

The potential role of soyfoods in weight and adiposity reduction: an evidence-based review

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Summary

Evidence concerning the relationship between soyfoods and weight loss was reviewed. Detailed searches of PubMed and Web of Science were performed to identify and evaluate evidence for or against four propositions related to soyfoods and weight loss (Data from *in vitro*, animal, epidemiologic, and clinical studies were evaluated and summarized). (1) Certain soyfoods will improve weight and/or fat loss when fed at isolcaloric levels (similar calories given across experimental conditions, but not necessarily at a level to maintain current body weight); generally supportive evidence in animal studies, but there is no compelling support in human studies. (2) Certain soyfoods will improve weight and fat loss when included as part of a diet by affecting caloric intake; limited supportive evidence in animal and human studies. (3) Certain soyfoods will prevent/improve risk factors related to glucoregulatory function and cardiovascular health during weight loss; some evidence supporting this proposition, but additional evidence is needed before conclusions can be made. (4) Certain soyfoods will minimize the loss of bone mass during weight loss; no data available pertinent to this proposition. Limitations in existing data make it difficult to reach conclusions regarding these four propositions. Overall, the current data suggest that soyfoods are as good as other protein sources for promoting weight loss and there is a suggestive body of evidence that soyfoods may confer additional benefits, but results must be carefully interpreted and additional evidence is needed before making firm conclusions concerning soyfoods and weight loss.

Keywords: Soyfoods, weight loss, obesity, adiposity.

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Introduction

Soy consumption is generally believed to have some health benefits (1,2). In 1999, the US Food and Drug Administration permitted food labels to state that soy protein was linked to health benefits related to reduction of coronary heart disease (3). However, in 2006 the American Heart Association stated that there was insufficient clinically relevant evidence to confirm that soy protein was more beneficial than other proteins (4), but in the same report concluded 'that many soy products should be beneficial to

cardiovascular and overall health because of their high content of polyunsaturated fats, fibre, vitamins, and minerals and low content of saturated fat' (4). While the relationship between soy and cardiovascular health has been acknowledged in the past, an area of investigation often overlooked is soy's potential effects on health outcomes in relation to body composition and weight loss among obese persons (5).

Reports in animal models (6–8) and humans (9–12) have examined the relationship between soy and weight loss. The main objective of this report is to evaluate the scientific evidence regarding soy use for or in the context of weight control or adiposity reduction. We evaluate evidence as to whether soy can promote weight loss or prevent weight

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Table 1 Propositions related to soy/weight loss and evidence summaries

	<i>In vitro</i>	Animal	Epidemiologic	Clinical
1. Certain soyfoods will improve weight and fat loss when fed at prescribed isocaloric* levels.	Limited support	Generally supportive when compared with casein; magnitude of effect varied among studies	Limited data; several studies with inverse associations (i.e. higher soy consumption associated with lower weight); self-reporting is a limitation of these observational studies	No compelling support; equivalent to other protein sources during low calorie intake
2. Certain soyfoods will improve weight and fat loss when included as part of a diet by affecting caloric intake.	Not applicable	Limited support; one study identified	No compelling support; one report showed equivalent caloric intake among people consuming higher and lower amounts of soy	Limited support for short-term effects; no data for long-term effects
3. Soy will prevent/improve risk factors related to gluco-regulatory function and cardiovascular health during weight loss				
a. Soy will improve indices of glucose metabolism.	Limited support; genistein may improve glucose metabolism	Limited support; two studies identified soy to be more beneficial than casein	No compelling support	No compelling support when controlling for weight loss
b. Soy will decrease LDL cholesterol levels.	Not applicable	Some support	Limited support	Some support, but weight loss may mask soy effects
c. Soy will increase HDL cholesterol levels.	Not applicable	Limited data	Limited support; one report indicated that genistein consumption positively associated with increased HDL	Some support; two studies indicated that soy increased HDL levels in postmenopausal women
d. Soy will decrease triglycerides.	Not applicable	Generally supportive	Limited data	Generally supportive
4. Soy will minimize the loss of bone mass during weight loss.	Not applicable	Limited support	No available data during weight loss	No available data during weight loss

*By 'isocaloric' we mean the consumption of a diet containing soy compared with a diet not containing soy where the two diets contain the same total energy.

LDL, low-density lipoprotein; HDL, high-density lipoprotein.

gain or regain. Moreover, we address whether during a weight loss programme, consuming soy-based products confers some additional benefit on a 'per unit-weight loss' basis. To provide context and requisite background information, we begin with a brief overview about soybeans; the nutritional composition of soy; the types of soyfoods consumed; and the putative general health benefits potential for soy consumption. A systematic approach is then used to give a clear account of soy's potential health benefits in the context of negative energy balance (weight loss). Several propositions related to soy's effects on body weight or body composition and the associated health benefits have been formulated (Table 1). Subsequently, literature searches (PubMed and Web of Science) were performed to identify any scientific evidence germane to these propositions (Table 2). Lastly, we present current scientific evi-

dence in detail (*in vitro*, animal, epidemiologic and clinical) either supporting or refuting the propositions about soy/weight loss and the related health benefits (Table 1) and give a summary about future directions based on these data (Table 3).

Soybeans

The exact date when the soybean was initially cultivated is not known; however, most believe this occurred 4000–5000 years ago (13). *Glycine max* is the soybean currently cultivated, whereas the ancestral wild soybean plant was *Glycine soja*. Soybeans contain macro constituents including protein (35%), oil (17%) and carbohydrate (31%) (13). Soy protein, after correcting for digestibility, has an amino acid score of 1, indicating that it meets the protein needs of

Table 2 Searches for evidence to support or refute the propositions

Search engine used	Keywords (combinations)	Number of references identified (some were excluded because of lack of body weight information)
PubMed	Soy, weight loss, fat loss, cholesterol, cardiovascular, glucose, LDL, HDL, bone, osteoporosis, isoflavone	211
ISI Web of Science	Soy, weight loss, fat loss, cholesterol, cardiovascular, glucose, LDL, HDL, bone, osteoporosis, isoflavone	12 that were different from the 211 identified by PubMed

LDL, low-density lipoprotein; HDL, high-density lipoprotein.

Table 3 Limitations of current data and suggestions for future research based on current data

Limitations	Suggestions
Choice of control or comparator condition	Most experiments compare soy to casein. When differences favouring soy are observed, this invites the question of whether we are really seeing a benefit of soy relative to other protein sources in general or just poor performance of casein. More testing with other protein sources is needed.
Nomenclature of soy constituents	Develop a universal language to describe the constituents used in animal and human studies.
Few long-term randomized clinical trials comparing soyfoods to other protein sources	Compare weight loss programmes using different protein sources following patients for several years during the weight loss phase as well as during a weight maintenance phase to determine the long-term metabolic effects of soyfoods compared with other protein sources.
Few longitudinal measures of body composition during long-term soyfood consumption	Measure body composition change (fat mass, lean mass, and bone) during soyfood-based weight loss programmes to determine the long-term effects of soyfoods on weight loss, but more importantly on fat mass and bone health.

infants and adults when consumed as the only source of protein at the recommended level of protein intake (14). Micro-constituents of the soybean that have received attention in scientific research are isoflavones, saponins, phytate, phytosterols, vitamins and minerals. Genistein and daidzein, the two major isoflavones found in soy, have been studied for their antioxidant (15) and phytoestrogenic properties (16). Saponins may be involved with reduced cholesterol absorption (17,18), phytate may reduce homocysteine (19), and the phytosterols have been reported to lower cholesterol levels (20,21).

Unfortunately, there is no standardized nomenclature for soy and its various components (22). Early epidemiologic studies examined the association of traditional soyfoods such as 'soymilk' and tofu on beneficial health outcomes, while more recent experimental research focused on the direct effects of isolated soy constituents on specific biomarkers related to beneficial health outcomes. A limitation of current soy research is that soy products being tested are often not standardized and likely have differences in both macro (protein, fat and carbohydrates) and micro (isoflavones, saponins, phytic acid, phytosterols, vitamins and minerals) constituents. Standardized nomenclature is needed to advance the study of which soy components are associated with health benefits.

Fermented soyfoods (miso, soy sauce, tempeh and natto) and non-fermented soyfoods (tofu, 'soymilk' and soy sprouts) can be produced from the soybean. Today, accord-

ing to The American Soybean Association, soy is used in hundreds of consumer and industrial products (<http://www.asasoya.org/Uses/UsesSoy.htm>). Soybean utilization has expanded with a variety of soyfoods now in production including meal replacement formulations (soy drinks/shakes), breakfast cereals, energy bars, infant formula and soy 'burgers'. On average, Asian populations consume more traditional soyfoods than do Americans (2). Asian populations frequently consume tofu, miso and tempeh while Americans consume soy drinks (meal replacement), breakfast cereals, energy bars and soy 'burgers' (2). The soyfoods consumed by Americans often have soy added in the form of soy protein isolate (~90% soy protein), soy concentrate (~60% soy protein) or textured soy protein (made of mixtures of soy flour and soy concentrates and extruded); therefore, soyfoods consumed by Americans tend to be quite different from the traditional Asian soyfoods.

Putative health benefits of soy

Soy and its constituents have been investigated for several decades; hundreds of reports have studied the connections between soy consumption and health benefits and disease prevention. The diseases commonly studied include cardiovascular disease (4,23), breast (24,25) and prostate cancer (26,27), and osteoporosis (28–30). Several studies have investigated the beneficial role of soyfoods on metabolic-

related conditions like obesity (6,9,10,31–33) and diabetes (12,34). Other proposed beneficial effects of soy have been studied in relation to menopausal symptoms (35). While there are reports (*in vitro*, animal and human investigations) regarding the connections between soy and health outcomes, many of the proposed benefits have yet to be clearly supported or clearly refuted by well controlled randomized clinical trials. Results and conclusions may be conflicting because of different formulations/nomenclature of soy constituents and this makes it difficult to determine if soyfoods are as beneficial with respect to many health outcomes as proposed. A comprehensive review of soy's health benefits related to each health outcome is outside the scope of this report. The remainder of this report will evaluate the evidence regarding several propositions about soyfoods' relationships with weight loss.

Propositions related to weight loss with soyfoods

Each proposition (Table 1) will be addressed to determine if there is evidence to support that soyfoods in the context of weight/fat loss can lead to health benefits; in other words, can soyfoods provide enhanced weight or fat loss and/or provide additional and improved health benefits beyond the benefits of weight loss in general?

Proposition no. 1 Certain soyfoods will increase weight and/or fat loss when fed at isocaloric levels

In vitro data

There are limited data from *in vitro* experiments analysing the specific effects of soy constituents (mostly genistein) on adipose tissue development and apoptosis. 3T3-L1 pre-adipocytes treated with genistein (100 μM in medium) had reduced adipocyte differentiation and enhanced adipocyte apoptosis; perhaps by activating a cyclic adenosine monophosphate (AMP)-activated kinase and by generating reactive oxygen species (36). It has been suggested that genistein (100 μM in medium) modulates adipocytes by inhibiting the proliferation of both preconfluent and post-confluent 3T3-L1 pre-adipocytes (37). Similarly, genistein administration (100 μM in medium) at the onset of differentiation blocked adipocyte formation through mechanisms involved with decreased expression and decreased activation of C/enhancer binding protein (EBP)-b and downstream adipogenic transcription factors (38). Thus, *in vitro* data support the conjecture that soy constituents may inhibit adipogenesis and therefore reduce *in vivo* adiposity. Nevertheless, Barnes *et al.* (39) reported pharmacokinetic calculations involving daily intake of isoflavones, absorption from the gut, distribution to peripheral tissues and excretion, and concluded that it is unlikely that blood

isoflavone concentrations even in high soy consumers could be greater than 1–5 μM . These *in vitro* data indicate how soy and more specifically the isoflavone, genistein, may have direct effects on the adipocyte; however, interpretation of the specific effects of genistein should be made cautiously because blood and tissue levels of most isoflavones may not reach 5 μM (39).

Animal data

Animal models of obesity have demonstrated that soy consumption, in an isocaloric setting, may produce weight and fat loss. Four groups of genetically obese male mice (yellow KK) were fed an energy-restricted (60% of normal) low-fat (5%) diet containing high-protein (milk whey isolate, milk whey hydrolysate, soy isolate, or soy hydrolysate) for 2 weeks and the food intake did not differ between groups (40). During the dietary intervention period, mice lost 9.1, 9.1, 10.0 and 11.1 g of initial body weight, respectively, with mice fed the soy hydrolysate losing significantly more weight than both groups of mice fed milk whey ($P < 0.01$). Mice fed soy isolate had lower per cent body fat than mice fed milk whey isolate ($P < 0.05$), and mice fed soy hydrolysate had lower per cent body fat than both groups fed milk whey ($P < 0.05$).

In another study, male Sprague-Dawley rats were fed high-fat diets (30%) for 12 weeks to induce obesity (6). Following 4 weeks of energy-restricted (60% of normal), low-fat (5%), high-protein (35% casein, soy protein isolate, or soy protein hydrolysate) dietary intervention, rats had similar body weights with a trend for soy protein groups to have more weight loss during the 4 weeks (6). Similarly, genetically obese male mice (yellow KK) were given high-fat diets for 31 days and then switched to energy-restricted diets (6). Mice fed soy protein hydrolysate diet lost more weight than mice fed casein diet during 3 weeks of intervention ($P < 0.05$). At the end of the intervention, mice fed soy protein diets (isolate and hydrolysate) had lower body fat levels compared with casein fed animals ($P < 0.05$).

Moriyama *et al.* investigated metabolic effects of the two main soybean protein components, β -conglycinin and glycinin in normal male (ICR) and obese (KK yellow) mice (41). Following 2 weeks of high-fat feeding (30% fat by weight), three groups of ICR and three groups of KK yellow mice received energy-restricted diets (2 g day⁻¹ – 20% protein and 30% fat) for 2 weeks. The energy-restricted diets differed in protein type (casein, β -conglycinin or glycinin). ICR and KK yellow mice fed β -conglycinin diet had lower body weights ($P < 0.05$ for both strains) and lower liver weights ($P < 0.05$ for both strains) than corresponding groups fed casein diet (41).

Obese male KK yellow mice fed soy protein isolate during calorie restricted dietary intervention had significantly lower body weights and less adipose tissue (mesen-

teric, epididymal and brown fat) compared with casein fed mice ($P < 0.05$) (42). Also, obese Wistar rats fed soy protein isolate in a diet containing hydrogenated fat (4% hydrogenated fat plus 1% corn oil) or corn oil (5%) had lower body weights and lipogenic enzymes than rats fed casein following 3 weeks of feeding (43). However, obese Wistar rats fed soy protein isolate as part of a calorie restricted dietary intervention did not differ in body weight compared with rats fed isocaloric casein diet (44).

Subcutaneous injections of genistein (80 and 200 mg kg⁻¹ day⁻¹) for 21 days in adult (12–13-week-old) ovariectomized (OVX) obese C57BL/6 mice caused reduced adipose weight ($P < 0.05$) without a difference in body weight (45). Likewise, juvenile (25–27-day-old) mice injected with genistein (20 and 80 mg kg⁻¹ day⁻¹) for 28 days had decreased parametrial fat pad weight ($P < 0.05$) and decreased adipocyte circumference ($P < 0.05$) compared with controls (45). This finding is potentially meaningful because adipocyte size has been shown to be a predictor of ill health even conditional on total adiposity (46). Similarly, OVX obese C57BL/6 mice (25–27-day-old) fed diets containing genistein (0–1500 p.p.m.) for 12 days had dose responsive decreases in fat pad weights compared with controls (45). Genistein serum concentrations from mice administered genistein did not exceed 4 μM for any dose (45) which are attainable levels in humans consuming high levels of soyfoods (39).

The effects of soy protein and exercise were evaluated in four groups of male Sprague-Dawley rats (casein diet/sedentary; casein diet/exercised; soy diet/sedentary; or soy diet/exercised) (47). Exercise training consisted of swimming 120 min day⁻¹ for 6 days week⁻¹ over a 2-week period. Retroperitoneal adipose tissue mass was less in the rats that exercised compared with sedentary rats; soy protein fed rats had less epididymal adipose tissue compared with rats fed casein diet (47). A similar experiment was performed to investigate effects of a combined intervention with dietary isoflavones (daidzin, genistin and glycitin plus glycitein – Fujiflavone P40) and exercise (treadmill; 30 min day⁻¹, 6 days week⁻¹ at 12 m min⁻¹ up a 10 degree slope) in obese OVX ddY mice fed a high cholesterol diet to induce obesity (8). Six groups of mice were studied: sham operated mice (lean controls), OVX (obese controls), OVX with isoflavone-supplemented diet, OVX with exercise, OVX with both isoflavone-supplemented diet and exercise, and OVX given estradiol injections (to mimic lean controls). Isoflavone supplementation partially protected the OVX mice from becoming obese; the combination of isoflavone and exercise completely reduced body fat mass back to the lean control level after 6 weeks of intervention (8).

Obese male Zucker rats were randomized into four groups ($n = 10$ /group) to investigate the effects of casein-based diets (control and rosiglitazone) and soy-based diets

(low and high isoflavone) on body weight and adiposity (34). Control and rosiglitazone-treated rats did not receive any soy protein or isoflavones during the 11-week treatment. Compared with controls, rats fed high isoflavone diet had decreased plasma lipids ($P < 0.05$), decreased liver weight ($P < 0.05$), decreased body weight ($P < 0.05$) and less body fat at the end of the intervention (34). Another study showed that obese female Zucker rats fed soy protein diet containing genistein (700 mg kg⁻¹ BW) gained more weight than rats fed casein protein diet ($P < 0.05$); however, visceral fat depots were not different between the two groups (48). Male rats treated with soy protein and high isoflavone did not differ from controls in body weight gain (48).

Male Wistar rats were fed a cholesterol-enriched diet for 3 weeks and then randomly assigned to one of the following four dietary groups for an additional 3 weeks: standard chow; standard chow plus fermented soy product with supplemented isoflavones (Isoflavin, Galena Quimica e Farmaceutica Ltda, Campinas, Brazil); standard chow plus placebo; and standard chow plus placebo with supplemented isoflavones (31). Isoflavin contained genistein, daidzein, glycitein and their glycoside derivatives. Two control groups were fed either chow or cholesterol-enriched diets over the entire 6 weeks. Food intake and body weight were not different among groups after 3 weeks of dietary intervention; however, both groups receiving supplemented isoflavones had smaller adipocyte circumference (larger adipocyte size has been associated with ill-health (46)) in epididymal and retroperitoneal fat pads compared with rats fed standard chow ($P < 0.05$) (31).

Dietary genistein (250 mg kg⁻¹ diet) was given to yellow agouti mice during gestation at levels attainable by humans consuming high soy diets (49). Genistein-supplemented offspring were protected from developing obesity in adulthood with 23% at normal weight compared with only 10% of un-supplemented offspring (49). This experiment suggests that *in utero* dietary genistein may influence gene expression and modify susceptibility to obesity in adulthood by permanently altering the epigenome.

Data from these animal models, when isocaloric diets are administered, although not perfectly consistent, are generally supportive for soy and/or its constituents to improve weight and fat loss.

Epidemiologic data

The Shanghai Women's Health Study reported that women consuming high amounts of soy protein (>12.61 g day⁻¹) did not have different body mass index (BMI) levels compared with women consuming less soy protein (50), while another report suggested that consumption of isoflavone-rich foods (based on self-reported food intake) was associated with lower BMI and lower waist and hip measures in women (51). Japanese women (both premenopausal and

postmenopausal) consuming no natto (fermented soybean) did not differ in weight or BMI compared with women who consumed 1–2 servings per week or >2 servings per week (52). Findings from the VITamins And Lifestyle cohort study (7633 men and 8022 women from western Washington state) showed that soy supplements did not reduce the amount of weight gained during an 8–12-year period in men or women regardless of starting BMI (53). Postmenopausal women consuming high levels of genistein (≥ 1.0 mg day⁻¹) had lower BMI than women consuming no genistein ($P < 0.05$) (54). Men and women categorized as soybean eaters participating in the World Health Organization-Cardiovascular Diseases and Alimentary Comparison Study had significantly lower BMI compared with non-soybean eaters (55).

These epidemiologic data provide inconsistent evidence for a relationship between soy consumption and lower body weights or reduced obesity.

Clinical data

Studies investigating weight loss in overweight and obese humans suggest that soy, as a source of dietary protein, may be used to achieve significant weight loss; however, there is no convincing evidence to show whether soy protein is better than other protein sources to achieve weight loss (10,56,57). Anderson *et al.* (10) evaluated the effects of soy-based and milk-based meal replacements on weight loss in women and men (BMI 27–40 kg m⁻²) who were assigned to low-energy diets (1200 kcal day⁻¹). During the 12-week randomized trial, the soy protein group was instructed to consume five soy-based shakes (Scan-Diet™) per day and the milk protein group was instructed to consume two milk-based shakes (Slim-Fast®) per day as part of the low-energy diet. Soy and milk consumers lost 9.0% (95% CI, 7.3–10.6%) and 7.9% (5.8–8.8%) of their initial body weights, respectively, with no significant differences in weight loss between the two groups over the intervention period. Soy and milk meal replacements resulted in significant reductions in waist circumferences ($P < 0.0001$), but the two groups were not different ($P = 0.21$). Both soy and milk protein, as a meal replacement during this weight loss trial, produced similar results on weight and central adiposity. However, it must be noted that isocaloric prescriptions are not necessarily equivalent to isocaloric feeding because of potential differences in compliance.

In a randomized trial, 43 women (BMI = 30–40) were placed on intensive dietary interventions using casein ($n = 21$) or soy ($n = 22$) shakes (58). Each participant was instructed to consume three shakes, one pre-packaged entrée, and five servings of fruits and vegetables daily to have a total energy intake between 4.5 and 5 MJ day⁻¹ over a 16-week period. The average weight loss among participants was 8.1% of initial weight at 8 weeks and 13.4% at

16 weeks. At the end, there was no difference in weight loss between groups with casein completers losing 14.0% and the soy completers losing 12.8%. Per cent body fat loss was not significantly different between groups with casein completers losing 23.7% and soy completers losing 21.8%. These data show that soy protein and casein meal replacement shakes can be used during a structured weight loss programme with no differences in outcome.

One hundred obese adults received either dietary counselling (controls) or a 1200 kcal day⁻¹ (soy-based meal replacement with Scan Diet Shakes™) diet plan for 12 weeks (9). Among completers, weight loss was significantly greater in the soy-based diet group compared with controls (-7.1 kg vs. -2.9 kg; $P = 0.0001$). There was a significant difference in fat mass loss at 8 and 12 weeks between the subjects on the soy-based diet compared with controls (-3.0 kg vs. -1.7 kg; $P = 0.011$ at 8 weeks and -4.3 kg vs. -1.4 kg; $P = 0.003$ at 12 weeks). These data indicate that soy meal replacement shakes can be used during a weight loss programme and this programme was better than dietary counselling.

Bosello *et al.* (56) evaluated 24 obese patients (60% above ideal body weight) aged 25–42 years for the effects of casein or soy protein on body weight. The patients received a 375 kcal day⁻¹ diet for 15 days followed by a 425 kcal day⁻¹ diet for 60 days; regardless of protein source (casein vs. soy) subjects lost equivalent weight ($-5.9 \pm 2.0\%$ vs. $-5.2 \pm 2.0\%$ after 15 days and $-14.1 \pm 3.6\%$ vs. $-13.5 \pm 4.0\%$ after 60 days) (56). Similarly, Yamashita *et al.* (57) tested the effects of protein source on weight loss in 36 overweight or obese women in a 16-week parallel-design trial with two isocaloric diets designed for weight loss. One group of women received red meat as their protein while the other group had soybeans as the protein. Regardless of protein source, weight loss (lost 9% of baseline in 16 weeks) and the metabolic benefits of weight loss occurred equally among the women (57).

In a randomized double-blind placebo-controlled study, subjects were given β -conglycinin (one of the major storage proteins in soy protein isolate) candy pieces (88% pure β -conglycinin, 5% soy protein, 2% minerals and 5% water) or taste matched placebo candy pieces (59). Weight (-2.7 kg - β -conglycinin vs. $+2.7$ kg - placebo) and visceral fat (-6.5 cm² - β -conglycinin vs. $+6.1$ cm² - placebo) were significantly reduced in the β -conglycinin group following a 20-week intervention ($P < 0.05$ for both).

Ninety obese subjects were placed into three treatment groups: lifestyle education (prescribed to consume 1200–1500 kcal day⁻¹ for women and 1500–1800 kcal day⁻¹ for men); soy protein diet (two meals per day were substituted with Almased®, a soy-yogurt-honey preparation, for the initial 6 weeks and one meal per day was substituted with Almased® for the final 18 weeks - prescribed to consume 1000–1200 kcal day⁻¹ for initial 6 weeks and 1500–

1700 kcal day⁻¹ for the final 18 weeks) plus exercise (two 60-min bouts of exercise per week); and soy protein diet without exercise (11). Both soy diet groups lost more weight than lifestyle education group (8.9 ± 3.9 kg vs. 6.2 ± 4.2 kg; $P = 0.048$) and there was a trend for subjects given soy diet to lose more fat mass than subjects given lifestyle education [8.8 ± 4.3 kg and 9.4 ± 4.5 kg (exercise) vs. 6.6 ± 4.6 kg; $P = 0.053$] (11). However, these results could be simply attributable to the effects of providing meal replacements as opposed to the soy or its constituents *per se*.

The effects of pork-meat protein, soy protein and carbohydrate on 24-h energy expenditure were evaluated in 12 healthy, overweight and mildly obese non-smoking men (60). In this randomized single-blind, three-way crossover study lasting 4 days, substituting carbohydrate (17–18% of energy) with either pork-meat or soy protein produced a 3% higher 24-h energy expenditure. Pork-meat consumption actually produced 2% higher 24-h energy expenditure than soy (60).

These clinical data suggest that soy protein may be as good as other protein sources for achieving weight loss in prescribed isocaloric settings, but suggest that soy consumption does not have a clear advantage over other protein sources for weight and fat loss when prescribed at isocaloric levels. In this light, it is noteworthy that the comparator in most of these studies is another protein source (i.e. milk protein) which is sensible if one wishes to determine whether soy has an effect through some property other than just being a good protein, but not if one is simply interested in soy as a good source of protein.

Proposition no. 2 Certain soyfoods will improve weight and fat loss when included as part of a diet by affecting caloric intake

In vitro data

N/A

Animal data

Semon *et al.* demonstrated that type of protein presented to rats may cause an initial reduction or an initial increase in food intake (61). Rats were acclimated to a high-protein mixture diet containing casein, lactalbumin, egg white and soy for 2 weeks. Food intake was measured during a 3-day pre-test period. Following the 3-day pre-test period, rats were given the diet containing the protein mixture or a diet containing only one of the four proteins. During the first 15-min interval, rats eating diets containing protein mixture, lactalbumin, egg white or soy protein depressed their intake significantly compared with the average intake from the 3-day pre-test period; whereas rats eating casein diet increased their intake (61).

These limited data make it difficult to confirm, but do suggest that soy protein, along with other protein sources, may reduce short-term caloric intake in animals.

Epidemiologic data

From the Shanghai Women's Health Study, women consuming greater than 12.61 g day⁻¹ of soy protein had equivalent caloric intake as women consuming less soy protein (50).

Clinical data

Lang *et al.* (59) examined the effects of three dietary protein types (casein, gelatin and soy) on satiety and food intake at two levels of loading (1.8 and 3.6 megajoules) (62). The meals were controlled for energy, macronutrients, fibre and palatability; all meals contained 23% energy as protein. Nine healthy normal weight men were administered the meals and had subjective satiety and hunger levels measured during 24 h following meal. The type of protein did not affect 24-h energy or macronutrient intakes and there were inconsistent effects on satiety and hunger levels (62).

To test the effects of protein preloads on short-term food intake, young men (18–35-year-old) were given isolates of whey, soy protein, or egg albumen in sweet and flavoured beverages (400 mL) at 09.00 h following an overnight fast; a pizza meal was then offered at 1 and 2 h after the preload and the amount of pizza consumed was measured. Subjects given whey and soy protein preloads, but not egg albumen, consumed less pizza than controls at 1 h after the preload (63); however, replacing half of the soy protein preload with either glucose or amylose did not cause a suppression of pizza intake as seen with the complete soy protein preload. When soy protein preload was given at 11.00 h rather than 09.00 h, the amount of pizza consumed at 1 h after the preload was not different from controls (63).

Forty-two overweight adult females were evaluated for the effects of preloading with mycoprotein (a food made by continuous fermentation of the fungus, *Fusarium graminearum*), tofu and chicken on hunger and satiety (64). Isocaloric preload meals were made from mycoprotein, tofu, or chicken and subjects were given these meals over a 3-day period before lunch each day. Following the complete consumption of the preload meal, subjects were given *ad libitum* access to sandwiches in the laboratory. Total food intakes at lunch and dinner were measured each day and hunger and satiety levels were accessed using visual analogue scales. Subjects given mycoprotein and tofu preload meals consumed less food during lunch compared with subjects given chicken, and this decrease at lunch was not compensated for during the subsequent dinner (64). Mycoprotein and tofu exhibited satiating properties that persisted for several hours following the meal.

These data give limited support that soy might increase short-term satiety, but extensive follow-up trials are needed to determine if soyfoods, as part of a dietary weight loss programme, actually cause increased satiating effects chronically which would result in weight loss.

Proposition no. 3 Soy will prevent/improve risk factors related to glucoregulatory function and cardiovascular health during weight loss

Several reviews have suggested that soyfood consumption and soy protein supplementation can improve health benefits related to cardiovascular disease (4,23,65); however, only a few studies have measured health benefits in the context of weight loss. Another major concern for overweight and obese individuals is the development of diabetes which involves abnormal insulin action and the progression of hyperglycemia. Bhathena and Velasquez reviewed, *in vitro*, animal and human data about the effects of soy and phytoestrogens on obesity and diabetes (66) and a comprehensive meta-analysis was performed by Reynolds *et al.* looking at the effect of soy protein supplementation on serum lipids (65). This section is devoted to discussing the role of soy in improving risk factors related to glucoregulatory function and cardiovascular health, specifically during weight loss.

Proposition no. 3a Soy will improve indices of glucose metabolism

In vitro data

Soybean extract (an ethanol extraction from Solbar Hatzor Ltd., Ashdod, Israel) inhibited glucose uptake in brush border membranes from rabbit intestines (67), and the isoflavone, genistein (100 μ M), increased basal insulin secretion in pancreatic islet cells (68). Similarly, Liu *et al.* (69) demonstrated that genistein, at concentrations that could be obtained in individuals consuming soy products, exerted a novel insulinotropic effect (regulated insulin secretion) on mouse pancreatic islet cells. In rat hepatocytes, genistein decreased incorporation of glucose into lipids and decreased the number of insulin receptors (70), and in rat adipocytes, genistein inhibited glucose conversion to total lipids, stimulated basal lipolysis and inhibited insulin-stimulated glucose oxidation (71). Szkudelski *et al.* found that genistein significantly affects lipogenesis and lipolysis in isolated rat adipocytes (72) and that adipocytes from Wistar rats administered genistein (5 mg kg⁻¹ BW) for 3 days had diminished leptin secretion (73). These data indicate that soy isoflavones, especially genistein, have an effect on both glucose and lipid metabolism *in vitro* and suggest that soy isoflavones may be effective at reducing diabetes by inhibiting lipogenesis and enhancing lipolysis in the hepatocyte and adipocyte (66).

Animal data

Serum glucose was lower in the ICR mice fed β -conglycinin compared with ICR mice fed casein ($P < 0.05$) and serum insulin was lower in ICR and KK yellow mice fed β -conglycinin compared with the groups fed casein ($P < 0.05$ for both strains) (41). Male obese KK yellow mice fed soy protein isolate had lower plasma glucose levels compared with casein fed mice (42). Male Sprague-Dawley rats were fed one of the following protein-carbohydrate sources for 28 days: casein-cornstarch, casein-sucrose, soy protein isolate-cornstarch, soy protein isolate-sucrose, cod protein-cornstarch, or cod protein-sucrose. Rats fed the soy protein-cornstarch diet had lower plasma glucose concentrations than rats fed casein-cornstarch or soy protein isolate-sucrose. These lower glucose levels were accompanied by trends for reduced energy intake and less fat gain in rats fed soy protein isolate (74).

To investigate the effects of protein diets on glucose tolerance, peripheral insulin sensitivity and postprandial plasma glucose and insulin responses, male Wistar rats were fed diets containing casein, cod, or soy protein for 28 days (isoenergetic diets to prevent weight gain loss⁻¹). Body weights and energy intake did not differ between the different protein-fed groups. Fasting plasma glucose was lower in the cod protein- and soy protein-fed rats compared with the casein protein-fed rats ($P < 0.05$). After intravenous glucose loading, cod protein- and soy protein-fed rats had lower incremental areas under glucose curves compared with casein-fed animals ($P < 0.05$). Using a hyperinsulinemic euglycemic clamp, peripheral insulin sensitivity was measured; higher glucose disposal rates were found in the cod protein- and soy protein-fed rats (15.2 ± 0.3 and 13.9 ± 0.6 mg kg⁻¹ min⁻¹ respectively) compared with casein-fed animals (6.5 ± 0.7 mg kg⁻¹ min⁻¹, $P < 0.05$), indicating that cod protein and soy protein diets improved peripheral insulin sensitivity (75). Plasma glucose levels in Wistar rats fed a soy protein diet containing either 9% partially saturated beef tallow (with 1% corn oil), 10% corn oil or 10% fish oil for 3 weeks were not different from casein-fed rats (76).

Obese male ZDF rats were randomized to four groups [$n = 12$; chow, chow plus stevioside (isolated from *Stevia rebaudiana*, Maringa, Parana, Brazil), chow plus 50% soy protein (Abalon, Nutri Pharma ASA, Oslo, Norway), and chow plus stevioside and soy] to compare the dietary effects of stevioside and soy protein on metabolic syndrome. Throughout the experiment, fasting glucose levels tended to be lower in the soy-treated groups compared with the chow only and chow plus stevioside groups (77).

These animal data provide some evidence for soy to have beneficial effects on glucose metabolism, especially when soy-based diets are compared with casein-based diets. However, extensive follow-up experiments will be needed to determine if soy intake actually causes positive

glucoregulatory function above and beyond those conferred by weight loss alone.

Epidemiologic data

Postmenopausal women enrolled in the Soy Health Effects (SHE) Study were categorized into one of the following for genistein intake: none, moderate (0.001–0.999 mg day⁻¹), or high (≥ 1.0 mg day⁻¹) (54). Fasting glucose levels were not different among the three groups. Data from the Shanghai Women's Health Study showed that postmenopausal women with low BMI (<25) who consume high amounts of soy protein (>12.61 g day⁻¹) have decreased risk of glycosuria when compared with women with low BMI (<25) who consume low levels of soy protein (<4.09) (50).

Clinical data

In a randomized clinical trial, soy-based meal replacement was compared with an individualized diet plan (American Diabetes Association) for weight loss and metabolic profile (12). In total, 104 subjects were randomized prospectively to the two treatments for a total of 12 months and 77 completed the study. The soy group lost a higher percentage of weight than the individualized diet plan group ($P < 0.05$; $4.57 \pm 0.81\%$ vs. $2.25 \pm 0.72\%$ respectively). Fasting plasma glucose was significantly reduced in the soy group compared with individualized diet plan group at 6 months ($P < 0.0001$; 126.4 ± 4.9 mg dL⁻¹ vs. 152.5 ± 6.6 mg dL⁻¹) but not at 12 months. These data suggest that a soy-based meal replacement protocol can be used for weight reduction in diabetic patients, and cause a positive effect on glycemic control (12).

In a randomized, placebo-controlled, double-blind crossover study, there were no effects of isoflavone enriched (Solbar Plant Extracts, Ltd, Ashdod, Israel; 50 mg day⁻¹) cereal bars (Efamol, Ltd, Manchester, United Kingdom; 2x day⁻¹ for 8 weeks) on lipids, glucose, or insulin in healthy postmenopausal women (78). Another randomized, double-blind, placebo-controlled clinical trial evaluated the effects of soy isoflavones and conjugated equine oestrogen on glucose and insulin in postmenopausal Taiwanese women (79). The soy isoflavone group ($n = 17$) received 100 mg isoflavone soft capsules (Novasoy, Archer Daniels Midland, Decatur, IL, USA), 300 mg calcium, and a blank vitamin capsule each day and the oestrogen replacement group ($n = 11$) received 0.625 mg conjugated oestrogen, 300 mg calcium, and blank isoflavone soft capsules each day for 6 months. Fasting glucose was significantly lower after isoflavone consumption ($P = 0.001$; 102 ± 18 mg dL⁻¹ at baseline vs. 81 ± 25 mg dL⁻¹ at 6 months). Estrogen treatment was also followed by significantly reduced fasting glucose ($P = 0.001$; 118 ± 46 mg dL⁻¹ at baseline vs. 92 ± 21 mg dL⁻¹ at 6 months). Insulin levels were also significantly reduced after isoflavone and oestrogen treatments ($P = 0.005$).

These results suggest that soy isoflavones (100 mg) and conjugated oestrogen (0.625 mg) may equally lower fasting blood glucose and insulin levels in postmenopausal women (79).

Proposition no. 3b Soy will decrease low-density lipoprotein (LDL) levels

In vitro data

N/A

Animal data

Obese female and male Zucker rats fed soy protein diet containing genistein (700 mg kg⁻¹ BW) had significant reductions in plasma cholesterol compared with their respective controls ($P < 0.05$) (48). Female rats, regardless of experiencing significant weight gain, had improved cholesterol levels during the 11 weeks of isoflavone dietary intervention (48).

Spontaneously hypertensive/NIH-corpulent rats (obese) and lean littermates were assigned to one of four dietary groups ($n = 8$ /group; 20% casein, 20% casein with 0.1% isoflavone mixture, 20% casein with 0.1% probiotic mixture, or 20% casein with 0.1% isoflavone mixture +0.1% probiotic mixture) and were fed these diets for 20 weeks (80). Obese and lean rats fed isoflavones (alone or with probiotic) had less fat deposition in several fat depots while probiotics alone had no significant effect on fat depots (80). Lean rats fed isoflavones had lower total, LDL and high-density lipoprotein (HDL) cholesterol compared with lean rats not fed isoflavones, while obese rats fed isoflavones had lower total and LDL cholesterol compared with obese rats not fed isoflavones; probiotics had no significant effect. These results indicate that soy isoflavones may lower plasma cholesterol and that probiotics did not enhance the effect of isoflavones (80).

To compare the dietary effects of stevioside and soy protein on metabolic syndrome (77), obese male ZDF rats were randomized to four groups for a 10-week dietary intervention: chow, chow plus stevioside, chow plus 50% soy protein, and chow plus stevioside and soy. Without significant differences in body weight or body composition, rats fed soy protein had lower fasting total cholesterol levels than rats fed chow only or chow plus stevioside ($P < 0.01$) (77).

These limited data give some support but do not give clear evidence that soyfood consumption will lower LDL cholesterol during weight loss in animal models.

Epidemiologic data

Total cholesterol and BMI were inversely related to 24-h urinary isoflavone excretion in men and women participating in the World Health Organization-Cardiovascular Diseases and Alimentary Comparison Study (55). Also,

subjects categorized as soybean eaters had lower total cholesterol and BMI compared with non-soybean eaters (55).

Clinical data

One hundred obese adults received either dietary counselling (controls) or a 1200 kcal day⁻¹ (soy-based meal replacement with Scan Diet Shakes) diet plan for 12 weeks (9). At the end of the 12-week trial, both total cholesterol ($P = 0.013$) and LDL cholesterol ($P = 0.009$) were reduced significantly in the diet group compared with controls. Total cholesterol was reduced by 26.1 mg dL⁻¹ in the diet group and 6.7 mg dL⁻¹ in the control group ($P = 0.0012$) and LDL was reduced by 21.6 mg dL⁻¹ in the diet group and 5.5 mg dL⁻¹ in the control group ($P = 0.0025$). These reductions in cholesterol remained significant even after accounting for the significant weight loss among the subjects on the soy-based diet (9).

The effects of a 12-week soy-based and milk-based meal replacement intervention (1200 kcal day⁻¹ diet plan) on lipids in women and men (BMI 27–40 kg m⁻²) were evaluated (10). Reductions from baseline in serum cholesterol and LDL-cholesterol values, respectively, at 6 weeks were significantly greater ($P < 0.015$) with soy meal replacement (15.2% and 17.4%) than with milk meal replacement (7.9% and 7.7%). Women (BMI 30–40 kg m⁻²) consuming either soy ($n = 22$) or casein ($n = 21$) meal replacements as part of an energy-restricted diet had significantly lower LDL-cholesterol values at 8 and 16 weeks of intervention compared with baseline; however, LDL-cholesterol values did not differ between treatments (58).

Ninety overweight/obese adults were randomized into two groups and prescribed one of the following patterns of calorie restriction for 40 weeks: (i) 12 weeks of 1200 kcal day⁻¹–16 weeks of 1500 kcal day⁻¹–12 weeks of 1800 kcal day⁻¹; and (ii) 28 weeks of 1500 kcal day⁻¹–12 weeks of 1800 kcal day⁻¹ (33). Scan Diet Shakes were used as the soy-based meal replacement formula during the dietary intervention for both groups. Both patterns of calorie restriction using the Scan Diet formula were associated with significant weight loss and reduced waist circumference. LDL and HDL cholesterol were reduced in the groups and the HDL/total cholesterol index was significantly improved (33).

A total of 156 hypercholesterolemic volunteers were put on the National Cholesterol Education Program Step I diet for 9 weeks (81). Each patient received one of five diets (25 g casein protein or 25 g of isolated soy protein with 3, 27, 37, or 62 mg of isoflavones). Subjects on the isolated soy protein diet with 62 mg of isoflavones had significantly lower levels of total cholesterol (4%) and LDL cholesterol (6%) compared with subjects on the casein diet ($P = 0.04$ and 0.01 respectively). Subjects with the highest LDL levels given the soy protein isolate with 62 mg of isoflavones had reductions of 9% for total cholesterol and 10% for LDL

which were significantly different from the casein group ($P < 0.001$ and $P < 0.03$ respectively). Similarly, subjects with elevated LDL levels at the beginning that were on the isolated soy protein containing 37 mg of isoflavones had significant reductions in total cholesterol and LDL compared with casein ($P = 0.007$ and $P = 0.02$ respectively) (81).

Subjects ($n = 13$) given a very low saturated fat portfolio diet (high plant sterols, soy protein, viscous fibres and almonds) compared with subjects ($n = 12$) on a low saturated fat control diet (whole-wheat cereals and low-fat dairy) had similar weight loss (1.0 and 0.9 kg respectively) (82). The portfolio diet group had significantly reduced LDL and LDL : HDL ratios compared with subjects on the control diet ($35.0 \pm 3.1\%$ vs. $12.1 \pm 2.4\%$; $P < 0.001$ and $30.0 \pm 3.5\%$ vs. $5.1 \pm 3.0\%$; $P < 0.001$) (82).

Postmenopausal women were randomized into three dietary supplementation groups (milk protein; soy protein without isoflavones; or soy protein with 80 mg aglycone isoflavones) and followed for 12 weeks (83). Women were instructed to not consume soyfoods during the supplementation period and advised to maintain their weight. The soy with isoflavones resulted in reduced LDL compared with the soy without isoflavones ($P < 0.005$), but was not different from the milk group (83).

To evaluate the effects of soy protein on cholesterol levels, postmenopausal women completed four 6-week diet interventions separated by 2-week washout periods (84). The following four diets were given to the women: soy protein isolate; soy protein isolate plus probiotic capsules; milk protein isolate; and milk protein isolate plus probiotic capsules. Soy protein isolate (SUPROSOY; The Solae Company, St. Louis, MO, USA) contained 1.16 mg isoflavones g⁻¹ powder (women were asked to substitute the protein isolates for their normal protein containing foods in order to prevent weight gain). Soy consumption significantly decreased plasma total cholesterol by 2.2% ($P = 0.02$) and LDL by 3.5% ($P = 0.005$); among hypercholesterolemic women, total cholesterol was significantly decreased by 3.3% ($P = 0.01$) and LDL by 4.5% ($P = 0.004$) (84).

These clinical data indicate that soy may have beneficial effects on LDL cholesterol, but more randomized clinical trials will be needed to make a conclusion about what type of soy and which populations will benefit most with soyfood consumption. Moreover, these studies have not carefully assessed whether soy causes a greater reduction in LDL independent of any weight loss effects or potentiates the effects of weight loss on LDL reduction.

Proposition no. 3c Soy will increase HDL levels

In vitro data

N/A

Animal data

Genistein (8 mg kg⁻¹ body weight day⁻¹) and control diets were administered to adult female and male NIH/S mice for 8 weeks (85). Females fed genistein had higher plasma HDL cholesterol compared with controls ($P < 0.05$; 3.34 ± 0.24 and 2.10 ± 0.35 mmol L⁻¹ respectively) while males fed genistein were not different from controls (2.64 ± 0.25 and 3.15 ± 0.18 mmol L⁻¹ respectively) (85). Obviously, more experiments will be needed to examine the effects of soy and its constituents on HDL in animal models during weight and fat loss experiments.

Epidemiologic data

The SHE study investigated the extent to which isoflavone use can improve heart disease risk in postmenopausal women (54). Subjects ($n = 208$) were screened for baseline levels of cholesterol, triglycerides, HDL and LDL. Dietary intake was evaluated using a standardized questionnaire; anthropometric measures and blood pressure were obtained; and a 75 g oral glucose tolerance test was administered. The levels of genistein consumption ranged from none to 13.9 mg day⁻¹ with a group average of 1.3 ± 2.4 mg day⁻¹. Genistein, daidzein and total isoflavone intake were positively associated with HDL cholesterol ($P = 0.05$) and inversely with postchallenge insulin ($P = 0.05$) (54).

Clinical data

After 8 weeks on an energy restricted diet with incorporation of either soy ($n = 22$) or casein ($n = 21$) meal replacement shakes, women (BMI 30–40 kg m⁻²) had significantly decreased HDL-cholesterol compared with baseline values; however, at 16 weeks on the intervention, HDL-cholesterol values were not significantly different from baseline in either group (58).

To determine the effects of soy protein on HDL, hypercholesterolemic, postmenopausal women were randomly assigned to the following three groups: isolated soy protein containing moderate concentrations of isoflavones (ISP56, Supro 675, Protein Technologies International, St. Louis, MO, USA), isolated soy protein containing higher concentrations of isoflavones (ISP90), or casein and non-fat dry milk (CNFDM; New Zealand Milk Products, Wellington, New Zealand) (86). After 6 weeks of intervention, women consuming the ISP56 had significantly higher HDL cholesterol than the CNFDM group ($P < 0.05$) and this elevation continued throughout the remainder of the 26-week intervention. Women on the ISP90 had significantly higher HDL than women given CNFDM at week 18 of the intervention ($P < 0.05$) and this continued to the end of the intervention (86).

The effects of soy protein on cholesterol levels were examined in postmenopausal women who completed four 6-week diet interventions separated by 2-week washout

periods (84). Overall, soy consumption significantly increased HDL cholesterol by 4.2% ($P = 0.006$) and hypercholesterolemic women had significantly increased HDL levels during soy consumption periods (4.2%; $P = 0.02$) (84).

Proposition no. 3d Soy will decrease triglycerides (TGs)

In vitro data

N/A

Animal data

Male and female obese Zucker rats were fed either casein control diet, low-isoflavone soy protein diet, or high-isoflavone soy protein diet (48). Female rats fed high-isoflavone soy diet gained significantly more weight than casein and low-isoflavone fed animals; however, both male and female rats fed high-isoflavone soy diets had improved lipid metabolism. Liver triglyceride and cholesterol concentrations were significantly lower in rats fed high-isoflavone compared with rats fed casein (48). Another study reported that an isoflavone supplement, Fujiflavone P40, significantly decreased total cholesterol, HDL cholesterol and triglyceride levels in OVX rats (87).

In ICR mice, serum triglyceride levels were significantly lower ($P < 0.05$) in β -conglycinin-fed mice (13.0 ± 1.3 mg dL⁻¹) compared with mice fed casein (21.8 ± 2.0 mg dL⁻¹) or glycinin (18.5 ± 3.4 mg dL⁻¹) following 28 days of treatment (41). KK yellow mice had significantly lower triglyceride levels ($P < 0.05$) when fed β -conglycinin (6.6 ± 1.0 mg dL⁻¹) compared with casein (9.6 ± 0.9 mg dL⁻¹) or glycinin (9.3 ± 1.0 mg dL⁻¹) (41). Similarly, obese KK yellow mice fed soy protein isolate as part of a caloric-restricted diet had lower plasma triglycerides compared with casein fed mice (42).

Obese male ZDF rats were randomized into these four groups: chow, chow plus stevioside, chow plus 50% soy protein, and chow plus stevioside and soy. At the end of the 10-week intervention, without significant differences in body weight or body composition, rats fed soy protein had lower fasting triglyceride levels than rats fed chow only or chow plus stevioside ($P < 0.01$) (77).

These animal data provide some supportive evidence for soy to lower triglycerides, but more experiments will be needed to determine if soy can lower triglycerides during weight loss.

Epidemiologic data

N/A

Clinical data

A randomized crossover dietary intervention study was performed to compare effects of lean meat (red meat;

150 g day⁻¹) and soy (tofu; 290 g day⁻¹) on lipids in healthy middle-aged men ($n = 42$) (88). Half of the subjects were first put on the lean meat diet for 4 weeks, followed by a 2-week washout, then they were put on the tofu diet for 4 weeks and the other half were put on the tofu first. Triglyceride levels were significantly lower in subjects while they were on the tofu diet ($P = 0.017$); however, HDL cholesterol was also lower on the tofu diet ($P = 0.01$) (88).

Bosello *et al.* (56) evaluated 24 obese patients for the effects of casein and soy protein on body weight during a very low energy diet programme. The patients received a 375 kcal day⁻¹ diet for 15 days followed by a 425 kcal-day⁻¹ diet for 60 days; regardless of which protein the subjects were given weight loss was equivalent (56). However, patients in the soy group had significantly reduced levels of total plasma triglycerides compared with the casein group (26% vs. 9%; $P < 0.01$) (56). Anderson *et al.* (10) found that soy-based meal replacement during a low-energy diet intervention (1200 kcal day⁻¹) was associated with significant reductions in serum triglycerides at 6 and 12 weeks while milk meal replacement did not cause this reduction. Neither soy nor casein meal replacement shakes when given as part of an energy-restricted diet caused significant reductions in serum triglycerides among women (BMI 30–40 kg m⁻²) (58).

In a crossover design, diabetic patients were put on either a soy-based diet or a meat-based diet for 8 weeks with a 4-week washout between the two dietary interventions (89). Soy-based dietary intake was associated with significant reductions in cholesterol ($P < 0.05$) and triglycerides ($P < 0.05$) (89). Subjects given β -conglycinin in the form of candies had reduced visceral fat (59). Serum triglyceride levels were significantly reduced in subjects given β -conglycinin during a 12-week intervention (59).

Proposition no. 4 Soyfoods will minimize the loss of bone mass during weight loss

In vitro data

N/A

Animal data

The effects of Fujiflavone P40 (a soybean isoflavone product which contains 46.6% isoflavones) on bone loss was evaluated in rats: (sham)-operated, OVX, OVX given Fujiflavone P40, OVX given 17- β -estradiol and OVX given the vehicle for 17- β -estradiol (87). Ovariectomy decreased the tibia bone mineral density by 22%. 17- β -estradiol recovered this tibia BMD decrease by 100% in OVX rats and Fujiflavone P40 recovered the decrease by 78% in OVX rats. The results suggest that this soybean product, Fujiflavone P40, may be useful as a preventive agent for osteoporosis (87). No data are available to indicate the effects of soy on bone loss during a weight loss experiment in animal models.

Epidemiologic data

N/A

Clinical data

Perimenopausal women were randomly assigned to one of three treatments (soy protein isolate with 80.4 mg aglycone components day⁻¹, soy protein isolate with 4.4 mg aglycone components day⁻¹, or control) for 24 weeks to evaluate the effects of isoflavones on bone mineral density and bone mineral content (28). Each group gained significant body weight during the intervention; however, there was not a significant treatment effect on body weight. Lumbar spine bone mineral density and content did not differ from baseline in the two soy protein isolate groups, but did decrease in the controls. This report suggests that perimenopausal women may have less bone loss with soy protein intake (28). In another study previously described (86), following 6 months of intervention, women on isolated soy protein containing higher concentrations of isoflavones (ISP90) had significant increases in bone mineral density in the lumbar spine compared with women on CNFDM diet ($P < 0.05$) (86). Mori *et al.* (90) reported that healthy Japanese women given isoflavone tablets (100 mg day⁻¹) had significantly increased bone mineral density compared with placebo.

Soy may reduce bone loss in women, but additional clinical trials are needed to determine the effects of soyfood consumption on bone during weight loss.

Summary and conclusions from findings

Proposition no. 1 (Weight and fat loss) Reports that soy and its constituents may be effective at reducing adipose tissue development are limited, but genistein may directly affect the adipocyte by blocking adipogenesis. In animal studies, soy and its constituents had a positive effect on weight loss and fat loss which was especially prominent when comparing casein-based diets to soy-based diets. Soyfood consumption was not associated with lower BMI or reduced body weight gain over time in epidemiologic reports. Clinical evidence indicated that soyfoods are as good as other protein sources for achieving weight loss when patients are on low-calorie diets (in negative energy balance). It is not clear that soyfoods will lead to weight and fat loss during *ad libitum* feeding paradigms; therefore, future studies should be designed to investigate this question.

Proposition no. 2 (Caloric intake) Soy, when included as part of dietary intervention, caused a decrease in caloric intake acutely, but there are no reports to indicate that soy will reduce caloric intake chronically. Clinical data are neutral with most studies demonstrating that soy protein is equivalent to other protein sources for reducing hunger and improving satiety.

Proposition no. 3a (Glucose metabolism) There is evidence for positive effects of soy on glucoregulatory function in *in vitro* models and in animal studies. It is not clear whether soy protein is more beneficial than other protein sources for glucoregulatory function during weight loss, nor is there enough evidence to show that soy directly affects glucose metabolism independent of weight and fat loss in animal models. Epidemiologic data in postmenopausal women indicate that soyfoods may not affect glucose levels unless very high amounts of soyfoods are consumed and clinical evidence demonstrates that soy isoflavone consumption may be related to improved glucoregulatory function in diabetic patients and in postmenopausal women.

Proposition no. 3b (LDL levels) Evidence from animal studies indicates that soy protein containing isoflavones will reduce LDL cholesterol and the results appear to be independent of weight loss. One epidemiologic report showed that isoflavone levels and soybean consumption were associated with lower total cholesterol. Soyfood consumption was associated with reduced LDL cholesterol among subjects that lost weight on soy-based meal replacements as well as in hypercholesterolemic subjects. Determining the beneficial effects of soy on cholesterol levels independent of weight loss and in normocholesterolemic subjects will require more clinical trials.

Proposition no. 3c (HDL levels) Some reports indicate that soy isoflavones may be associated with increased HDL levels in animal models, in epidemiologic studies and in clinical trials (postmenopausal women), but more experiments will be needed to conclude whether soyfood consumption actually improves HDL levels in all populations.

Proposition no. 3d (TG levels) Several animal studies demonstrated that soy may cause triglyceride reductions. Again, the data do not indicate precise components (isoflavone or protein) from soy that are involved with the beneficial effects on triglyceride reduction. Clinical trials have shown positive effects of tofu, soy protein, soy-based diets and β -conglycinin on triglyceride levels, but more studies will be required to make conclusions about soyfood's effects on triglycerides.

Proposition no. 4 (Bone loss) One animal study and one clinical trial indicated that consumption of soy isoflavones and soy protein may reduce bone loss; however, these studies were not performed during weight loss. Obviously, more long-term studies are needed to determine if soyfoods can prevent bone loss over time.

Several limitations in the existing research make it difficult to draw firm conclusions regarding these four propositions. Soyfood nomenclature is not standardized which makes it challenging to compare soy components across studies. Most of the animal and clinical studies use different formulations of soy products (differing in protein and

isoflavone content) and compare soy protein with milk protein sources. This could present another limitation because milk peptides may have active biological properties relevant to weight loss and obesity (91) and comparing two biologically active interventions (soy and milk) could introduce misleading conclusions; therefore, milk protein may not be an adequate 'placebo' for investigating the metabolic effects of soy in research studies. Also, few double-blind randomized clinical trials show the effects of long-term soyfood supplementation compared with other protein sources during weight loss programmes or as part of a normal *ad libitum* diet during weight maintenance. Animal and human studies typically do not report body composition changes during soyfood consumption/supplementation; therefore, it is difficult to conclude whether significant fat loss occurs with soyfood consumption.

These data do not allow us to conclude that soyfoods cause weight loss or fat loss, but there is enough positive preliminary data to warrant more research in this area. Current data give some indication that soyfoods are at least as good as other protein sources for weight loss during low-calorie diet interventions and soyfoods may be beneficial in promoting other positive metabolic consequences. The specific soy protein components and soy constituents that may cause these metabolic improvements are not known and it will require more extensive experimentation to determine which components and constituents are involved.

Will soyfoods be more beneficial if consumed throughout life compared with only during short-term weight loss programmes? Do soyfoods when consumed as part of a normal *ad libitum* diet promote beneficial metabolic outcomes? Are certain populations more receptive to the health benefits of soyfoods? – do only obese people, diabetics and postmenopausal women respond to soyfoods' beneficial effects? Better animal studies and more randomized clinical trials will be needed to answer these questions. Also, body composition will need to be monitored during intervention programmes to determine if soyfoods are causing beneficial effects on visceral adiposity and bone health. Current evidence suggests that soyfoods are at least as good as most other protein sources for use in diets for weight loss or weight gain prevention. Some data (especially in animals) suggest that soy protein is better in this regard than are other protein sources, but data, especially in humans, do not yet offer clear support for this proposition. Data further suggest the possibility that some soyfoods may have additional benefits in terms of either promoting lower weight or adiposity and/or promoting better values of other related variables during weight loss. Additional evidence is clearly required before firm conclusions about the benefits of soyfoods in the context of weight or adiposity control can be made.

Table 4 Additional references published after original submission of review

Authors	Publication	Description of Findings
St-Onge MP, Claps N, Wolper C, Heymsfield SB	Supplementation with soy-protein – rich foods does not enhance weight loss. <i>J Am Diet Assoc</i> 2007; 107 : 500–505	Two groups of overweight women were counselled to decrease caloric intake over a 12-week period. One group was counselled to consume 15 g of soy-protein-rich foods per day. Both groups lost similar amounts of weight ($-3.18 \pm 0.63\%$ -soy vs. $-4.04 \pm 0.95\%$ -controls).
Aubertin-Leheudre M, Lord C, Khalil A, Dionne IJ	Six month of isoflavone supplementation increases fat-free mass in obese-sarcopenic postmenopausal women: a randomized double-blind controlled trial. <i>Eur J Clin Nutrition</i> 2007; epub	Sarcopenic obese women consuming 70 mg of soy isoflavones per day for 24 weeks significantly increased appendicular leg fat-free mass and muscle mass index compared with women given placebo.
Aubertin-Leheudre M, Lord C, Khalil A, Dionne IJ	Effect of 6 months of exercise and isoflavone supplementation on clinical cardiovascular risk factors in obese postmenopausal women: a randomized, double-blind study. <i>Menopause</i> 2007; epub	Two groups of postmenopausal women were assigned either isoflavone (70 mg day^{-1}) or placebo for 1 year. Over the last 6 months, both groups participated in an exercise programme. The group on the isoflavones had significant improvements in body composition parameters during the exercise training compared with the placebo-exercised group.
Velasquez MT and Bhathena SJ	(Review) Role of Dietary Soy Protein in Obesity. <i>Int J Medical Sci.</i> 2007; 4 : 72–82	Described the literature suggesting there is a role of soy protein and its constituents on promoting a beneficial role in obesity. Some of the potential mechanisms were discussed.
Matsumoto K, Watanabe Y, Yokoyama SI	Okara, soybean residue, prevents obesity in a diet-induced murine obesity model. <i>Bioscience, Biotechnology and Biochemistry.</i> 2007; 71 : 720–727	Okara is a dried soybean residue. Male ICR mice were fed basal diet or a dried okara-supplemented basal diet (10, 20, or 40%) for 10 weeks. Okara intake dose-dependently suppressed the development of body weight and epididymal white adipose tissue, and prevented an increase of plasma lipids, including total cholesterol, LDL cholesterol and nonesterified fatty acid.

LDL, low-density lipoprotein.

Conflict of Interest Statement

No conflict of interest was declared.

Addendum

Additional papers (see Table 4 for summary) have been published since the original submission of this manuscript; however, the content of these new reports do not present any additional evidence to change the overall conclusions summarized in this review.

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