Functional Decline Risk Factors	Soy (n=12) Mean ± SE	Non-Soy (n=12) Mean ± SE	p-value
Cardiometabolic Risk Factors			
Systolic blood pressure (mmHg)	129.2 ± 3.7	124.2 ± 3.7	0.67**
Diastolic blood pressure (mmHg)	75.3 ± 2.7	66.7 ± 2.7	0.04
Total cholesterol (mg/dL)	192.8 ± 4.0	187.7 ± 4.0	0.37
LDL cholesterol (mg/dL)	116.3 ± 4.0	118.4 ± 4.0	0.71
HDL cholesterol (mg/dL)	53.5 ± 2.4	51.0 ± 2.4	0.46
Triglycerides (mg/dL)	114.1 ± 8.9	92.9 ± 8.9	0.11
Glucose (mg/dL)	94.6 ± 2.3	93.0 ± 2.3	0.64
Insulin (μIU/mL)	10.7 ± 1.2	9.5 ± 1.2	0.50
hsCRP (mg/L)	6.3 ± 1.5	2.5 ± 1.5	0.40**
Physical Performance Measures			
SPPB (score, 1–12)	11.4 ± 0.3	11.0 ± 0.3	0.24
400-meter walk time (s)	309.9 ± 12.8	306.2 ± 13.4	0.41**
Grip strength (kg)	29.2 ± 1.0	29.2 ± 1.0	0.99
Knee extensor strength (N/m)	108.4 ± 3.2	105.9 ± 3.6	0.62

All statistical comparisons based on either a parametric ANCOVA adjusted for baseline values of the outcome or the nonparametric Wilcoxon rank sum test, denoted by **.