

Unprocessed red meat in the dietary treatment of obesity: a randomized controlled trial of beef supplementation during weight maintenance after successful weight loss

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ABSTRACT

Background: Consumption of unprocessed red meat in randomized trials has no adverse effects on cardiovascular risk factors and body weight, but its physiological effects during weight loss maintenance are not known.

Objectives: We sought to investigate the effects of healthy diets that include small or large amounts of red meat on the maintenance of lost weight after successful weight loss, and secondarily on body composition (DXA), resting energy expenditure (REE; indirect calorimetry), and cardiometabolic risk factors.

Methods: In this 5-mo parallel randomized intervention trial, 108 adults with BMI 28–40 kg/m² (45 males/63 females) underwent an 8-wk rapid weight loss period, and those who lost ≥8% body weight ($n = 80$) continued to ad libitum weight maintenance diets for 12 wk: a moderate-protein diet with 25 g beef/d (B25, $n = 45$) or a high-protein diet with 150 g beef/d (B150, $n = 35$).

Results: In per protocol analysis ($n = 69$), mean body weight (−1.2 kg; 95% CI: −2.1, −0.3 kg), mean fat mass (−2.7 kg; 95% CI: −3.4, −2.0 kg), and mean body fat content (−2.6%; 95% CI: −3.1, −2.1%) decreased during the maintenance phase, whereas mean lean mass (1.5 kg; 95% CI: 1.0, 2.0 kg) and mean REE (51 kcal/d; 95% CI: 15, 86 kcal/d) increased, with no differences between groups (all $P > 0.05$). Results were similar in intention-to-treat analysis with multiple imputation for dropouts (20 from B150 compared with 19 from B25, $P = 0.929$). Changes in cardiometabolic risk factors were not different between groups, the general pattern being a decrease during weight loss and a return to baseline during weight maintenance (and despite the additional mild reduction in weight and fat mass).

Conclusions: Healthy diets consumed ad libitum that contain a little or a lot of unprocessed beef have similar effects on body weight, energy metabolism, and cardiovascular risk factors during the first 3 mo after clinically significant rapid weight loss. *Am J Clin Nutr* 2022;116:1820–1830.

Keywords: overweight, weight loss, meat intake, red meat, body composition, cardiovascular risk, prediabetes

Introduction

Maintenance of lost weight is the Achilles' heel in the management of obesity. Although it is not particularly difficult to lose weight by a variety of dietary regimens that focus on calorie restriction, maintaining the lost weight upon switching to an ad libitum diet has been an exercise in futility (1), inasmuch as 50–75% of the weight lost is regained within 3–5 y (2, 3). Greater reductions in metabolically active lean tissue mass and resting energy expenditure (REE) during weight loss have been associated with less effective weight loss maintenance (4–8). Higher-protein diets can mitigate the loss of lean body mass and the decline in REE during energy restriction and weight loss (9),

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Supplemental Tables 1–6 and Supplemental Figure 1 are available from the "Supplementary data" link in the online posting of the article and from the same link in the online table of contents at <https://academic.oup.com/ajcn/>.

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Abbreviations used: B25, weight maintenance diet supplemented with 25 g/d beef; B150, weight maintenance diet supplemented with 150 g/d beef; DASH, Dietary Approaches to Stop Hypertension; E%, percentage of total calories; HbA1c, glycated hemoglobin; ITT, intention-to-treat; RANOVA, repeated measures analysis of variance; REE, resting energy expenditure; VLCD, very-low-calorie diet.

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which could be responsible for their ability to attenuate weight regain after weight loss (10, 11) when compared with lower-protein diets.

Red meat is a rich source (>20% by weight) of high biological value protein—containing all essential amino acids—and accounts for about half of all meat consumption and 40% of all dietary protein in industrialized countries (12, 13). However, diets rich in meat, and particularly red meat, have been associated with increased risk of obesity, diabetes, and cardiovascular diseases in observational studies (14–17). Most of these are cross-sectional, retrospective, or longitudinal comparisons of meat eaters and non-meat eaters. These studies cannot prove causality and do not always distinguish between higher-fat and leaner meats, or between processed and unprocessed meats, even though industrial processing is known to alter the food matrix of meat and, consequently, result in final products with different composition, organoleptic properties (e.g., sensory attributes such as appearance, texture, smell, and taste), and possibly also health effects (18, 19). Additionally, there are differences in many other dietary factors—not only between meat eaters and non-meat eaters, but also between individuals who habitually consume a lot of meat compared with those who consume little meat (e.g., the former consume more sugary beverages, butter and butter-based fat spreads, and fewer fruits and vegetables than the latter) (20). Finally, the relation between meat intake and disease biomarkers, risk of cardiovascular disease, and all-cause mortality is not uniform in meat eaters; rather, it depends on the comparator diet (21) and the amount of daily meat consumption (22, 23).

Previous clinical trials have demonstrated that unprocessed red meat in amounts from ~15 g/d up to ~150 g/d can be included as part of a healthy dietary pattern without adverse effects on body weight and cardiovascular risk factors (19, 24–27), but the physiological effects of red meat consumption during weight loss maintenance are not known. Accordingly, the primary aim of this parallel randomized intervention trial was to investigate the effects of eating small (25 g/d) or large (150 g/d) amounts of red meat (beef) as part of a healthy diet—otherwise consumed ad libitum—on the maintenance of lost weight after successful weight loss, and secondarily on body composition, energy metabolism, and cardiometabolic risk factors.

Methods

Subjects

Apparently healthy males and females with overweight or obesity (BMI 28–40 kg/m²), aged 18–65 y, were recruited for this study. Subjects were excluded if they had experienced changes in body weight >5% within the past 3 mo (either weight gain or loss); if they were vegetarian or vegan; if they had been pregnant or lactating within the past 12 mo or were planning to become pregnant; if they had a history or diagnosis of diabetes, heart, liver, or kidney diseases, or eating disorders; if they had been diagnosed with cancer within the past 5 y (except adequately treated localized basal cell skin cancer); if they were planning to donate blood or were participating in other clinical trials during the course of this study; if they were using drugs that, in the opinion of the investigators, were likely to affect

outcomes; or if they were unable or unwilling to give informed consent, communicate with the study personnel, or follow the study protocol and instructions given by the study personnel. All subjects signed an informed consent form prior to participating in the study, which was approved by the regional Ethical Committee of the Capitol Region of Denmark and carried out in accordance with the Helsinki Declaration.

Design

This was a 5-mo parallel randomized controlled trial (clinicaltrials.gov # NCT04156165), which was initiated with an 8-wk weight loss period, followed by a 1-wk reintroduction to regular foods, and then a 12-wk period of weight maintenance (Figure 1). Clusters of 8–12 subjects were randomly assigned—by means of drawing a sealed envelope by a person not involved in the study—to a very-low-calorie diet (VLCD) with either standard or higher protein content for inducing rapid weight loss, followed by an ad libitum weight maintenance diet supplemented with either small or large amounts of beef (2 × 2 factorial design; allocation ratio 1:1:1:1). The trial was carried out from October 2019 to November 2020 at the University of Copenhagen, Denmark.

Diet interventions

Weight loss phase.

During the initial 8 wk, all subjects received 4 sachets daily of any combination of the following VLCD formula products (LighterLife): Shepherd's Pie, Oat Porridge, Spaghetti Bolognese, Vegetable Soup, Vanilla Shake, Strawberry Shake, Chocolate Shake, and Banana Shake; for an average total daily intake of approximately 600 kcal from 52 g protein [35% of all calories (35 E%)], 52 g carbohydrate (35 E%), 18 g fat (27 E%), and 14 g dietary fiber (5 E%). Subjects assigned to the higher-protein arm received an additional 25 g whey protein powder, for an average total daily intake of approximately 700 kcal from 77 g protein (44 E%), 52 g carbohydrate (30 E%), 18 g fat (23 E%), and 14 g dietary fiber (4 E%). Participants were also allowed to consume 50 g green salad, 125 g cucumber, and 200 g tomato daily, and any other noncaloric products to facilitate adherence. The VLCD formula products were handed out free of charge during onsite group meetings, during which the study dietitian also answered questions and provided advice for improving compliance. Results from the weight loss phase have been reported elsewhere (28). Subjects who successfully lost ≥8% of their initial body weight were allowed to continue to the weight maintenance phase.

Weight maintenance phase.

During the 12 wk of weight maintenance, subjects were prescribed diets supplemented with unprocessed red meat (beef) at either 25 g/d (B25) or 150 g/d (B150). These amounts of beef were chosen to result in diets that provided ~15% and ~25%, respectively, of total daily calories from protein. Fresh minced beef of Danish origin with a fat content of 8–12% by weight (i.e., mostly lean) was handed out free of charge during onsite group meetings with the study dietitian. Subjects were instructed

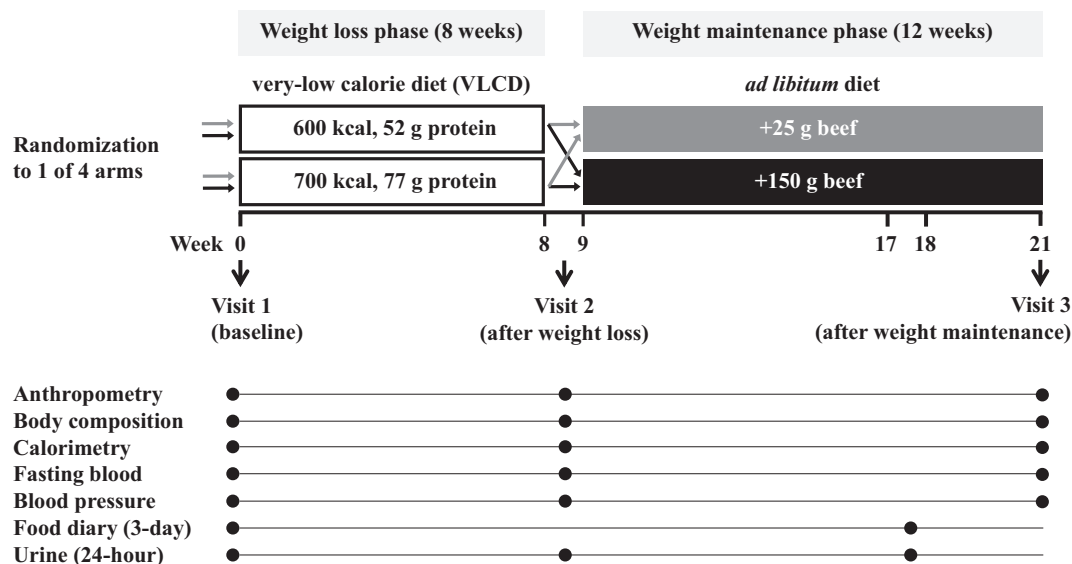


FIGURE 1 Study design, depicted in a chronological order (timeline).

to meet the target protein intake by consuming additional dairy, fish, eggs, and plant-based protein sources, but no extra meat. They had to purchase all other foods besides beef, received recipes in accordance with their allocation group, and were instructed to consume the diets *ad libitum*. Both diets emphasized consumption of fiber and whole grains and avoidance of free sugars. Dietary advice did not focus on calorie restriction, and the recommended food servings were based on individual calorie needs (estimated from indirect calorimetry) for maintaining the new, lower body weight achieved after completing the VLCD treatment.

Assessments and outcomes

All measurements were conducted 3 times during the study: at baseline (before weight loss), immediately after the 8-wk weight loss phase (during the week of food reintroduction), and after the 12-wk weight maintenance phase (Figure 1). For all visits, subjects were instructed to fast from 22:00 the evening before, and limit intake of water to ≤ 500 mL in the morning. Upon arrival to the laboratory, they emptied their bladder and changed into light clothing.

Weight was measured to the nearest 0.1 kg on a calibrated digital scale (WB-110MA; TANITA Corp). Height was measured to the nearest 0.5 cm on a wall-mounted stadiometer (Hultafors). Waist circumference (at the mid-point between the bottom of the rib cage and the top of the iliac crest in the mid-axillary line) and hip circumference (at the widest point between the hips and buttocks) were measured to the nearest 0.5 cm with a nonstretchable measuring tape, and the waist-to-hip ratio was calculated. Total body fat mass, bone-free lean mass, and visceral adipose tissue within the android region were measured by DXA (Lunar iDXA with CoreScan module; GE Healthcare) (29). During the whole-body scan, subjects were instructed to lie still with arms close to the body and legs kept in place by a Velcro fastener around the ankles. Blood pressure was measured in triplicate, 2 min apart, at the upper arm by trained personnel

using an electronic sphygmomanometer after the subjects rested quietly in a lying position for ≥ 5 min. Thereafter, fasting venous blood samples were drawn from the antecubital vein by a trained phlebotomist. All blood samples were processed for separation of plasma or serum and stored at -80°C until analyses for glucose, insulin, glycated hemoglobin (HbA1c), IL-6, TNF- α , total cholesterol, HDL cholesterol, LDL cholesterol, and triglyceride by standard methods at the Department of Nutrition, Exercise and Sports at the University of Copenhagen. Thereafter, subjects had their oxygen consumption and carbon dioxide production measured continuously for 30 min, while breathing under a ventilated hood, and their respiratory quotient and REE were determined by indirect calorimetry (Jaeger OxyconPro; Viasys Healthcare). The reproducibility of DXA and indirect calorimetry determinations in our laboratory, as reflected by the average CV of duplicate measurements in 16–25 subjects with similar characteristics as those recruited in the present study, is 0.7% for fat mass, 0.3% for lean mass, 2.5% for REE, and 4.0% for the respiratory quotient.

The daily energy requirements for weight maintenance at the new, lower body weight were estimated as the product of REE and the physical activity level (determined by questionnaire) at the end of the weight loss phase. Dietary intake was assessed at baseline (habitual diet) and during the ninth week of the 12-wk weight maintenance phase by means of a 3-d weighed food diary. Subjects were instructed to register all foods and drinks consumed during 3 d (consecutive or not) including 2 weekdays and 1 weekend day. Dietary data were analyzed for energy and nutrient intake by using Dankost (Kraftverk) and a food composition database (frida.fooddata.dk; DTU Food Institute). Subjects were given all required equipment and instructed to collect 24-h urine samples at baseline (before weight loss), after the 8-wk weight loss phase, and during the ninth week of the 12-wk weight maintenance phase. Urine samples were analyzed for urea according to a standard protocol at the Department of Nutrition, Exercise and Sports at the University of Copenhagen, and total urinary urea excretion was calculated

(urea concentration \times total urine volume, in millimoles per day) as a biomarker of dietary protein—and thus also beef—intake (30).

Statistics

The primary outcome of the study was weight loss maintenance. Power calculations for sample size determination were based on the weight change during this 12-wk period. Based on data from a previous weight maintenance trial (11), a total of 72 completers would be needed to detect a difference of 2.0 kg between diets with an SD of 3.0 kg, at the 5% level of significance with 80% power. Assuming a dropout rate of 20% during the initial weight loss phase, and an additional 20% during the weight maintenance phase, we planned to recruit 110 subjects.

Data for subjects who completed all study visits (per protocol analysis) were analyzed by using repeated measures analysis of variance (RANOVA), with 1 between-subjects factor (diet group: B25 compared with B150) and 1 within-subjects factor (time: baseline compared with after weight loss compared with after weight maintenance). The VLCD type (standard or higher protein content) (28) and sex (male or female) (31) were entered in the model as covariates, because they can affect the physiological responses to rapid weight loss. Significant main effects and time \times diet interactions were followed by Sidak post hoc tests to evaluate differences between time points and diets. Intention-to-treat (ITT) analysis was carried out in a similar manner including all subjects who started the study, regardless of when they dropped out. We first explored relations between baseline characteristics and changes in outcomes and found several significant correlations that led us to assume that data were missing at random and could be predicted from measured variables. We then performed missing data analysis to identify any patterns in data missingness; multiple imputation was performed accordingly and pooled estimates of the 5 “best-fit” iterations were used for analysis. Baseline characteristics between diet groups (before weight loss) were evaluated by independent *t* tests and ANOVA with sex as covariate. Normality of the data distributions was evaluated by using the Shapiro–Wilk test. The same test was used to assess normality of the standardized residuals in the RANOVA models. Nonnormally distributed datasets were log-transformed for analysis. Homogeneity of variance across the levels of the between-subjects factor (diet group) was assessed with the Levene test, and homogeneity of variance across the levels of the within-subjects factor (time) was assessed with the Mauchly test of sphericity (applying the Greenhouse–Geisser correction when necessary). Distributions of males/females and completers/noncompleters were compared between diet groups by Pearson χ^2 or Fisher exact tests. Two-sided *P* values <0.05 were considered statistically significant. Descriptive results are shown as means with SDs or as estimated marginal means with SEs or 95% CIs. All analyses were conducted with IBM SPSS Statistics version 28 (IBM Corp).

Results

A total of 108 randomly assigned subjects attended the baseline visit ($n = 56$ in B25 and $n = 52$ in B150, Table 1), and

TABLE 1 Baseline characteristics of subjects with overweight or obesity randomly assigned at baseline to an 8-wk weight loss intervention (very-low-calorie diet), followed by a 12-wk weight maintenance intervention of ad libitum diet supplemented with small (25 g/d, B25) or large (150 g/d, B150) amounts of beef¹

	B25 ($n = 56$)	B150 ($n = 52$)
Sex, M/F	21/35 (38/62%)	24/28 (46/54%)
Age, y	49.1 \pm 11.0	45.4 \pm 11.0
Height, cm	172 \pm 9	174 \pm 9
Weight, kg	100.3 \pm 15.4	101.4 \pm 12.5
BMI, kg/m ²	33.8 \pm 3.1	33.4 \pm 3.1
Body fat, %	42.4 \pm 6.2	40.5 \pm 6.2
Fat mass, kg	42.4 \pm 8.5	40.9 \pm 7.2
Lean mass, kg	55.0 \pm 11.1	57.4 \pm 10.4
Visceral adipose tissue, g	1812 \pm 964	1857 \pm 1083
Waist circumference, cm	109.0 \pm 12.2	108.0 \pm 9.5
Hip circumference, cm	114.4 \pm 10.1	113.5 \pm 8.3
Waist-to-hip ratio	0.96 \pm 0.10	0.96 \pm 0.11
Resting energy expenditure, kcal/d	1692 \pm 279	1747 \pm 274
Respiratory quotient	0.79 \pm 0.04	0.79 \pm 0.04

¹Values are means \pm SDs, except for sex distribution (absolute and relative frequencies).

84 completed the initial 8-wk weight loss phase (28), of which 4 did not meet the weight loss goal (2 for each VLCD type; Fisher exact test, $P = 1.000$). These 4 subjects were all females who had been allocated to B150 but lost only 5–7.5% body weight during the weight loss phase. The remaining 80 subjects who lost $\geq 8\%$ of their initial body weight continued to the weight maintenance phase ($n = 45$ in B25 and $n = 35$ in B150), and 69 completed the study. More subjects tended to discontinue the B25 than the B150 diet (9 and 2, respectively; Fisher exact test, $P = 0.101$), but the total attrition rate was $\sim 36\%$ in both groups (Pearson χ^2 , $P = 0.929$) (Figure 2). Noncompleters were younger, heavier, and had greater BMI, fat mass, and hip circumference than subjects who completed the entire study (Supplemental Table 1). Two serious (minor stroke and hernia) and 1 mild (benign growth in the breast) adverse events were recorded during the weight loss phase (which did not result in subjects dropping out) (28), and none were recorded during the weight maintenance phase.

There were no significant differences at baseline (before weight loss) in characteristics of subjects randomly assigned to the B25 and B150 diets (Table 1). However, the sex distribution of those who successfully lost $\geq 8\%$ body weight (Supplemental Table 2) and those who completed the study (Supplemental Table 3) tended to be different between groups (Pearson χ^2 test, $P = 0.094$ and $P = 0.077$, respectively), with more males in B150 than in B25. Accordingly, in subjects who completed the entire study, those allocated to the B150 diet tended to be taller and heavier and have greater lean mass, visceral adipose tissue, and REE at baseline (before weight loss) than those allocated to the B25 diet; however, these differences were abolished after adjusting for sex (Supplemental Table 3).

During weight maintenance (per protocol analysis), daily energy intake and the contribution from fat to total calories were reduced in both groups compared with their habitual intakes before weight loss (Table 2). The contribution from protein increased in B150 subjects but did not change in B25 subjects,

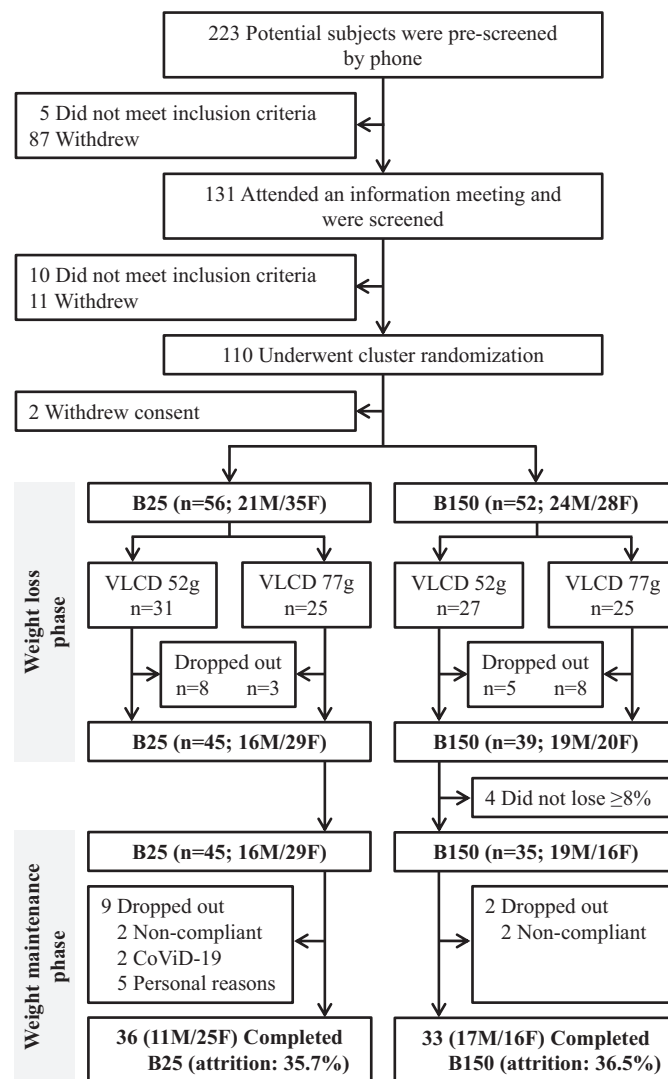


FIGURE 2 Flowchart of subjects through the study, according to beef supplementation group. Randomization was performed once, at the beginning of the study, into 1 of 4 arms (2×2 design): very-low-calorie diet (VLCD) with 52 or 77 g protein/d for the weight loss phase and supplementation with 25 or 150 g beef/d (B25 or B150, respectively) for the weight maintenance phase.

whereas the contribution from carbohydrate decreased in B150 and increased in B25 (P values for interaction <0.001 , [Table 2](#)). Both groups consumed 50–70 g more protein on top of that provided by beef (~ 7 g more in B25 and ~ 39 g more in B150, assuming an average beef protein content of 26% by weight). Added sugars decreased and fiber increased in both groups. Cholesterol intake decreased in B25 subjects but did not change in B150 subjects (P value for interaction = 0.022). Daily intakes of micronutrients relevant to meat consumption decreased in the B25 group (except for vitamin B-12) but increased in the B150 group (except for iron and phosphorus); and all were significantly greater in B150 compared with B25 subjects during the weight maintenance phase ([Table 2](#)). Time \times diet interactions, differences between groups, and changes over time were largely similar in ITT analysis ([Supplemental Table 4](#)). Changes in nutrient intakes were consistent with dietary advice and the different amounts of beef supplementation, as did those in 24-h urinary urea excretion ([Figure 3](#)). The latter were unaffected by

the type of VLCD during the weight loss phase ([Supplemental Figure 1](#)).

Changes in anthropometric, body composition, and energy metabolism outcomes (per protocol analysis) are shown in [Table 3](#). There were significant main effects of time but no significant differences between groups or time \times group interactions. During the weight loss phase, body fat content, fat mass, lean mass, visceral adipose tissue, waist and hip circumferences and the waist-to-hip ratio, REE, and the respiratory quotient all decreased ([Table 3](#)). Mean weight loss during the weight loss phase was 12.7% (95% CI: 11.8, 13.5%) and 13.1% (95% CI: 12.2, 13.9%) of initial body weight in B25 and B150 groups, respectively ($P = 0.523$). Body weight continued to decrease during the weight maintenance phase (mean loss = -1.2 kg; 95% CI: -2.1 , -0.3 kg), and so did mean body fat content (-2.6% ; 95% CI: -3.1 , -2.1%), mean fat mass (-2.7 kg; 95% CI: -3.4 , -2.0 kg), visceral adipose tissue, and waist and hip circumferences; by contrast, there were increases in mean lean

TABLE 2 Daily nutrient intakes at baseline and during a 12-wk weight maintenance diet supplemented with small (25 g/d, B25) or large (150 g/d, B150) amounts of beef¹

	B25 (n = 36)		B150 (n = 33)		P values		
	Baseline, before weight loss	During weight maintenance	Baseline, before weight loss	During weight maintenance	Time	Diet	Time × diet
Energy, kcal	2020 ± 95	1386 ± 73 ²	2116 ± 100	1634 ± 77 ²	<0.001	0.087	0.335
Protein, %	19 ± 1	17 ± 1	18 ± 1	28 ± 1 ^{2,3}	0.051	<0.001	<0.001
Protein, g	93 ± 5	57 ± 3 ²	93 ± 5	109 ± 4 ^{2,3}	0.006	<0.001	<0.001
Carbohydrate, %	44 ± 1	55 ± 1 ²	41 ± 1	35 ± 1 ^{2,3}	<0.001	<0.001	<0.001
Carbohydrate, g	207 ± 12	172 ± 9 ²	205 ± 12	132 ± 9 ^{2,3}	0.003	0.084	0.049
Fat, %	35 ± 1	27 ± 1 ²	40 ± 1 ³	36 ± 1 ^{2,3}	<0.001	<0.001	0.023
Fat, g	81 ± 5	43 ± 4 ²	95 ± 5 ³	67 ± 4 ^{2,3}	<0.001	0.001	0.194
Added sugars, g	20 ± 4	7 ± 2 ²	29 ± 4	6 ± 2 ²	0.003	0.177	0.091
Cholesterol, mg	321 ± 36	168 ± 32 ²	446 ± 38 ³	441 ± 33 ³	0.074	<0.001	0.022
Fiber, g	22 ± 1	30 ± 2 ²	21 ± 1	27 ± 2 ²	<0.001	0.185	0.424
Iron, mg	9.8 ± 0.5	7.6 ± 0.5 ²	10.0 ± 1.0	10.7 ± 0.5 ³	0.317	<0.001	0.001
Phosphorus, mg	1313 ± 69	1015 ± 68 ²	1378 ± 73	1372 ± 72 ³	0.228	0.015	0.014
Selenium, µg	41 ± 4	29 ± 4 ²	48 ± 4	61 ± 4 ^{2,3}	0.636	<0.001	0.001
Zinc, mg	11.5 ± 0.7	7.3 ± 0.5 ²	11.8 ± 0.8	13.9 ± 0.5 ^{2,3}	0.035	<0.001	<0.001
Niacin, mg	31.1 ± 1.9	19.5 ± 1.4 ²	28.8 ± 2.0	36.4 ± 1.5 ^{2,3}	0.122	<0.001	<0.001
Vitamin B-6, mg	1.4 ± 0.1	1.2 ± 0.1 ²	1.4 ± 0.1	1.8 ± 0.1 ^{2,3}	0.730	0.012	<0.001
Vitamin B-12, µg	4.7 ± 0.5	3.5 ± 0.5	5.8 ± 0.6	7.5 ± 0.6 ^{2,3}	0.989	<0.001	0.018

¹ Values are means ± SEs for 69 completers (per protocol analysis). Data were analyzed by repeated measures ANOVA (time × diet) and adjusted for sex and the very-low-calorie diet used during the weight loss phase.

² P < 0.05 vs. "Baseline" in the same diet group, from Sidak post hoc test.

³ P < 0.05 vs. "B25" at the same time point, from Sidak post hoc test.

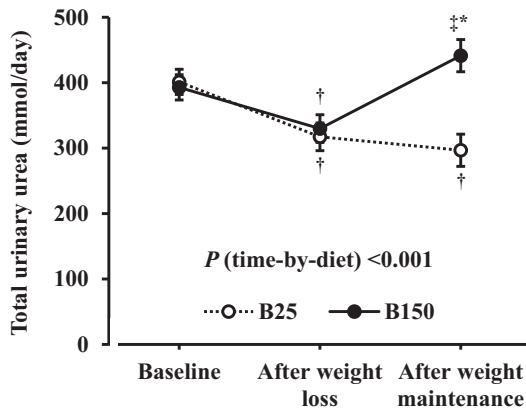


FIGURE 3 Effects of a 12-wk weight maintenance diet supplemented with small (25 g/d, B25) or large (150 g/d, B150) amounts of beef on 24-h urinary urea excretion. Values are means with SEs for 64 completers (per protocol analysis; $n = 32$ per group because of incomplete 24-h urine collection from 4 subjects in the B25 group and 1 subject in the B150 group). Data were analyzed by repeated measures ANOVA (time \times diet) and adjusted for sex and the very-low-calorie diet used during the weight loss phase. This was followed by Sidak post hoc tests: $^{\dagger}P < 0.05$ vs. “Baseline” in the same diet group; $^{\ddagger}P < 0.05$ vs. “After weight loss” in the same diet group; $^*P < 0.05$ vs. “B25” at the same time point.

mass (1.5 kg; 95% CI: 1.0, 2.0 kg), mean REE (51 kcal/d; 95% CI: 15, 86 kcal/d), and the respiratory quotient. The direction and magnitude of these changes were not significantly different between groups (Table 3); similar results were obtained in ITT analysis (Supplemental Table 5).

Cardiometabolic risk factors in completers improved during the study (Table 4). In both groups, resting systolic and diastolic blood pressures and fasting glucose and cholesterol concentrations (total, HDL, and LDL cholesterol) decreased during the weight loss phase; they rebounded during the weight maintenance phase but remained significantly lower compared with initial values (except HDL cholesterol in both groups and LDL cholesterol in B150, which returned to concentrations before weight loss). Fasting insulin and triglyceride concentrations decreased, and the ratio of HDL to LDL cholesterol increased with weight loss, and did not change thereafter. TNF- α and IL-6 concentrations did not change with weight loss, but TNF- α decreased during the weight maintenance phase. HbA1c (P value for interaction = 0.004) did not change in B150 subjects, whereas it decreased with weight loss in B25 subjects and increased thereafter to concentrations before weight loss (Table 4). Results from the ITT analysis were largely similar (Supplemental Table 6), except the HDL-to-LDL cholesterol ratio, which returned to concentrations before weight loss in both groups, and was overall greater in B150 than in B25 subjects.

Discussion

We evaluated the physiological effects of eating small or large amounts of mostly lean beef as part of a healthy diet consumed ad libitum after subjects with overweight or obesity lost clinically significant amounts of body weight. Our results indicate that diets with very different amounts of unprocessed red meat have largely similar effects on body weight, body composition, energy metabolism, and cardiovascular risk factors

TABLE 3 Effects of a 12-wk weight maintenance diet supplemented with small (25 g/d, B25) or large (150 g/d, B150) amounts of beef on anthropometric parameters, body composition, and resting energy metabolism¹

	B25 ($n = 36$)			B150 ($n = 33$)			P values	
	Baseline	After weight loss	After weight maintenance	Baseline	After weight loss	After weight maintenance	Time	Diet
Weight, kg	97.8 \pm 1.8	85.3 \pm 1.6 ²	84.0 \pm 1.7 ^{2,3}	100.3 \pm 1.9	87.3 \pm 1.7 ²	86.1 \pm 1.7 ^{2,3}	<0.001	0.381
BMI, kg/m ²	33.1 \pm 0.5	28.9 \pm 0.5 ²	28.4 \pm 0.5 ^{2,3}	33.3 \pm 0.5	28.9 \pm 0.5 ²	28.5 \pm 0.5 ^{2,3}	<0.001	0.825
Body fat, %	41.4 \pm 0.7	36.6 \pm 0.9 ²	34.4 \pm 1.0 ^{2,3}	40.9 \pm 0.8	36.0 \pm 1.0 ²	32.9 \pm 1.0 ^{2,3}	<0.001	0.504
Fat mass, kg	40.3 \pm 1.2	31.1 \pm 1.2 ²	28.7 \pm 1.2 ^{2,3}	41 \pm 1.3	31.4 \pm 1.3 ²	28.4 \pm 1.3 ^{2,3}	<0.001	0.866
Lean mass, kg	54.7 \pm 1.0	51.4 \pm 1.0 ²	52.5 \pm 1.1 ^{2,3}	56.3 \pm 1.1	52.8 \pm 1.0 ²	54.7 \pm 1.1 ^{2,3}	<0.001	0.252
Visceral adipose tissue, g	1790 \pm 132	1048 \pm 95 ²	997 \pm 102 ^{2,3}	1946 \pm 140	1168 \pm 101 ²	1092 \pm 109 ^{2,3}	<0.001	0.429
Waist circumference, cm	107.4 \pm 1.5	95.7 \pm 1.3 ²	94.7 \pm 1.4 ^{2,3}	109.0 \pm 1.5	97.6 \pm 1.3 ²	95.2 \pm 1.5 ^{2,3}	<0.001	0.508
Hip circumference, cm	111.3 \pm 1.2	106.1 \pm 1.2 ²	105.2 \pm 1.2 ^{2,3}	114.0 \pm 1.3	107.2 \pm 1.3 ²	106.1 \pm 1.2 ^{2,3}	<0.001	0.361
Waist-to-hip ratio	0.97 \pm 0.01	0.91 \pm 0.01 ²	0.90 \pm 0.01 ²	0.96 \pm 0.01	0.91 \pm 0.01 ²	0.90 \pm 0.01 ²	<0.001	0.977
Resting energy expenditure, kcal/d	1680 \pm 32	1504 \pm 26 ²	1550 \pm 32 ^{2,3}	1711 \pm 33	1556 \pm 27 ²	1611 \pm 34 ^{2,3}	<0.001	0.230
Respiratory quotient	0.80 \pm 0.01	0.72 \pm 0.01 ²	0.76 \pm 0.01 ^{2,3}	0.79 \pm 0.01	0.72 \pm 0.01 ²	0.76 \pm 0.01 ^{2,3}	<0.001	0.653
Time \times diet								0.642
								0.745
								0.144
								0.567
								0.166
								0.854
								0.370
								0.188
								0.167
								0.718

¹Values are means \pm SEs for 69 completers (per protocol analysis). Data were analyzed by repeated measures ANOVA (time \times diet) and adjusted for sex and the very-low-calorie diet used during the weight loss phase.

² $P < 0.05$ vs. “Baseline” in the same diet group, from Sidak post hoc test.

³ $P < 0.05$ vs. “After weight loss” in the same diet group, from Sidak post hoc test.

TABLE 4 Effects of a 12-wk weight maintenance diet supplemented with small (25 g/d, B25) or large (150 g/d, B150) amounts of beef on cardiometabolic risk factors¹

	B25 (n = 36)			B150 (n = 33)			P values		
	Baseline	After weight loss	After weight maintenance	Baseline	After weight loss	After weight maintenance	Time	Diet	Time × diet
Systolic blood pressure, mmHg	121 ± 3	109 ± 2 ²	116 ± 3 ^{2,3}	124 ± 3	111 ± 2 ²	116 ± 3 ^{2,3}	<0.001	0.585	0.484
Diastolic blood pressure, mmHg	81 ± 2	71 ± 1 ²	74 ± 1 ^{2,3}	83 ± 2	73 ± 1 ²	74 ± 1 ^{2,3}	<0.001	0.498	0.526
IL-6, pg/mL	2.5 ± 0.3	3.3 ± 0.6	2.5 ± 0.5	2.1 ± 0.4	1.9 ± 0.6	2.3 ± 0.5	0.207	0.262	0.253
TNF-α, pg/mL	0.69 ± 0.03	0.71 ± 0.03	0.63 ± 0.03 ^{2,3}	0.67 ± 0.03	0.68 ± 0.04	0.58 ± 0.03 ^{2,3}	<0.001	0.399	0.639
Insulin, pmol/L	94 ± 7	60 ± 6 ²	56 ± 6 ²	80 ± 8	42 ± 6 ²	51 ± 6 ²	<0.001	0.170	0.215
Glucose, mmol/L	5.80 ± 0.12	5.27 ± 0.10 ²	5.32 ± 0.09 ^{2,3}	5.60 ± 0.13	4.94 ± 0.10 ²	5.17 ± 0.10 ^{2,3}	<0.001	0.101	0.294
HbA1c, mmol/mol	42.5 ± 0.8	40.0 ± 0.8 ²	42.5 ± 0.7 ³	41.3 ± 0.8	41.3 ± 0.8	41.1 ± 0.7	0.021	0.664	0.004
Total cholesterol, mmol/L	5.36 ± 0.20	4.00 ± 0.13 ²	4.76 ± 0.16 ^{2,3}	5.10 ± 0.21	3.93 ± 0.14 ²	4.80 ± 0.17 ^{2,3}	<0.001	0.646	0.249
HDL cholesterol, mmol/L	1.25 ± 0.04	1.09 ± 0.04 ²	1.26 ± 0.04 ³	1.26 ± 0.04	1.08 ± 0.04 ²	1.31 ± 0.04 ³	0.002	0.787	0.455
LDL cholesterol, mmol/L	3.47 ± 0.17	2.37 ± 0.11 ²	2.92 ± 0.13 ^{2,3}	3.06 ± 0.17	2.28 ± 0.11 ²	2.91 ± 0.14 ³	<0.001	0.340	0.027
HDL/LDL cholesterol ratio	0.39 ± 0.02	0.49 ± 0.03 ²	0.45 ± 0.03 ²	0.44 ± 0.02	0.53 ± 0.03 ²	0.49 ± 0.03 ²	<0.001	0.223	0.820
Triglyceride, mmol/L	1.13 ± 0.11	0.83 ± 0.04 ²	0.95 ± 0.07 ²	1.32 ± 0.12	0.86 ± 0.04 ²	0.91 ± 0.07 ²	<0.001	0.498	0.286

¹Values are means ± SEs for 69 completers (per protocol analysis). Data were analyzed by repeated measures ANOVA (time × diet) and adjusted for sex and the very-low-calorie diet used during the weight loss phase. HbA1c, glycated hemoglobin.

²P < 0.05 vs. “Baseline” in the same diet group, from Sidak post hoc test.

³P < 0.05 vs. “After weight loss” in the same diet group, from Sidak post hoc test.

during the first 3 mo after rapid weight loss. These observations suggest that eating unprocessed red meat in amounts that far exceed population averages (e.g., 44 and 70 g/d among Danish females and males, respectively) (13) has no adverse effects on body weight and metabolic function when compared with a diet that contains much smaller amounts of beef, at least within the time frame of our study. Alternatively, eating relatively little beef as part of an ad libitum diet with adequate—but not necessarily high—protein content is as effective as eating a lot of beef as part of a protein-rich diet in maintaining weight loss and producing a favorable shift in body composition (loss of fat mass and increase in lean mass). These data imply that unprocessed red meat can be included in variable amounts within the context of a healthy dietary pattern for weight loss maintenance with very similar effects on body composition and cardiometabolic health.

Three randomized crossover trials evaluated the effects of including different amounts of mostly lean red meat as part of heart-healthy dietary patterns [i.e., Dietary Approaches to Stop Hypertension (DASH) and Mediterranean diets] during eucaloric feeding in individuals with normal weight, overweight, or obesity (19, 24, 27). All these trials included controlled feeding periods (4–5 wk long) with all foods provided that aimed at keeping body weight stable. Fleming et al. (24) evaluated Mediterranean-like diets with 14, 71, or 156 g lean beef/2000 kcal/d against a control diet while maintaining total protein content (17–20% of all calories), and found that all 3 experimental diets decreased LDL cholesterol and apoB, but did not affect HDL cholesterol, apoA-1, and triglyceride concentrations. Some differences were observed in the extent of reduction in total LDL particle number, but these were confined to the large LDL subclass; none of the diets decreased small LDL particles, which are particularly atherogenic (24). O’Connor et al. (27) evaluated 2 Mediterranean-like diets containing lean red meat (beef and pork) at either 28 or 68 g/d (18–19% of all calories from protein), and observed that the meat-rich pattern decreased LDL cholesterol and apoB concentrations to a greater extent than the meat-poor pattern, but this coincided with an unintended small yet significant reduction in body weight. Blood pressure improved with both diets, whereas glucose, insulin, and triglyceride concentrations did not change (27). Roussell et al. (19) found that compared with a control diet, the DASH diet with 28 g beef/d as well as 2 DASH-like diets with 113 or 153 g beef/d (18%, 19%, and 27% of all calories from protein, respectively) decreased LDL and HDL cholesterol similarly, and did not affect triglyceride, glucose, and insulin concentrations.

Two additional parallel randomized trials evaluated the effects of lean red meat consumption during hypocaloric feeding and weight loss. Sayer et al. (25) compared 2 equally calorie-restricted and high-protein diets (40–50% of all calories from protein)—one including beef at ~80 g/d and the other excluding all red meats—in men and women with overweight or obesity. After 16 wk of treatment, body weight, fat mass, LDL cholesterol, triglyceride, and blood pressure decreased significantly and to a similar extent with both diets; whereas lean body mass, glucose, and HbA1c did not change with either diet and despite weight loss (25). Hill et al. (26) evaluated DASH-like diets with 12, 139, or 196 g beef/2100 kcal/d (18%, 19%, and 27% of all calories from protein, respectively) in individuals with overweight or obesity and the metabolic syndrome, during 3 sequential phases: 5 wk of weight stability with all foods provided (eucaloric

diet), 5 wk of weight loss with all foods provided (hypocaloric diet), and 10 wk of free-living weight loss (hypocaloric diet advice only). These authors found no differences between diets in the changes in body weight, body composition, and metabolic syndrome criteria during each phase of the study (26). Our results extend these observations and demonstrate no differences in any clinically relevant outcomes between diets that contain small or large amounts of mostly lean beef, consumed ad libitum after weight loss. Further, it is evident that diet-induced changes in body composition, energy metabolism, and cardiometabolic risk factors largely depend on the physiological state with respect to energy balance and body weight homeostasis, rather than the amount of red meat in the diet (19, 24–27).

Interestingly, in our study, most cardiometabolic risk factors decreased during the weight loss phase, as expected, but several of them increased during the subsequent weight maintenance phase (i.e., rebounded towards baseline values); this was despite continued decreases in body weight and fat mass, albeit only modest ones (~1.5% weight loss). Although this apparent discrepancy can be taken to suggest an adverse effect of beef—or protein (32)—consumption, there were no significant differences between the B25 and B150 groups, and our B25 diet can hardly be considered as protein-rich or meat-rich. Rather, it represents a heart-healthy omnivorous diet of mixed macronutrient composition (19, 24, 27). Furthermore, previous studies with hypocaloric diets that led to greater amounts of weight loss (5–8%) found significant improvements in cardiometabolic risk factors that were similar for the experimental arms that contained large amounts of beef and the arms that contained little or no beef (25, 26). On the other hand, studies that examined physiological changes during 2–4 wk of weight maintenance after rapid weight loss induced by VLCDs observed an attenuation of the weight loss–induced improvements in several cardiometabolic risk factors (systolic blood pressure, fasting glucose and insulin concentrations) despite concurrent mild reductions in body weight (by an additional 0.3–0.6 kg) and fat mass (by an additional 1.2–1.9 kg), and regardless of the type of the refeeding diet (33–35); this is in agreement with our observations. We thus feel the apparent discrepancy between changes in cardiometabolic risk factor profile and changes in body weight and fat mass during the weight maintenance phase relates to the method of initial weight loss (VLCD-induced rapid weight loss) rather than to beef consumption during weight maintenance.

In our study, both diets were equally effective during the maintenance phase, independent of their beef and protein contents. In fact, body weight continued to decrease during this period, exclusively due to fat mass loss, whereas lean mass apparently increased, although some of this increase is likely because of restoration of body water content following VLCD-induced dehydration (36). Stabilization at the new, lower body weight following a period of severe negative energy balance and dynamic weight loss induced by VLCD treatment is accompanied by significant changes in body composition that are consistent with our observations—fat mass decreases and lean mass increases (33, 35). Our subjects experienced increases in REE and reported consuming significantly fewer calories during the weight maintenance period compared with their habitual intakes, changes that are likely associated with the observed changes in lean mass and body weight. Taken together, our results

demonstrate that neither meat-abundant nor high-protein diets are necessary to maintain or promote weight loss; diets with little meat and adequate protein of high biological value are sufficient. This is consistent with results from a multicenter study that evaluated the effects of high- or moderate-protein diets (25% or 15% of all calories, respectively) consumed ad libitum for ~3 y (148 wk) after subjects with prediabetes lost $\geq 8\%$ body weight (37). There were no differences in weight regain between diet arms; however, individuals consuming adequate amounts of protein (≥ 0.8 g/kg body weight/d) regained less weight than those with inadequate protein intakes (37).

Interpretation of our results is limited by the relatively short duration of the weight maintenance phase (3 mo), particularly when considering the time frame of weight regain after weight loss (3–5 y or more) (2, 3, 37). Still, this is comparable to previous studies with a similar end point—maintenance of lost weight—that followed up participants for 3–12 mo (10). Unfortunately, our study turned up slightly underpowered (69 completers as opposed to the planned 72) because of the higher than anticipated dropout rate during the weight loss phase—22% as opposed to the planned 20%—and also because 4 subjects did not meet the weight loss goal and were thus excluded from further participation. Moreover, we did not account for multiplicity, hence we cannot exclude the possibility of inflated type I error in the analyses of secondary outcomes. Nor can we rule out residual confounding due to unmeasured or unknown confounders. Our results are also limited by the greater (albeit not significantly different) discontinuation rate during weight maintenance from the B25 diet than from the B150 diet (20% and 6%, respectively; $P = 0.101$), although total attrition was identical (~36%, $P = 0.929$). Dropout rates in our study mirror those reported by Sayer et al. (25) during weight loss. In that study, twice as many participants withdrew from the “meatless” diet than the red meat diet, but differences in attrition were not statistically significant (25). These observations raise some concern about the feasibility of reducing or excluding red meat from the diet, because this food is particularly popular in industrialized countries (38, 39) and accounts for about half of all meat consumption in both sexes and all age groups (12, 13).

In conclusion, unprocessed red meat (mostly lean beef) in small or large amounts within the context of a healthy diet consumed ad libitum has similar effects on body weight, energy metabolism, and cardiovascular risk factors during the first 3 mo after clinically significant rapid weight loss. A better understanding of the dose–response in the physiological effects of meat consumption, but also of the behavioral factors that drive food choice relevant to meat, will be important for identifying a minimum amount of meat in the diet that is compatible with both individual and planetary health, and at the same time satisfies personal food preference. This information will be valuable to inform future meat reduction campaigns.

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Data Availability

Data described in the manuscript, code book, and analytic code will be made available upon request, pending approval by the corresponding and senior authors.

References

- Franz MJ, VanWormer JJ, Crain AL, Boucher JL, Histon T, Caplan W, et al. Weight-loss outcomes: a systematic review and meta-analysis of weight-loss clinical trials with a minimum 1-year follow-up. *J Am Diet Assoc* 2007;107(10):1755–67.
- Anderson JW, Konz EC, Frederich RC, Wood CL. Long-term weight-loss maintenance: a meta-analysis of US studies. *Am J Clin Nutr* 2001;74(5):579–84.
- Purcell K, Sumithran P, Prendergast LA, Bouniu CJ, Delbridge E, Proietto J. The effect of rate of weight loss on long-term weight management: a randomised controlled trial. *Lancet Diabetes Endocrinol* 2014;2(12):954–62.
- Pasman WJ, Saris WH, Westerterp-Plantenga MS. Predictors of weight maintenance. *Obes Res* 1999;7(1):43–50.
- Vogels N, Diepvens K, Westerterp-Plantenga MS. Predictors of long-term weight maintenance. *Obes Res* 2005;13(12):2162–8.
- Astrup A, Gotzsche PC, van de Werken K, Ranneries C, Toubro S, Raben A, et al. Meta-analysis of resting metabolic rate in formerly obese subjects. *Am J Clin Nutr* 1999;69(6):1117–22.
- Ravussin E, Lillioja S, Knowler WC, Christin L, Freymond D, Abbott WG, et al. Reduced rate of energy expenditure as a risk factor for body-weight gain. *N Engl J Med* 1988;318(8):467–72.
- Bosy-Westphal A, Schautz B, Lagerpusch M, Pourhassan M, Braun W, Goele K, et al. Effect of weight loss and regain on adipose tissue distribution, composition of lean mass and resting energy expenditure in young overweight and obese adults. *Int J Obes* 2013;37(10):1371–7.
- Wycherley TP, Moran LJ, Clifton PM, Noakes M, Brinkworth GD. Effects of energy-restricted high-protein, low-fat compared with standard-protein, low-fat diets: a meta-analysis of randomized controlled trials. *Am J Clin Nutr* 2012;96(6):1281–98.
- Magkos F. Protein-rich diets for weight loss maintenance. *Curr Obes Rep* 2020;9(3):213–18.
- Larsen TM, Dalskov SM, van Baak M, Jebb SA, Papadaki A, Pfeiffer AF, et al. Diets with high or low protein content and glycemic index for weight-loss maintenance. *N Engl J Med* 2010;363(22):2102–13.
- Daniel CR, Cross AJ, Koebernick C, Sinha R. Trends in meat consumption in the USA. *Public Health Nutr* 2011;14(4):575–83.
- Wyness L, Weichselbaum E, O'Connor A, Williams EB, Benelam B, Riley H, et al. Red meat in the diet: an update. *Nutr Bull* 2011;36(1):34–77.
- Micha R, Wallace SK, Mozaffarian D. Red and processed meat consumption and risk of incident coronary heart disease, stroke, and diabetes mellitus: a systematic review and meta-analysis. *Circulation* 2010;121(21):2271–83.
- Rouhani MH, Salehi-Abargouei A, Surkan PJ, Azadbakht L. Is there a relationship between red or processed meat intake and obesity? A systematic review and meta-analysis of observational studies. *Obes Rev* 2014;15(9):740–8.
- Zhang J, Hayden K, Jackson R, Schutte R. Association of red and processed meat consumption with cardiovascular morbidity and mortality in participants with and without obesity: a prospective cohort study. *Clin Nutr* 2021;40(5):3643–9.
- Zhong VW, Van Horn L, Greenland P, Carnethon MR, Ning H, Wilkins JT, et al. Associations of processed meat, unprocessed red meat, poultry, or fish intake with incident cardiovascular disease and all-cause mortality. *JAMA Intern Med* 2020;180(4):503–12.
- Geiker NRW, Bertram HC, Mejborn H, Dragsted LO, Kristensen L, Carrascal JR, et al. Meat and human health—current knowledge and research gaps. *Foods* 2021;10(7):1556.
- Roussel MA, Hill AM, Gaugler TL, West SG, Heuvel JP, Alaupovic P, et al. Beef in an optimal lean diet study: effects on lipids, lipoproteins, and apolipoproteins. *Am J Clin Nutr* 2012;95(1):9–16.
- Lehto E, Kaartinen NE, Saaksjarvi K, Mannisto S, Jallinoja P. Vegetarians and different types of meat eaters among the Finnish adult population from 2007 to 2017. *Br J Nutr* 2022;127(7):1060–72.
- Guasch-Ferre M, Satija A, Blondin SA, Janiszewski M, Emlen E, O'Connor LE, et al. Meta-analysis of randomized controlled trials of red meat consumption in comparison with various comparison diets on cardiovascular risk factors. *Circulation* 2019;139(15):1828–45.
- Lee JE, McLerran DF, Rolland B, Chen Y, Grant EJ, Vedanthan R, et al. Meat intake and cause-specific mortality: a pooled analysis of Asian prospective cohort studies. *Am J Clin Nutr* 2013;98(4):1032–41.
- Zhuang P, Jiao J, Wu F, Mao L, Zhang Y. Associations of meat consumption and changes with all-cause mortality in hypertensive patients during 11.4-year follow-up: findings from a population-based nationwide cohort. *Clin Nutr* 2021;40(3):1077–84.
- Fleming JA, Kris-Etherton PM, Petersen KS, Baer DJ. Effect of varying quantities of lean beef as part of a Mediterranean-style dietary pattern on lipids and lipoproteins: a randomized crossover controlled feeding trial. *Am J Clin Nutr* 2021;113(5):1126–36.
- Sayer RD, Speaker KJ, Pan Z, Peters JC, Wyatt HR, Hill JO. Equivalent reductions in body weight during the Beef WISE study: beef's role in weight improvement, satisfaction and energy. *Obes Sci Pract* 2017;3(3):298–310.
- Hill AM, Harris Jackson KA, Roussel MA, West SG, Kris-Etherton PM. Type and amount of dietary protein in the treatment of metabolic syndrome: a randomized controlled trial. *Am J Clin Nutr* 2015;102(4):757–70.
- O'Connor LE, Paddon-Jones D, Wright AJ, Campbell WW. A Mediterranean-style eating pattern with lean, unprocessed red meat has cardiometabolic benefits for adults who are overweight or obese in a randomized, crossover, controlled feeding trial. *Am J Clin Nutr* 2018;108(1):33–40.
- Magkos F, Hjorth MF, Asping S, Rosenkrans MI, Rasmussen SI, Ritz C, et al. A protein-supplemented very-low-calorie diet does not mitigate reductions in lean mass and resting metabolic rate in subjects with overweight or obesity: a randomized controlled trial. *Clin Nutr* 2021;40(12):5726–33.
- Kaul S, Rothney MP, Peters DM, Wacker WK, Davis CE, Shapiro MD, et al. Dual-energy X-ray absorptiometry for quantification of visceral fat. *Obesity* 2012;20(6):1313–18.
- Bingham SA. Urine nitrogen as a biomarker for the validation of dietary protein intake. *J Nutr* 2003;133(3):921S–4S.
- Christensen P, Meinert Larsen T, Westerterp-Plantenga M, Macdonald I, Martinez JA, Handjiev S, et al. Men and women respond differently to rapid weight loss: metabolic outcomes of a multi-centre intervention study after a low-energy diet in 2500 overweight, individuals with pre-diabetes (PREVIEW). *Diabetes Obes Metab* 2018;20(12):2840–51.
- Smith GI, Yoshino J, Kelly SC, Reeds DN, Okunade A, Patterson BW, et al. High-protein intake during weight loss therapy eliminates the weight-loss-induced improvement in insulin action in obese postmenopausal women. *Cell Rep* 2016;17(3):849–61.
- Coutinho SR, With E, Rehfeld JF, Kulseng B, Truby H, Martins C. The impact of rate of weight loss on body composition and compensatory mechanisms during weight reduction: a randomized control trial. *Clin Nutr* 2018;37(4):1154–62.
- Sumithran P, Prendergast LA, Delbridge E, Purcell K, Shulkes A, Kriketos A, et al. Ketosis and appetite-mediating nutrients and hormones after weight loss. *Eur J Clin Nutr* 2013;67(7):759–64.
- Vink RG, Roumans NJ, Arkenbosch LA, Mariman EC, van Baak MA. The effect of rate of weight loss on long-term weight regain in adults with overweight and obesity. *Obesity* 2016;24(2):321–7.
- Yang MU, van Itallie TB. Variability in body protein loss during protracted, severe caloric restriction: role of triiodothyronine and other possible determinants. *Am J Clin Nutr* 1984;40(3):611–22.

37. Raben A, Vestentoft PS, Brand-Miller J, Jalo E, Drummen M, Simpson L, et al. The PREVIEW intervention study: results from a 3-year randomized 2 x 2 factorial multinational trial investigating the role of protein, glycaemic index and physical activity for prevention of type 2 diabetes. *Diabetes Obes Metab* 2021;23(2):324–37.
38. Lennerz BS, Mey JT, Henn OH, Ludwig DS. Behavioral characteristics and self-reported health status among 2029 adults consuming a “carnivore diet.” *Curr Dev Nutr* 2021;5(12):nzab133.
39. Magkos F. Meat in the human diet: in transition from evolutionary hallmark to scapegoat. *Am J Clin Nutr* 2022;115(5):1263–5.