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# A PROPOSED MODEL TO TEST THE HYPOTHESIS OF EXERCISE-INDUCED LOCALIZED FAT REDUCTION (SPOT REDUCTION), INCLUDING A SYSTEMATIC REVIEW WITH META-ANALYSIS

review paper
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## ABSTRACT

**Purpose.** The process in which specific exercises reduce localized adipose tissue depots (targeted fat loss) and modify fat distribution is commonly termed spot reduction. According to this long-held popular belief, exercising a limb would lead to greater reduction in the adjacent adipose tissue in comparison with the contralateral limb. Aside from popular wisdom, scientific evidence from the 20th and 21st century seems to offer inconclusive results. The study aim was to summarize peer-reviewed literature assessing the effects of unilateral limb training, compared with the contralateral limb, on the localized adipose tissue depots in healthy participants, and to meta-analyse its results.

**Methods.** We followed the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses. We searched PubMed, Web of Science, and Scopus electronic databases using several relevant keyword combinations. Independent experts were contacted to help identify additional relevant articles. Following the PICOS approach, we included controlled studies that incorporated a localized exercise intervention (i.e., single-leg training) to cohorts of healthy participants (i.e., no restriction for fitness, age, or sex) compared with a control condition (i.e., contralateral limb), where the main outcome was the pre-to-post-intervention change of localized fat. The methodological quality of the studies was assessed with the Physiotherapy Evidence Database scale. Pre- and post-intervention means ± standard deviations of the fat-related outcome in the trained and control groups (limbs) were converted to Hedges' g effect size (*ES*; with 95% confidence intervals [CI]) by using a random-effects model. The impact of heterogeneity was assessed with the $I^2$ statistic. Extended Egger's test served to explore the risk of reporting bias. The statistical significance threshold was set at $p < 0.05$.

**Results.** From 1833 search records initially identified, 13 were included in the meta-analysis, involving 1158 male and female participants (age, 14–71 years). The 13 studies achieved a high methodological quality, and presented results with low heterogeneity ($I^2 = 24.3\%$) and no bias (Egger's test $p = 0.133$). The meta-analysis involved 37 comparisons, with 17 of these favouring (i.e., greater reduction of localized fat) the trained limb, and 20 favouring the untrained limb, but the *ES* ranged between –1.21 and 1.07. The effects were consistent, with a pooled *ES* = –0.03, 95% CI: –0.10 to 0.05, $p = 0.508$, meaning that spot reduction was not observed.

**Conclusions.** Localized muscle training had no effect on localized adipose tissue depots, i.e., there was no spot reduction, regardless of the characteristics of the population and of the exercise program. The popular belief concerning spot reduction is probably derived from wishful thinking and convenient marketing strategies, such as influencers seeking increased popularity and procedure sellers interested in increasing advertising.

**Key words:** exercise, human physical conditioning, resistance training, high-intensity interval training, body composition, subcutaneous fat

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## Introduction

> *A man may box and fence, and even walk, without losing his terrible abdominal accumulation; but if he centres his efforts at muscular exertion on the abdomen itself the fat cannot stand the attack and will gradually disappear.*
>
> (E. Checkley, 1895) [1]

Since (at least) the 19th century, the notion that specific exercises can reduce localized adipose tissue depots (i.e., targeted fat loss) and modify fat distribution has remained a very popular belief, with the process itself commonly termed spot reduction [2]. From the middle to nearly the end of the 20th century, several studies were performed on the subject, suggesting that spot reduction might be feasible [3–6]. However, during the same period, several studies disproved the notion of spot reduction [2, 7–13]. Toward the end of the 20th century, there seemed to be a consensus among the scientific community that spot reduction was a myth. Nonetheless, during the 21st century, new studies [14–24] have relaunched the debate.

Why is the notion of spot reduction so appealing across centuries [1, 25, 26]? Why have researchers not reached a definitive answer to the problem? This might be explained by 3 main factors. The first one may be the difficulty inherent in addressing the hypothesis of spot reduction. There are complex interactions among (i) different exercise programming characteristics (e.g., exercise modality, periodization, load management, adherence to the program); (ii) diverse regional responses of adipose tissue depots to exercise (i.e., lipolysis, re-esterification, mobilization of free fatty acids); and (iii) inter-individual differences in the modulators of the fat metabolism in response to exercise (e.g., sex, obesity) [19, 27–32]. The second factor of controversy may arise from the different concepts of spot reduction [16, 33]. Various models of study were used to test the hypothesis of spot reduction, such as cross-sectional studies [7, 14, 34, 35], as well as long-term intervention studies involving exercise compared with nutrition [22, 23], trunk-localized exercise [8, 20], limb-localized exercise [5, 9, 18, 21], and whole-body exercise [15, 16]. The third factor is the difficulty to conduct rigorous experimentation to test such a hypothesis (e.g., control the participants' diet and their compliance to the program, use valid measurement techniques [18]). The difficulty encountered by scientists is in contrast with the ease with which personal beliefs (or publicity) can be communicated [1, 25, 26]. Marketing and science often collide [33], and marketing the notion of exercise-based spot reduction to persons seeking a desperate solution to their problems [36] may be very appealing.

If the notion of spot reduction is correct, then performing a regimen of unilateral exercise should lead to higher reduction in adipose content in that region than in the contralateral limb. To the best of our knowledge, the debate regarding exercise-based spot reduction seems to be active, even after (at least) 3 centuries [1]. To contribute to settling down the debate, a systematic review with meta-analysis was conducted to qualitatively assess and quantitatively summarize the evidence in the field, but also circumvent the problem of most exercise-related studies: a reduced sample size [37]. Our aim was to summarize peer-reviewed literature assessing the effects of unilateral limb training, compared with the contralateral limb, on the localized adipose tissue depots in healthy participants across the life span, and to meta-analyse its results.

## Material and methods

We followed the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) [38, 39]. The methods were established before initiating the research, and protocol registration preceded the search.

### Search strategy

We searched through PubMed, Web of Science, and Scopus electronic databases from the inception of indexing to June 2021, with no restriction on language. Potentially relevant keywords were collected through authors' consensus on the basis of previous studies conducted in relation to spot reduction; organized vocabulary (i.e., Medical Subject Headings [MeSH]) was also incorporated. As a result, the following keywords were introduced in the electronic databases in different combinations by using Boolean search syntax with the operators 'AND,' 'OR': activity, arm, body, clinical, composition, conditioning, controlled, distribution, dominant, elbow, exercise, extension, fat, flexion, forearm, high, human, intensity, interval, knee, leg, local, localized, loss, mass, modalities, model, motor, movement, muscle, musculoskeletal, non-dominant, phenomena, physical, physiological, reduction, regional, resistance, running, single, sport, spot, strength, subcutaneous, targeted, therapy, thigh, training, treatment, trial, unilateral. Electronic searches were conducted in accordance with the specific characteristics of each electronic database search engine. For example, in the PubMed database, the following search syntax was used: controlled clinical trial [Publication Type] AND training [Title/Abstract] OR single-leg [Title/Abstract] AND body composition [MeSH Terms] AND fat [Title/Abstract].

After the initial search in June 2021, we created accounts in the respective databases. Through these accounts, the lead investigator received weekly automatically generated e-mails for updates regarding the search terms used (if available). All studies that were published before August 2021 were considered for inclusion. We excluded studies on the basis of the review of the title or abstract, or (when needed) after reading the full text. Conference proceedings were considered if the full-text was available. The reference list of included studies was searched for potentially relevant studies. Two authors (RRC, DCA) conducted the process independently, with potential discrepancies resolved by consensus.

Thereafter, the list of included articles and the inclusion criteria were sent to 2 independent world experts in the field of body composition (https://www.expertscape.com/ex/body+composition) to help identify additional relevant articles. Additionally, the experts (i) hold a Ph.D. in sports sciences or a related field (e.g., health sciences); (ii) have peer-reviewed publications on body composition in journals with impact factor according to the Journal Citation Reports®. The experts were not provided with our search strategy to avoid biasing their own searches. Upon completion of all these steps, the databases were again consulted in search for errata or retractions of any included study.

### Eligibility criteria

To elaborate the PICOS eligibility criteria, we first elaborated a definition of the investigated problem. Namely, spot reduction (in humans) is defined as a greater reduction of the non-intramuscular fat-related depot(s) (e.g., subcutaneous fat) adjacent to a voluntarily exercised muscle compared with the same depot from the contralateral non-exercised muscle, after an intervention period.

Accordingly, and following the PICOS criteria, we incorporated studies that:

(i) Included cohorts of healthy (e.g., with medical or ethics review board clearance to participate in a training programme) participants (humans), with no restriction for fitness/sport background, age, or sex. Excluded participants were those with a physical trauma (e.g., limb amputation [40]) or certain diseases (e.g., stroke leading to paretic limb [41], genetic conditions or syndromes potentially affecting adipose tissue or its response to training [24, 42, 43]).

(ii) Involved a localized exercise intervention (without restriction for the mode of exercise, e.g., resistance training, endurance training) where one limb was trained and the contralateral limb was the control. Interventions lasting a minimum of 2 weeks were considered [44, 45]. Studies that incorporated a non-localized exercise intervention (e.g., running, bilateral leg press) were excluded. Cross-sectional studies were also excluded. Studies were not excluded if they lacked dietary control and/or involved nutritional supplementation, as this is not a critical factor for experimental models using the contralateral limb as a control condition [46].

(iii) Compared localized exercise with a control condition (i.e., contralateral limb), with the only difference between the conditions being the exercise intervention.

(iv) Employed a pre-to-post-intervention assessment of at least 1 fat-related parameter (e.g., fat mass, fat volume) by using dual-energy X-ray absorptiometry, magnetic resonance imaging, computerized tomography, skinfold callipers, ultrasound, or the microscopic method (i.e., subcutaneous fat biopsy). Secondary outcomes were considered, including potential adverse effects derived from the intervention (e.g., injury).

(v) Utilized a randomized or non-randomized controlled design, as long as at least 1 comparator group existed.

### Data extraction

Two authors of the review (RRC, DCA) performed the data extraction independently, using a predefined form created in Microsoft Excel (Microsoft Corporation, Redmond, WA, USA). If there were any discrepancies between the authors in the extracted data, the accuracy of the information was re-checked in the studies. We extracted the following data: participants' sex, age (years), body mass (kg), height (cm), and previous experience with training. If applicable, information about the type and level (e.g., professional, amateur) of sports practice was also retrieved. Regarding training characteristics, the extracted data included training frequency (days/week) and training duration (weeks), intensity level and marker of intensity (e.g., % of one-repetition maximum [1RM]), total volume (e.g., repetitions, minutes), types of exercises performed, combination of exercise with diet, and progressive overload techniques (if any).

The means and standard deviations (*SDs*) of dependent variables were extracted at pre- and post-intervention time points from the included studies. In cases where the required data were not clearly or completely reported, the authors of the study were contacted for clarification. If no response was obtained from the authors (after 2 attempts) or if the authors could not provide the requested data, the study outcome was excluded from the analysis. However, even when no numerical data were provided by the authors upon contact, in cases where data were displayed in a figure [9], the meta-analysis used validated ($r = 0.99$, $p < 0.001$) [47] software (WebPlotDigitizer; https://apps.automeris.io/wpd/) [48] to derive the relevant numerical data.

### Methodological quality assessment

The Physiotherapy Evidence Database (PEDro) scale was used to assess the methodological quality of the included studies [49]. There are 11 items on the PEDro checklist, but item 1 is not included in the total score. Therefore, the methodological quality of the included studies was rated from 0 (lowest quality) to 10 (highest quality). The scale evaluates different aspects of the study design, such as participant eligibility criteria, randomization, blinding, attrition, and reporting of data. The validity and reliability of the PEDro scale was established previously [49–51]. Additionally, its agreement with other scales (e.g., Cochrane risk of bias tool) has been reported [52]. Also, the PEDro scale is probably one of the most frequently used scales in the literature, which helps to make comparisons between meta-analyses. In accordance with the cut-off scores, the methodological quality was rated as 'poor' (< 4), 'fair' (4–5), 'good' (6–8), or 'excellent' (9–10) in some subfields, however, it is not possible to satisfy all scale items in some areas of physiotherapy practice [53]. Moreover, in the context of this study, the definition of spot reduction, and the proposed experimental model to test the hypothesis of spot reduction, is not possible to blind the participants regarding whether they trained or not one of their limbs, which makes item 5 from the PEDro scale an unfair criterium to assess the methodological quality of studies involved in our review. Therefore, as outlined in previous systematic reviews in some sub-fields of physiotherapy [54, 55], the methodological quality of the studies was interpreted by using the following convention, based on the summary score: studies that scored ≤ 3 points were considered as being of 'poor quality,' studies scoring 4 or 5 points were considered as being of 'moderate quality,' and studies that scored 6–10 points were considered as being of 'high quality'. Two authors (RRC, DCA) performed the methodological quality assessment independently. Disagreements in the assessments between the reviewers were resolved through discussion and consensus.

### Statistical analysis

Pre- and post-intervention mean ± *SD* of a given fat-related outcome in the trained and control groups was converted to Hedges' *g* effect size (*ES*). A meta-analysis for a given fat-related outcome was conducted if at least 3 studies provided sufficient data for the calculation of *ES* [56–58]. The data were standardized by using post-score *SD*. For studies that reported standard errors, *SDs* were calculated by multiplying the standard error with the square root of the sample size [59]. In all analyses, we used the random-effects model to account for differences between studies that might affect the treatment effect [60, 61]. The *ES* values are presented with their respective 95% confidence intervals (CIs). The calculated *ES* values were interpreted with the following scale: < 0.2, trivial; 0.2–0.6, small; > 0.6–1.2, moderate; > 1.2–2.0, large; > 2.0–4.0, very large; > 4.0, extremely large [62]. The impact of heterogeneity was assessed with the $I^2$ statistic, with values of < 25%, 25–75%, and > 75% considered to represent low, moderate, and high levels of heterogeneity, respectively. Extended Egger's test (2-tailed) served to explore the risk of reporting bias [63]. To adjust for publication bias, a sensitivity analysis was conducted with the trim and fill method [64], with L0 as the default estimator for the number of missing studies [65]. All analyses were carried out by using the Comprehensive Meta-Analysis program (version 2; Biostat, Englewood, NJ, USA). The statistical significance threshold was set at $p < 0.05$.

## Ethical approval

The conducted research is not related to either human or animal use. The protocol for this systematic review with meta-analysis was registered at the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on June 28, 2021 (registration number: INPLASY202160103).

## Results

### Study selection

A total of 1833 search records were initially identified. After excluding the duplicates and studies on

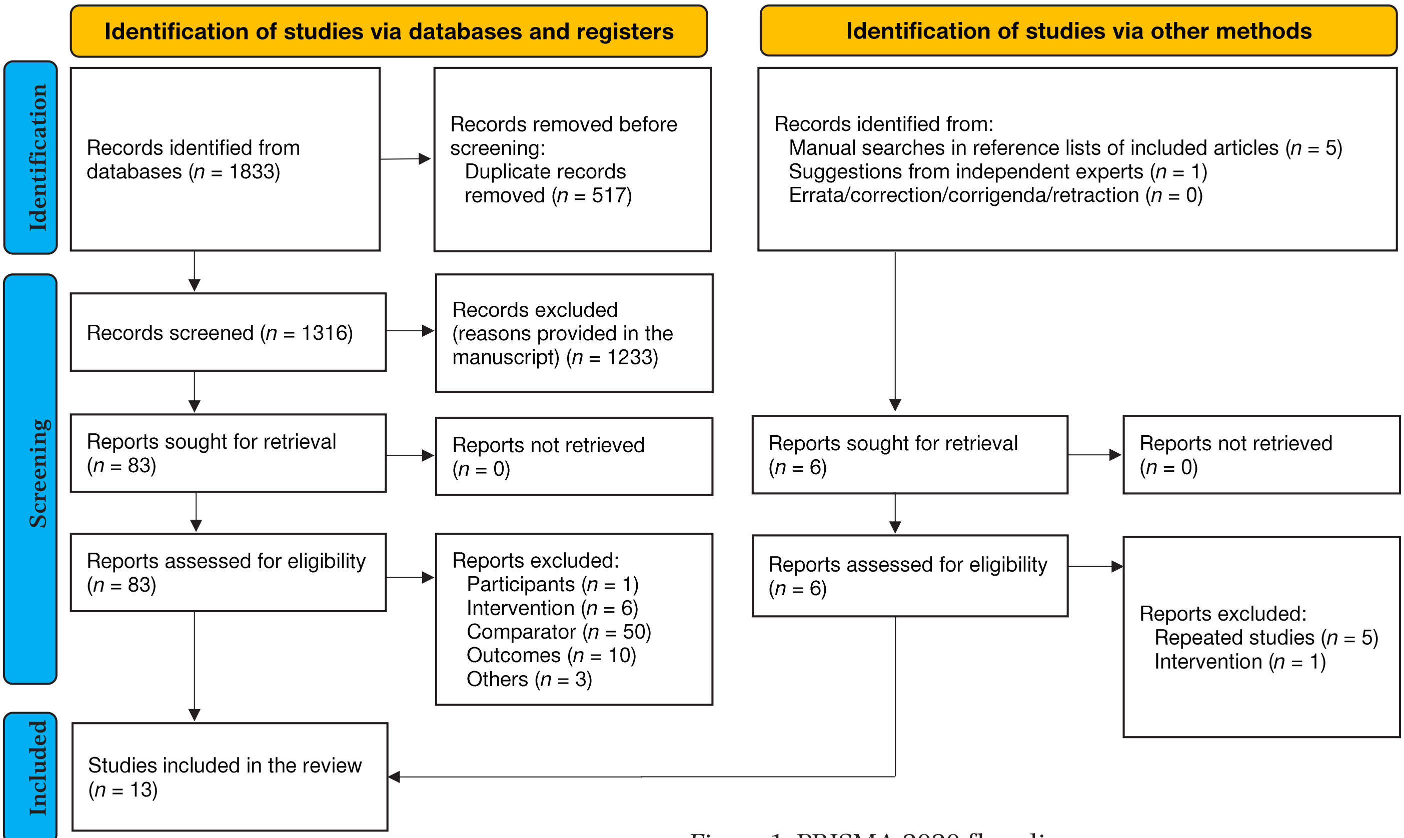


Figure 1. PRISMA 2020 flow diagram

the basis of the title or abstract, 83 studies remained, and their full texts were read. From these, 13 were included in the meta-analysis [5, 9, 10, 18, 21, 46, 66–72]. Figure 1 provides a diagram of the study selection process. The included studies involved 1158 participants (acting as both experimental and control groups). The characteristics of the participants from the included studies, the programming parameters of the training interventions, and the fat-related outcomes (for both the control and experimental limbs) are presented in Table 1.

Briefly, training interventions were applied during 2 up to 20 weeks, with a training frequency of 3 sessions per week, up to 7 sessions per week (i.e., daily training). The training intensity (i.e., single-leg) varied from 10% to 90% of 1RM for those interventions that applied resistance training exercises, and equalled ca. 40% of peak oxygen consumption (VO$_2$max) in the intervention that used endurance (i.e., cycling) training. Of note, the interventions with resistance training exercises commonly utilized elbow flexors/extensors-related exercises (e.g., dumbbell biceps concentration curls, overhead triceps extension) or knee extensors-related exercises (e.g., seated leg press, seated leg extension); none of the included studies applied knee flexors-related exercises. No major adverse effects were reported among the included studies; only mild-moderate delayed-onset muscle soreness was observed. However, most of the studies in this meta-analysis failed to report specific information regarding adverse health effects. This reflects a larger problem in sports sciences and produces unbalanced accounts, as authors present the main effects, but not the potential adverse health effects.

### Methodological quality

In accordance with the PEDro checklist, the 13 studies achieved 6–8 points and were classified as being of ‘high’ methodological quality (Table 2).

### Meta-analysis results

The meta-analysis included 13 controlled studies, involving 37 comparisons, with 17 of these favouring (i.e., greater reduction of localized fat) the trained limb, and 20 favouring the untrained limb, but the *ES* ranged between –1.21 and 1.07. The effects were consistent, with a pooled *ES* = –0.03, 95% CI: –0.10 to 0.05, $p$ = 0.508, $I^2$ = 24.3%, Egger’s test $p$ = 0.133 (Figure 2), meaning that spot reduction was not observed.

Table 1. Included studies characteristics

| Study | Participants | Training | Outcomes |
|---|---|---|---|
| Brinkworth et al., 2004 [66] | Healthy physically active men supplemented with bovine colostrum (*n* = 17; age, 21.4 years; height, 179 cm; body mass, 77.8 kg) or whey protein (*n* = 17; age, 23.8 years; height, 179 cm; body mass, 81.5 kg) | 8 weeks, 4 sessions per week. Muscle: elbow flexors non-dominant arm. Exercises: dumbbell biceps concentration curls. Velocity: controlled (slower during lengthening). Sets/repetitions/intensity: 6 sets to failure at 80% 1RM. Progressive overload: yes | Arm skin and subcutaneous fat ($cm^2$; MRI) |
| Devries et al., 2015 [67] | 30 healthy men (age, 70 years; height, 180 cm; body mass, 84 kg) | 2 weeks, 3 sessions/week. Unilateral leg press and leg extension. Equipment: air-resistance strength machines. Sets, intensity: 3, 30% 1RM until volitional fatigue | Leg fat mass (g; DEXA) |
| Hanson et al., 2009 [46] | Sedentary (without medical condition) women (*n* = 25; age, 71 years; height, 161 cm; body mass, 75.5 kg; BMI, 29.2 kg · $m^{-2}$) and men (*n* = 22; age, 71 years; height, 174 cm; body mass, 86.4 kg; BMI, 28.4 kg · $m^{-2}$) | 10 weeks, 3 sessions per week. Knee extensions for the dominant leg (pneumatic [air-powered] knee extension machine). Sets: 4–5 (4 for participants > 75 years of age and 5 for those < 75 years of age). First set: 5 repetitions, 50% 1RM. Second set: 5RM value (initially, 85% of basal 1RM). Third set: 5RM, then a drop-set of 1–2 repetitions until reaching 10 repetitions. Fourth set: 5RM, then a drop-set of 1–2 repetitions until reaching 15 repetitions. Fifth set: 5RM, then a drop-set of 1–2 repetitions until reaching 20 repetitions. Full ROM was required during repetitions. Repetition duration: 2–3 (shortening-lengthening). A seat belt was worn throughout the exercise session, with arms across the chest. Progressive overload was monitored session by session | Knee extensor subcutaneous fat ($cm^2$; CT)<br>Knee extensor intermuscular fat ($cm^2$; CT) |
| Kostek et al., 2007 [18] | 45 men and 59 women, Caucasian (94%) (age, 24.1 years; BMI, 24.2 kg · $m^{-2}$) | 12 weeks, 2 sessions per week (45–60 minutes per session). Progressive, supervised resistance training of the non-dominant arm. Exercises: biceps preacher curl, overhead triceps extension, biceps concentration curl, triceps kick-back, and standing biceps curl. Dose per exercise: 3 sets of 12 repetitions at 65–75% 1RM (i.e., 12RM). Each contraction involved 2 seconds for the concentric phase and 2 seconds for the eccentric phase. A 2-minute rest followed each set. The number of repetitions was decreased to 8 (i.e., 8RM) at week 5 and then to 6 (i.e., 6RM) at week 10. Consequently, the exercise intensity at weeks 5 and 10 increased to 75–82% and 83–90% 1RM, respectively. Experienced investigators supervised the training sessions and adjusted the weight accordingly | Biceps subcutaneous fat (mm; skinfold callipers)<br>Arm subcutaneous fat volume (ml; MRI) |
| Krotkiewski et al., 1979 [9] | 10 women (age, 24–29 years; height, 166.2 cm; body mass, 72–81 kg; body fat, 19–28 kg) | 5 weeks, performed daily. Three sets of 10 maximal voluntary isokinetic right knee extensions (constant angular velocity of 60° · $s^{-1}$) | Thigh adipose tissue thickness (cm; ultrasound)<br>Fat cell weight (µg; microscopic method) |
| Miura et al., 2009 [68] | 8 women, Japanese, sedentary (age, 21–23 years; height, 157 cm; body mass, 49.4 kg; $VO_2max$, 32.4 ml · $min^{-1}$ · $kg^{-1}$) | 12 weeks, 3 sessions per week (60 minutes per session). The right or left leg was assigned to cycling at 40% of single-leg peak $VO_2$ (i.e., below lactate threshold), equivalent to 25.3 W and a heart rate of 90–110 bpm | Thigh fat cross-sectional area ($cm^2$; ultrasound) |

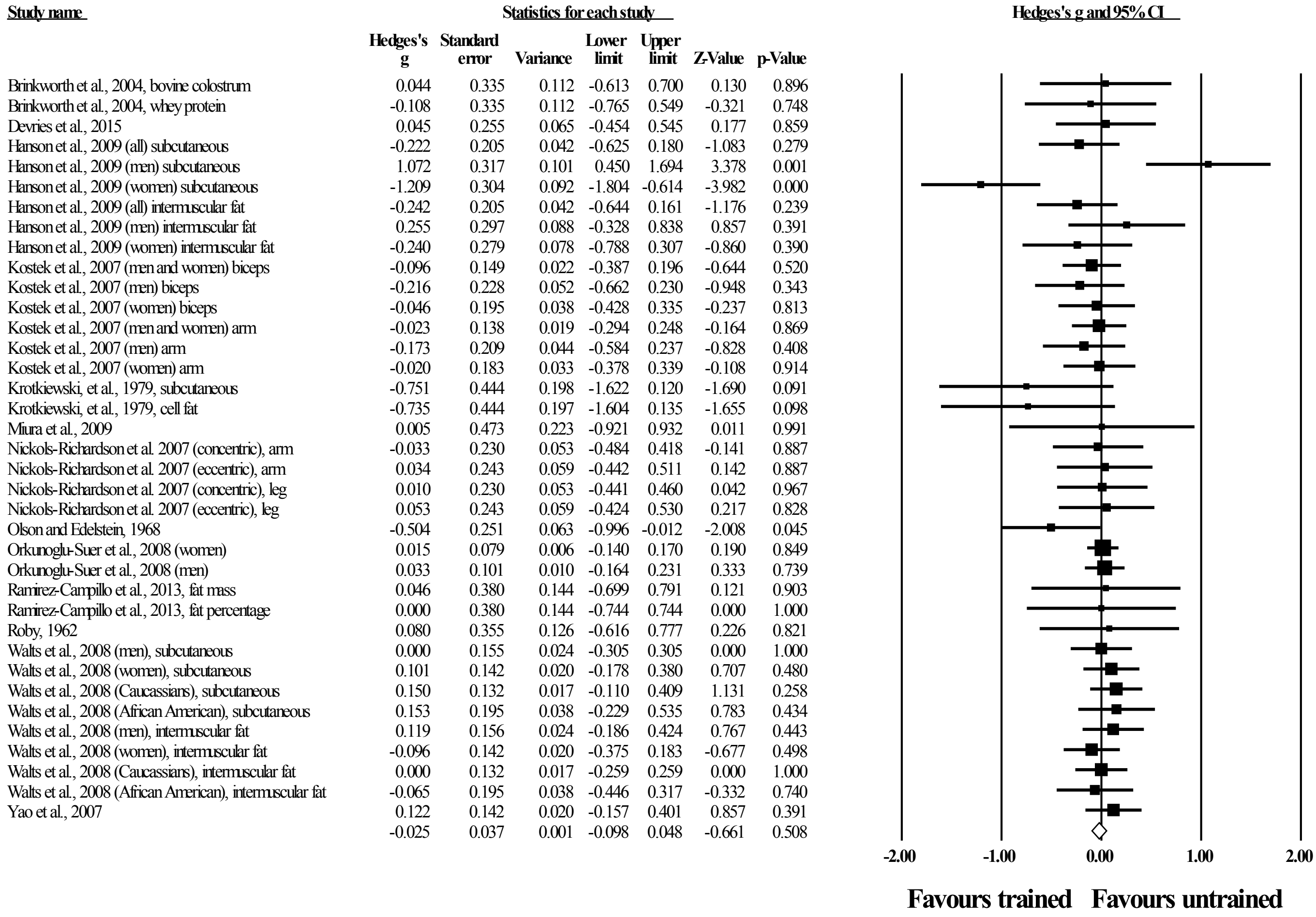
| | | | |
|---|---|---|---|
| Nickols-Richardson et al., 2007 [69] | 70 women, white (95%) (age, 20.2 years; BMI, 22.1 km · m$^{-2}$) | 20 weeks, 3 sessions per week. Concentric (or eccentric) slow-velocity (60° · s$^{-1}$) isokinetic training of the non-dominant leg and arm. During week 1, one set of 6 repetitions was performed for knee extension and elbow flexion. In weeks 2–5, one set was added each week, so by week 5, the participants completed 5 sets of 6 repetitions. In weeks 6–20, the volume was maintained. Torque output was not controlled during training, but was free to vary (i.e., increase) as participants performed each repetition at maximal volitional effort. Of note, one group of women (*n* = 37) performed concentric training, and the other group (*n* = 33) eccentric training | Arm fat mass (kg; DEXA)<br>Leg fat mass (kg; DEXA) |
| Olson and Edelstein, 1968 [5] | 32 boys, with no experience in weight training (age, 14–16 years) | 6 weeks, 3 or 5 days per week (half of the participants exercised 5 days a week and the other half exercised 3 days per week; however, data from all the participants were mixed). Right arm curl with dumbbell and triceps extension with dumbbell, for 3 sets of 7RM each exercise (with as many repetitions as possible in the second and third sets). When a sufficient gain in strength allowed 7 repetitions to be performed in all 3 sets, the resistance was increased. There was no warm-up prior to the exercises. The boys did not participate in physical education or in intramural or interscholastic athletics during the study | Triceps subcutaneous fat (mm; skinfold callipers) |
| Orkunoglu-Suer et al., 2008 [70] | 320 women (age, 22.9 years; body mass, 64.7 kg; height, 164.2 cm; BMI, 23.7 kg · m$^{-2}$) and 197 men (age, 23.9 years; body mass, 78.8 kg; height, 178.5 cm; BMI, 24.7 kg · m$^{-2}$); all European descents (white) | See: Kostek et al., 2007 [18] | Arm subcutaneous fat volume (mm$^3$; MRI) |
| Ramirez-Campillo et al., 2013 [21] | 11 physical education students (7 men and 4 women; Latin American) (age, 23.0 years; BMI, 25.0 kg · m$^{-2}$) | 12 weeks, 3 sessions per week (80 minutes per session). Localized muscle endurance resistance training for the non-dominant leg muscles. Subjects completed one set of leg press per session, at 10–30% 1RM (10% during weeks 1–4, 20% during weeks 5–6, and 30% during weeks 7–12). Subjects completed 960–1200 consecutive repetitions for their set (no rest between repetitions), with 4–5 seconds per repetition | Leg fat mass (kg; DEXA)<br>Leg fat percentage (DEXA) |
| Roby, 1962 [10] | 15 male college students (age, 21.1 years) | 10 weeks, 3 sessions per week. Dominant arm triceps extension, for 3 sets of 10–15 repetitions at 50% 1RM. Overload was applied when participants were able to perform 15 repetitions in all 3 sets | Triceps subcutaneous fat (mm; skinfold callipers) |
| Walts et al., 2008 [71] | Men (*n*: 78–82) and women (*n*: 95–98), relatively healthy, physically inactive (age, 63.0 years); self-reported Caucasians (*n* = 114) or African Americans (*n* = 52) | See: Hanson et al., 2009 [46] | Knee extensor subcutaneous fat (cm$^2$; CT)<br>Knee extensor intermuscular fat (cm$^2$; CT) |
| Yao et al., 2007 [72] | Men (*n* = 46; age, 64.4 years; height, 174 cm; body mass, 84 kg; % body fat, 27.4) and women (*n* = 52; age, 62.7 years; height, 163 cm; body mass, 73.2 kg; % body fat, 38.8) | See: Hanson et al., 2009 [46] | Knee extensor intermuscular fat (cm$^2$; CT) |

1RM – one-repetition maximum, BMI – body mass index, bpm – beats per minute, CT – computed tomography, DEXA – dual-energy X-ray absorptiometry, MRI – magnetic resonance imaging, ROM – range of motion, $VO_2$ – volume of oxygen consumption

Table 2. Methodological quality of the included studies based on the PEDro rating scale

| Study name | Q1 | Q2 | Q3[a] | Q4 | Q5 | Q6 | Q7 | Q8 | Q9 | Q10 | Q11 | Total* | Study quality |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Brinkworth et al., 2004 [66] | 1 | 0 | 1 | 1 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 8/10 | High |
| Devries et al., 2015 [67] | 1 | 1 | 1 | 1 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 7/10 | High |
| Hanson et al., 2009 [46] | 1 | 0 | 1 | 1 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 6/10 | High |
| Kostek et al., 2007 [18] | 1 | 0 | 1 | 1 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 8/10 | High |
| Krotkiewski, et al., 1979 [9] | 1 | 0 | 1 | 1 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 6/10 | High |
| Miura et al., 2009 [68] | 1 | 1 | 1 | 1 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 7/10 | High |
| Nickols-Richardson et al. 2007 [69] | 1 | 0 | 1 | 1 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 6/10 | High |
| Olson and Edelstein, 1968 [5] | 1 | 0 | 1 | 1 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 6/10 | High |
| Orkunoglu-Suer et al., 2008 [70] | 1 | 0 | 1 | 1 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 6/10 | High |
| Ramirez-Campillo et al., 2013 [21] | 1 | 0 | 1 | 1 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 6/10 | High |
| Roby, 1962 [10] | 1 | 0 | 1 | 1 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 6/10 | High |
| Walts et al., 2008 [71] | 1 | 0 | 1 | 1 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 8/10 | High |
| Yao et al., 2007 [72] | 1 | 0 | 1 | 1 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 6/10 | High |

A detailed explanation for each PEDro scale item can be accessed at https://www.pedro.org.au/english/downloads/pedro-scale. Q3 was considered to be attained even if concealed allocation was not reported, since the decision about whether or not to include a person in a trial could not be influenced by knowledge of whether the subject was to receive treatment or not.
[a] in the context of this study, * for a possible maximal punctuation of 10



| Study name | Statistics for each study | | | | | | | Hedges's g and 95% CI |
|---|---|---|---|---|---|---|---|---|
| | Hedges's g | Standard error | Variance | Lower limit | Upper limit | Z-Value | p-Value | |
| Brinkworth et al., 2004, bovine colostrum | 0.044 | 0.335 | 0.112 | -0.613 | 0.700 | 0.130 | 0.896 | |
| Brinkworth et al., 2004, whey protein | -0.108 | 0.335 | 0.112 | -0.765 | 0.549 | -0.321 | 0.748 | |
| Devries et al., 2015 | 0.045 | 0.255 | 0.065 | -0.454 | 0.545 | 0.177 | 0.859 | |
| Hanson et al., 2009 (all) subcutaneous | -0.222 | 0.205 | 0.042 | -0.625 | 0.180 | -1.083 | 0.279 | |
| Hanson et al., 2009 (men) subcutaneous | 1.072 | 0.317 | 0.101 | 0.450 | 1.694 | 3.378 | 0.001 | |
| Hanson et al., 2009 (women) subcutaneous | -1.209 | 0.304 | 0.092 | -1.804 | -0.614 | -3.982 | 0.000 | |
| Hanson et al., 2009 (all) intermuscular fat | -0.242 | 0.205 | 0.042 | -0.644 | 0.161 | -1.176 | 0.239 | |
| Hanson et al., 2009 (men) intermuscular fat | 0.255 | 0.297 | 0.088 | -0.328 | 0.838 | 0.857 | 0.391 | |
| Hanson et al., 2009 (women) intermuscular fat | -0.240 | 0.279 | 0.078 | -0.788 | 0.307 | -0.860 | 0.390 | |
| Kostek et al., 2007 (men and women) biceps | -0.096 | 0.149 | 0.022 | -0.387 | 0.196 | -0.644 | 0.520 | |
| Kostek et al., 2007 (men) biceps | -0.216 | 0.228 | 0.052 | -0.662 | 0.230 | -0.948 | 0.343 | |
| Kostek et al., 2007 (women) biceps | -0.046 | 0.195 | 0.038 | -0.428 | 0.335 | -0.237 | 0.813 | |
| Kostek et al., 2007 (men and women) arm | -0.023 | 0.138 | 0.019 | -0.294 | 0.248 | -0.164 | 0.869 | |
| Kostek et al., 2007 (men) arm | -0.173 | 0.209 | 0.044 | -0.584 | 0.237 | -0.828 | 0.408 | |
| Kostek et al., 2007 (women) arm | -0.020 | 0.183 | 0.033 | -0.378 | 0.339 | -0.108 | 0.914 | |
| Krotkiewski, et al., 1979, subcutaneous | -0.751 | 0.444 | 0.198 | -1.622 | 0.120 | -1.690 | 0.091 | |
| Krotkiewski, et al., 1979, cell fat | -0.735 | 0.444 | 0.197 | -1.604 | 0.135 | -1.655 | 0.098 | |
| Miura et al., 2009 | 0.005 | 0.473 | 0.223 | -0.921 | 0.932 | 0.011 | 0.991 | |
| Nickols-Richardson et al. 2007 (concentric), arm | -0.033 | 0.230 | 0.053 | -0.484 | 0.418 | -0.141 | 0.887 | |
| Nickols-Richardson et al. 2007 (eccentric), arm | 0.034 | 0.243 | 0.059 | -0.442 | 0.511 | 0.142 | 0.887 | |
| Nickols-Richardson et al. 2007 (concentric), leg | 0.010 | 0.230 | 0.053 | -0.441 | 0.460 | 0.042 | 0.967 | |
| Nickols-Richardson et al. 2007 (eccentric), leg | 0.053 | 0.243 | 0.059 | -0.424 | 0.530 | 0.217 | 0.828 | |
| Olson and Edelstein, 1968 | -0.504 | 0.251 | 0.063 | -0.996 | -0.012 | -2.008 | 0.045 | |
| Orkunoglu-Suer et al., 2008 (women) | 0.015 | 0.079 | 0.006 | -0.140 | 0.170 | 0.190 | 0.849 | |
| Orkunoglu-Suer et al., 2008 (men) | 0.033 | 0.101 | 0.010 | -0.164 | 0.231 | 0.333 | 0.739 | |
| Ramirez-Campillo et al., 2013, fat mass | 0.046 | 0.380 | 0.144 | -0.699 | 0.791 | 0.121 | 0.903 | |
| Ramirez-Campillo et al., 2013, fat percentage | 0.000 | 0.380 | 0.144 | -0.744 | 0.744 | 0.000 | 1.000 | |
| Roby, 1962 | 0.080 | 0.355 | 0.126 | -0.616 | 0.777 | 0.226 | 0.821 | |
| Walts et al., 2008 (men), subcutaneous | 0.000 | 0.155 | 0.024 | -0.305 | 0.305 | 0.000 | 1.000 | |
| Walts et al., 2008 (women), subcutaneous | 0.101 | 0.142 | 0.020 | -0.178 | 0.380 | 0.707 | 0.480 | |
| Walts et al., 2008 (Caucassians), subcutaneous | 0.150 | 0.132 | 0.017 | -0.110 | 0.409 | 1.131 | 0.258 | |
| Walts et al., 2008 (African American), subcutaneous | 0.153 | 0.195 | 0.038 | -0.229 | 0.535 | 0.783 | 0.434 | |
| Walts et al., 2008 (men), intermuscular fat | 0.119 | 0.156 | 0.024 | -0.186 | 0.424 | 0.767 | 0.443 | |
| Walts et al., 2008 (women), intermuscular fat | -0.096 | 0.142 | 0.020 | -0.375 | 0.183 | -0.677 | 0.498 | |
| Walts et al., 2008 (Caucassians), intermuscular fat | 0.000 | 0.132 | 0.017 | -0.259 | 0.259 | 0.000 | 1.000 | |
| Walts et al., 2008 (African American), intermuscular fat | -0.065 | 0.195 | 0.038 | -0.446 | 0.317 | -0.332 | 0.740 | |
| Yao et al., 2007 | 0.122 | 0.142 | 0.020 | -0.157 | 0.401 | 0.857 | 0.391 | |
| | -0.025 | 0.037 | 0.001 | -0.098 | 0.048 | -0.661 | 0.508 | |

Figure 2. Forest plot for changes in localized fat (spot reduction) in trained compared with untrained limbs. Negative values denote that the trained limb reduced more fat than the untrained limb. Values shown are effect sizes (Hedges' *g*) with 95% confidence intervals (CI). The size of the plotted squares reflects the statistical weight of each study. The white diamond reflects the overall result

## Discussion

In the context of the definition of our proposed model to test the hypothesis of spot reduction, our aim was to summarize peer-reviewed literature assessing the effects of unilateral limb training, compared with the contralateral limb, on the localized adipose tissue depots in healthy participants across the life span, and to meta-analyse its results. From the 13 studies included in our meta-analysis, all achieved 6 or more points in the PEDro scale. This may increase the perceived quality of research included in our analyses and the confidence in evidence. Further, results were obtained with low impact of heterogeneity ($I^2$ = 24.3%) and no significant risk of reporting bias (Egger's test $p$ = 0.133). In addition, a total of 1158 participants were included in the 13 studies, a strength when compared with the relatively reduced number of participants involved in sports sciences literature [37]. Although exercise is a potent contributor to fat reduction [73], our meta-analysis indicated no significant (trivial) effect of localized muscle training on localized adipose tissue depots, i.e., no spot reduction was observed. Therefore, long-term exercise-based localized adipose tissue reduction would not be an expected result of an adequately planned exercise intervention. The result of our meta-analysis is based on interventions with a mean duration of 11 weeks (range, 2–20 weeks) involving different training approaches (e.g., cycling, resistance training) in participants of different sex, age, and physical fitness level (e.g., sedentary, physically active). Despite the heterogeneity in samples, protocols, and study designs, the lack of effect was consistent, denoting a robust phenomenon that is largely independent of the characteristics of the population or of the exercise program. It is indeed intriguing from a physiological and anatomical perspective how exercise-based interventions may induce a localized effect on skeletal muscle tissue [74], bone tissue [75], or even skin tissue [76], but not on adipose tissue.

Such an intriguing phenomenon has generated controversy since (at least) the 19th century [1, 25, 26], with several studies performed on the subject from the middle of the 20th century up to recently [2–24]. It is possible that the controversy regarding spot reduction relates to its definition. For example, if spot reduction considers the intramuscular fat stores, a localized reduction may occur, contrary to the subcutaneous fat depot [24]. Considering our definition of voluntary exercise-based localized fat reduction (i.e., spot reduction; see methods section, eligibility criteria sub-section), a valid model to test the hypothesis of spot reduction would be one in which, essentially, the muscles in one part of the body are trained, whereas the muscles in the contralateral side are not. Indeed, the use of an appropriate research model is fundamental for researchers to avoid flawed experiments that may lead them to inappropriate (or even intended) results. For such definition and proposed model we considered [19, 27–30, 32, 71] (i) fat depots from different body regions are not equally comparable within a given individual (i.e., comparing arms and legs); (ii) for the same body fat depot, significant inter-individual differences might occur (e.g., abdominal fat may respond differently to exercise in males compared with females) [28, 77, 78]; (iii) contrary to neuromuscular-related outcomes, there is no evidence for a cross-education between subcutaneous fat depots through exercise; (iv) the effects of exercise training on one limb compared with the contralateral non-exercised limb allow a tight control for dietary (even if this is not manipulated) and other possible intervening factors (e.g., methodology, seasonal variation, genetics, biology, variations in attention and motivation between experimental and control groups) [46, 71]; (v) studies seeking to validly test the hypothesis of spot reduction should consider the size of the adipose tissue depots adjacent to the trained and respective non-trained muscles before and after an intervention period (with a relatively high volume of work to impact fat tissue), not just after an acute exercise bout [14]; (vi) valid studies should use valid measurement techniques, avoiding techniques that may provide biased results owing to changes in muscle mass [18] or other factors not related to biological changes in fat content [79]. For example, reductions of 3–14% (mean, 7.5%) were noted in the trained arm compared with the non-trained arm when subcutaneous fat was measured in the biceps with a skinfold calliper [18]. In contrast, when MRI was used to measure arm subcutaneous fat volume, the reduction was nearly 3-fold lower (range, 0–7%; mean, 2.8%) [18]. Additionally, valid studies should report the reliability of measurement (e.g., coefficient of variation, total error of measurement), as not all studies in this field have reported this essential element [4–6, 15].

In contrast to our proposed definition and model to test the hypothesis of exercise-induced localized fat reduction, 2 cross-sectional studies [14, 17] found acute localized lipolysis. However, the studies did not demonstrate spot reduction (i.e., localized reduction of adipose tissue). Moreover, in the 2 aforementioned cross-sectional studies [14, 17], although they reported that exercising one leg promoted an increase in lipolysis in the subcutaneous fat adjacent to the muscles being exercised (e.g., anterior thigh), the effect was highly local, meaning that any significant long-term effect (i.e., fat reduction) would be unlikely. Further, compared with the aforementioned cross-sectional studies [14, 17], some authors observed contradicting findings, with intense exercise (e.g., resistance training) reducing subcutaneous adipose tissue blood flow and lipolysis [31]. Aside the controversial findings, the fact that an acute increase in lipolysis does not translate into chronic reduction in fat depots is analogous to the fact that exercise at a given intensity may allow maximal acute rate of fat oxidation [80], without long-term effect on body composition [81]. Indeed, even if acute localized lipolysis occurs during exercise, several additional physiological processes are needed before free fatty acids enter the blood stream for later oxidation in tissues [28, 29, 82]. Moreover, the authors from one of the aforementioned cross-sectional studies [14] indicated that ‘More calories are expended during aerobic, whole body exercise than by exercise with local muscle groups, and, accordingly, a person seeking to loose fat must be advised to perform whole body exercise’ (p. E398). Indeed, high-intensity exercise has been found to promote large reduction in body fat in different body parts, with many different activities [83]. From a practical point of view, if the main aim of a training programme were to improve body composition, including reductions of adipose tissue, the most logically defendable approach would be to include a training programme allowing a considerable energy expenditure density. To this aim, compared with localized exercise, non-localized exercise involving large muscles groups would be preferable. Of course, localized exercise may still offer important practical relevance, improving the endurance of trunk muscles (e.g., abdominal muscle training), inducing a cross-education effect on injured limbs, or improving localized-peripheral adaptations with a minimization of central responses (e.g., blood pressure), among others. But the current literature does not support its use for regional fat reduction.

### Limitations

According to our definition, a valid model to test the hypothesis of spot reduction would be one in which the muscles in one limb are trained, whereas the muscles in the contralateral limb are not. To our knowledge, this model is less prone to bias compared with the rest of the models (e.g., cross-sectional, exercise compared with nutrition, trunk-localized exercise, whole-body exercise) currently proposed in the scientific literature to test the hypothesis of spot reduction through exercise training. Considering our proposed definition and model, we conducted a systematic review with meta-analysis that included studies with participants across a wide range of ages, with no restriction for sex or training status, and that included different protocols (e.g., training, assessment techniques). Owing to the high heterogeneity between the included studies, a high heterogeneity in results might been expected. However, the meta-analysis clearly denotes that lack of spot reduction is ubiquitous, i.e., the effect is very strong and seems to be sample- and protocol-independent. Although our results appear highly consistent, we discuss some potential limitations.

Firstly, exercising one limb might induce a partial activation of the contralateral limb [84], and contralateral strength gains have been reported [85–87]. How much activation of the control limb might have occurred and to what extent this affected study outcomes is unclear. Additionally, studies usually controlled for the correct technical execution of training exercise by proper spotters and researchers. Therefore, it is assumed that participants recruited for exercise interventions had an adequate exercise technique and supervision that made them able to activate the target muscle while maintaining the contralateral muscle relatively inactive. Secondly, the lack of nutritional control was not considered as an exclusion criterion in our meta-analysis. Nonetheless, the effects of exercise training on one limb compared with the contralateral non-exercised limb allow a tight control for dietary (even if this is not manipulated) and other possible intervening factors (e.g., seasonal variation, genetics, biology) [46, 71]. Thirdly, we only considered voluntary training protocols in this meta-analysis. Therefore, non-voluntary muscle activation strategies and their potential to affect the trained limb [88, 89] were not investigated. Fourthly, the studies included in our meta-analysis consisted of training programmes lasting 2–20 weeks; longer-term interventions were not addressed. However, on the basis of the current findings and those derived from some cross-sectional studies involving athletes with several years of training using one limb more than the contralateral one (e.g., tennis) [7, 35, 90], longer-term interventions would probably help to confirm the presented findings.

## Conclusions

Localized muscle training had no effect on localized adipose tissue depots, i.e., there was no spot reduction, regardless of the characteristics of the population and of the exercise program.

### Disclosure statement

No author has any financial interest or received any financial benefit from this research.

### Conflict of interest

The authors state no conflict of interest.

### Data availability

The datasets generated and/or analysed during the current study are available from the corresponding author on reasonable request.

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