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

3

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18 **List of Abbreviations**

19

20 % BF; Percentage Body Fat

21 ACSM; American College of Sports Medicine

22 AHA; American Heart Association

23 BIA; Bioelectrical Impedance Analysis

24 BMI; Body Mass Index

25 CT; Computerized Tomography

26 DXA; Dual-energy X-ray Absorptiometry

27 EPIDOS; EPIDemiologie de l'OSteoporose

28 EWGSOP; European Working Group on Sarcopenia in Older People

29 FM; fat mass;

30 GFR; Glomerular Filtration Rate

31 HD; Habitual Diet

32 HG, Handgrip

33 HSC; High Speed Circuit

34 IGF-1; Insulin-like Growth Factor 1

35 IADL; Instrumental Activities of Daily Living

36 LM; Lean Mass

37 MRI; Magnetic Resonance Imaging

38 MPS; muscle protein synthesis

39 mTOR; mechanistic Target of Rapamycin

40 PRISMA; Preferred Reporting for Systematic Reviews and Meta-analyses

41 PROSPERO; International prospective register of systematic reviews

- 42 RCH+HD; Ricotta Cheese plus Habitual Diet
- 43 RCTs; Randomized controlled trials
- 44 RPE; Rates of Perceived Exertion
- 45 RM; Repetition Maximum
- 46 SD; Standard Deviation
- 47 SGOT; Serum Glutamic Oxaloacetic Transaminase
- 48 SGPT; Serum Glutamic-Pyruvic Transaminase
- 49 SPPB; Short Physical Performance Battery test
- 50 SMI; Skeletal muscle index; SO, Sarcopenic Obesity
- 51 SH; Strength Hypertrophy
- 52 TASM; Total appendicular skeletal muscle

53 **Abstract**

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

74

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

76 **1. Introduction**

77

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

88

89 Another condition that can promote poor health is obesity, which is defined as ‘abnormal or
90 excess body fat accumulation’ [9], and is a growing concern due to its progressively rising
91 prevalence rates in older populations [10]. In 2010, 35 % and 28 % of the adults 65 years of
92 age and older were reported to be obese in the US and the UK, respectively [11][12]. Similar
93 to sarcopenia, obesity can increase the risk of falls and mobility limitations in older age
94 [13][14], and when used in conjunction with indices of body composition and fat distribution
95 (waist circumference or waist to hip ratio) it may be associated with adverse health effects,
96 such as cardiovascular disease, metabolic syndrome, diabetes mellitus and several cancers
97 [15]. Furthermore, adipose tissue can infiltrate the muscle tissue [16] and mediate an
98 inflammatory response [17], which can result in muscle atrophy, mobility losses and lower
99 strength and muscle quality [16][18][19].

100

101 The relationship between sarcopenia and obesity is complex, with the development/
102 progression of one condition being closely connected to the other (**Figure 1**). The condition
103 where sarcopenia and obesity occur together has been termed sarcopenic obesity (SO) [20]. It
104 has been suggested that SO can predispose older individuals to more physical disabilities, gait
105 and balance abnormalities, and an increased risk of falls compared with either of the two
106 conditions alone [21]. Individuals with SO are exposed to ~2.5 times higher risk of reporting
107 Instrumental Activities of Daily Living (IADL) disabilities compared with adults without
108 obesity but with sarcopenia, or adults with obesity but without sarcopenia [22]. This negative
109 synergistic effect of sarcopenia and obesity is in accordance with the findings from the
110 EPIDOS (EPIDemiologie de l'OSteoporose) study, which reported that among a cohort of
111 1,308 women divided in four groups: 1) without sarcopenia or obesity 2) with obesity but not
112 sarcopenia 3) with sarcopenia but not obesity and 4) with SO, the latter was the poorest in
113 terms of performing physical activities that required strength [23]. According to a meta-
114 analysis of 12 prospective cohort studies with a total number of 35,287 participants, the
115 adults with SO had a 24 % higher risk of all-cause mortality compared with their healthy
116 counterparts [24].

117

118 **Figure 1** Relationship between sarcopenia and obesity and associated outcomes

119

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

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

129

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

138

139 However, there are relatively few intervention studies utilizing exercise training and/or
140 nutritional regimens for older adults with SO [26][36]. It appears that most intervention trials
141 have aimed to attenuate muscle loss at an early stage rather than try to ‘reverse’ an
142 established condition related to advanced ageing such as sarcopenia or SO, which would be
143 far more challenging [37]. Furthermore, to the best of our knowledge, there has been no
144 systematic review to date assessing the effectiveness of nutritional and exercise strategies,
145 alone or combined, to improve body composition and strength/function indices in older
146 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

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

180

181 **2.2. Inclusion Criteria**

182

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

195 function identified by one of the following tests: handgrip strength, knee flexion/extension,
196 peak expiratory flow, gait speed, the Short Physical Performance Battery test (SPPB), the
197 timed up-and-go test or the stair climb power test . The mean age cut-off for inclusion was \geq
198 65 years based on how 'old age' is defined in the joint recommendations from the American
199 College of Sports Medicine (ACSM) and the American Heart Association (AHA) [39]. The
200 inclusion criterion for obesity was defined as mean percentage body fat (% BF) ≥ 28 % in
201 men and ≥ 40 % in women [22] or in the absence of % BF data, a BMI ≥ 27 kg·m⁻². For any
202 given BMI, a person with sarcopenia will have by definition more body fat compared with
203 their counterparts without sarcopenia, therefore, adults with sarcopenia can present high-
204 adiposity at BMIs substantially lower than 30 kg·m⁻² [40]. Moreover, it is not uncommon for
205 studies to recruit participants who would be classified as overweight or obese based on a BMI
206 cut-off ranging from 25 to 28 kg·m⁻² when the focus is on sarcopenic obesity and/or when
207 participants come from a non-Caucasian ethnic group [25][26]. Studies that presented neither
208 the % BF nor BMI were included only if these indices could be derived from the weight,
209 height and body fat mass values, or if the authors of the study when contacted provided the
210 essential information.

211

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

219

220 **2.3. Exclusion Criteria**

221

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

227

228 **2.4. Study Selection**

229

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

236

237 **2.5. Data Extraction**

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

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

246

247 **2.6. Quality Assessment**

248

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

257

258 **2.7. Principal Summary Measures**

259

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

263

264 **3. Results**

265

266 **3.1. Description of studies**

267

268 Our search strategy resulted in 1,440 potential articles. After the exclusion of 1,331 articles
269 based on titles and abstracts, 109 full-text articles reporting 109 studies were retrieved and
270 assessed for eligibility. The detailed flow chart of the selection process is presented in **Figure**
271 **2**. The authors of two potentially eligible studies [45][46] were contacted for further
272 information, but retrieval of all the essential body composition data was not possible for
273 reasons unrelated to this review, therefore, the articles were excluded. A total of $n=2$ studies
274 [47][48] including $n= 61$ participants met the inclusion criteria and were included in the
275 review. Study A[47] was a nutritional intervention and study B[48] an exercise training
276 intervention; neither of the studies combined exercise with diet.

277

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

280

281 **3.2. Quality Assessment**

282

283 The two studies were randomized control trials of moderate methodological quality based on
284 the modified Downs and Black rating scale [41][42]. The total score for each study was 18
285 out of 28. The summary key information of the methodological strengths and limitations is
286 presented in table 1 (**supplementary file 1** presents the complete breakdown of the scoring in
287 the different subsections of the scale). Both studies performed power calculations to
288 determine the population sample size prior to recruitment, however, study B[48] was
289 underpowered; target was $n=21$ per group, but the final analysis was conducted with $n=9$ and
290 $n=8$ for the control and intervention group, respectively. In study A[47] only the testers were

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

296

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

298

299 **3.3. Participant Characteristics**

300

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

308

309 **3.4. Study Design**

310

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

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

319

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

335

336 **3.5. Outcomes**

337

338 **3.5.1. Body composition**

339

340 No significant changes were seen in body composition, in either experimental or control
341 groups. In study A[47] the addition of ricotta cheese resulted in no significant changes in lean
342 mass, TASM or body fat in the intervention or control group (Table 2). Secondary analysis
343 by sex showed that although men ($n=8$) in the intervention group experienced an increase in
344 TASM by 490 g, this was not significantly different either from baseline or when compared
345 against the control group ($p=0.42$), which gained a non-significant 220 g of TASM.
346 Similarly, in study B[42] no statistically significant differences were detected in any of the
347 body composition indices, regardless of the exercise regimen (Table 2). Skeletal muscle
348 index (SMI) increased non-significantly in both groups (from $6.5 \pm 0.66 \text{ kg}\cdot\text{m}^{-2}$ to 6.6 ± 0.59
349 $\text{kg}\cdot\text{m}^{-2}$ in HSC and from $6.7 \pm 0.45 \text{ kg}\cdot\text{m}^{-2}$ to $6.8 \pm 0.42 \text{ kg}\cdot\text{m}^{-2}$ in SH).

350

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

352 **3.5.2 Strength and/ or function**

353

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

358

359 Study B[48] reported significant improvements in several aspects of strength and function in
360 both exercise groups (Table 2). In particular, the strength-hypertrophy (SH) control group
361 experienced significant improvements in leg press 1RM by 22 % ($p<0.01$), chest press 1RM
362 by 16 % ($p=0.03$), leg press peak power by 19 % ($p=0.03$) and chest press peak power by
363 15% ($p<0.01$) whereas a non-significant increase of 12% was detected in hand grip strength
364 (from $17.3 \pm 2.7 \text{ kg}$ to $19.4 \pm 4.6 \text{ kg}$; $p>0.05$). The HSC group had a significant improvement

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

370

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

375

376 **3.5.3 Secondary Outcomes**

377

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

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

391

392 The exercise intervention in study B[48] resulted in acute joint pain only in the SH group. In
393 addition, the HSC group reported significantly lower rates of perceived exertion (RPE) with a
394 mean difference of -1.5 (95 % CI -2.0,-0.12, p=0.04). Adherence rates were similar in the two
395 groups; 81 % in HSC and 85 % in SH. Regarding the Instrumental Activities of Daily Living
396 (IADLs) there were significant improvements within both groups (pre vs post); namely, time
397 needed for jacket on and off (from 11.5 ± 3.5 s to 10.2 ± 2.0 s; p=0.04), scarf pick-up ($5.2 \pm$
398 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
399 significantly within the control group, while the HSC group experienced significant
400 improvements in time for sit-to-stand (from 16.1 ± 5.7 s to 13.4 ± 3.9 s; p=0.02) and pan
401 carry (5.4 ± 1.3 s to 4.5 ± 1.2 s; p<0.01). No differences were observed between the two
402 groups in the aforementioned IADLs.

403

404 In summary, neither of the studies had a significant effect on body composition. The
405 introduction of ricotta cheese in the habitual diet of participants in study A[47] aimed to
406 increase their protein intake but it was not reported whether or not this was achieved, and if
407 so to what extent. In the same study, there was a trend for an increase in strength in the
408 intervention group, but this was not significant. The only significant improvement reported
409 was the fasting insulin levels, but that was reported only in men in the intervention group.

410 Despite the lack of body composition changes, in study B[48], the high speed circuit
411 resistance training and strength hypertrophy resistance training protocols significantly
412 improved strength, power and function indices. Finally, due to the limited data extracted and

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

415 **4. Discussion**

416

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

427

428 **4.1 Effects of protein intake on body composition and function in sarcopenic obesity**

429

430 Study A[47] attempted to utilize the effects of protein on increased skeletal muscle mass
431 accretion rates. Although the authors acknowledged that the suggested recommendations for
432 protein intake in older individuals with sarcopenia are $1.2\text{-}1.5\text{ g} \cdot \text{kg} \text{ bw}^{-1} \cdot \text{day}^{-1}$ [47], they did
433 not report the participants' daily protein intake, therefore, it was not corroborated whether
434 such intakes were achieved. It has been suggested that maximal muscle protein synthesis
435 (MPS) rates in older adults can be achieved using $\sim 35\text{-}40\text{ g protein} \cdot \text{meal}^{-1}$ [49-51] or 0.4 g
436 $\text{protein} \cdot \text{kg} \text{ bw}^{-1} \cdot \text{meal}^{-1}$ [51]. A valid question would be whether a daily addition of 210 g
437 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

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

469

470 **4.2 Effects of exercise training on body composition and function in sarcopenic obesity**

471

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

479

480 In study B[48], the aim was to assess the effect of high-speed resistance exercise training on
481 indices of SO. In spite of possible methodological limitations, the improvements in strength,
482 power and IADL reported in study B[42], provide some evidence that exercise can improve
483 several domains of physical performance such as strength and power in older adults with SO.
484 This is in agreement with previous reports supporting the benefits of resistance exercise
485 training on clinically important outcomes, even in the absence of increased muscle mass
486 [8][31][57]. This may be partly accounted for by the adaptive plasticity in the neuromuscular
487 system and skeletal muscle tissue in response to resistance exercise even in advanced older

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

496

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

508

509 These data support the potential benefit of a resistance exercise program within lifestyle
510 intervention protocols due to its positive effect on muscle strength, power and function in
511 older adults with SO. Although no statistically significant body-composition changes were
512 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

538 Maltais et al. [68] was the only one that recruited older overweight adults with a low
539 appendicular lean mass index. The authors concluded that 16-weeks of a whole body
540 resistance exercise regimen (at 80% 1RM) followed by the consumption of ~13 g dairy
541 supplement (chocolate milk with added milk powder) increased lean mass and reduced fat
542 mass even at the absence of caloric restriction ($n=8$). In the same study, the group that
543 received a soy-based beverage (matched for energy, protein, essential amino acids,
544 carbohydrate and calcium content) ($n=8$), reported significant increases only in lean mass but
545 no changes in fat mass. Similar results, but in pre-menopausal women, have been reported by
546 Josse et al. [66]. After 16 weeks of mixed exercise training (aerobic and resistance) combined
547 with a caloric restriction (500 kcal daily deficit), only the high protein group (30% of total
548 energy intake came from protein, half of which was derived from dairy products) experienced
549 lean gains concomitant with fat losses. Albeit in younger adults, a recent four-week
550 intervention combining $2.4 \text{ g protein} \cdot \text{kg bw}^{-1} \cdot \text{day}^{-1}$ (achieved by consuming 3-4 whey-
551 based protein beverages daily) with a mixed resistance, plyometric and high-intensity interval
552 training alongside an energy deficit regimen resulted in significantly higher lean mass and
553 lower body fat [67]. The control group which differed only in protein intake ($1.2 \text{ g protein} \cdot$
554 $\text{kg bw}^{-1} \cdot \text{day}^{-1}$) did not experience a significant change in lean mass [67].

555

556 Although the effectiveness of the aforementioned paradigms needs to be evaluated in older
557 adults with SO, they provide the framework for an initial approach to combat this condition.
558 What is primarily lacking from the literature is trials recruiting older adults with SO.
559 Additionally, protocols combining a high protein diet (potentially using whey or dairy
560 proteins) with a modest caloric deficit along with a well structured exercise training regimen
561 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

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

594

595 **4.5 Conclusion**

596

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

610

611 **Supplementary material**

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

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

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

616

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621

622 **Authors' contributions**

623

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

630

631 **Competing interests**

632

633 The authors have no competing interests to declare

634

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641

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643

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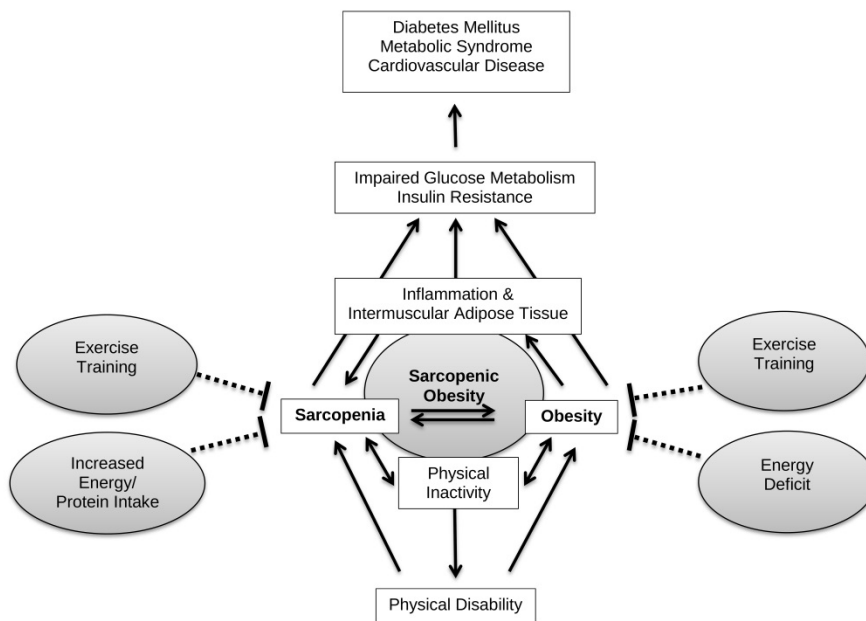
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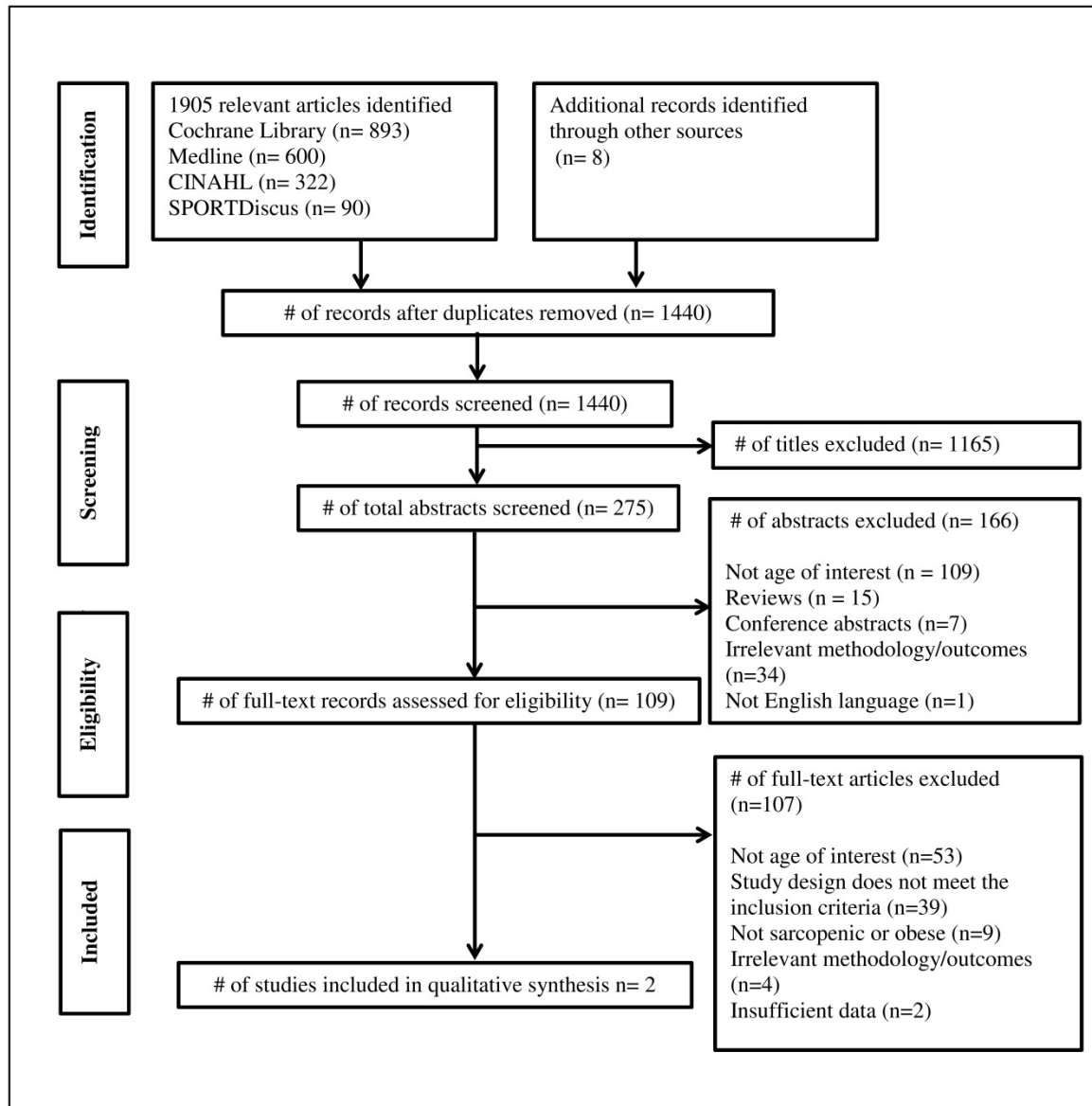
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882

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:



886

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

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

Study	Summary	Strengths	Limitations
<p>Study A Aleman-Mateo et al. [47]</p>	<ul style="list-style-type: none"> ○ Nutritional Intervention ○ 40 participants ○ 3 months ○ Habitual diet plus 210g Ricotta cheese ·day⁻¹ (intervention) vs habitual diet (control) 	<ul style="list-style-type: none"> ○ Intention to treat analysis ○ Body composition by dual-energy xray absorptiometry ○ Physically-independent participants. ○ Baseline and follow up clinical tests for kidney and liver function ○ Blinded personnel delivering the assessment tests. 	<ul style="list-style-type: none"> ○ Lack of baseline and follow up dietary intake and physical activity data
<p>Study B Balachandran et al. [48]</p>	<ul style="list-style-type: none"> ○ Exercise Intervention ○ 21 participants ○ 15 weeks ○ High speed circuit resistance (HSC) training (intervention) vs strength hypertrophy (SH) resistance training (control) 	<ul style="list-style-type: none"> ○ Independent living community-dwellers. ○ Participants were partially blinded to the intervention. ○ Testing personnel blinded ○ All sessions supervised by 2 physiology majors 	<ul style="list-style-type: none"> ○ No allocation concealment ○ Per-protocol analysis ○ Underpowered ○ Characteristics of participants lost to follow-up not described ○ No description of the exercise setting

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→

891 **Notes: → no significant change, ↑significant increase, ↓significant decrease, *<0.05, **<0.01, † significantly better than the control group;**
892 **%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,**
893 **repetition maximum; SPPB, short physical performance battery test; TASM, total appendicular skeletal muscle.**

