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Section: Scholarly Review

Article Title: No Difference Between the Effects of Supplementing With Soy Protein Versus Animal Protein on Gains in Muscle Mass and Strength in Response to Resistance Exercise

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Title:

No difference between the effects of supplementing with soy protein versus animal protein on gains in muscle mass and strength in response to resistance exercise

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SHORT TITLE: Soy protein and lean tissue accretion and strength

Abstract

Much attention has been given to determining the influence of total protein intake and protein source on gains in lean body mass (LBM) and strength in response to resistance exercise training (RET). Acute studies indicate that whey protein, likely related to its higher leucine content, stimulates muscle protein synthesis (MPS) to a greater extent than proteins such as soy and casein. Less clear is the extent to which the type of protein supplemented impacts strength and LBM in longer term studies (≥6 weeks). Therefore, a meta-analysis was conducted to compare the effect of supplementation with soy protein to animal protein supplementation on strength and LBM in response to RET. Nine studies involving 266 participants suitable for inclusion in the meta-analysis were identified. Five studies compared whey with soy protein and four compared soy protein with other proteins (beef, milk or dairy protein). Meta-analysis showed that supplementing RET with whey or soy protein resulted in significant increases in strength but found no difference between groups (bench press Chi^2 = 0.02, p=0.90; squat Chi^2=0.22, p =0.64). There was no significant effect of whey or soy alone (n=5) on LBM change, and no differences between groups (Chi^2=0.00, p=0.96). Strength and LBM both increased significantly in the 'other protein' and the soy groups (n=9), but there were no between group differences (bench Chi^2=0.02, p=0.88; squat Chi^2=0.78, p=0.38 and LBM Chi^2=0.06, p=0.80). The results of this meta-analysis indicate that soy protein supplementation produces similar gains in strength and LBM in response to RET as whey protein.

Key words: Animal protein, soy protein, lean body mass

INTRODUCTION

For a variety of reasons, dietary protein has been the subject of increased research attention in recent years. There is evidence that consuming protein in excess of the US recommended dietary allowance (RDA) may lead to health benefits and that for many population groups the RDA for protein (0.8 g/kg body weight) may be too low (Wolfe, et al. 2017). Higher protein intakes may help to prevent and/or delay the onset of sarcopenia and because protein is more satiating than carbohydrate and fat, higher-protein diets may also help with weight management (Cuenca-Sanchez, et al. 2015).

In addition to total protein intake research has focused on the effects of different types of protein, in particular plant vs animal protein, on the risk of developing various chronic diseases (Richter, et al. 2015; Shang, et al. 2016a; Shang, et al. 2016b; Sucher, et al. 2017). Western health authorities have generally called for economically-advantaged countries to consume a more plant-based diet for health and environmental reasons (Springmann, et al. 2016). However, per capita meat consumption is predicted to increase as the global population becomes wealthier (Shi, et al. 2015), although animal protein will likely still be beyond the economic reach of billions of people (Speedy 2003). Consequently, much of the world will continue to rely primarily on plants to meet their dietary protein needs.

For millions of Asians (Messina, et al. 2006) and for many Western vegetarians and health-conscious individuals, soyfoods are an important source of protein (Rizzo, et al. 2013). Soybeans are not only higher in protein than other legumes (Messina 1999) but the quality of soy protein is superior to that of other plant proteins and relatively similar to that of animal proteins (Hughes, et al. 2011; Rutherfurd, et al. 2015). Soy protein is often considered to be the quintessential plant protein and as such is often compared to animal proteins in animal and human studies.

Although foods such as tofu, miso and soymilk, are the most popular forms of soy throughout Asia, intervention and animal studies typically rely upon the use of soy protein products (SPPs) to evaluate the health effects of soy protein. SPPs include isolated soy protein (ISP), soy protein concentrate (SPC), and soy flour and textured vegetable protein® (TVP). On a dry weight basis, these products range in protein content from approximately 56-59% (soy flour/TVP), 65-72% (SPC) and 90-92% (ISP). ISP is an especially convenient product for incorporating large amounts of soy protein into the diet and for that reason is most commonly used for experimental purposes.

Plant proteins such as soy protein may have a number of advantages over animal protein, such as lowering blood cholesterol levels (Tokede, et al. 2015); however, a general view within the sports nutrition community is that animal proteins and whey protein in particular, are more effective at building muscle in response to RET (Devries, et al. 2015; Hulmi, et al. 2010; van Vliet, et al. 2015). That whey protein is considered by some to be superior to soy protein at building muscle and increasing strength is not surprising given the results of acute studies monitoring changes in muscle protein synthesis (MPS) over a 3-4 hour period. To the authors' knowledge, seven such studies (Gran, et al. 2014; Luiking, et al. 2011; Mitchell, et al. 2015; Rittig, et al. 2017; Tang, et al. 2009; Wilkinson, et al. 2007; Yang, et al. 2012b) involving both younger (Luiking, et al. 2011; Rittig, et al. 2017; Tang, et al. 2009; Wilkinson, et al. 2007) and older men (Gran, et al. 2014; Mitchell, et al. 2015; Yang, et al. 2012b) have compared whey to soy. Three of these studies focused on markers of MPS such as phosphorylation of ribosomal protein S6 kinase beta-1 (p70S6 kinase) (Gran, et al. 2014; Mitchell, et al. 2015) or the mammalian/mechanistic target of rapamycin (mTOR) (Gran, et al. 2014; Rittig, et al. 2017), whereas three did not involve an exercise component (Gran, et al. 2014; Luiking, et al. 2011; Rittig, et al. 2017). Important to note, in two of these studies (Mitchell, et al. 2015; Yang, et al. 2012b) the data for whey protein were derived from previously published research (D'Souza, et al. 2014; Yang, et al. 2012a).

There may be a number of possible factors, such as greater systemic availability of amino acids (Devries, et al. 2015), that account for the greater effect of whey protein in comparison to soy protein on MPS. However, much of the difference between the two proteins is likely attributable to the higher leucine content of whey protein (Norton, et al. 2012; Tang, et al. 2009). Leucine, one of the three branched chain amino acids (BCAA), has been extensively investigated for its ability to activate MPS. In particular, leucine activates MPS through the mTOR complex 1 (mTORC1) (Anthony, et al. 2000) and possibly also through an mTORC1-independent process (Bolster, et al. 2004). Recognition of the important role of leucine in stimulating MPS (Katsanos, et al. 2006) has given rise to the "leucine threshold" hypothesis, which refers to the leucine intake required to reach a muscle intracellular leucine concentration that triggers a robust increase in MPS following protein consumption (Phillips 2014). Once this threshold is met further increases in leucine do not lead to further increases in the muscle anabolic response (Glynn, et al. 2010).

The International Society of Sports Nutrition (ISSN) recommends that the post-exercise meal contain as much as 3g of leucine in addition to a balanced array of indispensable amino acids (IAA) (Jäger, et al. 2017). The amount of leucine required to maximally stimulate MPS may be affected by a number of factors including age (Burd, et al. 2013; Moore, et al. 2009; Witard, et al. 2014) as older individuals most likely require more dietary protein and leucine to stimulate MPS than younger people (Breen, et al. 2011; D'Souza, et al. 2014; Glynn, et al. 2010; Moore, et al. 2015; Volpi, et al. 1999). In theory, proteins with a higher BCAA content will lead to greater MPS (Fouillet, et al. 2002; Luiking, et al. 2005). Because of the key role of leucine, adding this BCAA to lesser amounts of total protein can stimulate MPS to a similar extent as a larger amount of protein that provides a similar amount of leucine (Churchward-Venne, et al. 2014; Katsanos, et al. 2006; Wilkinson, et al. 2013).

Although acute studies evaluating MPS may provide valuable insight, MPS following protein supplementation and resistance exercise may last for at least 24 h (Burd, et al. 2011). Thus, it is important to determine how protein source affects changes in strength and lean tissue accretion in longer-term studies. Knowing how these metrics are affected by protein type is an important public health consideration because greater lean tissue is associated with overall health (Wolfe, et al. 2017) and with the prevention of functional decline with aging (Bradlee, et al. 2017). Strength may actually be a much more important barometer than muscle mass as research indicates that among older adults, low muscle strength is independently associated with elevated risk of all-cause mortality regardless of muscle mass (Li, et al. 2017; Newman, et al. 2006). Therefore, to determine whether supplementation with soy protein or other animal proteins differentially impacts the response to RET, we performed a meta-analysis of longer-term studies specifically comparing supplementation with soy protein to whey protein and other animal proteins on lean tissue accretion and strength in response to RET. This analysis was undertaken in part to evaluate the recent conclusion by Morton et al. (Morton, et al. 2017) that protein source likely plays a minor role in determining the impact of protein supplementation on gains in LBM and strength in response to RET

Materials and methods

Criteria and search strategy

The meta-analysis was carried out in accordance with the PRISMA guidelines (Moher, et al. 2009). The literature search (through November 2017) was performed without date restrictions on articles published in peer reviewed journals using Web of Science, PubMed and Google

Scholar. Search terms were: 'soy', 'whey', 'protein', 'animal protein', 'muscle', 'training', 'exercise', and 'lean mass'. References listed in papers identified by the search and that came to the attention of the authors through other means were also considered for inclusion.

Non-human studies and those including participants aged less than 18 years were excluded from the meta-analysis, which was comprised of two separate comparisons: changes in muscular strength and changes in LBM. Studies could be included in one or both comparisons but it was not required that those studies reporting strength also reported LBM or vice versa. To be included, study participants were required to undertake a RET program of at least six weeks in duration, training at least twice per week, prior to which they were randomly allocated to a nutritional supplementation protocol in which the addition of soy protein to the diet was compared with the addition of non-soy protein. Studies were required to provide the necessary data for the calculation of effect sizes (pre-training and post-training means and standard deviations) for outcome measures. Outcome measures were assessment of maximal muscular strength (upper body or lower body) and assessments of LBM. Strength was measured as 1-repetition maximum (RM in kg) in all studies that assessed changes in muscle strength. LBM was assessed via DEXA in four studies (Candow, et al. 2006; Kalman, et al. 2007; Maltais, et al. 2016; Volek, et al. 2013) and one study each used air displacement plethysmography (Haub, et al. 2002), skinfold (Denysschen, et al. 2009) and hydrostatic weighing (Brown, et al. 2004). Studies could be included if they provided the data necessary to calculate LBM, for example, it could be derived from body mass and measures of percentage body fat.

Data extraction

Data extraction was performed by MM and KR. MM collated all the data and KR verified data accuracy and confirmed eligibility for inclusion. For each outcome measure pre- and post-training means and standard deviations (SDs) were extracted for the soy protein-supplemented group and control (comparator) protein group and used in the analysis. In all cases the last available measurement was used for comparison; e.g., in the study Volek et al. (Volek, et al. 2013) changes at 3, 6 and 9-month periods were reported but only the 9-month time point was used for analysis.

Data analysis

Statistical analysis was performed in RevMan (Review Manager Version 5.3). A fixed effects model of the inverse variance method for meta-analysis was used to analyze the data. This method assigns a proportionate weight to studies according to the magnitude of standard error, and permits analysis while controlling for heterogeneity. Outcome measures of change (post intervention (kg) – pre intervention (kg)) in strength and lean mass were expressed as the standardized mean difference with 95% confidence intervals (95% CI).

Bias and Heterogeneity

Within each comparison heterogeneity using the I^2 statistic was calculated (Moher, et al. 2009). It was assumed that a value of I^2 <25% demonstrated low heterogeneity; 25-50% was considered moderate and 75% or more demonstrated high heterogeneity. Bias was examined using funnel plots for each outcome variable. With a low number of studies, statistical tests to determine bias would likely be underpowered, so a visual inspection using a funnel plot was used.

RESULTS

Of the 62 studies originally identified by the literature search, nine met the criteria for inclusion in the meta-analysis (Brown, et al. 2004; Candow, et al. 2006; Denysschen, et al. 2009; Hartman, et al. 2007; Haub, et al. 2002; Kalman, et al. 2007; Maltais, et al. 2016; Thomson, et al.

2016; Volek, et al. 2013). Reasons for exclusion are shown in Figure 1. Studies reported a range of strength measures so the most frequently assessed were identified and used for statistical comparisons. All studies reported bench press (upper body) or a measure of lower body strength such as squat (lower body) or incline press in kg. Funnel plots showed no evidence of publication bias (data not shown).

Of the nine studies included in the analysis, the comparator protein to soy was whey in five studies, and beef or dairy or milk protein in four (table 1). As the soy vs whey comparison is the most common, and of primary interest, separate forest plots were created for this analysis. Data from 106 participants aged 18 to 50 were included in the soy vs whey only analysis (Figures 2-4). Data from 266 individuals aged 18-70 were included in the extended analysis (soy vs other proteins, Figures 5-7).

With respect to prior experience with RET, in the study by Brown et al. (Brown, et al. 2004) the participants were trained weight lifters, in the study by Kalman et al. (Kalman, et al. 2007) the participants included a mix of trained and untrained individuals but they were matched per group, and in the study by Haub et al. (Haub, et al. 2002) the training background of the participants was not indicated but they appeared to be untrained. In the other six studies the participants were described as having not previously participated in RET for at least one year. Five of the nine studies were conducted in the United States (Brown, et al. 2004; Denysschen, et al. 2009; Haub, et al. 2002; Kalman, et al. 2007; Volek, et al. 2013), three in Canada (Candow, et al. 2006; Hartman, et al. 2007; Maltais, et al. 2016) and one in Australia (Thomson, et al. 2016). The studies ranged in duration from 6 (Candow, et al. 2006) to 36 (Volek, et al. 2013) (mean 13.6 +/- 8.6) weeks and protein supplementation ranged from 12 g/d (plus IAA) (Maltais, et al. 2016) to 86 g/d (Candow, et al. 2006). Six studies included only men (Brown, et al. 2004; Denysschen, et al.

2009; Hartman, et al. 2007; Haub, et al. 2002; Kalman, et al. 2007; Maltais, et al. 2016), three included both genders(Candow, et al. 2006; Thomson, et al. 2016; Volek, et al. 2013) and three included participants who were older than 50 years of age (Haub, et al. 2002; Maltais, et al. 2016; Thomson, et al. 2016); in one of these studies the participants were described as sarcopenic (Maltais, et al. 2016) and in another, the dropout rate in the soy group exceeded 50% (Thomson, et al. 2016). In the study involving sarcopenic men, the milk and soy beverages were supplemented with IAA providing 3.5 g leucine (Maltais, et al. 2016).

Whey vs soy protein

As noted, five studies compared soy protein with whey (Brown, et al. 2004; Candow, et al. 2006; Denysschen, et al. 2009; Kalman, et al. 2007; Volek, et al. 2013). The within study heterogeneity (I2) was low to moderate within each subgroup ranging from 45% to 0% (Figures 2-5).

There were significant increases in strength (1RM), but not LBM in each subgroup as a result of the interventions. Subgroup analysis was carried out to look for differences in change in strength or lean mass according to protein type. As shown in Figure 2, there was no significant (Chi^2 =0.02, p = 0.90) difference in the change in bench press 1RM in the whey vs soy subgroup comparison. There were also no significant subgroup differences between whey and soy groups for the change in squat strength (Figure 3; Chi^2 = 0.22, p=0.64) or for increases in LBM (Figure 4; Chi^2 = 0.00, p = 0.96).

Other proteins vs soy protein

Nine studies compared soy protein vs all other proteins (whey, beef and dairy). (Brown, et al. 2004; Candow, et al. 2006; Denysschen, et al. 2009; Hartman, et al. 2007; Haub, et al. 2002;

Kalman, et al. 2007; Maltais, et al. 2016; Thomson, et al. 2016; Volek, et al. 2013). Again, within study heterogeneity (I^2) was low to moderate ranging between 88% and 0%.

There were significant increases in both strength and LBM in each subgroup as a result of the interventions. None of the subgroup comparisons resulted in significant differences between soy and the other proteins groups. These between subgroup comparisons were bench press (Figure 5; $Chi^2 = 0.02$, $p = 0.88$); squat (Figure 6; $Chi^2 = 0.78$, $p = 0.38$) and LBM (Figure 7; $Chi^2 = 0.06$, $p = 0.80$).

DISCUSSION

Acute studies show that when matched for nitrogen content, soy protein stimulates MPS to a lesser extent than whey protein (Gran, et al. 2014; Luiking, et al. 2011; Mitchell, et al. 2015; Rittig, et al. 2017; Tang, et al. 2009; Wilkinson, et al. 2007; Yang, et al. 2012b), a difference likely mostly due to the lower leucine concentration of the former. Consequently, these differences have led to speculation that soy protein is inferior to milk and whey protein at building muscle and increasing strength in response to RET (Devries, et al. 2015; Jäger, et al. 2017). However, the results of the current meta-analysis do not support such speculation as strength (bench press and squat) and lean tissue accretion in response to RET were similar between whey and soy protein supplementation (Brown, et al. 2004; Candow, et al. 2006; Denysschen, et al. 2009; Hartman, et al. 2007; Haub, et al. 2002; Kalman, et al. 2007; Maltais, et al. 2016; Thomson, et al. 2016; Volek, et al. 2013) .

To the knowledge of the authors, no previous meta-analysis of studies comparing the effects of soy protein with a control protein on strength and LBM has been published. Nevertheless, for at least two reasons the results are not surprising. First, gains in strength in response RET, especially among novice weight lifters which comprised most of the study participants in the meta-analysis, are due to a combination of neurological and morphological factors, not just increases in muscle size (Folland, et al. 2007). These factors may not be influenced by protein source or overall protein intake (Reidy, et al. 2016). Second, in two of the nine studies included in the meta-analysis soy protein was compared to milk protein (Hartman, et al. 2007; Maltais, et al. 2016) and in another study, soy protein was compared to protein from a mix of dairy products (Thomson, et al. 2016). Given that dairy protein is comprised of 80% casein (Mackle, et al. 1999) and that soy protein is at least as effective as casein at stimulating MPS in acute studies (Luiking, et al. 2011; Tang, et al. 2009), there is little reason for soy protein and dairy protein to differentially affect strength or lean tissue accretion. Furthermore, in one of these studies, both the soy and milk groups were supplemented with leucine (Maltais, et al. 2016). Therefore, the results of the current meta-analysis are actually consistent with existing understanding of the effect of dietary protein type on strength and lean tissue accretion in response to RET.

The current meta-analysis found that supplementation with whey or soy protein during RET results in similar increases in LBM and strength (Figures 2-4). Although this finding contrasts with the results of acute studies, it is supported by previous work that has shown a lack of correlation between acute changes in MPS and gains and LBM among individuals (Mayhew, et al. 2009; Mitchell, et al. 2014). It should be noted that many acute studies assess MPS over a 3-5 h post-exercise period (Gran, et al. 2014; Luiking, et al. 2011; Mitchell, et al. 2015; Rittig, et al. 2017; Tang, et al. 2009; Wilkinson, et al. 2007; Yang, et al. 2012b), whereas MPS can remain elevated for up to 72 h post exercise (Miller, et al. 2005). Consequently, the acute studies may not capture the entire hypertrophic period and therefore, differences among proteins sources in acute MPS may be exaggerated in the early post-exercise period. To that end, Damas et al. (Damas, et al. 2016) recently performed correlational analyses between changes in fiber cross-sectional area (CSA) after 10 weeks of RET and acute measures of myofibrillar protein synthesis. Importantly, myofibrillar protein synthesis was assessed over a 24 h time course at three time points during the RET: pre training, at 3 weeks of training, and at 10 weeks of training. While Damas et al. (Damas, et al. 2016) did observe a correlation between fiber CSA and acute measures of myofibrillar protein synthesis made after 3 and 10 weeks of training, no correlation was observed between acute measures of myofibrillar protein synthesis assessed during the initial exercise session (i.e., pre-training) and fiber CSA after 10 weeks of RET. Consequently, the MPS response to unaccustomed exercise may also make correlational analyses between acute MPS and chronic adaptions more difficult. In addition, muscle hypertrophy is governed by the relationship between protein synthesis and protein breakdown, and often protein breakdown is not assessed or cannot be assessed to the same degree of precision using current techniques. Whether the observed differences in MPS observed between whey and soy protein in acute exercise studies would manifest in different muscle adaptations over a longer RET period than was evaluated in the studies included in the current meta-analysis requires further study.

A recently published meta-analysis by Morton et al. (Morton, et al. 2017), which included 49 intervention studies involving 1,863 participants examined the effect of protein supplementation on changes in muscle mass and strength in conjunction with resistance training. The authors found that consumption of protein supplements alongside RET resulted in greater increases in fat free mass and muscle strength than resistance training alone, and that the effect of protein supplementation was more pronounced among trained participants and attenuated with increasing age. In their analysis, Morton et al. (Morton, et al. 2017) did not distinguish among protein sources, but rather looked at the effect of protein vs no protein supplementation on effect size.

The meta-regression also conducted by these authors, including 15 studies, which investigated the influence of protein source (soy vs whey) on change in LBM or strength, concluded it is potentially a very minor determinant (Morton, et al. 2017). Meta-regression is seen by some authors to be hypothesis generating rather than hypothesis testing (Baker, et al. 2009) and thus, the current work sought to further determine the contribution of protein source to change in LBM or strength by conducting meta-analyses using selected studies that compared changes in these parameters in response to supplementing with soy protein vs whey protein, and soy protein vs different animal proteins. The studies used in the current analyses were randomized trials where a soy protein experimental arm was compared with another experimental arm that intervened with a different animal protein. One issue with meta-regression is that potential correlation characteristics among variables may not be adequately identified (Thompson, et al. 2002). Therefore, characteristics that may differ among trials (such as trial duration or protein dose) would be taken into account in the current meta-analyses to a greater extent.

In the current study, two meta-analyses were conducted; one that directly compared soy protein with whey protein (the 'gold standard' protein supplement) and one that compared soy protein with all other animal proteins. The present results both confirm the observation by Morton et al. (Morton, et al. 2017) and extend it by showing not only that differences do not exist between soy protein and whey, but also, between soy protein and animal protein in general.

It is noteworthy that in three of the five studies intervening with whey included in our meta-analysis, the participants were young and untrained (Candow, et al. 2006; Denysschen, et al. 2009; Volek, et al. 2013) and in another (Kalman, et al. 2007), the number of trained participants was unclear. Recent data show that protein supplementation following RET is primarily effective only in highly trained individuals. The proposed reason being that the effect of protein supplementation is overwhelmed by the very robust response to RET that occurs in novice weight lifters (Morton, et al. 2017). This point is supported by a recent12-wk trial by Mobley et al. (Mobley, et al. 2017) involving untrained college-aged males that found RET led to increases in LBM and strength, but neither whey nor soy protein supplementation affected these changes. Further research is needed to determine more definitively whether protein type affects strength and LBM in highly trained individuals.

The ISSN recommends that acute protein doses should contain as much as 3 g leucine (Jäger, et al. 2017), although the optimal leucine dose depends upon factors such as age and body weight (Burd, et al. 2013; Moore, et al. 2009; Witard, et al. 2014). To obtain 3 g leucine from soy protein requires consuming approximately 38 g. The results of the current meta-analysis suggest that this upper limit may not be necessary with regards to gains in strength and LBM during RET as only three (Candow, et al. 2006; Haub, et al. 2002; Kalman, et al. 2007) of the nine studies intervened with an amount of soy protein that would have provided 3 g leucine. When considering only those studies in which soy was compared to whey, two studies (Candow, et al. 2006; Kalman, et al. 2007) provided ≥38 g/d soy protein and three (Brown, et al. 2004; Denysschen, et al. 2009; Volek, et al. 2013) less than this amount, and yet the meta-analysis showed there were no significant difference between whey and soy protein. Therefore, it would appear lower amounts of leucine than are recommended by the ISSN are capable of facilitating gains in strength and LBM during RET.

One criticism of soyfoods as a source of protein for increasing strength and LBM is that the isoflavones naturally present in the soybean will inhibit mTOR activation (Jäger, et al. 2017).

The isoflavone concentration in traditional Asian soyfoods is approximately 3.5 mg/g protein whereas as a result of processing, in most concentrated sources of soy protein it is much lower (<1 mg/g) (Messina, et al. 2006). Interestingly, two studies have shown that isoflavones do inhibit mTOR (Cederroth, et al. 2008; Liu, et al. 2015); however, both of these were conducted in mice. In addition to the normal caveats about extrapolating findings from rodents to humans (Liu, et al. 2015), mice are a poor model for understanding the effects of isoflavones in humans because these two species metabolize isoflavones so differently (Gu, et al. 2006; Setchell, et al. 2011). Furthermore, in one of the mouse studies (Liu, et al. 2015), mice were given 160 mg/d genistein (the predominant isoflavone in soybeans) per kg body weight. Average genistein intake among native Japanese following a traditional diet is only about 0.3 mg/d (Messina, et al. 2006). Even when acknowledging the faster metabolism of rodents compared to humans (Reagan-Shaw, et al. 2008), the dose used in this study is clearly pharmacological and therefore of questionable relevance (Liu, et al. 2015). The results of the current analysis, which shows supplementation of soy protein containing isoflavones leads to similar gains in strength and LBM in response to RET as does animal protein, also argues against isoflavones inhibiting muscle growth in response to RET, at least in untrained adult men and women. However, further research is necessary to determine whether similar or different molecular processes are involved.

Finally, it is important to acknowledge limitations of the data. In particular, we recognize that the studies described in table 1 varied markedly in experimental design, such as the pre-intervention training status, age and gender, and often involved very small participant numbers and for some measures, the statistical comparisons between whey and soy protein were limited to only three studies. Further, the relatively low number of studies and participants that met the criteria for our meta-analysis did not provide appropriate power to identify the independent influence of age or gender on our outcomes. Specifically, there is a particular need for more research focused on the protein needs of older individuals since their leucine requirements are higher, their caloric and protein intake often suboptimal, and many are at risk of developing sarcopenia (Leidy 2017). Another possible limitation is that the meta-analysis included the study by Maltais et al. (Maltais, et al. 2016) even though as noted, the participants in both the milk and soy groups were supplemented with IAA including leucine. Although we chose to include this study, when it is eliminated from the analysis the results are not appreciably altered (data not shown).

In conclusion, the current meta-analysis is consistent with the totality of evidence regarding protein supplementation and RET. Our meta-analysis identified that soyfoods and soy protein supplements can be viewed as sources of protein suitable for building strength and increasing lean tissue in response to RET. Overall, the results indicate that protein source is not likely an important factor influencing gains in strength and LBM in response to RET. Since two dietary principles are moderation and variety, rather than relying on just one source, including soy protein an option for meeting protein needs for those wanting to increase strength and LBM makes overall nutritional sense. Whether a mix of soy and dairy protein might actually increase strength and LBM relative to a single protein remains to be established (Reidy, et al. 2016; Reidy, et al. 2013).

Acknowledgements

MM and KER conducted the literature search to identify studies for inclusion in the meta-analysis and extracted the necessary data. KER conducted the statistical analysis. MM, KER, HL and JMD participated in the writing of the manuscript and reviewed the literature cited. All authors approved the final version of the paper.

Conflict of interest.

KER, HL and JMD have no conflicts. MM is the executive director of the Soy Nutrition Institute, an organization that is partially funded by the soy industry.

References

Standardised effect sizes… Higgins JPT, Green S (editors) Cochrane Handbook for systematic Reviews of Interventions Version 5.1.0. The Cochrane Collection, Updated March 2011, available from www.cochrane-handbook.org.

Anthony, J. C., Yoshizawa, F., Anthony, T. G., Vary, T. C., Jefferson, L. S., & Kimball, S. R. (2000). Leucine stimulates translation initiation in skeletal muscle of postabsorptive rats via a rapamycin-sensitive pathway. *J Nutr*, 130, 2413-9.

Baker, W. L., White, C. M., Cappelleri, J. C., Kluger, J., & Coleman, C. I. (2009). Understanding heterogeneity in meta-analysis: the role of meta-regression. *Int J Clin Pract*, 63, 1426-34.

Bolster, D. R., Vary, T. C., Kimball, S. R., & Jefferson, L. S. (2004). Leucine regulates translation initiation in rat skeletal muscle via enhanced eIF4G phosphorylation. *J Nutr*, 134, 1704-10.

Bradlee, M. L., Mustafa, J., Singer, M. R., & Moore, L. L. (2017). High-Protein Foods and Physical Activity Protect Against Age-Related Muscle Loss and Functional Decline. *J Gerontol A Biol Sci Med Sci*, 73, 88-94.

Breen, L., & Phillips, S. M. (2011). Skeletal muscle protein metabolism in the elderly: Interventions to counteract the 'anabolic resistance' of ageing. *Nutr Metab (Lond)*, 8, 68.

Brown, E. C., Disilvestro, R. A., Babaknia, A., & Devor, S. T. (2004). Soy versus whey protein bars: Effects on exercise training impact on lean body mass and antioxidant status. *Nutr J*, 3, 22.

Burd, N. A., Gorissen, S. H., & van Loon, L. J. (2013). Anabolic resistance of muscle protein synthesis with aging. *Exerc Sport Sci Rev*, 41, 169-73.

Burd, N. A., West, D. W., Moore, D. R., Atherton, P. J., Staples, A. W., Prior, T., Tang, J. E., Rennie, M. J., Baker, S. K., & Phillips, S. M. (2011). Enhanced amino acid sensitivity of myofibrillar protein synthesis persists for up to 24 h after resistance exercise in young men. *J Nutr*, 141, 568-73.

Candow, D. G., Burke, N. C., Smith-Palmer, T., & Burke, D. G. (2006). Effect of whey and soy protein supplementation combined with resistance training in young adults. *Int J Sport Nutr Exerc Metab*, 16, 233-44.

Cederroth, C. R., Vinciguerra, M., Gjinovci, A., Kuhne, F., Klein, M., Cederroth, M., Caille, D., Suter, M., Neumann, D., James, R. W., Doerge, D. R., Wallimann, T., Meda, P., Foti, M., Rohner-Jeanrenaud, F., Vassalli, J. D., & Nef, S. (2008). Dietary phytoestrogens activate AMP-activated protein kinase with improvement in lipid and glucose metabolism. *Diabetes*, 57, 1176-85.

Churchward-Venne, T. A., Breen, L., Di Donato, D. M., Hector, A. J., Mitchell, C. J., Moore, D. R., Stellingwerff, T., Breuille, D., Offord, E. A., Baker, S. K., & Phillips, S. M. (2014). Leucine supplementation of a low-protein mixed macronutrient beverage enhances myofibrillar protein synthesis in young men: a double-blind, randomized trial. *Am J Clin Nutr*, 99, 276-86.

Cuenca-Sanchez, M., Navas-Carrillo, D., & Orenes-Pinero, E. (2015). Controversies surrounding high-protein diet intake: Satiating effect and kidney and bone health. *Adv Nutr*, 6, 260-266.

D'Souza, R. F., Marworth, J. F., Figueiredo, V. C., Della Gatta, P. A., Petersen, A. C., Mitchell, C. J., & Cameron-Smith, D. (2014). Dose-dependent increases in p70S6K phosphorylation and intramuscular branched-chain amino acids in older men following resistance exercise and protein intake. *Physiol Rep*, 2.

Damas, F., Phillips, S. M., Libardi, C. A., Vechin, F. C., Lixandrao, M. E., Jannig, P. R., Costa, L. A., Bacurau, A. V., Snijders, T., Parise, G., Tricoli, V., Roschel, H., & Ugrinowitsch, C. (2016). Resistance training-induced changes in integrated myofibrillar protein synthesis are related to hypertrophy only after attenuation of muscle damage. *J Physiol*, 594, 5209-22.

Denysschen, C. A., Burton, H. W., Horvath, P. J., Leddy, J. J., & Browne, R. W. (2009). Resistance training with soy vs whey protein supplements in hyperlipidemic males. *J Int Soc Sports Nutr*, 6, 8.

Devries, M. C., & Phillips, S. M. (2015). Supplemental protein in support of muscle mass and health: advantage whey. *J Food Sci*, 80 Suppl 1, A8-A15.

Folland, J. P., & Williams, A. G. (2007). The adaptations to strength training : morphological and neurological contributions to increased strength. *Sports Med*, 37, 145-68.

Fouillet, H., Mariotti, F., Gaudichon, C., Bos, C., & Tome, D. (2002). Peripheral and splanchnic metabolism of dietary nitrogen are differently affected by the protein source in humans as assessed by compartmental modeling. *J Nutr*, 132, 125-33.

Glynn, E. L., Fry, C. S., Drummond, M. J., Timmerman, K. L., Dhanani, S., Volpi, E., & Rasmussen, B. B. (2010). Excess leucine intake enhances muscle anabolic signaling but not net protein anabolism in young men and women. *J Nutr*, 140, 1970-6.

Gran, P., Larsen, A. E., Bonham, M., Dordevic, A. L., Rupasinghe, T., Silva, C., Nahid, A., Tull, D., Sinclair, A. J., Mitchell, C. J., & Cameron-Smith, D. (2014). Muscle p70S6K phosphorylation in response to soy and dairy rich meals in middle aged men with metabolic syndrome: a randomised crossover trial. *Nutr Metab (Lond)*, 11, 46.

Gu, L., House, S. E., Prior, R. L., Fang, N., Ronis, M. J., Clarkson, T. B., Wilson, M. E., & Badger, T. M. (2006). Metabolic phenotype of isoflavones differ among female rats, pigs, monkeys, and women. *J Nutr*, 136, 1215-21.

Hartman, J. W., Tang, J. E., Wilkinson, S. B., Tarnopolsky, M. A., Lawrence, R. L., Fullerton, A. V., & Phillips, S. M. (2007). Consumption of fat-free fluid milk after resistance exercise promotes greater lean mass accretion than does consumption of soy or carbohydrate in young, novice, male weightlifters. *Am J Clin Nutr*, 86, 373-81.

Haub, M. D., Wells, A. M., Tarnopolsky, M. A., & Campbell, W. W. (2002). Effect of protein source on resistive-training-induced changes in body composition and muscle size in older men. *Am J Clin Nutr*, 76, 511-7.

Hughes, G. J., Ryan, D. J., Mukherjea, R., & Schasteen, C. S. (2011). Protein digestibility-corrected amino acid scores (PDCAAS) for soy protein isolates and concentrate: Criteria for evaluation. *J Agric Food Chem*, 59, 12707-12.

Hulmi, J. J., Lockwood, C. M., & Stout, J. R. (2010). Effect of protein/essential amino acids and resistance training on skeletal muscle hypertrophy: A case for whey protein. *Nutr Metab (Lond)*, 7, 51.

Jäger, R., Kerksick, C. M., Campbell, B. I., Cribb, P. J., Wells, S. D., Skwiat, T. M., Purpura, M., Ziegenfuss, T. N., Ferrando, A. A., Arent, S. M., Smith-Ryan, A. E., Stout, J. R., Arciero, P. J., Ormsbee, M. J., Taylor, L. W., Wilborn, C. D., Kalman, D. S., Kreider, R. B., Willoughby, D. S., Hoffman, J. R., Krzykowski, J. L., & Antonio, J. (2017). International Society of Sports Nutrition Position Stand: protein and exercise. *J Internal Soc Sports Nutr*, 14, 1-25.

Kalman, D., Feldman, S., Martinez, M., Krieger, D. R., & Tallon, M. J. (2007). Effect of protein source and resistance training on body composition and sex hormones. *J Int Soc Sports Nutr*, 4, 4.

Katsanos, C. S., Kobayashi, H., Sheffield-Moore, M., Aarsland, A., & Wolfe, R. R. (2006). A high proportion of leucine is required for optimal stimulation of the rate of muscle protein synthesis by essential amino acids in the elderly. *Am J Physiol Endocrinol Metab*, 291, E381-7.

Leidy, H. J. (2017). Consumption of protein beverages as a strategy to promote increased energy intake in older adults. *Am J Clin Nutr*, 106, 715-716.

Li, R., Xia, J., Zhang, X., Gathirua-Mwangi, W. G., Guo, J., Li, Y., McKenzie, S., & Song, Y. (2017). Associations of muscle mass and strength with all-cause mortality among US older adults. *Med Sci Sports Exerc*.

Liu, M., Qi, Z., Liu, B., Ren, Y., Li, H., Yang, G., & Zhang, Q. (2015). RY-2f, an isoflavone analog, overcomes cisplatin resistance to inhibit ovarian tumorigenesis via targeting the PI3K/AKT/mTOR signaling pathway. *Oncotarget*, 6, 25281-94.

Luiking, Y. C., Deutz, N. E., Jakel, M., & Soeters, P. B. (2005). Casein and soy protein meals differentially affect whole-body and splanchnic protein metabolism in healthy humans. *J Nutr*, 135, 1080-7.

Luiking, Y. C., Engelen, M. P., Soeters, P. B., Boirie, Y., & Deutz, N. E. (2011). Differential metabolic effects of casein and soy protein meals on skeletal muscle in healthy volunteers. *Clin Nutr*, 30, 65-72.

Mackle, T. R., Bryant, A. M., Petch, S. F., Hooper, R. J., & Auldist, M. J. (1999). Variation in the composition of milk protein from pasture-fed dairy cows in late lactation and the effect of grain and silage supplementation. *New Zealand Journal of Agricultural Research*, 42, 147-154.

Maltais, M. L., Ladouceur, J. P., & Dionne, I. J. (2016). The effect of resistance training and different sources of postexercise protein supplementation on muscle mass and physical capacity in sarcopenic elderly men. *J Strength Cond Res*, 30, 1680-7.

Mayhew, D. L., Kim, J. S., Cross, J. M., Ferrando, A. A., & Bamman, M. M. (2009). Translational signaling responses preceding resistance training-mediated myofiber hypertrophy in young and old humans. *J Appl Physiol (1985)*, 107, 1655-62.

Messina, M., Nagata, C., & Wu, A. H. (2006). Estimated Asian adult soy protein and isoflavone intakes. *Nutr Cancer*, 55, 1-12.

Messina, M. J. (1999). Legumes and soybeans: overview of their nutritional profiles and health effects. *Am J Clin Nutr*, 70, 439S-450S.

Miller, B. F., Olesen, J. L., Hansen, M., Dossing, S., Crameri, R. M., Welling, R. J., Langberg, H., Flyvbjerg, A., Kjaer, M., Babraj, J. A., Smith, K., & Rennie, M. J. (2005). Coordinated collagen and muscle protein synthesis in human patella tendon and quadriceps muscle after exercise. *J Physiol*, 567, 1021-33.

Mitchell, C. J., Churchward-Venne, T. A., Parise, G., Bellamy, L., Baker, S. K., Smith, K., Atherton, P. J., & Phillips, S. M. (2014). Acute post-exercise myofibrillar protein synthesis is not correlated with resistance training-induced muscle hypertrophy in young men. *PLoS One*, 9, e89431.

Mitchell, C. J., Della Gatta, P. A., Petersen, A. C., Cameron-Smith, D., & Markworth, J. F. (2015). Soy protein ingestion results in less prolonged p70S6 kinase phosphorylation compared to whey protein after resistance exercise in older men. *J Int Soc Sports Nutr*, 12, 6.

Mobley, C. B., Haun, C. T., Roberson, P. A., Mumford, P. W., Romero, M. A., Kephart, W. C., Anderson, R. G., Vann, C. G., Osburn, S. C., Pledge, C. D., Martin, J. S., Young, K. C., Goodlett, M. D., Pascoe, D. D., Lockwood, C. M., & Roberts, M. D. (2017). Effects of whey, soy or leucine supplementation with 12 weeks of resistance training on strength, body composition, and skeletal muscle and adipose tissue histological attributes in college-aged males. *Nutrients*, 9.

Moher, D., Liberati, A., Tetzlaff, J., & Altman, D. G. (2009). Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *BMJ*, 339, b2535.

Moore, D. R., Churchward-Venne, T. A., Witard, O., Breen, L., Burd, N. A., Tipton, K. D., & Phillips, S. M. (2015). Protein ingestion to stimulate myofibrillar protein synthesis requires greater relative protein intakes in healthy older versus younger men. *J Gerontol A Biol Sci Med Sci*, 70, 57-62.

Moore, D. R., Robinson, M. J., Fry, J. L., Tang, J. E., Glover, E. I., Wilkinson, S. B., Prior, T., Tarnopolsky, M. A., & Phillips, S. M. (2009). Ingested protein dose response of muscle and albumin protein synthesis after resistance exercise in young men. *Am J Clin Nutr*, 89, 161-8.

Morton, R. W., Murphy, K. T., McKellar, S. R., Schoenfeld, B. J., Henselmans, M., Helms, E., Aragon, A. A., Devries, M. C., Banfield, L., Krieger, J. W., & Phillips, S. M. (2017). A systematic review, meta-analysis and meta-regression of the effect of protein supplementation on resistance training-induced gains in muscle mass and strength in healthy adults. *Br J Sports Med*, 52, 376-84.

Newman, A. B., Kupelian, V., Visser, M., Simonsick, E. M., Goodpaster, B. H., Kritchevsky, S. B., Tylavsky, F. A., Rubin, S. M., & Harris, T. B. (2006). Strength, but not muscle mass, is associated with mortality in the health, aging and body composition study cohort. *J Gerontol A Biol Sci Med Sci*, 61, 72-7.

Norton, L. E., Wilson, G. J., Layman, D. K., Moulton, C. J., & Garlick, P. J. (2012). Leucine content of dietary proteins is a determinant of postprandial skeletal muscle protein synthesis in adult rats. *Nutr Metab (Lond)*, 9, 67.

Phillips, S. M. (2014). A brief review of critical processes in exercise-induced muscular hypertrophy. *Sports Med*, 44 Suppl 1, S71-7.

Reagan-Shaw, S., Nihal, M., & Ahmad, N. (2008). Dose translation from animal to human studies revisited. *FASEB J*, 22, 659-61.

Reidy, P. T., Borack, M. S., Markofski, M. M., Dickinson, J. M., Deer, R. R., Husaini, S. H., Walker, D. K., Igbinigie, S., Robertson, S. M., Cope, M. B., Mukherjea, R., Hall-Porter, J. M., Jennings, K., Volpi, E., & Rasmussen, B. B. (2016). Protein supplementation has minimal effects on muscle adaptations during resistance exercise training in young men: A double-blind randomized clinical trial. *J Nutr*, 146, 1660-9.

Reidy, P. T., Walker, D. K., Dickinson, J. M., Gundermann, D. M., Drummond, M. J., Timmerman, K. L., Fry, C. S., Borack, M. S., Cope, M. B., Mukherjea, R., Jennings, K., Volpi, E., & Rasmussen, B. B. (2013). Protein blend ingestion following resistance exercise promotes human muscle protein synthesis. *J Nutr*, 143, 410-6.

Richter, C. K., Skulas-Ray, A. C., Champagne, C. M., & Kris-Etherton, P. M. (2015). Plant protein and animal proteins: do they differentially affect cardiovascular disease risk? *Adv Nutr*, 6, 712-28.

Rittig, N., Bach, E., Thomsen, H. H., Moller, A. B., Hansen, J., Johannsen, M., Jensen, E., Serena, A., Jorgensen, J. O., Richelsen, B., Jessen, N., & Moller, N. (2017). Anabolic effects of leucine-rich whey protein, carbohydrate, and soy protein with and without beta-hydroxy-beta-methylbutyrate (HMB) during fasting-induced catabolism: A human randomized crossover trial. *Clin Nutr*, 36, 697-705.

Rizzo, N. S., Jaceldo-Siegl, K., Sabate, J., & Fraser, G. E. (2013). Nutrient profiles of vegetarian and nonvegetarian dietary patterns. *J Acad Nutr Diet*, 113, 1610-9.

Rutherfurd, S. M., Fanning, A. C., Miller, B. J., & Moughan, P. J. (2015). Protein digestibility-corrected amino acid scores and digestible indispensable amino acid scores differentially describe protein quality in growing male rats. *J Nutr*, 145, 372-9.

Setchell, K. D., Brown, N. M., Zhao, X., Lindley, S. L., Heubi, J. E., King, E. C., & Messina, M. J. (2011). Soy isoflavone phase II metabolism differs between rodents and humans: implications for the effect on breast cancer risk. *Am J Clin Nutr*, 94, 1284-94.

Shang, X., Scott, D., Hodge, A., English, D. R., Giles, G. G., Ebeling, P. R., & Sanders, K. M. (2016a). Dietary protein from different food sources, incident metabolic syndrome and changes in its components: An 11-year longitudinal study in healthy community-dwelling adults. *Clin Nutr*.

Shang, X., Scott, D., Hodge, A. M., English, D. R., Giles, G. G., Ebeling, P. R., & Sanders, K. M. (2016b). Dietary protein intake and risk of type 2 diabetes: results from the Melbourne Collaborative Cohort Study and a meta-analysis of prospective studies. *Am J Clin Nutr*, 104, 1352-1365.

Shi, M., BAI, J.-F., & Seale, J. W., T (2015). Demographics, societal aging, and meat consumption in China. *J Integrative Agric*, 14, 995-1007.

Speedy, A. W. (2003). Global production and consumption of animal source foods. *J Nutr*, 133, 4048S-4053S.

Springmann, M., Godfray, H. C., Rayner, M., & Scarborough, P. (2016). Analysis and valuation of the health and climate change cobenefits of dietary change. *Proc Natl Acad Sci U S A*, 113, 4146-51.

Sucher, S., Markova, M., Hornemann, S., Pivovarova, O., Rudovich, N., Thomann, R., Schneeweiss, R., Rohn, S., & Pfeiffer, A. F. (2017). A comparison of the effects of diets high in animal or plant protein on metabolic and cardiovascular markers in type 2 diabetes - a randomized clinical trial. *Diabetes Obes Metab*, 19, 944-952.

Tang, J. E., Moore, D. R., Kujbida, G. W., Tarnopolsky, M. A., & Phillips, S. M. (2009). Ingestion of whey hydrolysate, casein, or soy protein isolate: effects on mixed muscle protein synthesis at rest and following resistance exercise in young men. *J Appl Physiol*, 107, 987-92.

Thompson, S. G., & Higgins, J. P. (2002). How should meta-regression analyses be undertaken and interpreted? *Stat Med*, 21, 1559-73.

Thomson, R. L., Brinkworth, G. D., Noakes, M., & Buckley, J. D. (2016). Muscle strength gains during resistance exercise training are attenuated with soy compared with dairy or usual protein intake in older adults: A randomized controlled trial. *Clin Nutr*, 35, 27-33.

Tokede, O. A., Onabanjo, T. A., Yansane, A., Gaziano, J. M., & Djousse, L. (2015). Soya products and serum lipids: a meta-analysis of randomised controlled trials. *Br J Nutr*, 114, 831-43.

van Vliet, S., Burd, N. A., & van Loon, L. J. (2015). The skeletal muscle anabolic response to plant- versus animal-based protein consumption. *J Nutr*, 145, 1981-91.

Volek, J. S., Volk, B. M., Gomez, A. L., Kunces, L. J., Kupchak, B. R., Freidenreich, D. J., Aristizabal, J. C., Saenz, C., Dunn-Lewis, C., Ballard, K. D., Quann, E. E., Kawiecki, D. L., Flanagan, S. D., Comstock, B. A., Fragala, M. S., Earp, J. E., Fernandez, M. L., Bruno, R. S., Ptolemy, A. S., Kellogg, M. D., Maresh, C. M., & Kraemer, W. J. (2013). Whey protein supplementation during resistance training augments lean body mass. *J Am Coll Nutr*, 32, 122-35.

Volpi, E., Mittendorfer, B., Wolf, S. E., & Wolfe, R. R. (1999). Oral amino acids stimulate muscle protein anabolism in the elderly despite higher first-pass splanchnic extraction. *Am J Physiol*, 277, E513-20.

Wilkinson, D. J., Hossain, T., Hill, D. S., Phillips, B. E., Crossland, H., Williams, J., Loughna, P., Churchward-Venne, T. A., Breen, L., Phillips, S. M., Etheridge, T., Rathmacher, J. A., Smith, K., Szewczyk, N. J., & Atherton, P. J. (2013). Effects of leucine and its metabolite beta-hydroxy-beta-methylbutyrate on human skeletal muscle protein metabolism. *J Physiol*, 591, 2911-23.

Wilkinson, S. B., Tarnopolsky, M. A., Macdonald, M. J., Macdonald, J. R., Armstrong, D., & Phillips, S. M. (2007). Consumption of fluid skim milk promotes greater muscle protein accretion after resistance exercise than does consumption of an isonitrogenous and isoenergetic soy-protein beverage. *Am J Clin Nutr*, 85, 1031-40.

Witard, O. C., Jackman, S. R., Breen, L., Smith, K., Selby, A., & Tipton, K. D. (2014). Myofibrillar muscle protein synthesis rates subsequent to a meal in response to increasing doses of whey protein at rest and after resistance exercise. *Am J Clin Nutr*, 99, 86-95.

Wolfe, R. R., Cifelli, A. M., Kostas, G., & Kim, I. Y. (2017). Optimizing protein intake in adults: Interpretation and application of the recommended dietary allowance compared with the acceptable macronutrient distribution range. *Adv Nutr*, 8, 266-275.

Yang, Y., Breen, L., Burd, N. A., Hector, A. J., Churchward-Venne, T. A., Josse, A. R., Tarnopolsky, M. A., & Phillips, S. M. (2012a). Resistance exercise enhances myofibrillar protein synthesis with graded intakes of whey protein in older men. *Br J Nutr*, 108, 1780-8.

Yang, Y., Churchward-Venne, T. A., Burd, N. A., Breen, L., Tarnopolsky, M. A., & Phillips, S. M. (2012b). Myofibrillar protein synthesis following ingestion of soy protein isolate at rest and after resistance exercise in elderly men. *Nutr Metab (Lond)*, 9, 57.

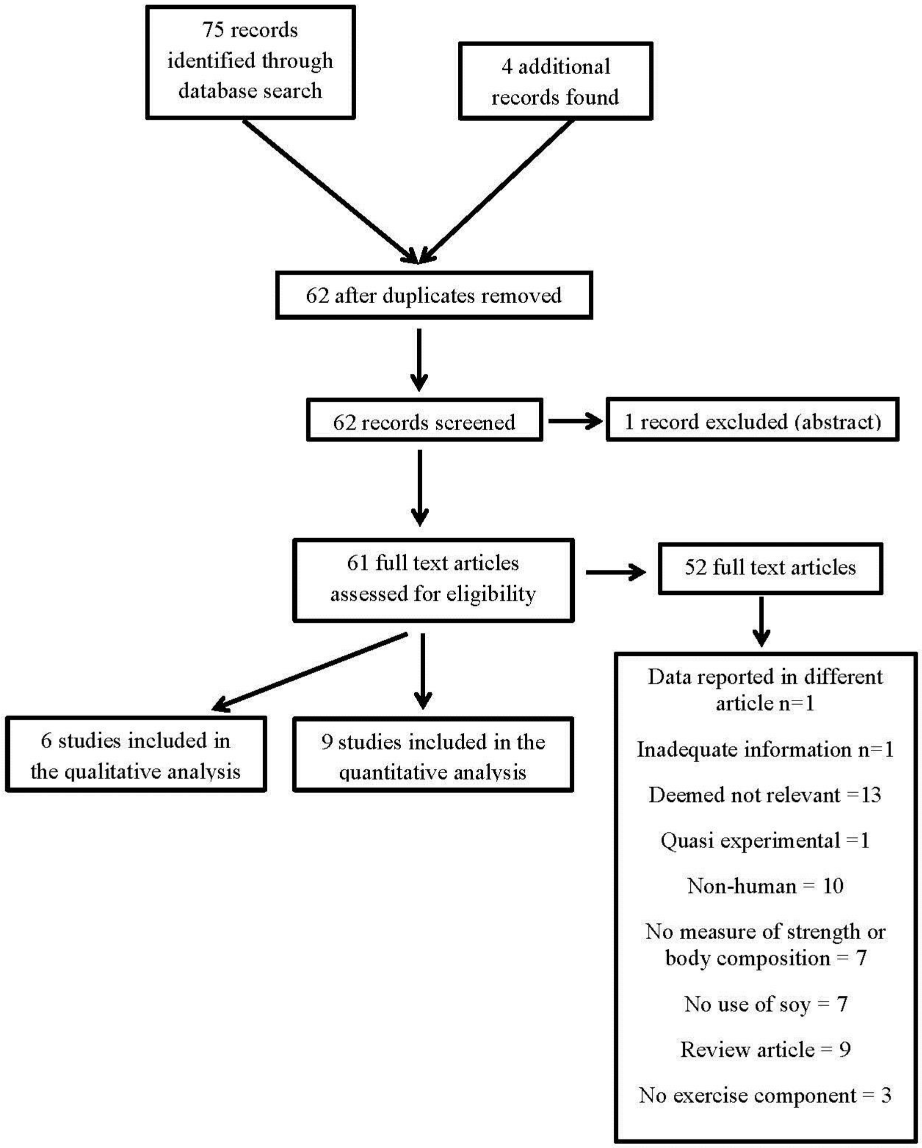

Figure 1. Flow diagram showing outcomes of literature search and inclusion/exclusion of studies at each stage.

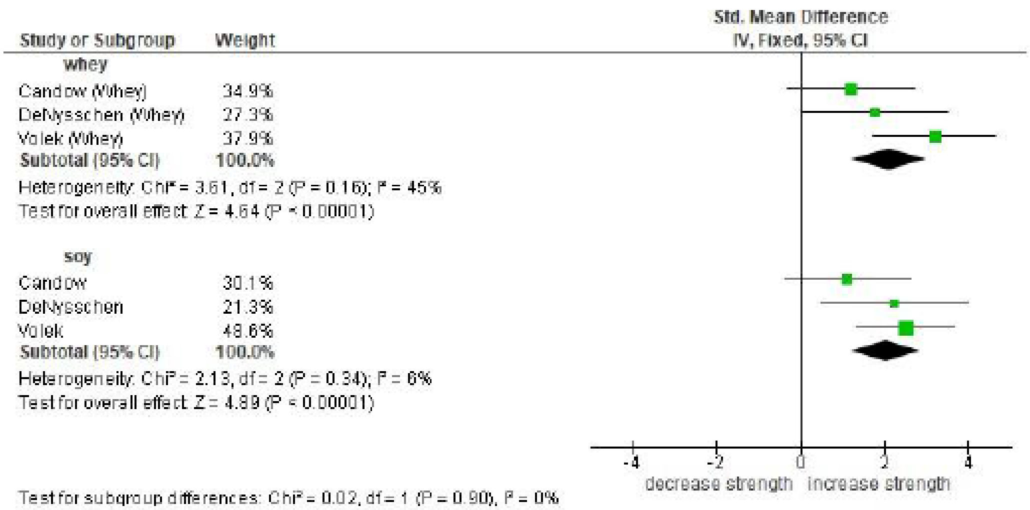

Figure 2. Forest plot showing the effect of protein source supplementation (whey vs soy) combined with RET, on change (SMD) in bench press strength (1 RM). Figure shows effect for each group and a comparison of change between groups (Chi^2).

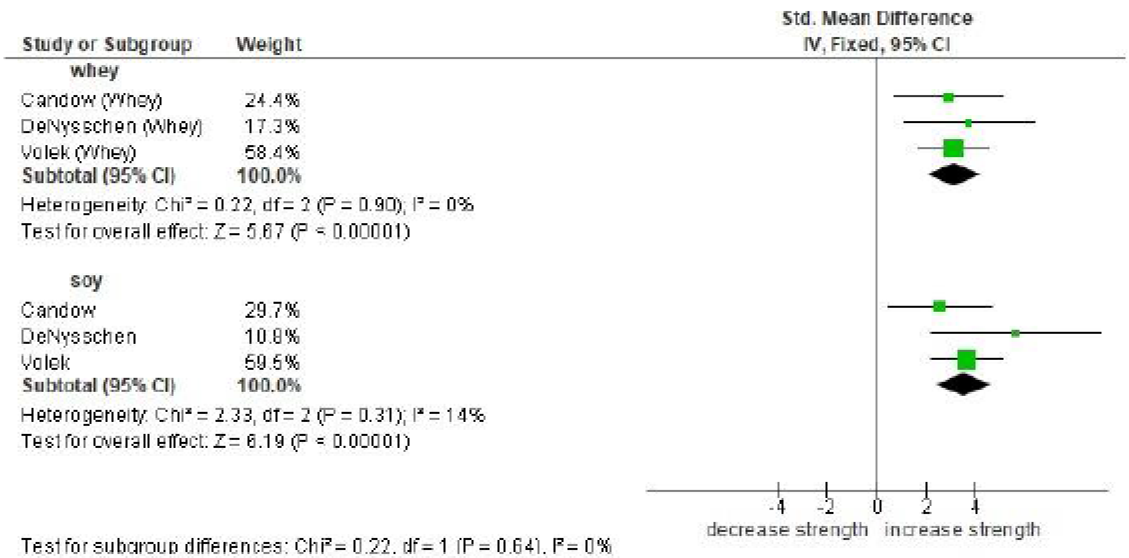

Figure 3. Forest plot showing the effect of protein source supplementation (whey vs soy) combined with RET, on change (SMD) in squat/leg press strength (1 RM). Figure shows effect for each group and a comparison of change between groups (Chi^2).

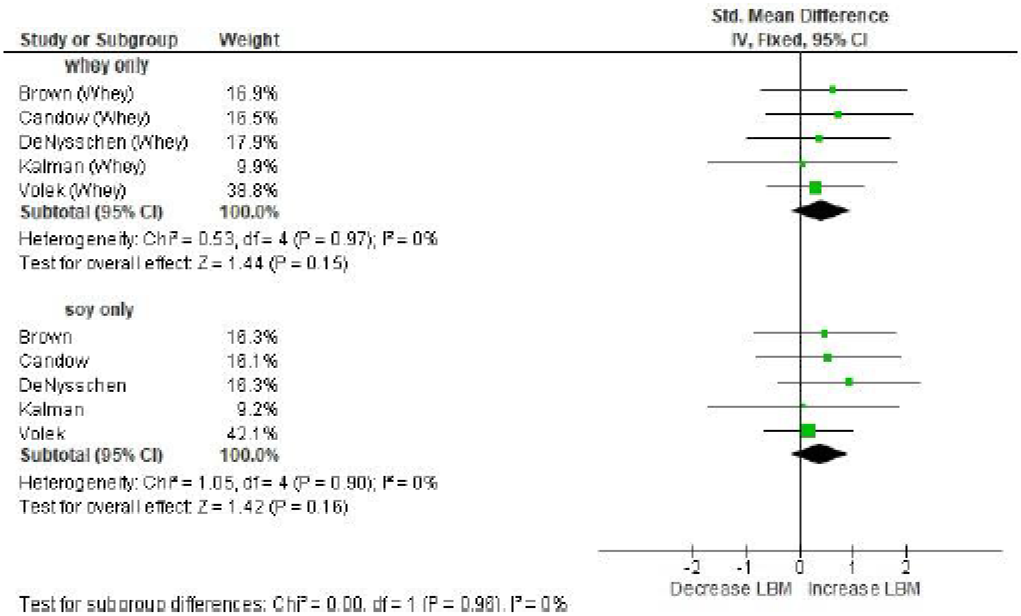

Figure 4. Forest plot showing the effect of protein source supplementation (whey vs soy) combined with RET, on change (SMD) lean body mass (LBM). Figure shows effect for each group and a comparison of change between groups (Chi^2).

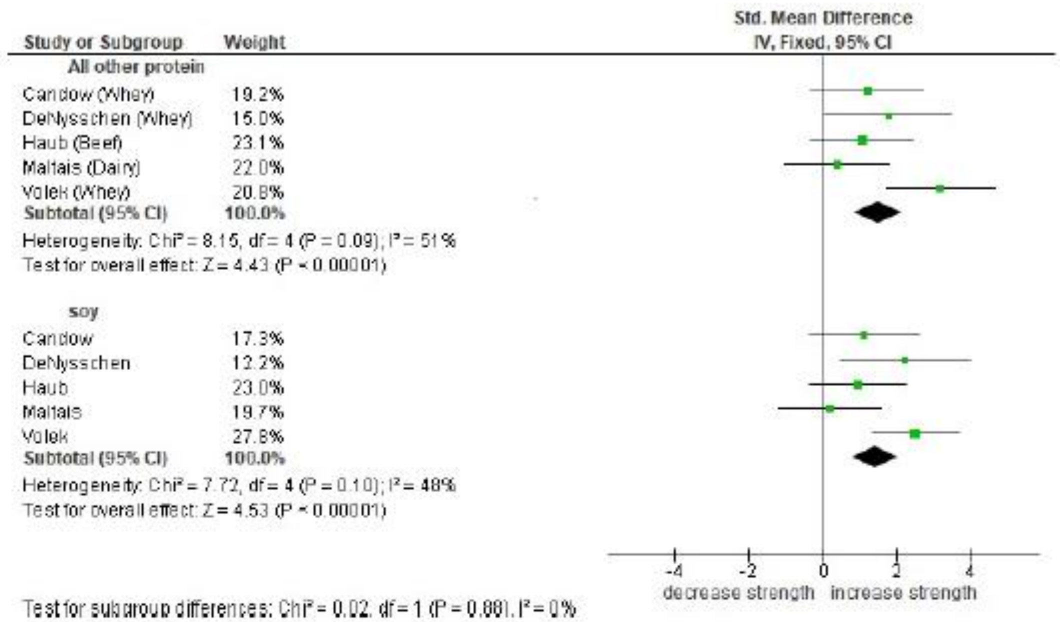

Figure 5. Forest plot showing the effect of protein source supplementation (other proteins vs soy) combined with RET, on change (SMD) in bench press strength (1 RM). Figure shows effect for each group and a comparison of change between groups (Chi^2).

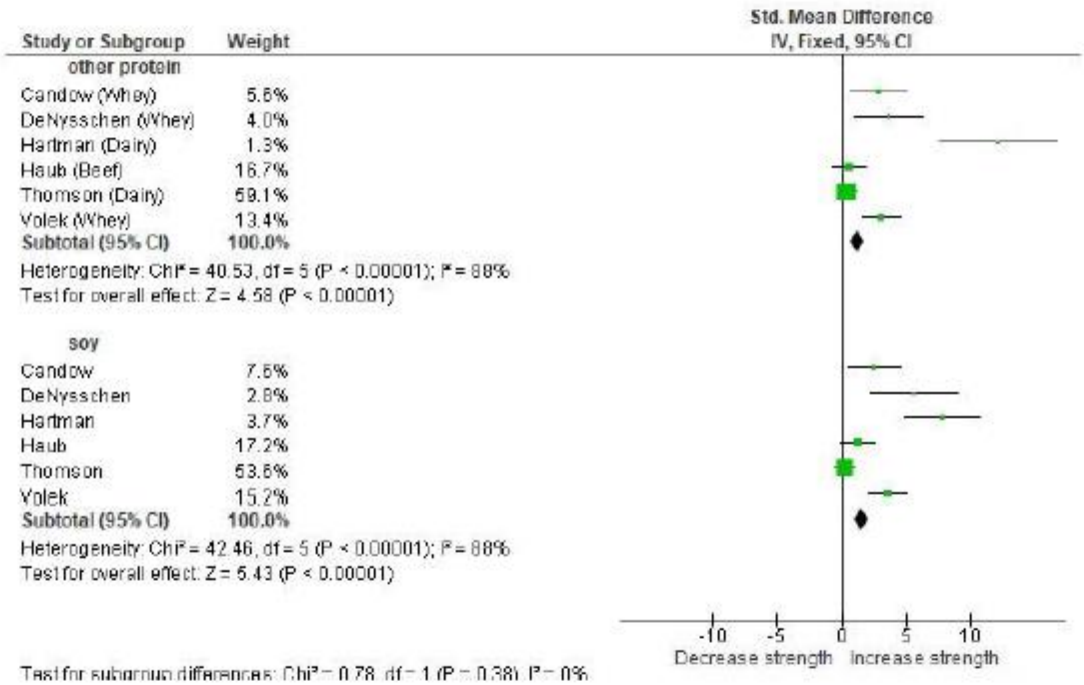

Figure 6. Forest plot showing the effect of protein source supplementation (other proteins vs soy) combined with RET, on change (SMD) in squat/leg press strength (1 RM). Figure shows effect for each group and a comparison of change between groups (Chi^2).

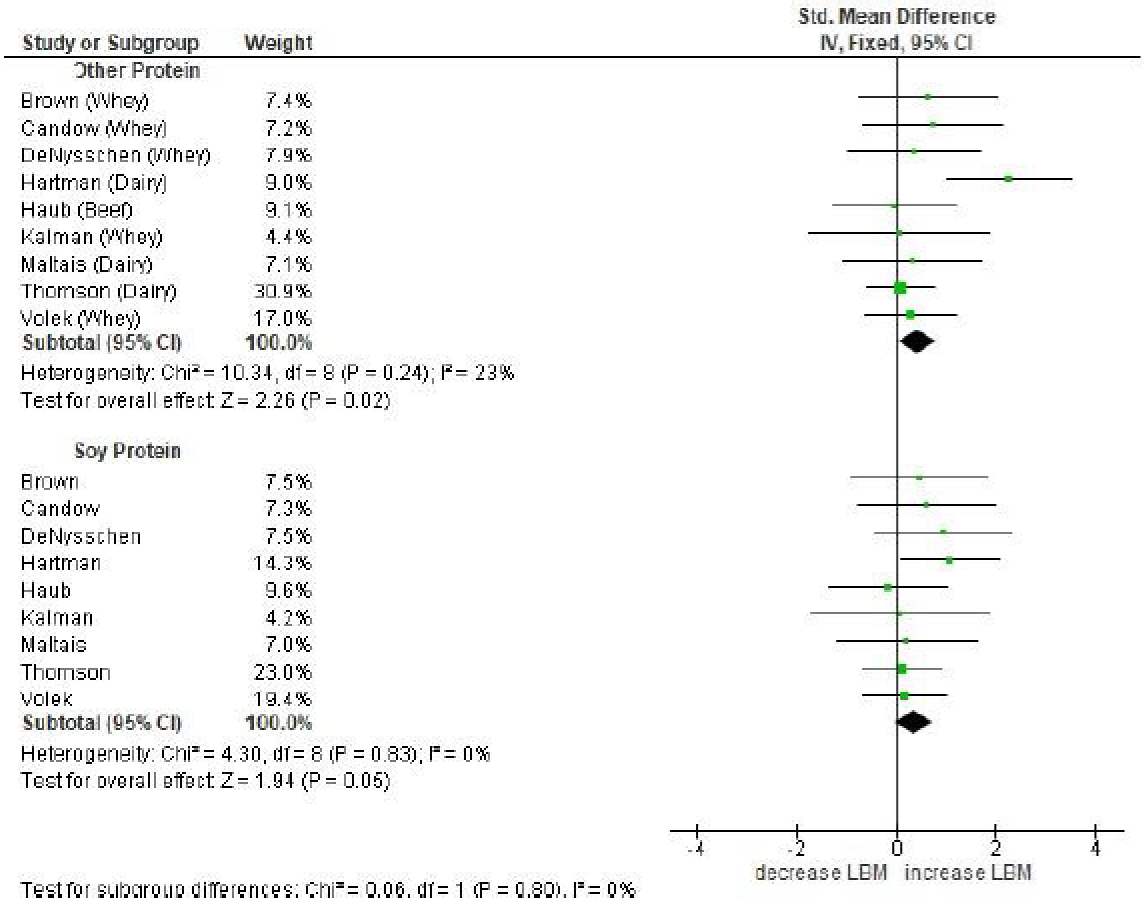

Figure 7. Forest plot showing the effect of protein source supplementation (other proteins vs soy) combined with RET, on change (SMD) in lean body mass (LBM). Figure shows effect for each group and a comparison of change between groups (Chi^2).

Table 1. Description of studies included in the meta-analysis

Author, year	Country	RET duration (wks)	RET (d/wk)	Trained (yes/no)	Timing of test protein	n/Gender	Age mean ± SD or range	Intervention (g/d)	Total protein intake (g/kg) unless otherwise indicated
Haub, 2002	USA	12	5	No	NI[1]				Initial Final
						10/M	63 ± 3	Beef, ~52 g	1.00 1.03
						11/M	67 ± 6	TVP, ~53 g[2]	1.06 1.15
Thomson, 2016	Australia	12	3	No	Immediately after RET	23/M,F[3]	61.5 ± 6.9	Usual diet	1.08 g/kg
						34/M,F[3]	61.3 ± 6.9	Dairy, 27 g[4]	1.42
						26/.M,F[3]	61.7 ± 8.3	Soy, 27 g[5]	1.45
Hartman, 2007	Canada	12	5	No	Within 1 h post RET				Initial Final
						19/M	18 – 30	Maltodextrin	1.4 1.6
						18/M	18 – 30	Milk, 17.5 g	1.4 1.8
						19/M	18 – 30	Soy, 17.5 g[6]	1.2 1.6
Maltais, 2016	Canada	16	3	No	Immediately after RET				Initial Final
						10/M	64 ± 4.5	Rice milk, ~0	1.32 1.05
						8/M	68 ± 5.6	Milk, 12 g + 7 g IAA[7]	1.04 0.95
						8/M	64 ± 4.8	Soy, 12 g + 7 g IAA[7]	1.26 1.21
Candow, 2006	Canada	6	2	No	1/3 ~30 min before RET, 1/3 ~30 min post RET & 1/3 at bedtime				Initial Final
						9/6 F, 3 M	23.0 ± 6	Maltodextrin, ~83 g	1.7 1.7
						9/6 F, 3 M	24.0 ± 6	Whey, ~83 g	1.6 1.9
						9/6 F, 3 M	22.5 ± 6	Soy, ~86 g	1.8 1.8
Brown, 2004	USA	9	NI	Yes	1/3 at participant's discretion 3x/d	9/M	20.4 ± 0.6	Usual diet	NI
						9/M	20.4 ± 0.3	Whey, 33 g	
						9/M	21.7 ± 0.2	Soy, 33 g	
Kalman, 2007	USA	12	3	Matched for training	½ within 1 h post RET, ½ later in day				Post vs Pre
						5/M	31.6 ± 5.9	Whey, 50 g	23 g/d
						5/M	31.6 ± 5.9	Soy (ISP) + Whey, 50 g	-21 g/d
						5/M	31.6 ± 5.9	Soy (concentrate), 50 g	63 g/d
						5/M	30.3 ± 8.1	Soy (ISP), 50 g	-21 g/d
DeNysschen, 2009	USA	12	3	No	Within 1 h of RET				Initial Final
						9/M	38, 21-50	Carbohydrate, 25 g	1.0 1.0
						9/M	38, 21-50	Whey, 26.6	1.0 1.2
						10/M	38, 21-50	Soy, 25.8 g	0.92 1.1

Author, year	Country	RET duration (wks)	RET (d/wk)	Trained (yes/no)	Timing of test protein	n/Gender	Age mean ± SD or range	Intervention (g/d)	Total protein intake (g/kg) unless otherwise indicated
Volek, 2013	USA	36	2-3	No	Immediately post RET				Initial Final
						22/M, F	22.3 ± 3.1	Maltodextrin, 45 g	1.14 1.06
						19/M, F	22.8 ± 3.7	Whey, 21.6	1.27 1.39
						22/M, F	24.0 ± 2.9	Soy, 20.0	1.27 1.35

[1]Not indicated [2]TVP, textured vegetable protein [3]55% women at baseline; no gender breakdown given at study end [4]Yogurt and milk [5]Soy yogurt, soymilk, soy protein powder [6]Source of soy protein not indicated [7]Indispensible amino acids providing 3.5 g leucine.