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SYSTEMATIC REVIEW

Association Between Muscular Strength and Bone Health from Children to Young Adults: A Systematic Review and Meta-analysis

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Abstract

Background Osteoporosis is a major worldwide health concern. The acquisition of bone mass during growth decreases the risk of osteoporosis later in life. Muscular strength is an important and modifiable factor to improve bone development in this period.

Objective The aim of this review was to summarize the relationship between muscular strength and bone health.

Methods Cross-sectional data from studies addressing this association from childhood to young adulthood were systematically searched. The DerSimonian and Laird method was used to compute pooled estimates of effect size and respective 95% CI. The meta-analyses were conducted separately for upper limbs or lower limbs muscular strength and for bone regions. Additionally, a regression model was used to estimate the influence of determinants such as age, lean mass, fat mass, height, weight and cardiorespiratory fitness in this association.

Results Thirty-nine published studies were included in the systematic review. The pooled effect size for the association of upper limbs muscular strength with upper limbs, spine and total body BMD ranged from 0.70 to 1.07 and with upper limbs, spine and total body BMC ranged from 1.84 to 1.30. The pooled effect size for the association of lower limbs muscular strength with lower limbs, spine and total body BMD ranged from 0.54 to 0.88 and with lower limbs, spine and total body BMC ranged between 0.81 and 0.71. All reported pooled effect size estimates were statistically significant.

Conclusion This systematic review and meta-analysis supports that muscular strength should be considered as a useful skeletal health marker during development and a target outcome for interventions aimed at improving bone health.

1 Introduction

Osteoporosis is a systemic skeletal disease that consists of low bone mass and microarchitectural deterioration of bone tissue, which increases bone fragility and the risk of fracture [1]. Because of its high morbidity and mortality, osteoporosis is one of the most important health problems in terms of the global burden of disease [1, 2]. It has been clearly established that high bone mass during childhood and adolescence has an important positive effect on adult skeletal health [3]. Peak bone mass, defined as the amount of bone attained at the end of skeletal development, usually occurs between the 2nd and 3rd decade of life [4, 5], and has been proposed as a key determinant of future fracture risk during adulthood [3, 6].

While peak bone mass is mainly determined by genes, behavioral factors such as hormones, diet and physical activity may act as modifiers. Thus, it is essential to know which modifiable factors improve and maximize peak bone mass to optimize bone health. Lean mass has been consistently associated with bone mineral content (BMC) and bone mineral density (BMD) due to the mechanical loading placed on bones by lean mass [7, 8]. Closely related to lean mass is the muscle mass and therefore the expression of their physical condition, muscular strength, which has been associated

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Key Points

Muscular strength is associated with bone health during growth. This positive association was site-to-site and distant to the contraction in both males and females.

Overall, upper limbs muscular strength showed a stronger relationship with bone results than lower limbs muscular strength.

The meta-regression analyses showed that determinants such as age, lean mass, height and weight positively influenced lower limbs muscular strength and skeletal health association.

with bone development in children and adolescents. Furthermore, strengthening activities are related to both lean mass and muscular strength, according to the mechanostat theory [9], which exert tensile forces that strain the bones they are attached to and induce adaptations that improve the bones' resistance. During growth, the primary mechanical challenges to the mechanostat result from increases in bone length and muscle force [10].

A wide variety of tests is applied to express muscular strength and its relationship to bone health. ALPHA battery includes handgrip strength and standing long jump tests, which have been previously validated and used to assess musculoskeletal fitness [11]; also isokinetic testing and one maximal repetition have been recommended for the assessment of muscle strength.

Previous reviews have addressed the health benefits of muscular strength for children and adolescents [12, 13]. However, no previous study has comprehensively examined the information regarding the site-specific and systemic association between both upper and lower limbs muscular strength and bone development taking into account the influence of potential confounders in this link in a growing skeleton, using a meta-analysis approach.

For these reasons, this systematic review and meta-analysis aimed to synthesize in a reproducible way the consistency of the associations of muscular strength to bone health during growth at local and remote sites of DXA measurements and to examine the influence of participants' characteristics (i.e., sex, age, lean mass, fat mass, height, weight, physical activity and cardiorespiratory fitness) in this relationship.

2 Methods

This systematic review and meta-analysis was performed according to the Meta-analysis of Observational Studies in Epidemiology statements (MOOSE) [14], Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) [15], and the Cochrane Collaboration Handbook [16] recommendations. This systematic review and meta-analysis was previously registered with the International Prospective Register of Systematic Reviews (PROSPERO) database (Registration number: CRD42018097051).

2.1 Search Strategy

A literature search was conducted in MEDLINE (via PubMed), EMBASE, the Cochrane Central Register of Controlled Trials, the Cochrane Database of Systematic Reviews and the Web of Science databases from inception to April 2019. The search strategy used was: ("physical activity" OR "muscle strength" OR endurance OR "grip strength" OR jump OR fitness) AND (adolescen* OR teen* OR child* OR student* OR youth* OR young*) AND ("bone density" OR "bone mineral content" OR "bone mineral density" OR "bone mass"). The reference lists of the articles included and of previous relevant systematic reviews and meta-analyses were reviewed for additional studies.

2.2 Selection Criteria

Original research articles analyzing the relationship between muscular strength and bone outcomes during growth were included in this systematic review and meta-analysis. The following inclusion criteria were used: (i) study participants: healthy individuals aged 8–30 years, since this age range has been previously used to estimate the peak bone mass [4] in accordance with data that suggest that bone mass is still being accrued in the 3rd decade of life [17]; and (ii) study design: data obtained from either cross-sectional studies or baseline measurements of cohort studies. The exclusion criteria were: (i) not using dual-energy X-ray absorptiometry (DXA) to assess bone health; (ii) studies reporting adjusted associations; and (iii) studies not written in English or Spanish.

Where more than one report provided data for the same sample, only the publication with the most detailed results or providing data for the largest sample size was included. However, sample characteristics could be extracted from the multiple reports to obtain the most complete descriptive information. The literature search was performed independently by two reviewers (ATC and PLM) and inconsistencies were solved by consensus.

2.3 Data Extraction

The main characteristics of the selected studies were summarized in an ad hoc table including information regarding: (1) author identification; (2) country of study; (3) year of publication; (4) participants' characteristics (i.e., age, number, lean and fat mass, height and weight); (5) physical activity level: non-active (< 2 or 3 h/week of extracurricular activity participation), active (> 2 or 3 h/week of extracurricular activity participation) or mixed (studies analyzing non-active and active population together). Studies that did not report participants' physical activity level were considered as a mixed group; (6) cardiorespiratory and muscular strength measurements; (7) DXA model; and (8) bone outcomes.

2.4 Risk of Bias Assessment

The Quality Assessment tool for Observational Cohort and Cross-sectional Studies from the National Heart, Lung and Blood Institute [18] was used to evaluate the risk of bias for cohort and cross-sectional studies, which include criteria about the research question, population definition, participation rate, recruitment, sample size, analysis, time frame, exposure levels, measures and assessment, outcome measures and blinding, loss of follow up, and confounding variables. Each study was rated as good (i.e., most criteria met and with a low risk of bias), fair (i.e., some criteria met and with a moderate risk of bias), or poor (i.e., few criteria met and with a high risk of bias).

Data extraction and quality assessment were independently performed by two researchers (ATC and PLM) and inconsistencies were solved by consensus or involving a third researcher (CAB).

2.5 Data Synthesis and Analysis

The DerSimonian and Laird method [19] was used to compute pooled estimates of effect size (ES) and respective confidence intervals (95% CI) for the association of muscular strength with BMD and BMC. ES was calculated regardless of whether studies estimated this association by correlation coefficients, regression models or mean value trends by group. ES values around 0.2 were considered to be a weak effect, values around 0.5 a moderate effect, values around 0.8 a strong effect and values larger than 1.0 a very strong effect.

Considering differences between regional muscular strength in the values of BMD and BMC, meta-analyses were conducted separately for upper and lower limbs muscular strength. Furthermore, considering differences between BMD and BMC regions (upper limbs, lower limbs, spine and total body), a meta-analysis was done for each region. For upper limbs muscular strength, BMD and BMC from the same region were considered, and similarly for lower limbs muscular strength. At least four studies in each group were required to conduct the meta-analysis. The heterogeneity of results across studies was evaluated using the I^2 statistic [20], which was interpreted as: 0–40% (minimal), 30–60% (moderate), 50–90% (substantial) and 75–100% (considerable). The corresponding p values were also considered [16].

Sensitivity analyses (systematic re-analysis while removing studies one at a time) and subgroup analyses were conducted to assess the robustness of the summary estimates. Additionally, sensitivity analyses provided insight as to whether any particular study or subgroup accounted for a large proportion of heterogeneity in the correlation pooled estimates. Subgroup analyses were performed according to participants' sex, physical activity level (non-active, active and mixed group; non-active and active participants analysed together) and test used (ALPHA-fitness battery tests versus others tests groups such as isokinetic testing, Sargent jump test, vertical jump, 1RM, maximal isometric leg extension force, isometric force with a force plate, multi-station weight machine testing, total hip machine).

Random-effects meta-regression analyses were conducted to assess whether age, lean mass, fat mass, height, weight or cardiorespiratory fitness significantly influenced the association of muscular strength with BMD and BMC. Finally, to assess publication bias, Egger's regression asymmetry test was used [21]. A level of <0.10 was used to determine if publication bias might be present.

Statistical analyses were performed using Stata/SE software, version 14 (StataCorp, Chicago, IL, USA).

3 Results

3.1 Systematic Review

The systematic review and meta-analyses flow diagram is presented in Fig. 1. From the 117 full-text articles identified, only 39 studies [22–60], which included a total of 5785 participants, met the inclusion criteria and were included in the systematic review. Most studies were conducted in European countries [23, 24, 31–34, 37, 42–45, 48–50, 52, 53, 55–58]. Eight were conducted in North America [29, 30, 39, 40, 51, 54, 59, 60], two in South America [35, 36], six in Asia [22, 25–27, 38, 41], one in Africa [47] and one in Australia [28]. Participants in the studies were healthy people whose age ranged from 9.3 to 25.0 years. Upper limbs muscular strength was examined in 16 studies [22, 26, 27, 30–32, 37, 40, 41, 48, 51, 53–55, 57, 59] and lower limbs muscular strength in 32 studies [23–25, 27–30, 32–36, 38–40, 42–52, 54–56, 58–60]. Additionally, 12 studies reported results related to upper limbs, 29 related to spine, 26 related to total body and 30 related to lower limbs bone outcomes.

Handgrip was the most used test to assess upper limbs muscular strength, while a wide variety of tests was used to assess lower limbs muscular strength. All studies used DXA as the tool to assess bone health (Table 1).

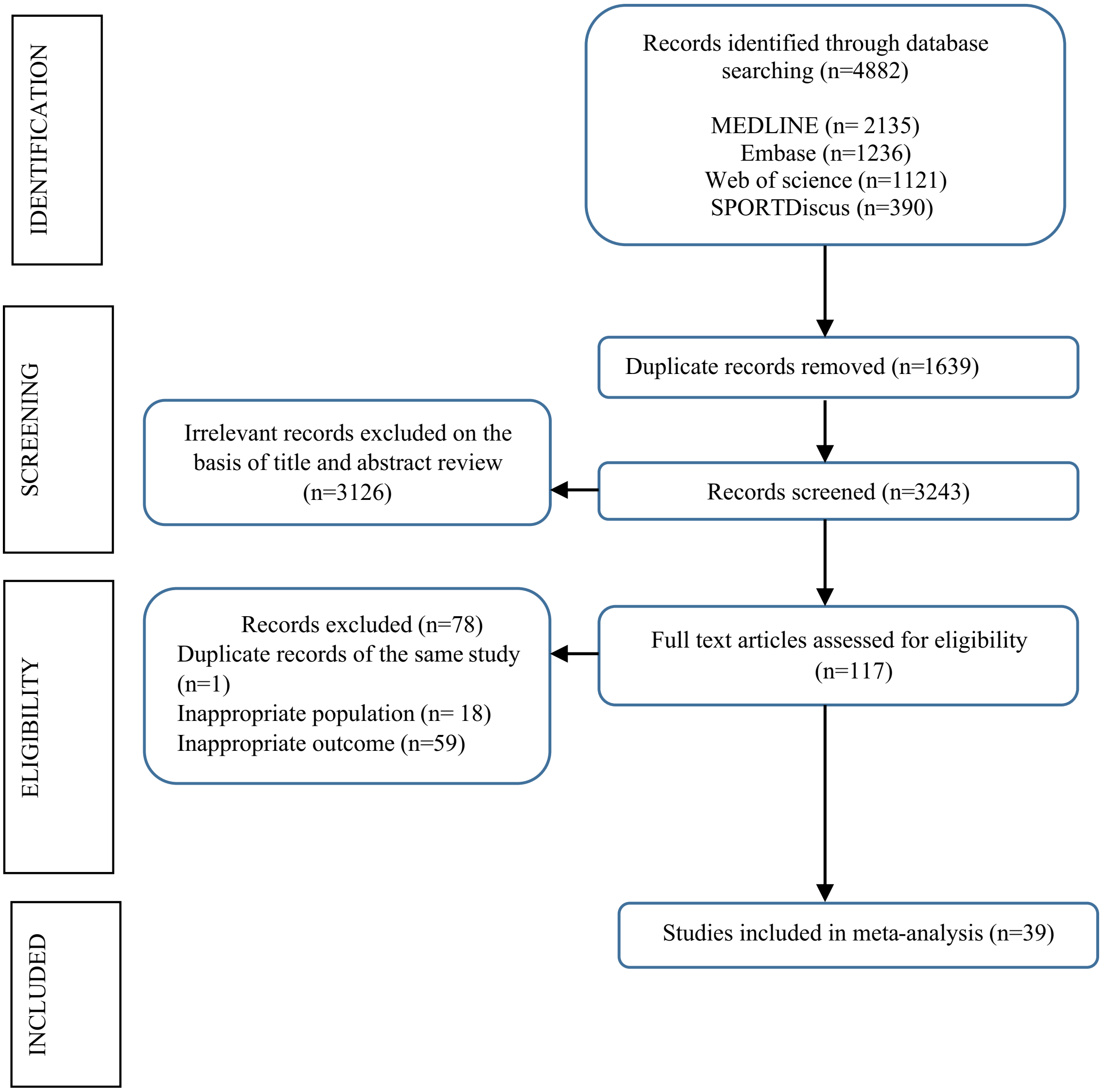

Fig. 1 PRISMA flow diagram

3.2 Risk of Bias

Risk of bias was evaluated with the Quality Assessment tool for Observational Cohort and Cross-sectional Studies from the National Heart, Lung and Blood Institute, which showed that 84.62 % of the studies had a moderate risk of bias [22–25, 27–31, 35, 36, 38–51, 53, 54, 56–60], and 15.38 % a low risk of bias [26, 32–34, 37, 42, 52, 55]. When studies were analysed by individual domains, 71.79 % of the studies had shortcomings in the exposure level domain (Electronic Supplementary Material (ESM) Appendix S1).

3.3 Meta-analysis

Forests plots including the pooled ES estimates for upper and lower limbs muscular strength, the corresponding 95% CI and the I^2 heterogeneity statistic for BMD and BMC are shown in Figs. 2, 3, 4, 5.

3.3.1 Upper Limbs Muscular Strength

For the BMD analysis, the pooled ES were 0.87 (95% CI 0.56–1.17) with considerable heterogeneity ($I^2 = 90.0\%$; $p < 0.001$) for upper limbs BMD, 1.07 (95% CI 0.81–1.33) with substantial heterogeneity ($I^2 = 84.3\%$; $p < 0.001$) for spine BMD and 0.70 (95% CI 0.54–0.87) with important

Table 1 Characteristics of the studies included in the systematic review and meta-analysis

Reference	Country	*N* (M, F)	Age (years)	Lean mass (kg)	Fat mass (kg)	Height (cm)	Weight (kg)	PA level	CRF measure(s)	MF measure (s)	Outcomes	
											DXA scan tool	Zone
Afghani et al. (2003) [22]	China	466 (300, 166)	M: 14.4 ± 0.52 F: 14.2 ± 0.48	M: 47.6 ± 8.57 F: 38.2 ± 4.38	M: 5.1 ± 2.65 F: 9.8 ± 3.45	M: 163.8 ± 8.17 F: 157.2 ± 5.38	M: 52.8 ± 10.43 F: 48.1 ± 6.88	Mixed*	NR	Handgrip: Preston: Jackson, MI	PIXI, Lunar Corporation: Madison, WI	Forearm, heel: BMD, BMC
Alfredson et al. (1996) [23]	Sweden	13 (0, 13)	25.0 ± 2.4	44.4 ± 4.6	26.7 ± 6.3 %	171.2 ± 4.3	64.0 ± 7.7	Non-active	NR	Isokinetic muscle strength (quadriceps, hamstrings): Biodex isokinetic dynamometer (Biodex Co, New York, USA)	Lunar DPX-L (Lunar Co. WI)	Total body, head, femoral neck, Ward's triangle, trochanter, lumbar spine (L1–L4), femur, humerus: BMD
Alfredson et al. (1997) [24]	Sweden	13 (0, 13)	20.9 ± 3.7	47.5 ± 3.0	27.1 ± 5.3%	174.4 ± 6.8	68.6 ± 6.9	Active	NR	Isokinetic muscle strength (quadriceps, hamstrings): Biodex isokinetic dynamometer (Biodex Co, New York, USA)	Lunar DPX-L (Lunar Co. WI)	Total body, head, femoral neck, Ward's triangle, trochanter, lumbar spine (L1–L4), femur, humerus: BMD
Al Rassy et al. (2018) [25]	Lebanon	57 (0, 57) L-BMI: 13 N-BMI: 24 H-BMI: 20	L-BMI: 22.7 ± 2.67 N-BMI: 23.28 ± 2.41 H-BMI: 23.66 ± 4.26	L-BMI: 32.82 ± 2.49 N-BMI: 35.45 ± 3.18 H-BMI: 40.93 ± 5.56	NR	L-BMI: 163 ± 5 N-BMI: 162 ± 6 H-BMI: 159 ± 7	L-BMI: 47.31 ± 2.43 N-BMI: 54.02 ± 5.04 H-BMI: 77.48 ± 14.02	Mixed	VO_{2max}	Sargent jump test	GE Healthcare, Lunar iDXA System, version 13.60	Total body: BMD, BMC Lumbar spine: BMD, BMC, TBS Femoral neck: BMD, BMC, CSA, CSMI, Z

Table 1 (continued)

Reference	Country	*N* (M, F)	Age (years)	Lean mass (kg)	Fat mass (kg)	Height (cm)	Weight (kg)	PA level	CRF measure(s)	MF measure (s)	Outcomes	
											DXA scan tool	Zone
Chan et al. (2008) [26]	China	342 (169, 173)	M: 11.65 ± 0.37 F: 10.68 ± 0.37	NR	NR	M: 148.13 ± 7.95 F: 143.6 ± 7.9	M: 41.17 ± 9.21 F: 36.27 ± 8.27	NR	NR	Handgrip: Jamar Hard dynamometer (Sammons Preston, Canada)	QDR Model 4500W, Hologic Inc, Waltham, MA	Hip, spine, total body: BMD, BMC
Cheng et al. (1998) [27]	China	179 (92, 87)	12–13	NR	NR	NR	NR	Mixed	NR	Handgrip: Grip D 5101 dynamometer Takei, Tokyo, Japan) Vertical jump Isokinetic knee test: Cybex II$^+$ dynamometer (Cybex, Lumex Inc Ronkonkoma, New York, USA)	Model XR-26 (Norland Corporation)	L2–L4 vertebrae: BMD
Duncan et al. (2002) [28]	Australia	76 (0, 76)	Control: 16.9 ± 0.9 Swimmers: 16.7 ± 1.3 Cyclists: 16.5 ± 1.4 Runners: 17.6 ± 1.4 Triathletes: 17.7 ± 1.1	Control: 37.4 ± 5.1 Swimmers: 41.3 ± 5.3 Cyclists: 43.8 ± 5.2 Runners: 42.6 ± 6.0 Triathletes: 42.4 ± 3.6	Control: 31.3 ± 10.2% Swimmers: 27.1 ± 6.0% Cyclists: 23.6 ± 8.6% Runners: 25.3 ± 5.3% Triathletes: 26.3 ± 6.2%	Control: 166 ± 7 Swimmers: 167 ± 6 Cyclists: 166 ± 4 Runners: 168 ± 4 Triathletes: 167 ± 4	Control: 57.8 ± 10.5 Swimmers: 58.6 ± 7.7 Cyclists: 60.3 ± 7.6 Runners: 60.7 ± 6.4 Triathletes: 59.4 ± 5.9	Active	NR	Isokinetic knee test: Cybex Norm isokinetic dynamometer (Lumex, Inc., Ronkonkoma, NY)	DPX, pencil beam; Lunar Radiation Corp., Madison, WI	Total body, lumbar spine, femoral neck and leg: BMD

Table 1 (continued)

Reference	Country	*N* (M, F)	Age (years)	Lean mass (kg)	Fat mass (kg)	Height (cm)	Weight (kg)	PA level	CRF measure(s)	MF measure (s)	Outcomes	
											DXA scan tool	Zone
Eickhoff et al. (1993) [29]	USA	81 (0, 81)	24.8 ± 3.0	NR	NR	165.1 ± 5.6	62.5 ± 9.8	Non-active	NR	Isometric trunk strength: Wagner Dynamometer or Cable Tensiometer Isokinetic knee test: Cybex II Isokinetic dynamometer (Lumex Inc., New York)	DPX-Lunar Radiation Corporation, Madison, WI	Lumbar spine femoral neck:(L2–L4), BMD
Emslander et al. (1998) [30]	USA	63 (0,63)	Runners: 20.3 ± 0.36 Swimmers: 20.5 ± 0.32 Controls: 20.4 ± 0.32	NR	From skinfolds: Runners: 19.7 ± 1.14% Swimmers: 17.5 ± 0.98% Controls: 21.8 ± 1.7 %	Runners: 163.6 ± 1.06 Swimmers: 171.7 ± 1.64 Controls: 167.0 ± 1.47	Runners: 58.7 ± 0.94 Swimmers: 64.7 ± 1.33 Controls: 62.0 ± 2.45	Active	VO_{2max}	Shoulder and hip strength: Cybex IT isokinetic dynamometer (Lumex, Ronkonkoma, New York) Back strength: strain-gauge dynamometer (BID-2000). Grip strength: Jamar grip dynamometer	Lunar DP4B, Lunar Corp., Madison, WI	Total body, lumbar spine, femoral neck and trochanter: BMD

Table 1 (continued)

Reference	Country	*N* (M, F)	Age (years)	Lean mass (kg)	Fat mass (kg)	Height (cm)	Weight (kg)	PA level	CRF measure(s)	MF measure (s)	Outcomes	
											DXA scan tool	Zone
Ginty et al. (2005) [31]	United Kingdom	128 (128, 0)	16.8 ± 0.5	NR	NR	177.4 ± 6.4	68.0 ± 10.2	Active	VO_{2max}	Isometric dynamometry: Back and grip strength	Hologic QDR 1000/W	Total body, lumbar spine (L1–L4), total hip, femoral neck, trochanter, intertrochanter, total radius, ultradistal radius, midradius, one-third radius: BMC, BA, BMD
Gracia-Marco et al. (2011) [32]	Spain	373 (182, 191)	14.8 ± 1.2	40.4 ± 8.6	NR	163.2 ± 18.1	58.3 ± 13.2	Mixed	20 m shuttle run test VO_{2max}	Handgrip test Standing broad jump test	Hologic Explorer scanner, QDR-Explorer, Hologic Corp., Software version 12.4, Waltham, MA, USA	Total body, upper limbs and lower limbs: BMC
Gruodyté et al. (2009) [33]	Estonia	CONT: 43(0,43) SG: 56 (0,56) SPR: 25 (0,25) GYM: 29 (0,29) SW: 32 (0, 32) CCS: 17 (0,17)	CONT: 14.2 ± 1.2 SG: 14.2 ± 1.0 SPR: 14.2 ± 1.1 GYM: 14.4 ± 0.9 SW: 13.8 ± 1.3 CCS: 13.9 ± 0.9	NR	NR	CONT: 162.4 ± 6.9 SG: 167.2 ± 7.8 SPR: 168.1 ± 5.9 GYM: 165 ± 7.0 SW: 164.1 ± 7.1 CCS: 162.8 ± 6.4	CONT: 53.7 ± 8.8 SG: 57.6 ± 9.3 SPR: 54.2 ± 6.5 GYM: 53.6 ± 10.5 SW: 54.2 ± 9.1 CCS: 52.7 ± 9.5	Active	NR	Vertical jumps: CMJ, RJ15s, RJ30S	DPX-IQ, Lunar Corporation, Madison, WI, USA	Lumbar spine (L2–L4), femoral neck: BMD

Table 1 (continued)

Reference	Country	*N* (M, F)	Age (years)	Lean mass (kg)	Fat mass (kg)	Height (cm)	Weight (kg)	PA level	CRF measure(s)	MF measure (s)	Outcomes	
											DXA scan tool	Zone
Gruodyté et al. (2010) [34]	Estonia	Pre-menar: 33 (0, 36) Post-menar: 77 (0,77)	Pre-menar: 13.6 ± 0.9 Post-menar: 14.4 ± 0.9	NR	NR	Pre-menar: 163.1 ± 7.7 Post-menar: 167.7 ± 6.7	Pre-menar: 49.7 ± 7.7 Post-menar: 57.8 ± 8.6	Active	NR	Vertical jumps: CMJ, RJ15s, RJ30S	DPX-IQ, Lunar Corporation, Madison, WI, USA	Lumbar spine (L2–L4), femoral neck: BMD
Guimarães et al. (2018) [35]	Brazil	36 (36, 0)	24.9 ± 8.6	55.41 ± 7.64	NR	175.2 ± 5.1	71.2 ± 12.6	NR	NR	1RM tests: Flat bench-press, lat pull-down, knee extension, leg curl, leg press 45°	Hologic®, QDR Descoberta Wi®	Total body, trunk, upper limb, lower limb, thoracic V, lumbar V, pelvis: BMC, BMD
Guimarães et al. (2018) [36]	Brazil	15 (0, 15)	24.9 ± 7.2	37.52 ± 2,71	NR	162.4 ± 5.0	59.1 ± 6.2	NR	NR	1RM tests: horizontal bench-press, lat pull-down, knee extension, leg-curl, leg press 45°	Hologic model, QDR Discovery Wi	Total body, trunk, upper limb, lower limb, thoracic V, lumbar V, pelvis: BMC, BMD
Kardinaal et al. (2000) [37]	Denmark, Finland, France, Italy, the Netherlands, Poland	1652 1116 girls (11–15 years) 526 women (20–23 years)	T1: 11.7 ± 0.7 T2: 11.8 ± 0.7 T3: 12.3 ± 0.9 T4: 13.4 ± 1.3 T5: 14.3 ± 1.2 W: 22.0 ± 1.1	NR	NR	T1: 148 ± 7 T2: 150 ± 7 T3: 153 ± 7 T4: 160 ± 8 T5: 162 ± 7 W: 166 ± 7	T1: 36.4 ± 6.5 T2: 40.2 ± 7.9 T3: 42.5 ± 7.6 T4: 50.3 ± 8.9 T5: 57.2 ± 8.9 W: 60.8 ± 9.2	NR	NR	Handgrip	p-DXA Osteoscan, Nederburgh BV, Bunschoten, Netherlands	Mid-distal and ultradistal radius: BMC, BMD

Table 1 (continued)

Reference	Country	*N* (M, F)	Age (years)	Lean mass (kg)	Fat mass (kg)	Height (cm)	Weight (kg)	PA level	CRF measure(s)	MF measure (s)	Outcomes	
											DXA scan tool	Zone
Khawaja et al. (2019) [38]	Lebanon	201 (53, 148)	M: 24.3 ± 4.9 F: 24.1 ± 3.9	M: 55.30 ± 12.02 F: 39.75 ± 8.64	M: 26.64 ± 14.88 F: 25.19 ± 8.63	M: 173 ± 8 F: 162 ± 7	M: 84.9 ± 20.0 F: 67.0 ± 13.7	NR	NR	Vertical jump: Sargent test	GE Healthcare, Madison, WI	Total body: BMD, BMC L1–L4: BMD, BMC, TBS Femoral neck: BMD, BMC, CSA, CSMI, Z Total hip: BMD, BMC
Madsen et al. (1998) [39]	USA	60 (0,60)	LW athletes: 20.8 ± 2.5 LW sedentary: 20.8 ± 2.5 AW sedentary: 20.8 ± 2.5	LW athletes: 45.0 ± 3.9 LW sedentary: 40.0 ± 4.1 AW sedentary: 45.0 ± 3.7	LW athletes: 7.3 ± 2.1 LW sedentary: 12.2 ± 2.8 AW sedentary: 16.9 ± 4.2	LW athletes: 165.2 ± 6.2 LW sedentary: 165.8 ± 6.4 AW sedentary: 165.3 ± 6.4	LW athletes: 52.3 ± 5.2 LW sedentary: 52.2 ± 5.5 AW sedentary: 62.0 ± 5.6	Active	NR	Peak isometric torque of the torso, dominant arm and leg: LIDO Active Isokinetic Rehabilitation System	DPX-L with version 3.6R software, Lunar Radiation Corp., Madison, WI	Total body: BMD Lumbar spine: BMD Femoral neck: BMD

Table 1 (continued)

Reference	Country	*N* (M, F)	Age (years)	Lean mass (kg)	Fat mass (kg)	Height (cm)	Weight (kg)	PA level	CRF measure(s)	MF measure (s)	Outcomes	
											DXA scan tool	Zone
Miller et al. (2004) [40]	USA	76 (0, 76)	20.3 ± 1.8	40.0 ± 3.9	15.8 ± 3.3	164 ± 6	57.4 ± 6.1	Active	NR	Strength testing (thigh, upper arm): Isokinetic dynamometer (Multi-Joint system 3 Pro, Biodex Medical Systems, Inc., Shirley, NY, USA)	QDR4500A, Hologic, Inc., Bedford, MA	Total body, femoral neck, trochanter, intertrochanter, Ward's triangle, total hip, ultradistal forearm, midshaft forearm, 1/3 proximal forearm, total forearm: BMD
Naka et al. (2005) [41]	Japan	404 (129, 275) Pre: (31,79) JH1: (38,22) E6: (47,106) E5: (12, 55) E4: (1,13)	12.8 ± 0.3 M: 12.9 ± 0.3 Pre: 12.7 ± 0.3 JH1: 12.9 ± 0.3 E6: 12.09 ± 02 E5: 13.0 ± 0.2 E4: 13.3 F: 12.8 ± 0.3 Pre: 12.7 ± 0.3 JH1: 12.8 ± 0.3 E6: 12.8 ± 0.3 E5: 12.8 ± 0.3 E4: 12.9 ± 0.3	NR	NR	M: 158.7 ± 8.1 Pre: 151.9 ± 6.7 JH1: 158.1 ± 6.9 E6: 161.5 ± 6.6 E5: 166.3 ± 6.0 E4: 174.8 F: 154.4 ± 5.7 Pre: 151.5 ± 5.6 JH1: 154.9 ± 5.3 E6: 154.6 ± 5.4 E5: 156.8 ± 5.0 E4: 158.7 ± 5.1	M: 47.4 ± 10.4 Pre: 42.9 ± 11.4 JH1: 45.2 ± 7.7 E6: 50.3 ± 10.4 E5: 52.5 ± 8.5 E4: 71.6 F: 44.6 ± 7.7 Pre: 39.0 ± 5.7 JH1: 42.2 ± 4.7 E6: 46.1 ± 7.5 E5: 48.5 ± 4.7 E4: 54.6 ± 9.7	NR	NR	Handgrip: strain gauge hand dynamometer (T.K.K. 5401;Takei, Tokyo, Japan)	QDR4500A; Hologic, Waltham, MA, USA	Lumbar spine (L2–L4), femoral neck, total hip: BMD

Table 1 (continued)

Reference	Country	*N* (M, F)	Age (years)	Lean mass (kg)	Fat mass (kg)	Height (cm)	Weight (kg)	PA level	CRF measure(s)	MF measure (s)	Outcomes	
											DXA scan tool	Zone
Nordström et al. (1995) [42]	Sweden	26 (26, 0)	15.9 ± 0.3	55.0 ± 6.6	12.1 ± 8.0	179 ± 6	70.1 ± 13.3	Non-active	NR	Isokinetic muscle strength (quadriceps, hamstrings): Biodex isokinetic dynamometer (Biodex Co, New York, USA)	Lunar DPX-L (Lunar Co., Wisconsin, USA)	Total body, humerus, spine, femur, tibia/fibula, head: BMD
Nordström et al. (1996) [43]	Sweden	54 (54,0)	RG 15.9 ± 0.3 HAG 15.9 ± 0.3	RG 55.1 ± 6.6 HAG 57.2 ± 6.1	RG 12.7 ± 8.1 HAG 10.0 ± 4.7	RG 179 ± 6 HAG 177 ± 6	RG 70.8 ± 13.5 HAG 70.4 ± 10	Non-active	NR	Isokinetic muscle strength (quadriceps, hamstrings): Biodex isokinetic dynamometer (Biodex Co, New York, USA)	Lunar DPX-L (Lunar Co., Wisconsin, USA)	Lumbar spine (L2–L4), total body, femoral neck, Ward´s triangle, trochanter, humerus, head: BMD
Nordström et al. (1997) [44]	Sweden	33 (33, 0)	24.8 ± 2.3	61.4 ± 5.0	13.3 ± 4.3	184 ± 6	77.4 ± 7.6	Non-active	NR	Isokinetic muscle strength (quadriceps, hamstrings): Biodex isokinetic dynamometer (Biodex Co, New York, USA)	Lunar DPX-L (Lunar Co., Wisconsin, USA)	Lumbar spine (L2–L4), total body, femoral neck, Ward´s triangle, trochanter, humerus, head: BMD

Table 1 (continued)

Reference	Country	*N* (M, F)	Age (years)	Lean mass (kg)	Fat mass (kg)	Height (cm)	Weight (kg)	PA level	CRF measure(s)	MF measure (s)	Outcomes	
											DXA scan tool	Zone
Pettersson et al. (1999) [45]	Sweden	RG: 20 (20, 0) HAG: 20 (20,0)	RG: 24.6 ± 2.3 HAG: 23.4 ± 4.9	RG: 62.6 ± 5.1 HAG:66.02 ± 4.3	RG: 15.0 ± 4.2 HAG:12.2 ± 4.2	RG: 183 ± 5.7 HAG: 182 ± 6.1	RG: 81.2 ± 6.9 HAG: 82.2 ± 7.1	Non-active Active	NR	Isokinetic muscle strength (quadriceps, hamstrings): Biodex isokinetic dynamometer (Biodex Co, New York, USA)	Lunar DPX-L, software version 1.3, (Lunar Co, Wisconsin, USA)	Total body, head, humerus, spine, pelvis, femur, femoral neck, femur diaphysis, Ward's triangle, trochanter, proximal tibia, tibia diaphysis: BMD
Pettersson, et al. (2000) [46]	Sweden	RG:16 (0, 16) CCS: 16 (0, 16)	RG:16.4 ± 0.7 CCS:16.2 ± 0.3	RG:36.9 ± 2.5 CCS: 4.9 ± 4.0	RG:20.4 ± 4.1 CCS:15.2 ± 2.9	RG:167 ± 4.0 CCS:168 ± 5.5	RG:59.8 ± 5.3 CCS:62.8 ± 4.7	Non-active Active	NR	Isokinetic muscle strength (quadriceps, hamstrings): Biodex isokinetic dynamometer (Biodex Co, New York, USA)	Lunar DPX-L, software version 1.3y, (Lunar Co. Wisconsin, USA).	Total body, head, spine, femoral neck, trochanter, Ward´s triangle, femoral diaphysis, humerus diaphysis, distal femur, proximal tibia, tibia diaphysis: BMD Humerus diaphysis, femoral neck: BMAD

Table 1 (continued)

Reference	Country	*N* (M, F)	Age (years)	Lean mass (kg)	Fat mass (kg)	Height (cm)	Weight (kg)	PA level	CRF measure(s)	MF measure (s)	Outcomes	
											DXA scan tool	Zone
Rebai et al. (2012) [47]	Tunisia	RG: 22(0,22) Athletes: 29 (0,29)	RG: 21.4 ± 1.5 Athletes: 21.9 ± 9.1	RG: 38.2 ± 31.7 Athletes: 45.9 ± 60.5	RG: 17.7 ± 38.8 Athletes: 19.9 ± 63.7	RG: 163.7 ± 5.4 Athletes: 173.7 ± 7.8	RG: 59.0 ± 6.1 Athletes: 68.4 ± 10.4	Non-active Active	NR	Isokinetic muscle strength (quadriceps, hamstrings): Cybex Norm isokinetic dynamometer (Lumex, Inc., New York, USA)	Lunar Prodigy, WI, Madison,WI,USA, software version 3.6	Total body, lumbar spine, total femur, total humerus: BMD
Ribom et al. (2004) [48]	Sweden	125 (61, 64)	M: 21 ± NR F: 21 ± NR	M: 64.0 ± 5.97 F: 45.74 ± 4.59	M: 8.23 ± 0.85 F: 13.79 ± 0.76	M: 182.1 ± 6.1 F: 167.8 ± 6.5	M: 75.1 ± 10.0 F: 62.2 ± 9.3	NR	NR	Handgrip: JAMAR hydraulic hand dynamometer (5030Jl, Jackson, MI, USA) Isokinetic knee strength (FX, EXT): Cybex III dynamometer (Lumex Corp., Bay Shore, NY, USA)	DPX-L™ (Lunar Co., Madison WI, USA) (Mazess, 1995).	Total body: BMD, BMC

Table 1 (continued)

Reference	Country	*N* (M, F)	Age (years)	Lean mass (kg)	Fat mass (kg)	Height (cm)	Weight (kg)	PA level	CRF measure(s)	MF measure (s)	Outcomes	
											DXA scan tool	Zone
Sandström et al. (2000) [49]	Sweden	RG: 14 (0, 14) Ice-hockey: 14 (0, 14)	RG:21.5 ± 3.8 Ice-hockey: 22.2 ± 4.3	RG: 41.9 ± 5.3 Ice-hockey: 41.8 ± 3.2	NR	RG:167.8 ± 7.1 Ice-hockey: 169.6 ± 5.1	RG:64.4 ± 6.5 Ice-hockey: 65.0 ± 6.8	Non-active Active	NR	Isokinetic muscle strength (quadriceps, hamstrings): Biodex isokinetic dynamometer (Biodex Co, New York, USA)	Lunar DPX-L (Lunar Co, Wisconsin, USA)	Total body, head, lumbar spine (L2–L4), femoral neck, Ward's triangle, trochanter: BMD
Seabra et al (2012) [50]	Portugal	RG:34 (34, 0) Soccer group: 117 (117,0)	RG:13.3 ± 1.3 Soccer group: 13.8 ± 1.5	RG:40.2 ± 8.9 Soccer group: 45.9 ± 10.8	NR	RG:160.6 ± 10.1 Soccer group: 161.2 ± 10.1	RG.53.7 ± 12.7 Soccer group: 55.1 ± 12.0	Non-active Active	NR	Isokinetic dynamometry (knee EXT and FX): Biodex System 2, NY, USA	Hologic QDR 4500A, Hologic Inc., Waltham, MA, USA	Total body, lumbar spine, dominant lower limb, non-dominant lower limb: BMD, BMC

Table 1 (continued)

Reference	Country	*N* (M, F)	Age (years)	Lean mass (kg)	Fat mass (kg)	Height (cm)	Weight (kg)	PA level	CRF measure(s)	MF measure (s)	Outcomes	
											DXA scan tool	Zone
Snow-Harter et al. (1990) [51]	USA	59 (0, 59)	23 ± 0.58	NR	NR	163.7 ± 0.74	61.7 ± 1.2	NR	NR	Hip (ABD, ADD, EXT, FX): total hip machine (Model 9907, Universal Gym Equipment, Cedar Rapids, IA) Back extensors: Lower Back Machine, Nautilus Sports/Medical Industries, Inc., Dallas, TX Leg EXT and biceps curl: Multi-station Weight Machine (Model 9066, Universal Gym Equipment, Cedar Rapids, IA) Isometric grip strength: hand-held dynamometer (J.A. Preston, Clifton, NJ)	Hologic QDR 1O00, Waltham, MA	Lumbar spine (L2–L4), total hip, femoral neck, trochanter: BMD

Table 1 (continued)

Reference	Country	*N* (M, F)	Age (years)	Lean mass (kg)	Fat mass (kg)	Height (cm)	Weight (kg)	PA level	CRF measure(s)	MF measure (s)	Outcomes	
											DXA scan tool	Zone
Söderman et al. (2000) [52]	Sweden	Non-active 41 (0, 41) Soccer players 51 (0, 51)	16.2 ± 1.3 G≤16 years: 14.9 ± 0.5 G>16 years: 17.2 ± 0.8 16.3 ± 1.4 G≤16 years: 14.9 ± 0.6 G>16 years: 17.4 ± 0.7	36.4 ± 3.1 G≤16 years: 35.4 ± 2.9 G>16 years: 37.3 ± 3.0 41.9 ± 2.9 G≤16 years: 40.0 ± 3.3 G>16 years: 42.7 ± 3.2	19.3 ± 4.4 G≤16 years: 19.5 ± 4.7 G>16 years: 19.2 ± 4.2 15.4 ± 3.5 G≤16 years: 14.0 ± 3.5 G>16 years: 16.5 ± 3.2	166.5 ± 5.5 G≤16 years: 165.4 ± 6.5 G>16 years: 167.4 ± 4.6 166.1 ± 4.3 G≤16 years: 165.2 ± 4.2 G>16 years: 166.8 ± 4.3	58.3 ± 6.0 G≤16 years: 57.3 ± 6.5 G>16 years: 59.0 ± 5.7 58.3 ± 6.0 G≤16 years: 57.3 ± 6.2 G>16 years: 61.9 ± 3.9	Non-active Active	NR	Isokinetic muscle strength (quadriceps, hamstrings): Biodex isokinetic dynamometer (Biodex Co, New York, USA)	Lunar DPX-L (Lunar Co, Wisconsin, USA)	Total body, head, lumbar spine (L2–L4), femoral neck, Ward's triangle, trochanter: BMD
Sutter, et al. (2019 [53]	France	100 (100, 0)	24.4 ± 2.81	61.91 ± 7.48	11.40 ± 4.67	176.4 ± 6.19	72.9 ± 9.34	NR	NR	Handgrip strength: Jamar hydraulic hand dynamometer (Jamar Plus +, Sammons Preston, Bolingbrook, Il, USA)	Hologic Discovery A, Hologic Inc., Bedford, MA, US	Total body, femoral neck, total hip, lumbar spine: BMD

Table 1 (continued)

Reference	Country	*N* (M, F)	Age (years)	Lean mass (kg)	Fat mass (kg)	Height (cm)	Weight (kg)	PA level	CRF measure(s)	MF measure (s)	Outcomes	
											DXA scan tool	Zone
Taaffe et al. (2004) [54]	USA	Control 22 (22, 0) Gymnasts 18 (18,0)	Control 19.9 ± 1.6 Gymnasts 19.2 ± 1.2	NR	Control 24.8 ± 3.4% Gymnasts 17.9 ± 1 .7%	Control 164.4 ± 5.5 Gymnasts 159.2 ± 4.6	Control 58.5 ± 6.9 Gymnasts 56.5 ± 3.7	Non-active Active	NR	1RM (bench and leg press): Multi-station weight machine (Universal Gym Equipment, Cedar Rapids, IA, USA) Knee EXT and FX: Cybex 6000 isokinetic dynamometer (Cybex Division of Lumex, Inc., NY, USA) Handgrip: dynamometry (Jamar, TEC, Clifton, NJ, USA)	Hologic QDR 1O00/W, Waltham, MA, USA	Lumbar spine (L2–L4), femoral neck, arm, leg, total body: BMD
Torres-Costoso et al. (2014) [55]	Spain	132 (62, 70)	9.43 ± 0.72 M: 9.38 ± 0.78 F: 9.47 ± 0.67	26.11 ± 4.00 M: 26.84 ± 4.44 F: 25.44 ± 3.48	NR	140.16 ± 6.63 M: 139.46 ± 6.85 F: 140.74 ± 6.42	37.28 ± 9.17 M: 38.18 ± 10.85 F: 36.52 ± 7.47	Active	NR	Handgrip: hand dynamometer TKK 5401 Grip D; Takey, Tokyo, Japan Standing long jump tests	Lunar iDXA, GE Medical Systems Lunar, Madison, WI, USA	Total body, upper and lower limbs, spine, pelvis: BMD, BMC

Table 1 (continued)

Reference	Country	*N* (M, F)	Age (years)	Lean mass (kg)	Fat mass (kg)	Height (cm)	Weight (kg)	PA level	CRF measure(s)	MF measure (s)	Outcomes	
											DXA scan tool	Zone
Ubago-Guisado et al. (2017) [56]	England	121 (121,0)	Swimmers 13.4 ± 1.0 Footballers 12.8 ± 0.9 Cyclists 13.2 ± 1.0 Nonathletes 12.3 ± 0.5	Swimmers 41.6 ± 9.1 Footballers 35.4 ± 7.2 Cyclists 37.7 ± 7.5 Nonathletes 31.7 ± 5.5	NR	Swimmers 165.5 ± 9.7 Footballers 155.2 ± 9.3 Cyclists 160.8 ± 9.9 Nonathletes 154.5 ± 9.9	Swimmers 52.4 ± 9.0 Footballers 44.3 ± 7.6 Cyclists 49.5 ± 12.3 Nonathletes 48.3 ± 13.0	Active	20-m shuttle run test VO_{2max}	Vertical and standing long jump	GE Healthcare Inc, Madison, WI, USA	Whole body minus the head, total hip, lumbar spine, trochanter and femoral neck BMD
Valdimarsson et al. (1999) [57]	Iceland	254	G1 (71): 16 years G2 (64): 18 years G3 (119): 20 years	G1: 37.4 ± 4.2 G2: 38.8 ± 4.1 G3: 39.2 ± 4.3	G1: 17.4 ± 6.7 G2: 19.8 ± 6.8 G3: 22.8 ± 9.6	G1: 165.8 ± 5.8 G2: 167.5 ± 5.5 G3: 167.4 ± 6.2	G1: 57.8 ± 9.4 G2: 61.6 ± 9.0 G3: 65.0 ± 11.8	Active	NR	Grip strength: Jamar adjustable hand-held dynamometer	Hologic QDR-2000 plus, Hologic Inc., Waltham, MA	Spine (L2–L4), femoral neck, Ward's triangle, hip total, forearm total, total skeleton: BMD, BMC
Vicente-Rodriguez et al. (2003) [58]	Spain	104 (104,0)	Control: 9.3 ± 0.2 Footballers: 9.3 ± 0.2	NR	NR	Control: 135.2 ± 1.2 Footballers: 137.1 ± 1.3	Control: 31.9 ± 0.9 Footballers: 35.5 ± 1.6	Active	NR	Maximal isometric leg extension force	QDR-1500, Hologic Corp., Software version 7.10, Waltham, MA	Arm, lower limb, femoral neck BMC and lower limb BMD
Whittngton et al. (2009) [59]	USA	7 (4,3)	M: 20.1 ± 1.2 F: 20.1 ± 0.8	M:91.6 ± 4.0 F:69.3 ± 7.9	M:19.2 ± 7.0% W:29.6 ± 3.2%	M: 179.5 ± 7.1 W: 179.1 ± 3.8	M: 114.0 ± 10.1 W:98.5 ± 11.2	Active	NR	Isometric force mid-thigh pull: force plate, Rice Lake Scales, Rice Lake, WI Ball throw	Lunar Prodigy, GE Health Care Systems	Total body, spine, leg, arm: BMC, BMD

Table 1 (continued)

Reference	Country	*N* (M, F)	Age (years)	Lean mass (kg)	Fat mass (kg)	Height (cm)	Weight (kg)	PA level	CRF measure(s)	MF measure (s)	Outcomes	
											DXA scan tool	Zone
Witzke et al. (1999) [60]	USA	54 (0, 54)	14.6 ± 0.5	42.1 ± 5.3	14.1 ± 5.2	164.2 ± 6.0	59.3 ± 9.7	Mixed	NR	Leg strength (knee EXT): Kin-Com 500H (Chattex Corp., Hixson, TN)	Hologic QDR-1000/W	Total body, femoral neck, greater trochanter, lumbar spine (L2–L4), femoral shaft: BMD, BMC

Values are presented as mean ± SD. Inconsistencies in the reporting of study summary data between studies are attributable to differences in presentation between the original articles

PA physical activity, *M* male, *F* female, *MF* muscular fitness, *CRF* cardiorespiratory fitness, *DXA* dual-energy X-ray absorptiometer, *BMC* bone mineral content, *BMD* bone mineral density, *NR* not reported, *BA* bone area, *L-BMI* low body mass index, *N-BMI* normal body mass index, *H-BMI* high body mass index, *CSA* cross-sectional area, *CSMI* cross-sectional moment of inertia, *Z* section modulus, *TBS* trabecular bone score, *V* vertebrae, *CMJ* countermovement jump, *T1, T2, T3, T4, T5* Tanner 1, 2, 3, 4, 5, CONT control, *SG* sport games group, *SPR* sprinters, *GYM* gymnasts, *SW* swimmers, *CCS* cross-country skiers, *pre-menar* pre-menarcheal, *post-menar* post-menarcheal, *LW* low weight, *AW* average weight, *postPre* prepuberty, *JH1* pubertal onset first year of junior high school, *E6* pubertal onset sixth year of elementary school, *E5* pubertal onset fifth year of elementary school, *E4* pubertal onset fourth year of elementary school, *W* women, *RG* reference group, *HAG* high-activity group, *FX* flexion, *EXT* extension, *ABD* abduction, *ADD* adduction, *BMAD* bone mineral apparent density

*Mixed: non-active + active analysed together

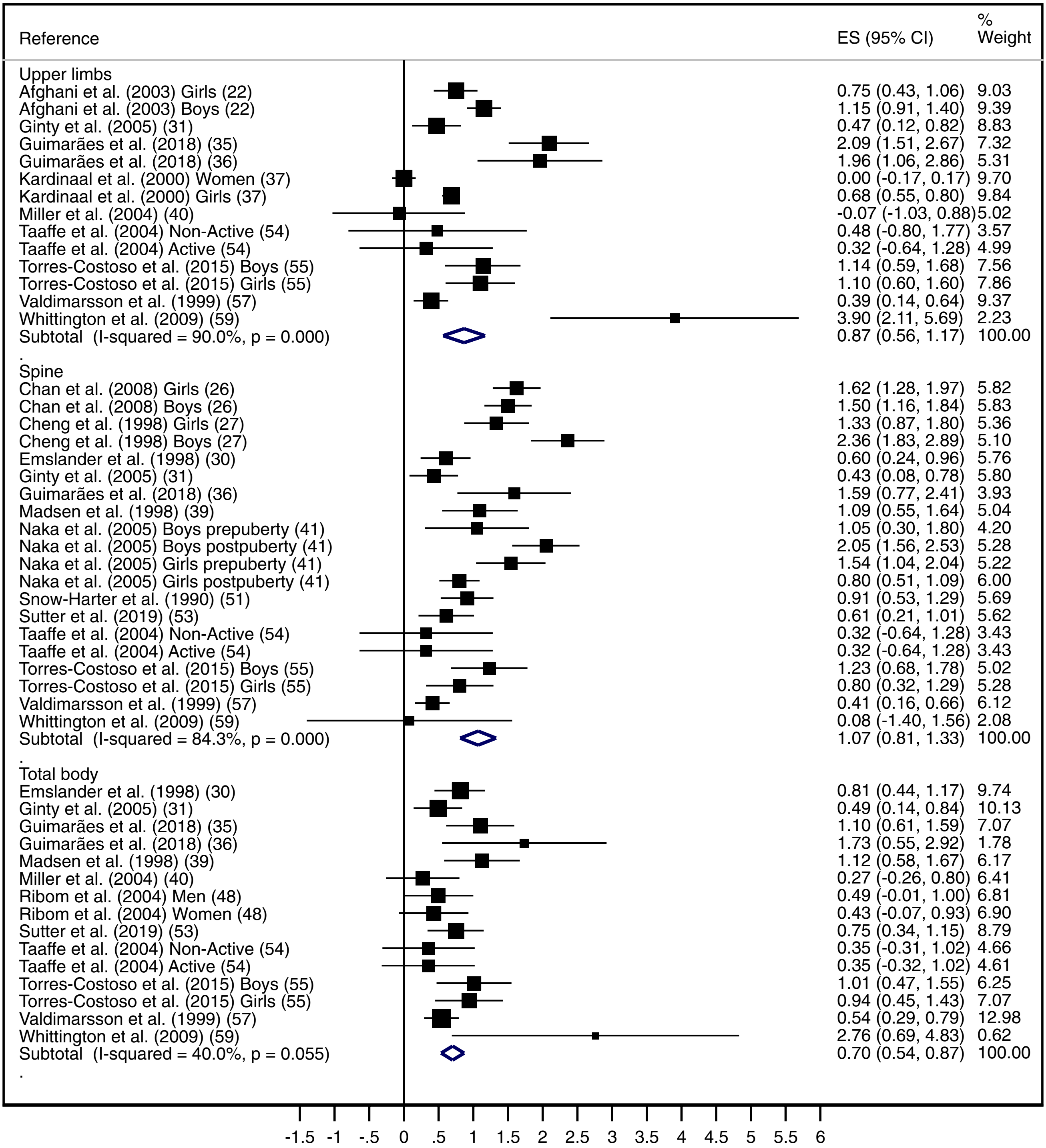

Fig. 2 Forest plot including correlation between upper limb muscular fitness and BMD (bone mineral density) outcomes. The effect size and 95% CI (confidence interval) for fully adjusted random effects are depicted for each study

heterogeneity ($I^2 = 40.0\%$; $p = 0.055$) for total body BMD (Fig. 2). Considering the BMC analysis, the pooled ES were 1.84 (95% CI 1.11–2.57) with considerable heterogeneity ($I^2 = 98.2\%$; $p < 0.001$) for upper limbs BMC, 1.38 (95% CI 0.88–1.87) with substantial heterogeneity ($I^2 = 89.6$ %; $p < 0.001$) for spine BMC and 1.30 (95% CI 0.90–1.70) with considerable heterogeneity ($I^2 = 90.4\%$; $p < 0.001$) for total body BMC (Fig. 3).

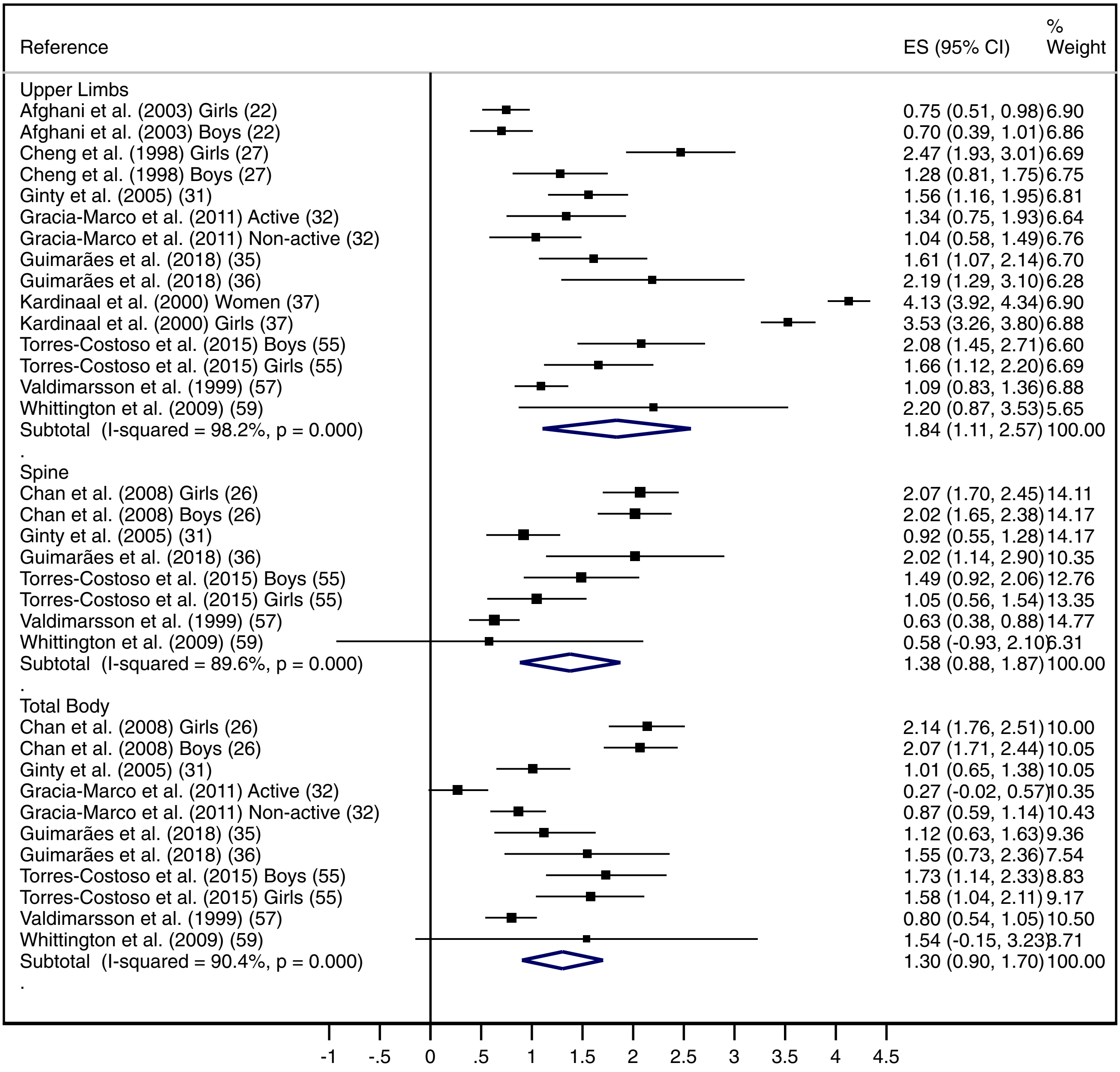

Fig. 3 Forest plot including correlation between upper limb muscular fitness and BMC (bone mineral content) outcomes. The effect size and 95% CI (confidence interval) for fully adjusted random effects are depicted for each study

3.3.2 Lower Limbs Muscular Strength

For the BMD analysis, the pooled ES were 0.67 (95% CI 0.54–0.80), with substantial heterogeneity ($I^2 = 86.5\%$; $p < 0.001$) for lower limbs BMD, 0.54 (95% CI 0.36–0.72) with substantial heterogeneity ($I^2 = 81\%$; $p < 0.001$) for spine BMD and 0.88 (95% CI 0.65–1.11) with substantial heterogeneity ($I^2 = 81.5\%$; $p < 0.001$) for total body BMD (Fig. 4). Considering the BMC analysis, the pooled ES were 0.81 (95% CI 0.52–1.09) with substantial heterogeneity ($I^2 = 82.7\%$; $p < 0.001$) for lower limbs BMC, 0.71 (95% CI 0.37–1.06) with substantial heterogeneity ($I^2 = 74.5\%$; $p < 0.001$) for spine BMC and 0.77 (95% CI 0.49–1.06) with substantial heterogeneity ($I^2 = 77.3\%$; $p = 0.001$) for total body BMC (Fig. 5).

3.3.3 Sensitivity Analysis

The pooled ES estimates for the association between upper limbs muscular strength and BMD and BMC were not significantly modified in magnitude or direction when individual study data were removed from the analysis one at a time.

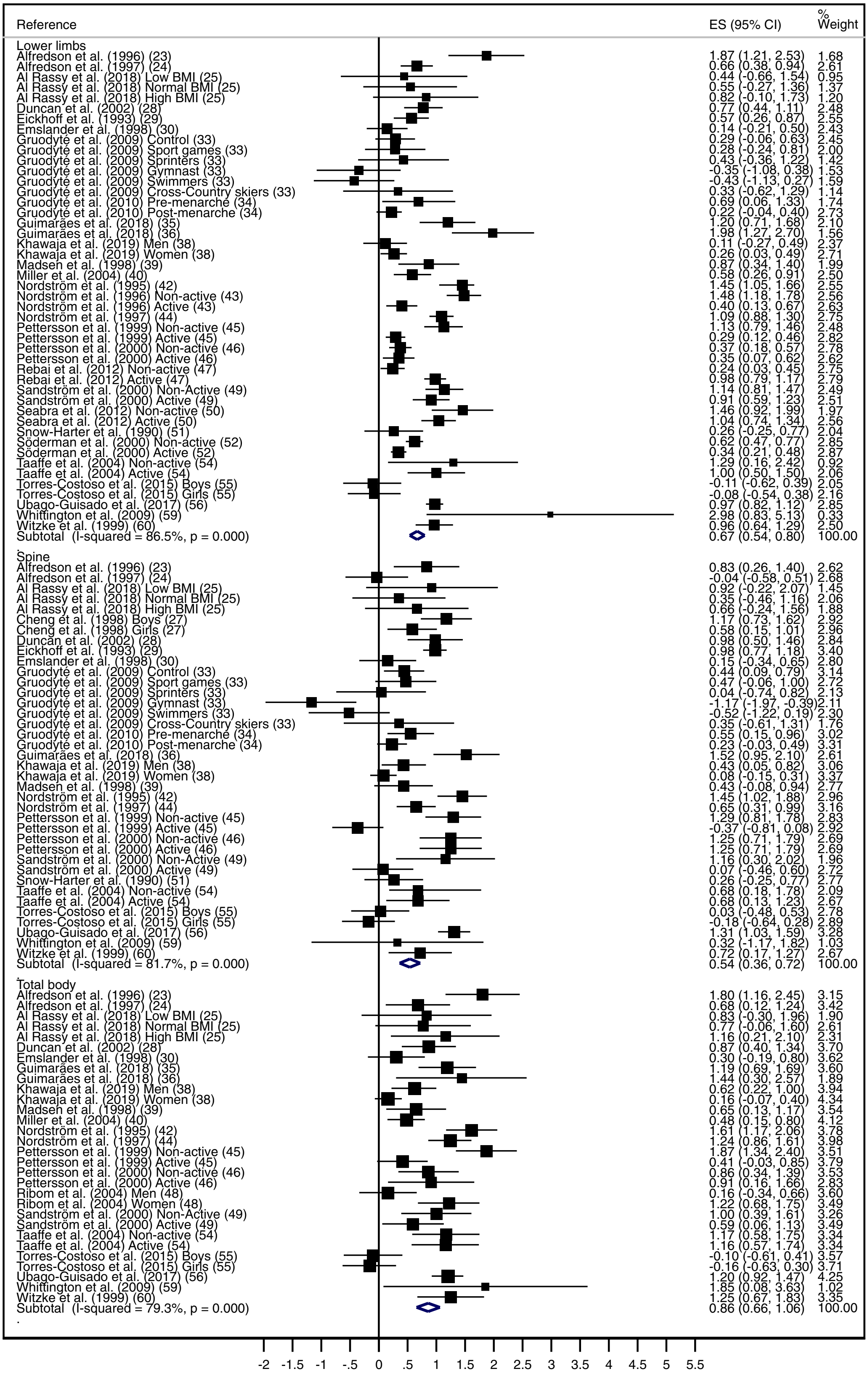

Fig. 4 Forest plot including correlation between lower limb muscular fitness and BMD (bone mineral density) outcomes. The effect size and 95% CI (confidence interval) for fully adjusted random effects are depicted for each study

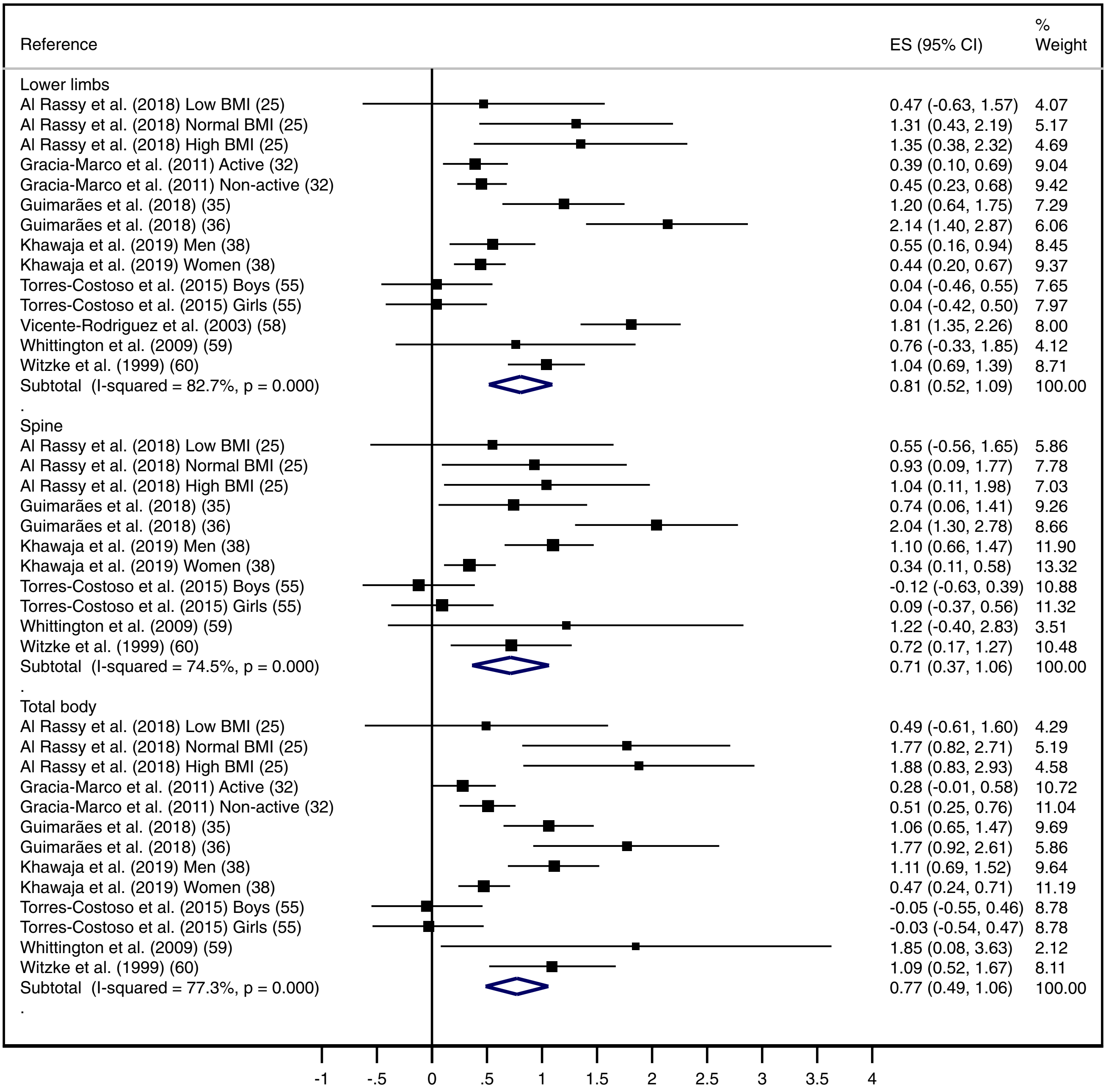

Fig. 5 Forest plot including correlation between lower limb muscular fitness and BMC (bone mineral content) outcomes. The effect size and 95% CI (confidence interval) for fully adjusted random effects are depicted for each study

3.3.4 Subgroup Analysis and Meta-regression

Based on participants' sex, all BMD regions for upper limbs muscular strength showed higher ES values in boys (e.g., 1.18 for upper limbs, 1.31 for spine and 0.74 for total body) than in girls (e.g., 0.59 for upper limbs, 0.96 for spine and 0.65 for total body). Also, most BMC regions for upper limbs muscular strength showed similar ES values in boys (e.g., 1.67 for upper limbs, 1.49 for spine and 1.50 for total body), whereas in girls, upper limbs had higher ES estimates (e.g., 2.09 for upper limbs, 1.39 for spine and 1.49 for total body).

Furthermore, all BMD regions for lower limbs muscular strength showed higher ES values in boys (e.g., 0.88 for lower limbs, 0.75 for spine and 0.92 for total body) than among girls (e.g., 0.56 for lower limbs, 0.48 for spine and 0.80 for total body). Conversely, all BMC regions for lower limbs muscular strength showed higher ES values in girls (e.g., 0.92 for lower limbs, 0.76 for spine and 0.98 for total body) than in boys (e.g., 0.90 for lower limbs, 0.58 for spine and 0.72 for total body) (ESM Appendix S2).

Regarding participants' physical activity levels, because of the scarcity of studies (none or only one), analysis of non-active participants was not possible except for BMD regions and lower limbs muscular strength; in this case, the ES for the associations were higher in non-active participants (from 1.00 to 1.36) than in active participants (from 0.28 to 0.60) and in mixed participants (from 0.64 to 0.81). When analyses were possible only for active and mixed groups, the ES for the association were higher in mixed participants (from 0.64 to 1.91) than in active participants (from 0.06 to 1.59) (ESM Appendix S3).

Based on muscular strength tests used, other tests group showed higher ES (from 0.54 to 1.83) than ALPHA-fitness test battery (from −0.01 to 1.80), except for upper limbs BMC and upper limbs muscular strength, in which results were similar (ESM Appendix S4).

The random-effects meta-regression models indicated that age ($\beta = -0.05$, $p = 0.043$), height ($\beta = -0.02$, $p = 0.035$) and weight ($\beta = -0.02$, $p = 0.011$) were inversely related to the association between upper limbs muscular strength and spine BMD. Likewise, height ($\beta = -0.03$, $p = 0.035$) and weight ($\beta = -0.02$, $p = 0.019$) were inversely related to the association between upper limbs muscular strength and total body BMC.

The association between lower limb muscular strength and all BMD regions was positively influenced by most of the variables, e.g., lean mass ($\beta = 0.02$, $p = 0.040$), height ($\beta = 0.02$, $p = 0.026$) and weight ($\beta = 0.02$, $p = 0.040$) for lower limb BMD, and height ($\beta = 0.02$, $p = 0.013$) for total body BMD. Furthermore, age ($\beta = 0.07$, $p = 0.008$), height ($\beta = 0.03$, $p = 0.028$) and weight ($\beta = 0.03$, $p = 0.021$) were related to the association between lower limbs muscular strength and total body BMC. Finally, age was related to the association between lower limbs muscular strength and the BMC of the spine ($\beta = 0.06$, $p = 0.037$) and height ($\beta = 0.03$, $p = 0.037$) (ESM Appendix S5).

3.3.5 Publication Bias

Evidence of publication bias was found by funnel plot asymmetry and Egger's test (total body BMC $p = 0.063$ and total body BMD $p = 0.093$ for lower limb muscular fitness and total body BMD for upper limb muscular fitness $p = 0.081$; ESM Appendix S6).

4 Discussion

Bone mass accrual during the growing years is a strong determinant of osteoporosis risk later in life. This systematic review identified and pooled cross-sectional data from studies addressing the relationship between muscular strength and bone health during skeletal development. This systematic review and meta-analysis found a site-to-site and total positive association between muscular strength and bone outcomes in both males and females.

Current evidence supports that muscular strength is a marker of skeletal health in children and adolescents [12, 13]. Our meta-analysis, in accordance with these prior findings, confirms a consistent association of muscular strength with BMC and BMD. Moreover, our review supports the consistency of this association across different sites, including spine and total body, which are the preferred skeletal sites for DXA measurements during growth as they are highly accurate and reproducible [61]. In this sense, the results showed an association at local and distant anatomical sites with muscular action. The cause–effect relationship seems to be primarily associated with powerful muscle contractions and powerful osteogenic stimuli for the adjacent bone [43]. Furthermore, a remote relationship has been suggested indicating that not only a pure mechanical stimulus, but also muscle glycogen metabolism and systemic-related changes are involved factors [42, 62, 63].

Overall, upper limbs muscular strength showed a stronger relationship with BMC results than lower limbs muscular strength. The most used test to assess upper limbs muscular strength was the handgrip test [64] and the cutoff points of this test have been recently proposed for screening healthy bone development in adolescents [65]. Regarding lower limbs muscular strength, the wide variability of tests used to measure it could have some influence in our estimates. In this line, our analyses determined a positive association between muscular strength and bone health using both the ALPHA-battery test and other tests group (mainly isokinetic strength testing). However, higher estimates were found for the other tests group, probably because during growth isokinetic strength is closely related to body size, since isokinetic actions are dependent on muscle moment limb length [66].

Our subgroup analyses determined that both males and females showed a significant positive association between muscular strength and bone health. Overall, associations among boys were stronger than among girls; these results could be explained by sex differences in muscular strength and lean mass linked to sex steroid hormones and their positive association with bone development [67]. However, the association between BMC and upper and lower limbs muscular strength showed higher estimates in girls than in boys, which might be explained by the sex-dependent maturational timing effect on total body BMC development. The rise of serum oestrogens in early maturity women is believed to influence the accrual of bone mass during growth, but the differences in maturity do not have any influence in men [68].

The level of physical activity seems to have an important influence on bone health through the bone piezoelectric effect [69]. In this sense, our data showed a positive association between muscular strength and bone health in both non-active and active participants, although ES estimates were higher in non-active participants than in active participants. In those cases in which it was possible to compare active and mixed participants, ES estimates were higher in the mixed group, probably by influence of non-active participants. This is in accordance with previous studies that have reported strongest associations among sedentary individuals than those with higher levels of physical training, while little or no relationship has been observed in highly trained individuals [48, 49].

The meta-regression analyses showed that determinants such as age, lean mass, height and weight positively influenced the lower limbs muscular strength and skeletal health association. However, age, height and weight negatively influenced the association with upper limbs muscular strength, in spite of these variables being strongly related with upper limbs muscular strength [70] and bone development [71]. Some confounders, such as pubertal status or diet behavior, related to both muscular strength and bone health, may account for the lack of positive effect of muscular strength on bone health [45].

Osteoporosis-related fractures are very common and are associated with high direct and indirect costs to the global economy [72]. DXA is a cost-effective screening tool for early detection of low bone mass [73]. A routine bone assessment that could be initiated at age 50–60 would be expected to improve health outcomes at an acceptable cost [74, 75].

4.1 Limitations

This review has several limitations, thus, its results should be interpreted cautiously. Some of these are common to meta-analyses (e.g., publication bias, selection bias and limited availability of complete information from study reports). First, because of the cross-sectional design of included studies, temporal ambiguity represents an insurmountable threat to cause–effect inferences. Second and related to total body bone assessment, there is a consensus that the total body minus the head instead of the total body including the head should be obtained because the skull constitutes a large percentage of the skeleton and is not related to environmental factors; [76] however, most of the studies included only showed data for total body bone measurement. Third, it is known that pubertal status plays an important role in bone development; however, this was not considered in our analysis because most of the included studies did not report this information. The same occurs with other important factors such as nutrition and ethnic differences. Finally, the included studies used different DXA models to collect bone outcomes and this could be important, since there have been differences shown between bone measurements depending on DXA scanner tools [77].

5 Conclusion

Muscular strength should be considered a useful skeletal health marker during development and maturation. Physical activity programs should emphasize promoting muscular strength to maximize peak bone mass in this period. Notwithstanding, more research is needed to establish an optimal level of muscular strength in this population to identify high-risk individuals in whom exercise interventions aimed at improving muscular strength could be more beneficial.

Data Availability Statement The data that support the findings of this review are available on reasonable request from the corresponding author (Vicente Martínez-Vizcaíno).

Compliance with Ethical Standards

Conflict of interest Ana Torres-Costoso, Purificación López-Muñoz, Celia Alvarez-Bueno, Iván Cavero-Redondo and Vicente Martínez-Vizcaíno declare that they have no conflict of interest.

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