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Published in:
Nutrition Research

DOI:
10.1016/j.nutres.2017.05.002

Publication date:
2017

Effectiveness of nutritional and exercise interventions to improve body composition and muscle strength or function in sarcopenic obese older adults: A systematic review

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List of Abbreviations

% BF; Percentage Body Fat

ACSM; American College of Sports Medicine

AHA; American Heart Association

BIA; Bioelectrical Impedance Analysis

BMI; Body Mass Index

CT; Computerized Tomography

DXA; Dual-energy X-ray Absorptiometry

EPIDOS; EPIDemiologie de l'OSteoporose

EWGSOP; European Working Group on Sarcopenia in Older People

FM; fat mass;

GFR; Glomerular Filtration Rate

HD; Habitual Diet

HG, Handgrip

HSC; High Speed Circuit

IGF-1; Insulin-like Growth Factor 1

IADL; Instrumental Activities of Daily Living

LM; Lean Mass

MRI; Magnetic Resonance Imaging

MPS; muscle protein synthesis

mTOR; mechanistic Target of Rapamycin

PRISMA; Preferred Reporting for Systematic Reviews and Meta-analyses

PROSPERO; International prospective register of systematic reviews

RCH+HD; Ricotta Cheese plus Habitual Diet

RCTs; Randomized controlled trials

RPE; Rates of Perceived Exertion

RM; Repetition Maximum

SD; Standard Deviation

SGOT; Serum Glutamic Oxaloacetic Transaminase

SGPT; Serum Glutamic-Pyruvic Transaminase

SPPB; Short Physical Performance Battery test

SMI; Skeletal muscle index; SO, Sarcopenic Obesity

SH; Strength Hypertrophy

TASM; Total appendicular skeletal muscle

Abstract

Although sarcopenic obesity (SO) poses a major public health concern, a robust approach for the optimization of body composition and strength/function in SO has not yet been established. The purpose of this systematic review was to assess the effectiveness of nutritional (focusing on energy and protein modulation) and exercise interventions, either individually or combined, on body composition and strength/function in older adults with SO. MEDLINE, the Cochrane Central Register of Controlled Trials, CINAHL and SPORTDiscus were searched. Main inclusion criteria comprised sarcopenia as defined by the European Working Group on Sarcopenia in Older People (EWGSOP) and obesity defined as % body fat ≥ 40 % (women) and ≥ 28 % (men). Randomized controlled trials (RCTs), randomized controlled crossover trials and controlled clinical trials with older adults (mean age ≥65 years) following a nutritional regimen and/or an exercise training program were considered. Out of 109 full text articles identified, only two RCTs (61 participants) met the inclusion criteria. One study was a nutritional intervention adding 15 g protein·day^{-1} (via cheese consumption) to the participants' habitual diet. The second study was a high-speed circuit resistance training intervention. Body composition did not change significantly in either of the studies. However, the exercise intervention improved significantly muscle strength and physical function. Although this review was limited by the small number of eligible studies, it provides evidence for the potential benefits of exercise and highlights the necessity for future research to develop effective interventions including dietary and exercise regimens to combat sarcopenic obesity.

Keywords: Aged; sarcopenia; obesity; dietary proteins; exercise; systematic review

1. Introduction

Sarcopenia is defined by the European Working Group on Sarcopenia in Older People (EWGSOP) as the age-related decline of muscle mass and strength or function [1]. Low strength and muscle mass are associated with poor functional status, physical impairments, frailty, increased risk of falls, loss of independence and higher mortality risk [1][2]. It has been suggested that in older people, strength is a stronger predictor of functional impairment and mortality rates than absolute changes in muscle mass or lean mass alone [3-6]. Secondary to functional impairments, muscle atrophy may also contribute to insulin resistance as muscle tissue plays the main role in glucose uptake and utilization [7]. According to a recent systematic review, the prevalence of sarcopenia may vary from 1 % to 29 % in community-dwellers and 14-33 % in long-term care populations [8].

Another condition that can promote poor health is obesity, which is defined as ‘abnormal or excess body fat accumulation’ [9], and is a growing concern due to its progressively rising prevalence rates in older populations [10]. In 2010, 35 % and 28 % of the adults 65 years of age and older were reported to be obese in the US and the UK, respectively [11][12]. Similar to sarcopenia, obesity can increase the risk of falls and mobility limitations in older age [13][14], and when used in conjunction with indices of body composition and fat distribution (waist circumference or waist to hip ratio) it may be associated with adverse health effects, such as cardiovascular disease, metabolic syndrome, diabetes mellitus and several cancers [15]. Furthermore, adipose tissue can infiltrate the muscle tissue [16] and mediate an inflammatory response [17], which can result in muscle atrophy, mobility losses and lower strength and muscle quality [16][18][19].

The relationship between sarcopenia and obesity is complex, with the development/ progression of one condition being closely connected to the other (**Figure 1**). The condition where sarcopenia and obesity occur together has been termed sarcopenic obesity (SO) [20]. It has been suggested that SO can predispose older individuals to more physical disabilities, gait and balance abnormalities, and an increased risk of falls compared with either of the two conditions alone [21]. Individuals with SO are exposed to ~2.5 times higher risk of reporting Instrumental Activities of Daily Living (IADL) disabilities compared with adults without obesity but with sarcopenia, or adults with obesity but without sarcopenia [22]. This negative synergistic effect of sarcopenia and obesity is in accordance with the findings from the EPIDOS (EPIDemiologie de l'OSteoporose) study, which reported that among a cohort of 1,308 women divided in four groups: 1) without sarcopenia or obesity 2) with obesity but not sarcopenia 3) with sarcopenia but not obesity and 4) with SO, the latter was the poorest in terms of performing physical activities that required strength [23]. According to a meta-analysis of 12 prospective cohort studies with a total number of 35,287 participants, the adults with SO had a 24 % higher risk of all-cause mortality compared with their healthy counterparts [24].

Figure 1 Relationship between sarcopenia and obesity and associated outcomes

Although SO has gained significant attention from the scientific community in recent years, and a plethora of existing definitions and cut-offs for sarcopenia and obesity exist, there is no universally accepted definition for SO [1][25][26]. Depending on the definition criteria and

cut-offs used the prevalence rates of SO can vary up to 26-fold, which makes detection and management of the condition challenging for healthcare practitioners [27]. Moreover, there are operational challenges around the management of SO. While exercise training can be beneficial for both obesity and sarcopenia, the dietary management of obesity may require energy restriction, whilst management of sarcopenia requires an increased intake of macronutrients, especially protein [28].

This has resulted in a growing body of evidence highlighting potentially beneficial nutritional and exercise strategies, aiming to reverse or attenuate the negative effects of ageing on body composition and physical function [29-31]. Particular focus has been placed on protein intake, energy modulation and resistance exercise [32][33]. With regard to protein intake, there seems to be a consensus for the benefits of increased protein intake, ranging from 1.0 g· kg bw^{-1}· day^{-1} to 1.5 g· kg bw^{-1}· day^{-1}, with the higher values appropriate for those older adults with chronic conditions, sarcopenia and malnutrition, or when combined with resistance exercise [28][34][35].

However, there are relatively few intervention studies utilizing exercise training and/or nutritional regimens for older adults with SO [26][36]. It appears that most intervention trials have aimed to attenuate muscle loss at an early stage rather than try to 'reverse' an established condition related to advanced ageing such as sarcopenia or SO, which would be far more challenging [37]. Furthermore, to the best of our knowledge, there has been no systematic review to date assessing the effectiveness of nutritional and exercise strategies, alone or combined, to improve body composition and strength/function indices in older individuals with SO. Therefore, the purpose of this systematic review was to assess the

147 evidence for the use of diets modulating energy and protein (or amino acids) content, exercise
148 training regimens, or diet and exercise training combined, in older adults with SO.

149

150 The focus of this systematic review was to determine the effectiveness of protein or energy-
151 modulating regimens, with or without exercise training on body composition and function in
152 adults, 65 years of age and older with SO. In particular, our aims were to 1) determine
153 changes in absolute muscle mass, total appendicular skeletal muscle (TASM), skeletal muscle
154 index (SMI), fat mass, % body fat, body weight and body mass index (BMI), 2) assess
155 changes in muscle strength and/or physical function (including muscle strength, power, gait
156 speed and balance and 3) evaluate the effect of these interventions on quality of life,
157 metabolic profile, activities of daily living, adverse effects of supplementation or food
158 choices, compliance rates and changes in habitual dietary intake during or after the
159 interventions.

160

161 **2. Approach**

162

163 This systematic review was performed according to the Preferred Reporting for Systematic
164 Reviews and Meta-analyses (PRISMA) guidelines [38]. The protocol was registered with the
165 International prospective register of systematic reviews (PROSPERO registration number:
166 CRD42015017311).

167

168 **2.1. Search Strategy**

169

The Cochrane Central Register of Controlled Trials, MEDLINE (via EBSCOhost Research Databases), CINAHL and SPORTDiscus were searched up to and including May 2016. The last search was conducted on 22 May 2016. No limits were applied for date of publication. Combinations of key terms with Medical Subject Headings (MeSH) and Boolean operators were used. The main keywords and terms used were: Age*/ Adult*/ Old*/ Elderly/ Senior, Sarcopeni*/ Lean/ Frail/ Atrophy/ Weakness, Obes*/ Overweight/ Body Mass Index, Exercise/ Training/ Strength/ Muscle/ Mass/ Hypertrophy/ Size/ Body Composition, Diet/ Supplements/ Protein/ Amino Acids/ Energy, Life Quality/ Intervention. The search limiters were English language and studies with human participants [the complete search strategy is presented in supplementary file 2].

2.2. Inclusion Criteria

We included randomized control trials (RCTs), randomized control crossover trials and controlled clinical trials using prospective nutritional and/or exercise interventions to attenuate/ reverse the loss of muscle mass, reduce adipose tissue and optimize muscle strength or function. Given that there are no universally adopted definition criteria for SO, some authors may have used different terms to define the participants, e.g. ‘weak and overweight’ or ‘obese frail’ etc. Such studies were included only if the participants had a sarcopenic phenotype based on the definition criteria and cut-off scores recommended by the EWGSOP [1]. Therefore, studies were included only if they presented data for a) body composition (data on absolute muscle mass, appendicular muscle mass, Total Appendicular Skeletal Muscle (TASM) or Skeletal Muscle Index (SMI) assessed by Dual-energy X-ray Absorptiometry (DXA), Bioelectrical Impedance Analysis (BIA), Computerised Tomography (CT) or Magnetic Resonance Imaging (MRI) and b) muscular strength and/ or physical

function identified by one of the following tests: handgrip strength, knee flexion/extension, peak expiratory flow, gait speed, the Short Physical Performance Battery test (SPPB), the timed up-and-go test or the stair climb power test . The mean age cut-off for inclusion was ≥ 65 years based on how 'old age' is defined in the joint recommendations from the American College of Sports Medicine (ACSM) and the American Heart Association (AHA) [39]. The inclusion criterion for obesity was defined as mean percentage body fat (% BF) ≥ 28 % in men and ≥ 40 % in women [22] or in the absence of % BF data, a BMI ≥ 27 $kg \cdot m^{-2}$. For any given BMI, a person with sarcopenia will have by definition more body fat compared with their counterparts without sarcopenia, therefore, adults with sarcopenia can present high-adiposity at BMIs substantially lower than 30 $kg \cdot m^{-2}$ [40]. Moreover, it is not uncommon for studies to recruit participants who would be classified as overweight or obese based on a BMI cut-off ranging from 25 to 28 $kg \cdot m^{-2}$ when the focus is on sarcopenic obesity and/or when participants come from a non-Caucasian ethnic group [25][26]. Studies that presented neither the % BF nor BMI were included only if these indices could be derived from the weight, height and body fat mass values, or if the authors of the study when contacted provided the essential information.

Nutritional interventions aiming to promote muscle hypertrophy by macronutrient profile modification or weight loss via energy restriction were of primary interest. Studies providing extra macronutrients (especially proteins or amino acids and their metabolites) either in the form of whole foods or dietary supplements administered through the oral route only were considered. Exercise regimens including resistance, balance, aerobic and mixed exercise protocols influencing lean mass, fat mass, muscle hypertrophy, strength, power, speed and/ or physical functional were also of primary interest.

2.3. Exclusion Criteria

Studies were excluded if the protocol involved administration of any kind of prescription only/pharmaceutical agents, or any type of supplementation administered via a route other than oral. Studies including participants with cachexia or with serious mental and cognitive conditions prohibiting adherence to a structured exercise/ nutrition regimen, such as Alzheimer's or dementia, were excluded.

2.4. Study Selection

The titles and abstracts were screened for eligibility (CT), and the full text copies of potentially eligible articles were obtained for further inspection. The full-text articles were independently assessed for eligibility by two reviewers (CT and JJ). The reference lists of eligible articles and review papers as well as journals specializing in older age were hand searched for potential articles. Any disagreement between the two reviewers was resolved by a third reviewer (CAG).

2.5. Data Extraction

Data were extracted from each eligible article by two reviewers (CT and CAG). Any disagreements between the two reviewers were resolved by discussion until consensus was reached. Demographic (age, sex, ethnicity/host country and habitation), methodological (study design, sample sizes, duration, nutritional/dietary and/or exercise intervention plan, supplement type, dosing/frequency of administration, exercise training

type/frequency/volume, assessment method, blinding) and outcome data (changes within and between groups, significance, dropout rates, compliance, adverse effects) were compiled in a standardized Excel spreadsheet.

2.6. Quality Assessment

The quality of the studies was assessed by two independent reviewers using a modified version of the Downs and Black rating scale [41][42]. The Downs and Black scale is one of the most credible instruments for the quality assessment of randomized [43] and non-randomized intervention trials [44]. Modified scoring for Question 27 was performed as detailed by Eng et al. [42]: the original scale had a maximum score of 32 but in this review Question 27 was modified to score either 0 or 1 point instead of the original 0-5 points. Therefore, the maximum total score for the five sections of the scale (reporting, external validity, internal validity/bias, internal validity/confounding, power) was 28.

2.7. Principal Summary Measures

The primary outcome measures were 1) differences in mean of skeletal muscle mass (either absolute, relative or appendicular) and body fat or BMI, and 2) differences in mean of muscle strength and physical function/performance

3. Results

3.1. Description of studies

Our search strategy resulted in 1,440 potential articles. After the exclusion of 1,331 articles based on titles and abstracts, 109 full-text articles reporting 109 studies were retrieved and assessed for eligibility. The detailed flow chart of the selection process is presented in **Figure 2**. The authors of two potentially eligible studies [45][46] were contacted for further information, but retrieval of all the essential body composition data was not possible for reasons unrelated to this review, therefore, the articles were excluded. A total of n=2 studies [47][48] including n= 61 participants met the inclusion criteria and were included in the review. Study A[47] was a nutritional intervention and study B[48] an exercise training intervention; neither of the studies combined exercise with diet.

Figure 2. Information flow through the phases of the systematic review according to PRISMA guidelines.

3.2. Quality Assessment

The two studies were randomized control trials of moderate methodological quality based on the modified Downs and Black rating scale [41][42]. The total score for each study was 18 out of 28. The summary key information of the methodological strengths and limitations is presented in table 1 (**supplementary file 1** presents the complete breakdown of the scoring in the different subsections of the scale). Both studies performed power calculations to determine the population sample size prior to recruitment, however, study B[48] was underpowered; target was *n*=21 per group, but the final analysis was conducted with *n=9* and *n=8* for the control and intervention group, respectively. In study A[47] only the testers were

blinded but not the participants. In study B[48] the two groups were exercising at different times, therefore, participants were partially blinded. Study A[47] reported and tested for a range of potential confounders, but failed to report essential information regarding the participants' dietary intake at baseline and follow-up. The results in Study A were based on an intention-to-treat analysis, whereas in Study B the analysis conducted was per-protocol.

Table 1. Summary key points of the included study designs.

3.3. Participant Characteristics

Participants in study A[47] were physically-independent individuals living in Mexico. Their mean± SD age and TASM were 76± 5.4 years and 15.5± 2.9 kg, respectively. The mean % BF of men and women was 33.3± 6.2 % and 47.8± 6.6 %, respectively. At baseline two men had a % BF < 28 % and three women < 40 %. All participants in study B[48] were independent-living community dwellers from South Miami (USA). The mean ± SD age and BMI of participants was 71.3 ± 7.8 years and 32.6 ± 4.7 kg · m^{-2}, respectively and their mean SMI 6.6 ± 1.0 kg · m^{-2}.

3.4. Study Design

The aim of study A[47] was to assess whether the addition of a protein rich food to the habitual diet could increase TASM and strength in older individuals with sarcopenia. The study was a 3-month RCT with a control (habitual diet; HD) and an intervention group (habitual diet + 210 g ricotta cheese per day; RCH+HD). The cheese provided 15.7 g extra protein (including 8.6 g of essential amino acids), 10.4 g carbohydrate, 18.4 g fat and a total

of 267 kcal per day. Cheese was divided into three 70 g portions and participants were instructed to consume each portion along with their usual breakfast, lunch and dinner. Dual-energy x-ray absorptiometry was used to measure TASM and body composition changes.

Study B[48] was a 15-week single blind RCT, which aimed to assess the effectiveness of a novel exercise regime based on a high speed circuit (HSC) resistance training program (intervention) on body composition, muscular performance and IADL compared with a conventional strength hypertrophy (SH) regime (control group) in community-dwellers with SO. Body composition was assessed by single frequency BIA. Both groups performed exercises at 11 pneumatic gym machines twice per week. The SH protocol involved three sets of 10-12 repetitions at 70 % of 1RM with a 1-2 min recovery break between sets. Participants were instructed to keep a similar speed of contraction for both the concentric and eccentric phase (2 seconds per phase). The HSC group performed 10-12 repetitions at the same 11 exercises, but in a circuit pattern (i.e. moving from one exercise to the other) with no break in between exercises, unless one full circuit was complete. Three full circuits were performed in total. The resistance load was selected based on maximum power output for each machine. The concentric phase was performed as fast as possible while the eccentric in 2 seconds. No dietary or nutritional element was introduced in the study, and neither dietary patterns nor intakes were reported.

3.5. Outcomes

3.5.1. Body composition

No significant changes were seen in body composition, in either experimental or control groups. In study A[47] the addition of ricotta cheese resulted in no significant changes in lean mass, TASM or body fat in the intervention or control group (Table 2). Secondary analysis by sex showed that although men (*n*=8) in the intervention group experienced an increase in TASM by 490 g, this was not significantly different either from baseline or when compared against the control group (p=0.42), which gained a non-significant 220 g of TASM. Similarly, in study B[42] no statistically significant differences were detected in any of the body composition indices, regardless of the exercise regimen (Table 2). Skeletal muscle index (SMI) increased non-significantly in both groups (from 6.5 ± 0.66 $kg \cdot m^{-2}$ to 6.6 ± 0.59 $kg \cdot m^{-2}$ in HSC and from 6.7 ± 0.45 $kg \cdot m^{-2}$ to 6.8 ± 0.42 $kg \cdot m^{-2}$ in SH).

Table 2. Summary of the included studies

3.5.2 Strength and/ or function

In study A[47], the group receiving the extra protein noted a non-significant trend towards an increase in strength (+ 0.9 % relative increase). Although the control group experienced a drop in strength (-3.5 %), the difference between the two groups did not achieve statistical significance (p=0.06).

Study B[48] reported significant improvements in several aspects of strength and function in both exercise groups (Table 2). In particular, the strength-hypertrophy (SH) control group experienced significant improvements in leg press 1RM by 22 % (p<0.01), chest press 1RM by 16 % (p=0.03), leg press peak power by 19 % (p=0.03) and chest press peak power by 15% (p<0.01) whereas a non-significant increase of 12% was detected in hand grip strength (from 17.3 ± 2.7 kg to 19.4 ± 4.6 kg; p>0.05). The HSC group had a significant improvement

in chest press 1RM by 21 % ($p<0.01$), leg press peak power by 41% ($p<0.01$) chest press peak power by 24 % ($p<0.01$) but hand grip strength did not change significantly (increased by 10 %, from 17.7 ± 7.8 kg to 19.4 ± 6.6 kg; $p>0.5$). Between group differences were detected only for leg press peak power, with the HSC group performing better than the control by 158 W [95 % CI (2, 315), $p=0.005$].

The Short Physical Performance Battery (SPPB) test improved significantly over time only within the HSC group from 8.0 ± 1.5 to 9.6 ±1.2 ($p=0.02$). Between group differences favored the HSC group [mean difference 1.1 (95 % CI (-0.1, 2.4), $p=0.08$], although this was not statistically significant.

3.5.3 Secondary Outcomes

Consumption of ricotta cheese in study A[47], resulted in significantly lower fasting insulin levels in men ($p=0.05$) but not in women. There were no other significant changes in hepatic markers (Serum Glutamic Oxaloacetic Transaminase (SGOT), Serum Glutamic-Pyruvic Transaminase (SGPT) and Alkaline Phosphatase), kidney function (blood urea, uric acid, creatinine and Glomerular Filtration Rate (GFR)), anabolism (Insulin-like Growth Factor-1 (IGF-1)) or insulin resistance. No cases of microalbuminuria were present in the RCH+HD group after the intervention period. In the intervention group, 25 % of women reported early satiety after the consumption of ricotta cheese, however, dietary intakes were not reported. Eight participants from the intervention group dropped out; five were due to personal health issues, two could not eat the entire portion of ricotta cheese, and one had to relocate. In the control group three people dropped out (two for personal reasons and one for modifying the

habitual diet). However, all participants were measured pre- and post-intervention according to an intention-to-treat analysis.

The exercise intervention in study B[48] resulted in acute joint pain only in the SH group. In addition, the HSC group reported significantly lower rates of perceived exertion (RPE) with a mean difference of -1.5 (95 % CI -2.0,-0.12, p=0.04). Adherence rates were similar in the two groups; 81 % in HSC and 85 % in SH. Regarding the Instrumental Activities of Daily Living (IADLs) there were significant improvements within both groups (pre vs post); namely, time needed for jacket on and off (from 11.5 ± 3.5 s to 10.2 ± 2.0 s; p=0.04), scarf pick-up (5.2 ± 1.1 s to 4.7 ± 0.91 s; p<0.01 and pan carry (4.9 ± 0.61 s to 3.9± 0.77 s; p<0.01) improved significantly within the control group, while the HSC group experienced significant improvements in time for sit-to-stand (from 16.1 ± 5.7 s to 13.4 ± 3.9 s; p=0.02) and pan carry (5.4 ± 1.3 s to 4.5 ± 1.2 s; p<0.01). No differences were observed between the two groups in the aforementioned IADLs.

In summary, neither of the studies had a significant effect on body composition. The introduction of ricotta cheese in the habitual diet of participants in study A[47] aimed to increase their protein intake but it was not reported whether or not this was achieved, and if so to what extent. In the same study, there was a trend for an increase in strength in the intervention group, but this was not significant. The only significant improvement reported was the fasting insulin levels, but that was reported only in men in the intervention group. Despite the lack of body composition changes, in study B[48], the high speed circuit resistance training and strength hypertrophy resistance training protocols significantly improved strength, power and function indices. Finally, due to the limited data extracted and

diversity of methodologies, statistical pooling was not feasible and therefore, a narrative analysis was conducted.

4. Discussion

The aim of this systematic review was to assess the effectiveness of nutritional and/or exercise interventions on body composition and strength or function in older adults with obesity and sarcopenia. Although only two studies were identified, the lack of intervention trials clearly highlights the need for more research in this area, especially trials combining exercise with nutritional approaches targeting this population group. With regard to the main outcomes, neither an increase in protein intake by 15g · day^{-1} nor a 15-week resistance exercise protocol produced significant improvements in body composition indices. However, the exercise intervention (both the control group following a strength-hypertrophy resistance exercise protocol and the intervention group utilizing a high-speed power-orientated circuit resistance training) reported significant improvements in both strength and function.

4.1 Effects of protein intake on body composition and function in sarcopenic obesity

Study A[47] attempted to utilize the effects of protein on increased skeletal muscle mass accretion rates. Although the authors acknowledged that the suggested recommendations for protein intake in older individuals with sarcopenia are 1.2- 1.5 g ·kg bw^{-1} ·day^{-1} [47], they did not report the participants' daily protein intake, therefore, it was not corroborated whether such intakes were achieved. It has been suggested that maximal muscle protein synthesis (MPS) rates in older adults can be achieved using ~35- 40 g protein · $meal^{-1}$ [49-51] or 0.4 g protein · kg bw^{-1} · $meal^{-1}$ [51]. A valid question would be whether a daily addition of 210 g ricotta cheese (delivering 15.7 g protein [47]) to the habitual diet could practically augment

438 muscle mass in older adults with sarcopenia. It is important to note that the cheese servings
439 were not consumed in one meal, instead they were spread over the three main meals, that is,
440 70 g cheese (~5 g of extra protein per meal) consumed with breakfast, lunch and dinner.
441 Protein intakes in Study A[47] were not reported, but if we extrapolate data from studies in
442 similar population cohorts [52], it has been suggested that older individuals are not likely to
443 consume an adequate amount of protein during all main meals. Tieland et al. [52] reported
444 mean protein intakes of ~8 g, ~18 g and ~29 g for breakfast, lunch and dinner, respectively.
445 Therefore, it is uncertain whether the addition of 5 g protein in the main meals in study A[47]
446 was enough to significantly augment MPS.
447
448 Another confounder may have been the potential impact of the addition of cheese on the
449 habitual diet given the fact that 25 % of women in Study A[47] experienced early satiety. It
450 could be consequently speculated that women's habitual diet was modified with the addition
451 of ricotta, potentially displacing the intake of other foods. However this cannot be confirmed
452 as the habitual diet was not reported.
453
454 In study A [47], even though there was a trend towards increased strength, it could be argued
455 that higher -and perhaps different distributions of- protein intake [31] were needed to enhance
456 muscle strength and accretion of skeletal muscle mass. It should be also noted that the power
457 calculation for sample size was based on lean mass as the primary outcome, rather than
458 muscle strength. Therefore, it is unknown whether a larger sample size was needed to reveal
459 a significant change in handgrip strength.
460
461 It has been previously reported that protein supplementation can enhance function in older
462 adults. Namely, Tieland et al. [53] provided an oral supplement delivering 15 g of protein

twice daily (with breakfast and lunch) to older frail adults. This addition resulted in significantly enhanced physical performance. The potential for high protein meals to maintain or increase muscle mass and strength in older adults has been recently reported by Loenneke et al. [54] who showed that one or two meals containing 30-45 g protein · day^{-1} were associated with higher lean mass and strength compared with those who did not consume any meals over the threshold of 30g protein.

4.2 Effects of exercise training on body composition and function in sarcopenic obesity

The mechanisms underpinning the effects of exercise on body composition and function in older age are mainly accounted for by regulation of genes, circulating hormone levels (e.g. testosterone, IGF-1) and metabolic pathways (especially by activating the mechanistic target of rapamycin (mTOR), which is a pathway also activated by leucine-rich protein meals [31]) and have been reviewed in detail by Garatachea et al. [55] and McGlory and Phillips [56]. However, it is still unclear whether the modulation of these pathways can translate into real-world benefits for adults with SO.

In study B[48], the aim was to assess the effect of high-speed resistance exercise training on indices of SO. In spite of possible methodological limitations, the improvements in strength, power and IADL reported in study B[42], provide some evidence that exercise can improve several domains of physical performance such as strength and power in older adults with SO. This is in agreement with previous reports supporting the benefits of resistance exercise training on clinically important outcomes, even in the absence of increased muscle mass [8][31][57]. This may be partly accounted for by the adaptive plasticity in the neuromuscular system and skeletal muscle tissue in response to resistance exercise even in advanced older

age [58]. A significant improvement particularly in power can be very important for individuals with SO since muscle power can be a predictor of mobility skills and a more influential indicator of physical capacity compared with absolute changes in strength [59]. Another interesting finding from study B[48] was the large effect size observed in peak leg power achieved by exercising at 50 % 1RM. To a certain extent, this finding may be explained by the novel aspect of the study design, that is, the resistance exercise progression protocol. Resistance load would increase only when a power plateau was reached [48]. Therefore, the protocol was designed in such a way as to favor maximum power output.

The lack of significant changes in lean mass or muscle mass after exercise training in adults with sarcopenia, (which has also been reported elsewhere [8]), may be accounted for by protocol-specific differences such as: duration, type, intensity, volume and frequency of exercise, as well as the availability of adequate nutrients (protein/amino acids), which are needed to elicit an anabolic response and consequently muscle hypertrophy [31]. One limitation of study B[48] was the lack of control for dietary intake, which could have partly explained the lack of effect on body composition. It has been shown that a bout of resistance exercise can stimulate muscle protein synthesis (MPS) to a higher degree than protein breakdown, however, in the absence of post-workout provision of nutrients (especially protein) it can result in negative net muscle protein balance [60][61], and is a limitation of study designs to date.

These data support the potential benefit of a resistance exercise program within lifestyle intervention protocols due to its positive effect on muscle strength, power and function in older adults with SO. Although no statistically significant body-composition changes were reported in the included studies, the significant improvements in strength, power and function

513 may be more important for the quality of life of adults with SO than absolute changes in body
514 fat or lean mass per se.
515

516 **4.3 Recommendations for future research**
517

518 More intervention trials should be undertaken to identify effective lifestyle strategies in adults
519 with SO, that will inform more robust approaches to combat this condition. Future research
520 should also bridge the gap in knowledge with respect to multimodal approaches combining
521 resistance exercise training with dietary strategies modulating protein intakes, in order to
522 augment muscle mass and strength [32] or fat free mass [62], and potentially alongside an
523 energy-deficit diet to promote fat loss [33].
524

525 It is important to note that although the need to augment muscle mass is paramount, a
526 reduction in fat mass and especially fat infiltrating the muscle tissue is equally important,
527 since intermuscular fat can result in mobility limitations [16]. Exercise training can
528 preferentially reduce intermuscular adipose tissue more effectively than caloric-restriction
529 alone [63]. However, a combination of exercise with caloric-restriction can lead to greater
530 losses of total fat mass, which in turn may result in greater improvements in physical
531 function, sometimes even at the expense of lean tissue [64][65]. Nevertheless, it is currently
532 unknown whether this loss of lean mass may be detrimental in the long term for the life
533 quality of an older individual with sarcopenia who has already experienced a large decline in
534 muscle mass and strength.
535

536 To our knowledge only three studies to date, have reported significantly increased muscle or
537 lean mass while concomitantly reducing fat mass [66-68]. The pilot study conducted by

Maltais et al. [68] was the only one that recruited older overweight adults with a low appendicular lean mass index. The authors concluded that 16-weeks of a whole body resistance exercise regimen (at 80% 1RM) followed by the consumption of ~13 g dairy supplement (chocolate milk with added milk powder) increased lean mass and reduced fat mass even at the absence of caloric restriction (*n=8*). In the same study, the group that received a soy-based beverage (matched for energy, protein, essential amino acids, carbohydrate and calcium content) (*n=8*), reported significant increases only in lean mass but no changes in fat mass. Similar results, but in pre-menopausal women, have been reported by Josse et al. [66]. After 16 weeks of mixed exercise training (aerobic and resistance) combined with a caloric restriction (500 kcal daily deficit), only the high protein group (30% of total energy intake came from protein, half of which was derived from dairy products) experienced lean gains concomitant with fat losses. Albeit in younger adults, a recent four-week intervention combining 2.4 g protein · kg bw^{-1} · day^{-1} (achieved by consuming 3-4 whey-based protein beverages daily) with a mixed resistance, plyometric and high-intensity interval training alongside an energy deficit regimen resulted in significantly higher lean mass and lower body fat [67]. The control group which differed only in protein intake (1.2 g protein · kg bw^{-1} · day^{-1}) did not experience a significant change in lean mass [67].

Although the effectiveness of the aforementioned paradigms needs to be evaluated in older adults with SO, they provide the framework for an initial approach to combat this condition. What is primarily lacking from the literature is trials recruiting older adults with SO. Additionally, protocols combining a high protein diet (potentially using whey or dairy proteins) with a modest caloric deficit along with a well structured exercise training regimen could be adopted. Moreover, long-term and follow-up studies with adults with SO who have

562 intentionally lost weight should be undertaken, in order to assess the impact of weight loss
563 (especially if it comes from lean tissue) on life quality and other comorbidities.
564

565 **4.4 Limitations**

566

567 The main limitation of this review is the scarcity of data and studies undertaken in older
568 groups with SO. We reviewed only studies with participants presenting the sarcopenic
569 phenotype, as defined by the EWGSOP [1], using an appropriate methodology to assess body
570 composition. Although the EWGSOP reached a consensus in 2010 on the definition and
571 assessment of sarcopenia, adopting criteria for low muscle and low strength or function, there
572 are recent studies [68][69] that use solely the criterion of low muscle mass to define
573 sarcopenia as it was initially proposed [70], without taking into consideration low strength or
574 function. In addition, one study conducted before 2010 was excluded because muscle mass
575 was assessed using urinary creatinine [71], a method not included in the EWGSOP definition.
576 Regarding the two studies included in this review, study B[48] aimed to recruit specifically
577 participants with sarcopenic obesity. Study A[47] used sarcopenia as an inclusion criterion,
578 and although the mean % BF values met our cut-off criteria for obesity, after personal
579 communication with the authors it was reported that although the majority of participants had
580 the sarcopenic obesity phenotype, a small proportion (5 out of 40) had a % BF below our cut-
581 off.

582 Although of vital importance, there is an apparent lack of interventions with older adults with
583 SO. This is in accordance with Finger et al. [62] who commented that interventions may refer
584 to or discuss sarcopenia, however, the number of studies recruiting adults specifically with
585 sarcopenia is very limited. This is even more complex with respect to studies on sarcopenic
586 obesity, with a number of reviews [26][36][33][72] presenting interventions with participants

who either had none or only one of the conditions (sarcopenia or overweight/obesity but not both) and extrapolate these results to propose ways to improve the sarcopenic obesity phenotype. An example of an intervention study is that by Gadelha et al. [73] investigating the effect of exercise training on changes in the sarcopenic obesity index (assessed by the residuals method initially presented by Newman et al. [40] and adopted by the EWGSOP) of older Brazilian women. However, older age was the main inclusion criterion and no criteria specific for sarcopenia or obesity were adopted.

4.5 Conclusion

This review assessed studies investigating the effectiveness of exercise or nutritional interventions to improve the body composition and strength/function of older adults with sarcopenia and obesity. None of the included studies significantly reduced body fat or increased either skeletal muscle mass or lean mass. Although the number of included studies was low, it is evident that exercise training can elicit significant improvements in aspects of physical fitness such as muscle strength and power, and consequently improve performance in activities of daily living in adults with SO. The addition of 15 g protein·day^{-1} to the habitual diet via cheese consumption revealed a non-statistically significant trend towards increased handgrip strength, and a significantly better insulin response in men, but not in women. The lack of published data highlights the necessity for new research adopting universally accepted cut-offs for sarcopenic obesity, with the inclusion of appropriately designed exercise programs and dietary regimens, and with detailed assessments of dietary patterns and protein intakes for the targeted population group.

Supplementary material

Supplementary file 1 (.pdf) **S1 Table**. Assessment of the methodological quality of the included studies with the modified Downs and Black Scale.

Supplementary file 2 (.pdf) **S1 Appendix**. Search strategy

Supplementary file 3 (.doc) **PRISMA Checklist**

Acknowledgements

We would like to thank Queen Margaret University's librarians and especially Sheila Williams for the guidance they provided during the initial stages of this systematic review.

Authors' contributions

CT, CAG, EB and JJ designed the study protocol and contributed to the writing of the manuscript. CT conducted the search and screening of titles, abstracts, full-text articles, the study selection, data extraction and quality assessment and prepared the manuscript. JJ screened the full-text articles and assessed the eligibility of the studies. CAG conducted the extraction, analysis and interpretation of data and risk of bias (quality) assessment. All authors read the final version of the manuscript.

Competing interests

The authors have no competing interests to declare

Funding

Queen Margaret University, Edinburgh provided support in the form of a studentship for the main author [CT], but did not have any role in the decision to produce and publish this manuscript or in the conceptualization, methodology, analysis and interpretation of data presented.

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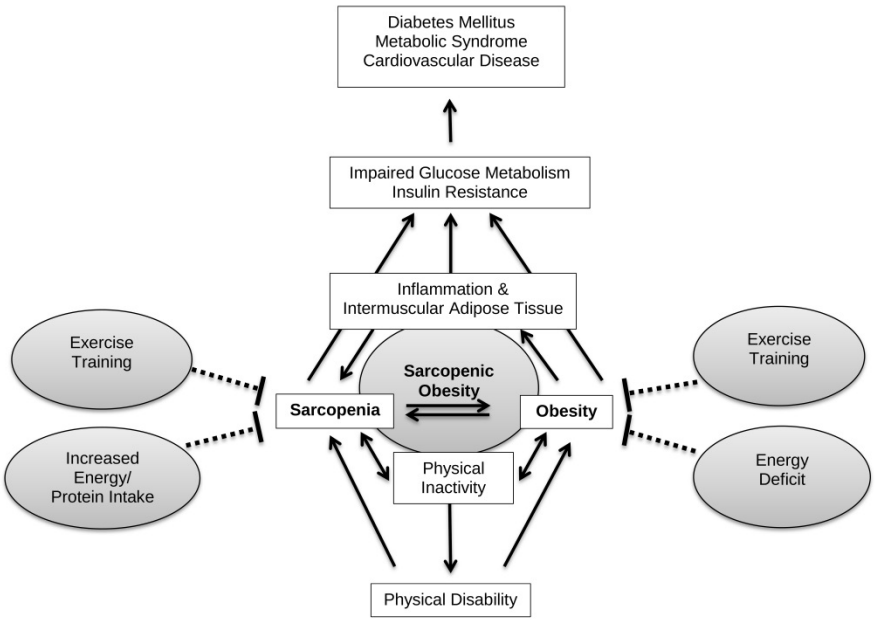

882

883 **Figure 1.** Relationship between sarcopenia and obesity and associated risks as well as

884 management strategies. Notes: Solid arrow: direct and positive association; Dashed line

885 management strategy attenuating/reversing the condition:

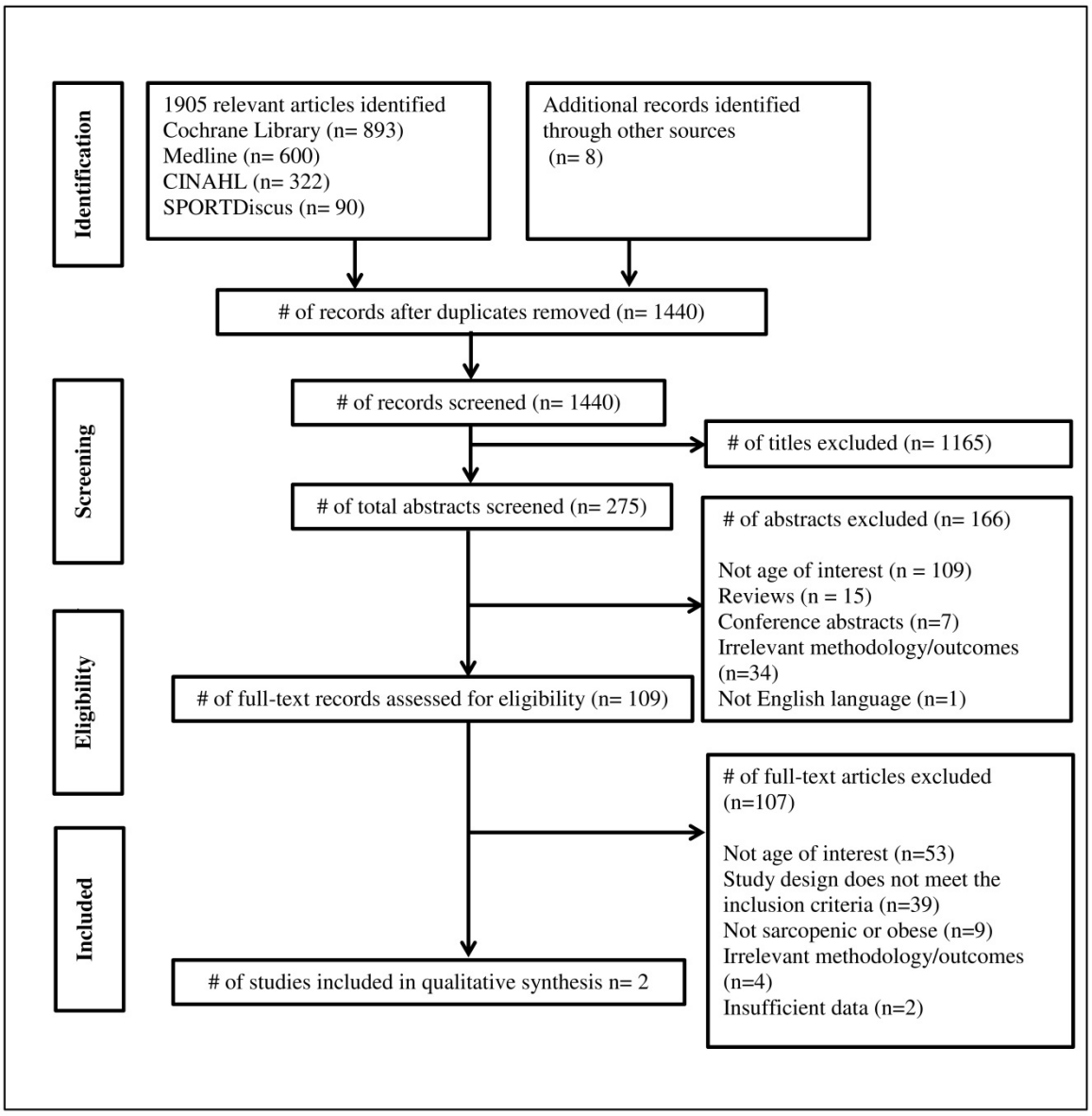

Figure 2. Information flow through the phases of the systematic review according to PRISMA guidelines.

889 **Table 2. Summary key points of the included study designs.**

Study	Summary	Strengths	Limitations
Study A Aleman-Mateo et al. [47]	o Nutritional Intervention o 40 participants o 3 months o Habitual diet plus 210g Ricotta cheese ·day^{-1} (intervention) vs habitual diet (control)	o Intention to treat analysis o Body composition by dual-energy xray absorptiometry o Physically-independent participants. o Baseline and follow up clinical tests for kidney and liver function o Blinded personnel delivering the assessment tests.	o Lack of baseline and follow up dietary intake and physical activity data
Study B Balachandran et al. [48]	o Exercise Intervention o 21 participants o 15 weeks o High speed circuit resistance (HSC) training (intervention) vs strength hypertrophy (SH) resistance training (control)	o Independent living community-dwellers. o Participants were partially blinded to the intervention. o Testing personnel blinded o All sessions supervised by 2 physiology majors	o No allocation concealment o Per-protocol analysis o Underpowered o Characteristics of participants lost to follow-up not described o No description of the exercise setting

890 **Table 2. Summary of the included studies**

Study	Setting/ Study Design/ Duration	Group	Participants Mean Age (SD)/ characteristics	Exercise Training	Nutritional Intervention	Sample Size (n) Drop-out (DO n) Female (F n) Adherence (%)	Assessment of a)body composition b) strength or function	Outcome Measure
Study A (Aleman-Mateo et al. [47])	Mexico/ RCT: two arms, one control, one intervention / 3 months	Control	76.7 (5.8) / physically-independent, sarcopenic based on low TASM and strength, obese based on %BF	No	Habitual diet (HD)	Baseline n=20, Final n= 12 DO n= 3 F n=12 N/A	a) DXA b) HG strength	TASM→, FM→, LM→, HG→
		Intervention	75.4 (5.0)/ independent living sarcopenic based on low TASM and strength, obese based on %BF	No	HD plus 210 g of ricotta cheese/day, (providing 15.7 gr extra protein/day)	Baseline n=20, Final n=17 DO n=8 F n=11 N/A		TASM→, FM→ , LM→, HG→
Study B (Balachandran et al. [48])	USA/ RCT: Two arms, one control, one intervention/ 15 weeks	Control	71 (8.2)/ independent living community dwellers from South Miami, sarcopenic based on SMI and strength, obese based on %BF and BMI	Strength-hypertrophy (SH) training, 11 exercises, 3 sets of 10-12 reps per set at 70% 1RM	No	Baseline n=10, Final n=9 DO n= 1 F n=8 85%	a) BIA b) HG strength, SPPB, Leg press 1RM, Chest press 1RM, Leg press power, Chest press power,	SMI→, %BF→, SPPB→, Leg 1RM↑**, Leg Power↑*, Chest 1RM↑*, Chest Power↑**, HG→
		Intervention	71.6 (7.8)/ independent living community dwellers from South Miami	High speed circuit (HSC) training, 11 exercises: 3 circuits of 10-12 reps per exercise at loads that maximised peak power output	No	Baseline n=11, Final n= 8 DO n= 3 F n =8 81%		SMI→, %BF→, SPPB↓*, Leg 1RM→, Leg Power↑**‡, Chest 1RM↑**, Chest power↑**, HG→

Notes: → no significant change, ↑significant increase, ↓significant decrease, *<0.05, **<0.01, ǂ significantly better than the control group;
%BF, percent body fat; BMI, body mass index; DXA, dual-energy xray absorptiometry; FM, fat mass; HG, handgrip; LM, lean mass; RCT, randomised control Trial; RM, repetition maximum; SPPB, short physical performance battery test; TASM, total appendicular skeletal muscle.