

Effects of Physical Exercise on Bone Mineral Density in Older Adults: A Systematic Review and Meta-Analysis of Randomized Controlled Trials

Diego Gama Linhares^{1,2}, Giulio César Pereira Salustiano Mallen da Silva², Bruno Gama Linhares³, Ana Beatriz Moreira de Carvalho Monteiro², Claudio Joaquim Borba Pinheiro⁴, Elirez Bezerra da Silva², Rodrigo Gomes de Souza Vale^{1,2}

¹ Health Sciences Laboratory (Labics), Estácio de Sá University, Campos dos Goytacazes, Rio de Janeiro, Brazil

² Exercise and Sports Sciences Laboratory (Labees), State University of Rio de Janeiro, Rio de Janeiro, Brazil

³ Pará State University and Federal Institute of Pará, Pará, Brazil

⁴ Porto University, Porto, Portugal

CORRESPONDING AUTHOR:

Diego Gama Linhares
Health Sciences Laboratory (Labics)
Estácio de Sá University
Av. Vinte e Oito de Março, 423 - Centro
Rio de Janeiro, Brazil 28020-740
E-mail: diegamalin@gmail.com

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SUMMARY

Objective. Verify the effects of different physical exercises on bone mineral density in the older.

Methods. The PRISMA criteria were followed, and the study was registered with PROSPERO. The databases used were MEDLINE (via PubMed), Scopus, Cochrane, Web of Science, Embase, and Pedro.

Results. A total of 4,118 publications were found from the database search, and 13 RCTs were included in the present systematic review. The estimated average standardized mean difference was 0.26 (95%CI 0.00 to 0.52). The average result differed significantly from zero ($p = 0.05$) and heterogeneity was estimated at $I^2 = 43\%$.

Conclusions. Until now, physical exercise has shown low efficacy and moderate evidence for gaining total bone mineral density in the elderly population.

KEY WORDS

Body mineral density; exercise; older; bone remodeling; Physical exercise

INTRODUCTION

The numbers of older adults and adults with age-related chronic diseases are expected to more than double between 2019 and 2050 (1). Although populations around the world are rapidly ageing, evidence that increasing longevity is accompanied by an extended period of good health is scarce (2, 3). Unfortunately, many people are subject to some type of frailty during the aging process (4, 5).

Fractures related to osteoporosis constitute a major health problem in our aging society, often causing the individual to lose independence. There is an increase in morbidity and mortality in elderly people with osteoporosis, especial-

ly in women, and prevention should occur from the age of 65 regardless of sex. Physical exercise and drug therapies are strategies used in the prevention and treatment of bone diseases (6, 7).

Aging, a natural physiological process, can cause some unfavorable morphofunctional changes, such as a reduction in total mineral density (total BMD) and physical fitness, thereby increasing the risk of developing disorders such as osteopenia, osteoporosis and decreased functional capacity (8).

Bones should be strong, to prevent fractures. Bone turnover markers predict fracture risk and treatment-induced changes in specific markers account for a substantial

proportion of fracture risk reduction (5). Bone modeling is sensitive to mechanical loading, emphasizing the importance of physical activity throughout growth. Physical exercise can improve bone health in middle-aged and postmenopausal women (9, 10).

This study is justified by the existence of approximately 25 published meta-analyses that have examined the effect of physical exercise on bone mineral density (11-35). Only 3 of these meta-analyses measured total bone mineral density, those by (19, 21, 34). However, the number of studies included in these meta-analyses was very small to measure total bone mineral density, contributing to the imprecision of the findings. The study (19) included two studies, (21) included four studies, and (34) included four studies, three of which involved participants using medications. Despite the recent nature of these meta-analyses, new RCTs measuring total bone mineral density have already been published, providing 8 new results (36-43) to be meta-analyzed.

With this, the objective of this study was to verify the effects of physical exercise on bone mineral density in the older.

METHODS

This systematic review and meta-analysis followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) criteria (44) (**figure 1**), and was approved by the international prospective registry of systematic reviews (PROSPERO) under number CRD42023495223 - approval date: December 19, 2023.

Inclusion criteria

The PICOS strategy was used, the population of older adults (aged ≥ 60 years) of both sexes, the intervention with physical exercise practitioners, the comparison with a control group, the outcome bone mineral density, the study design with randomized controlled trials (RCTs). Systematic review and meta-analysis studies, animal studies, participants under the age of 60 and studies that did not use physical exercise as the main intervention were excluded.

Search strategy

The databases used were MEDLINE (via PubMed), Scopus, Cochrane, Web of Science, Science Direct, Embase, SciELO, and PEDro from November 01 to 15, 2024. The elec-

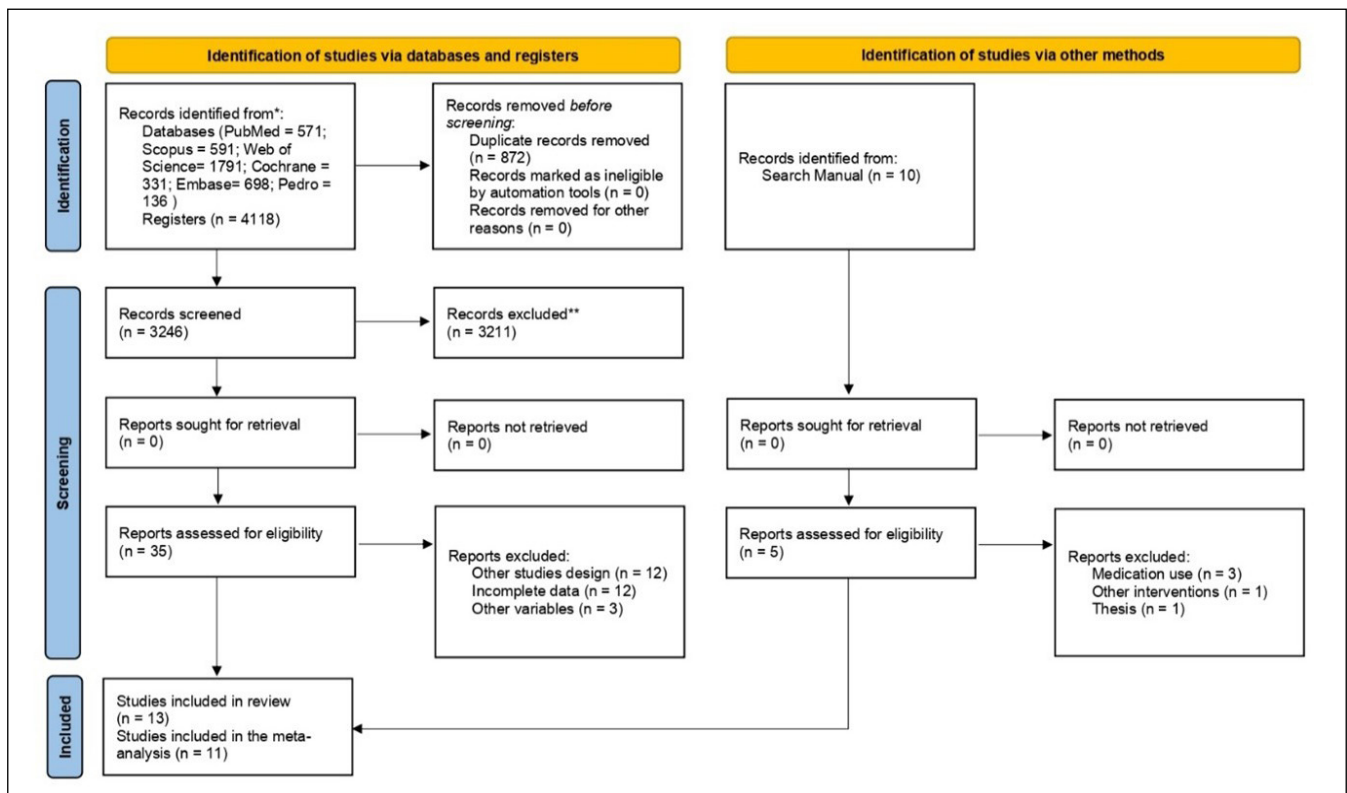


Figure 1. Flowchart of the 13 studies included in the meta-analysis according to PRISMA recommendations.

tronic search was conducted by two independent and experienced evaluators without language or time filters, and any conflict was resolved by a third reviewer. The search terms used were grouped with the operators (AND, OR) in a single Boolean phrase, the descriptors used were Older, Exercise, “Bone mineral density” and AND operator between descriptors and OR between their synonyms (**supplement 1**). Keywords related to the topic were selected based on a literature review and verified by Medical Subject Headings (MeSH) metadata systems. The selection of studies was carried out in three phases: 1) Identification and exclusion of duplicate studies using the Zotero 6.0.30 application; 2) Reading the titles and abstracts to see if the studies met the established inclusion criteria; and 3) Reading the entire text of the remaining studies with the same purpose.

Bibliometric analysis by network visualization

The software used for this analysis was VOSviewer 1.6.20, the keywords are represented by the circle, the size of the circle indicates the weight of the item. The clusters are separated by color according to the group the item belongs to and the lines between the items represent the existing

connections. The relationship between keywords is proportional to the distance, the closer they are, the greater the relationship between the terms (**figure 2**).

Risk of bias assessment

Eligible RCTs in this study were assessed using the Cochrane Collaboration risk-of-bias tool, available at <https://training.cochrane.org/handbook/>. Two experienced authors independently assessed them, and any discrepancies were resolved by a third author. The bias of the following sources was evaluated: 1) random sequence generation; 2) allocation concealment; 3) blinding of participants and staff; 4) concealment of outcome assessments; 5) incomplete outcome data; 6) selective notification; 7) another bias. Each domain has the risk of bias set as low, uncertain, or high (**figure 3**).

Assessment of methodological quality

The quality assessment tool for studies and reports on physical exercise (TESTEX) is a 15-point scale used in experimental studies, including internal validity assessment criteria and presentation of the statistical analysis

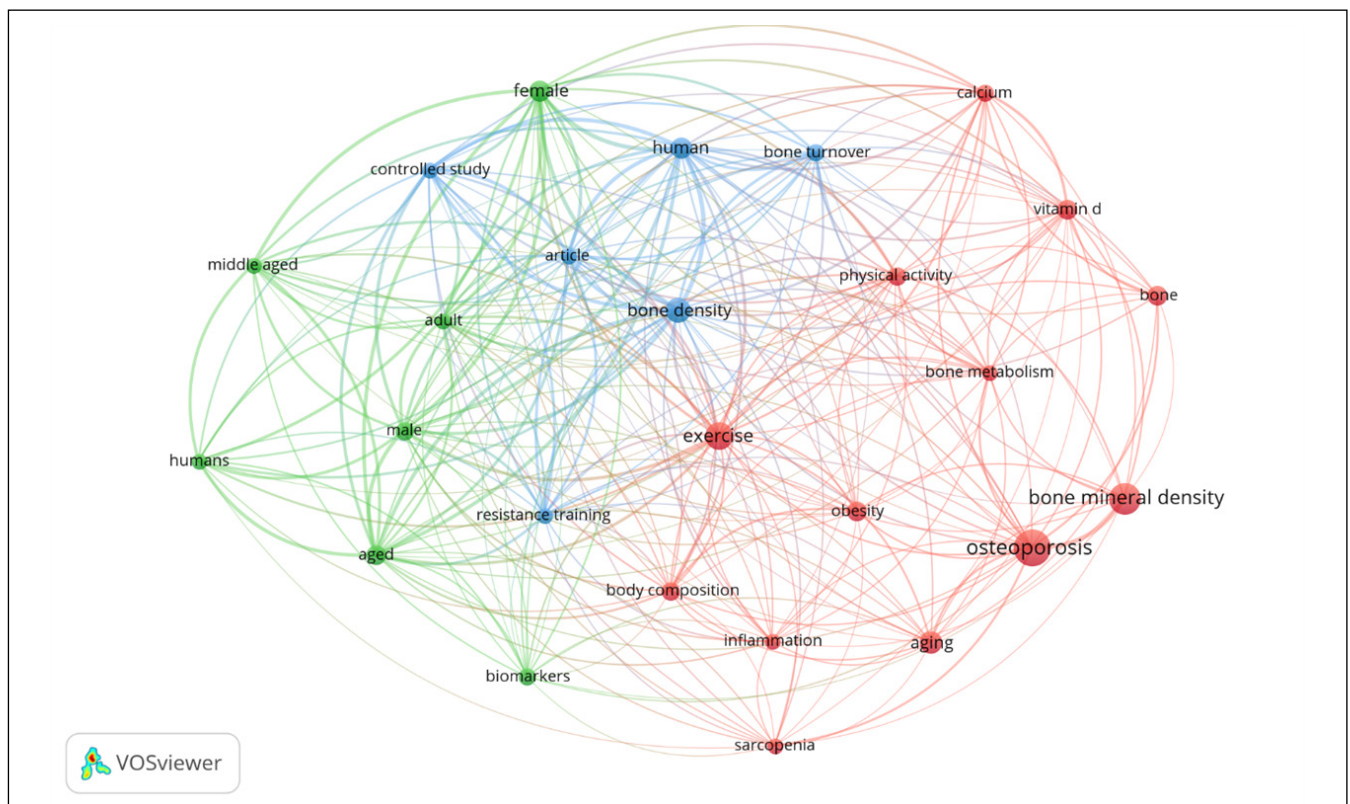


Figure 2. Network visualization, among the bases used in this meta-analysis.

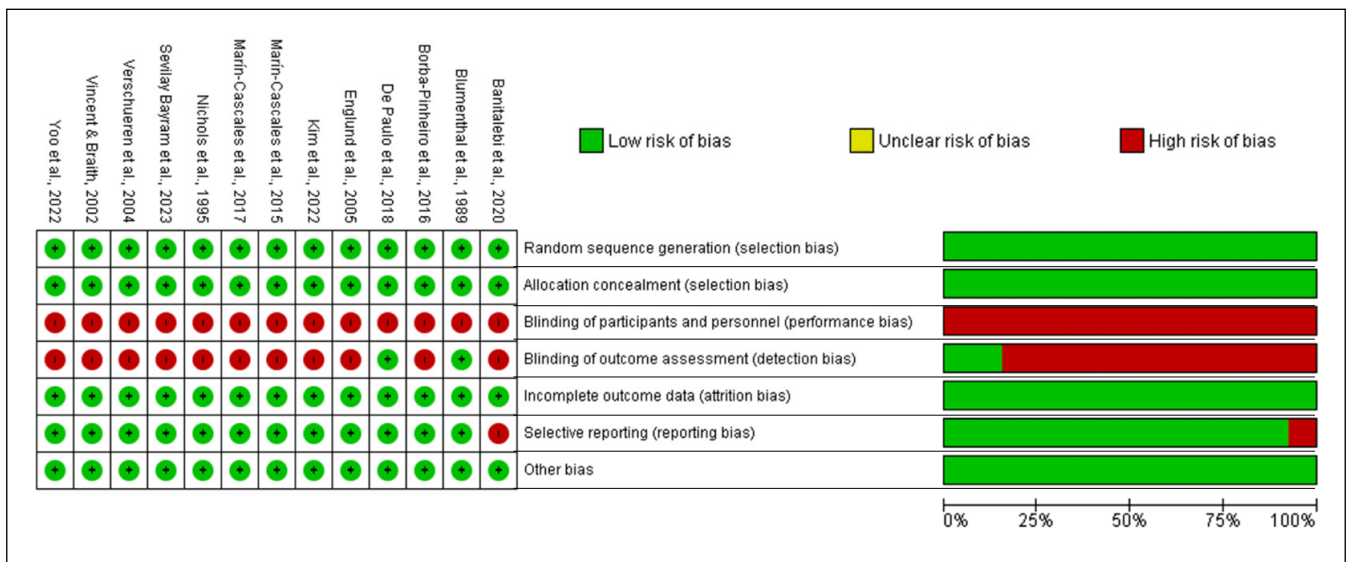


Figure 3. Risk of bias analysis for randomized studies.

used. In this tool, one point is assigned for each criterion defined on the scale and zero in the absence of these indicators (46) (**table III**).

Data extraction

For better understanding, the extracted data was divided by authors, year of publication, country of origin, characteristics of the study population, intervention data including details of general and specific exercises, evaluation method and results.

Meta-analysis

The Review Manager (RevMan), version 5.4, the Cochrane Collaboration, 2020 was used to analyze the effects of physical exercise bone mineral density in the older. Despite the total bone mineral density (BMD) having the same unit of measurement across all studies, the standardized mean difference (SMD) was chosen to classify the effect size according to Cohen (47). Each standardized mean difference (SMD) was weighted according to the inverse variance method. The SMD values in each study were pooled using a random model because the heterogeneity was significant. Heterogeneity between studies was analyzed using I^2 statistics. I^2 values are interpreted as low heterogeneity (0-50%), moderate heterogeneity (50-74%), and high heterogeneity ($\geq 75\%$) (45, 48). SMD values were interpreted as: $0.2 \leq TE < 0.5$ (weak); $0.5 \leq TE \leq 0.8$ (moderate); $TE \geq 0.8$ (strong) (47). A statistically significant effect was indicated by P -value < 0.05 .

Evidence-level assessment

Two authors independently assessed the certainty of evidence using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) approach with the GRADE PRO website, available at <https://grade.pro.org>. GRADE specifies four categories: “high”, “moderate”, “low”, and “very low”, applied to a body of evidence. RCTs begin with high-quality evidence. Five aspects can decrease the quality of evidence: methodological limitations, inconsistency, indirect evidence, inaccuracy, and publication bias (49).

RESULTS

A total of 4,118 publications were found from the database search following the proposed research methodology (MEDLINE via PubMed = 571; Scopus = 591; Web of Science = 1,791; Cochrane = 331; Embase = 698; Pedro = 136). After using the selection criteria, a total of 13 RCTs were included in the present systematic review, and in the meta-analysis there were 11 studies and 13 results (**figure 1**).

Figure 2 shows the network visualization, among the bases used in this meta-analysis. 1,999 keywords were found, of which 26 appear with at least 15 occurrences. Red circles indicate cluster 1 (13 circles). The terms “osteoporosis” and “bone mineral density” have the greatest weight. The green circles represent cluster 2 (7 circles) The term “female” has the highest weight and the other circles have balanced weight in both clusters. Blue circles indi-

cate cluster 3 (6 circles). The keywords “bone density” and “human” have the highest weight, not differing much from the other keywords in this cluster.

Figure 3 presents the results of the risk of bias analysis of randomized studies using the Cochrane Collaboration tool. All studies were classified as “high risk”, not shielding participants and/or evaluators due to the difficulty of this procedure with interventions in humans.

Table I presents the methodological quality assessment using the TESTEX tool. All studies included in this systematic review obtained a score ≥ 10 . The domain “Exercise volume and energy expenditure were reported” did not

score 100% of the studies because they did not present data regarding caloric expenditure.

In **table II**, the study variables are arranged by author and year, country of origin, study design, age, sex, and number of participants per group. The average age of participants in the CG was 67 and EG was 66 years old. The studies appear in different countries, Iran (36), USA (42, 43, 50), Brazil (37, 38), Sweden (51), Spain (40, 41), Turkey (52), Korea (39), Belgium (53, 54).

Table III contains the data extracted from the studies included in this review. The details of the intervention, the type of exercise, the total duration of the intervention, the

Table I. TESTEX study quality assessment.

Study	Study Quality					Sub-Total (0 to 5)	Study Reporting										Sub-Total (0 to 10)	Total (0 a 15)
	1	2	3	4	5		6a	6b	6c	7	8a	8b	9	10	11	12		
(36)	1	1	1	1	0	4	1	1	1	1	1	1	1	1	1	0	9	13
(50)	1	1	1	1	0	4	1	1	1	1	1	1	1	1	1	0	9	13
(37)	1	1	1	1	0	4	1	1	1	1	1	1	1	1	1	0	9	13
(38)	1	1	1	1	1	5	1	1	1	1	1	1	1	1	1	0	9	14
(51)	1	1	1	1	0	4	1	0	1	1	1	1	1	1	1	0	8	12
(39)	1	1	1	1	0	4	1	1	1	1	1	1	1	1	1	0	9	13
(40)	1	1	1	1	0	4	1	1	1	1	1	1	1	1	1	0	9	13
(41)	1	1	1	1	0	4	1	1	1	1	1	1	1	1	1	0	9	13
(42)	1	1	1	1	0	4	1	1	1	1	1	1	1	1	1	0	9	13
(52)	1	1	1	1	0	4	1	1	1	1	1	1	1	1	1	0	9	13
(43)	1	1	1	1	0	4	1	1	1	1	1	1	1	1	1	0	9	13
(53)	1	1	1	1	0	4	1	0	1	1	1	1	1	1	1	0	8	12
(54)	1	1	1	1	0	4	1	0	1	1	1	1	1	1	1	0	8	12

Study quality: 1 = specific eligibility criteria; 2 = type of randomization specified; 3 = hidden allocation; 4 = similar groups at baseline; 5 = raters were blinded (at least one main outcome); 6 = outcomes assessed in 85% of participants (6a = 1 point if more than 85% completed; 6b = 1 point if adverse events were reported; 6c = if exercise attendance was reported); 7 = intention-to-treat statistical analysis; 8 = statistical comparison between groups was reported (8a = 1 point if between-group comparisons are reported for the primary outcome variable of interest; 8b = 1 point if statistical comparisons between groups are reported for at least one secondary measure); 9 = point measures and measures of variability for all outcome measures that were reported; 10 = activity monitoring in the control group; 11 = relative exercise intensity remained constant; 12 = exercise volume and energy expenditure were reported.

Table II. Population characteristics.

Author/ year	Country	Age (media/ SD)	Population	BMI (Kg/m ²)	n
(36)	Iran	CG: 64.05 ± 3.35 EG: 64.11 ± 3.81	Osteosarcopenic obese women	CG: 33 EG: 34	CG: 31 EG:32
(50)	USA	CG: 66.8 ± 4.3 EG1: 66.5 ± 4.3 EG2: 67.8 ± 5.9	Healthy men	NI	CG: 34 EG1: 33 EG2: 34
(37)	Brazil	CG: 56.3 ± 5.2 EG1: 60.6 ± 7.5 EG2: 55.3 ± 6.8	Postmenopausal women	CG: 28 EG1: 26 EG2: 29	CG: 16 EG1: 20 EG2: 16
(38)	Brazil	CG: 66.6 ± 9.6 EG: 63.2 ± 7.1	Women with breast cancer	CG: 32 EG: 29	CG: 18 EG:18
(51)	Sweden	CG: 73.2 ± 4.9 EG: 72.8 ± 3.6	Postmenopausal Women	CG: 26 EG: 25	CG: 19 EG: 21
(39)	Korea	CG: 81.6 ± 4.78 EG: 79.6 ± 5.19	Obese women	CG: 34 EG: 35	CG: 15 EG:15
(40)	Spain	CG: 62.4 ± 5.1 EG: 57.7 ± 7.1	Postmenopausal Women	CG: 29 EG: 29	CG: 10 EG: 14
(41)	Spain	CG: 60.0 ± 6.3 EG: 60.0 ± 6.3	Postmenopausal Women	CG: 27 EG: 28	CG: 10 EG: 13
(42)	USA	CG: 67.8 ± 1.6 EG: 65.2 ± 1.2	Healthy women	CG: 27 EG: 26	CG: 17 EG:17
(52)	Turkiye	CG: 71.5±4.5 EG: 70.2±3.8	Healthy women	CG: 31 EG: 30	CG: 10 EG: 13
(43)	USA	CG: 71 ± 5 EG1: 67.6 ± 6 EG2: 66.6 ± 7	Healthy men and women	CG: 25 EG1: 27 EG2: 24	CG: 16 EG1: 24 EG2: 22
(53)	Belgium	CG: 64.2 ± 3.1 EG: 63.90 ± 3.8	Postmenopausal Women	CG: 27 EG: 27	CG: 24 EG: 22
(54)	Korea	CG: 71.1 ± 2.7 EG: 70.9 ± 2.7	Postmenopausal women	CG: 25 EG: 27	CG: 10 EG: 11

EG: experimental group; CG: control group.

training volume indicating the session time and the number of sessions per week, and the results found in the experimental group of each study. The average time per session was 53 min, 3 sessions per week and the total intervention time was 27 weeks.

In **figure 4**, 13 results from 11 included studies were analyzed. The observed standardized mean differences ranged from -0.15 to 1.72, with the majority of estimates being positive (69%). The estimated average standardized mean difference

based on the random-effects model was 0.26 (95%CI 0.00 to 0.52). Therefore, the average outcome differed significantly from zero ($z = 1.99$, $p = 0.05$). According to the Q-test, the true outcomes appear to be heterogeneous ($Q(15) = 21.17$, $p = 0.05$, $\tau^2 = 0.09$, $I^2 = 43\%$). Hence, although the average outcome is estimated to be positive, in some studies the true outcome may in fact be negative. Neither the rank correlation nor the regression test indicated any funnel plot asymmetry ($p = 0.06$ and $p = 0.10$, respectively) (**figure 5**).

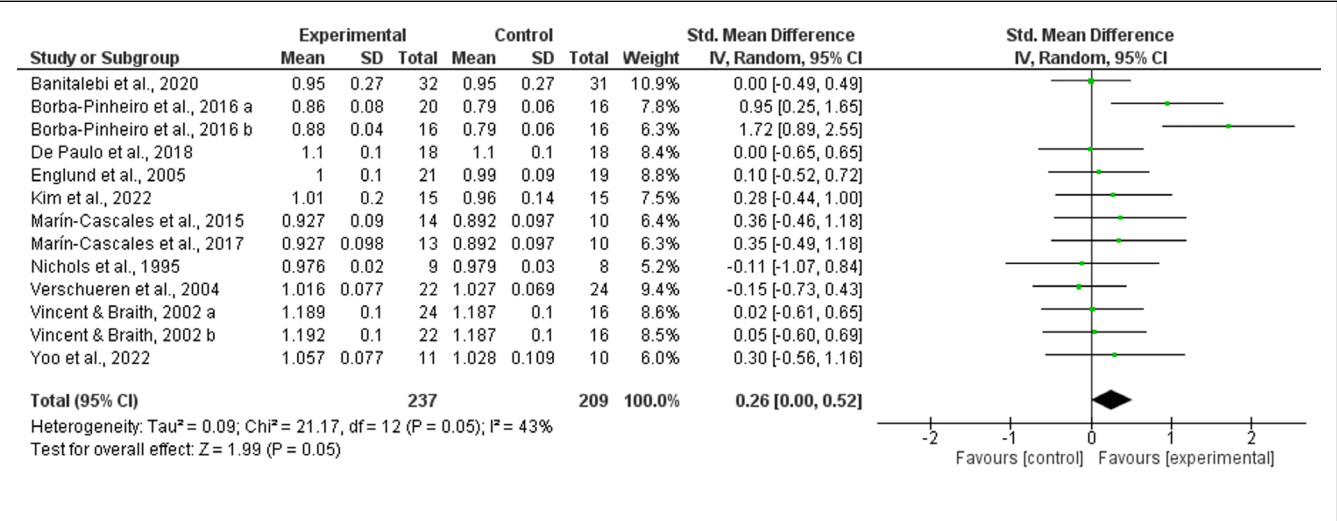


Figure 4. Forest plot (BMD Total) of 11 studies with 13 results that evaluated bone mineral density by subgroups of type of physical exercise: RT (Resistance training), Aerobic, Combined (with more than one exercise modality) and Pilates.

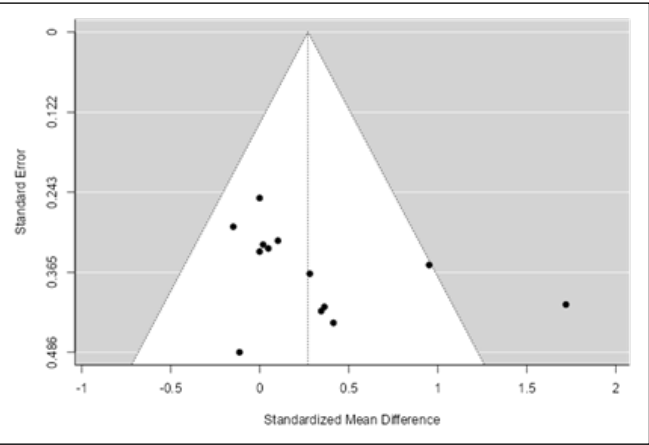


Figure 5. Funnel plot (total BMD) of 11 studies with 13 results that were meta-analyzed. Each result was plotted by SE(SMD) on the Y axis and SMD on the X axis.

DISCUSSION

The objective of this meta-analysis was to analyze the possible effects of physical exercise on bone mineral density in the older.

The result of this meta-analysis, after considering the 11 studies with 13 results, showed a standardized mean difference = 0.26 [0.00 to 0.52]; p = 0.05, with a low and significant heterogeneity of 43 %; p = 0.05 (figure 4). Despite the statistical significance obtained, the clinical significance was low (55).

The result of this meta-analysis, involving 446 participants, provided a more precise confirmation of the results from previous meta-analyses by (21) with a mean difference = 0.00 [-0.03 to 0.03] g/cm²; p = 0.96 with I² = 0 %; p = 1.00; (19) with a mean difference = 0.04 [-0.00 to 0.08] g/cm²; p = 0.06 with I² = 0 %; p = 0.82; and (34) with a standardized mean difference = 0.257 [0.05 to 0.461]; p = 0.014 with I² = 0 %; p = 0.83.

The studies (50, 52) were included in this systematic review but were not included in this meta-analysis because they presented a significant difference in initial total bone mineral density between the exercise group (GE) and the control group (GC) (table III). This initial heterogeneity in total bone mineral density between the groups may have affected the final outcomes of this outcome between the GE and GC, to be considered in the meta-analysis.

An important point for discussion is the fact that the total bone mineral density between the groups was primarily driven by the loss of total bone mineral density in the control groups. This occurred in six studies: (36,39,42,43,53,54), with the only significant decrease (p = 0.01) observed in one study (42) (table III).

This could lead to the following question: *were the results in the forest plot of standardized mean differences in favor of the exercise group due to the greater total bone mineral density loss in these control groups, making the relative difference appear to favor the exercise group?* So, this could lead to obtaining a significant total bone mineral density between the exercise and control groups. Yes, this can happen, espe-

Table III. Data extracted from the included studies.

Study/year	Intervention	Duration(weeks)	VT	BMD Total (g/cm ² ± sd)	
(36)	EG: elastic band RT CG: no exercise	12	60 min x session; 3 x week	GC: Pre: 1.005 ± 0.450 Post: 0.947 ± 0.274	p = 0.54***
				GE: Pre: 0.929 ± 0.245 Post: 0.945 ± 0.271	p = 0.41**
(50)*	EG1: aerobic EG2: Yoga and Flexibility CG: no exercise	16	60 min x session; 3 x week	GC: Pre: 1.08 ± 0.04 Post: 1.05 ± 0.05	p = 0.008***
				EG1: Pre: 1.10 ± 0.06 Post: 1.11 ± 0.03	p = 0.11**
				EG2: Pre: 1.14 ± 0.05 Post: 1.13 ± 0.05	p = 0.00001**
(37)	EG1: RT 3 x semana EG2: RT 2 x semana CG: no exercise	52	60 min x session; 2 x week	GC: Pre: 1.00 ± 0.03 Post: 1.00 ± 0.03	p = 1.00***
				EG1: Pre: 0.99 ± 0.03 Post: 1.03 ± 0.04	p = 0.33**
				EG2: Pre: 1.00 ± 0.04 Post: 1.04 ± 1.02	p = 1.00**
(38)	EG: RT + aerobic CG: no exercise	36	100 min x session; 3 x week	CG: Pre: 1.1 ± 0.08 Post: 1.1 ± 0.1	p = 1.00***
				EG : Pre: 1.1 ± 0.1 Post: 1.1 ± 0.1	p = 1.00**
(51)	EG: strengthening, aerobic, balance and coordination exercise CG: no exercise	48	50 min x session; 2 x week	GC: Pre: 0.98 ± 0.10 Post: 1.00 ± 0.10	p = 0.54***
				EG: Pre: 0.97 ± 0.09 Post: 0.99 ± 0.09	p = 0.74**
(39)	EG: RT CG: no exercise	24	NI x session; 2 x week	CG: Pre: 0.97 ± 0.14 Post: 0.96 ± 0.14	p = 0.85***
				EG: Pre: 1.00 ± 0.21 Post: 1.01 ± 0.20	p = 0.65**
(40)	EG: Aerobic 50 – 60% HRR + RT CG: no exercise	12	30-45 min x session; 3 x week	GC: Pre: 0.886 ± 0.091 Post: 0.892 ± 0.097	p = 0.89***
				EG: Pre: 0.918 ± 0.103 Post: 0.927 ± 0.090	p = 0.44**

Study/year	Intervention	Duration(weeks)	VT	BMD Total (g/cm ² ± sd)	
(41)	EG: Aerobic 50 – 60% HRR + Drop Jump CG: no exercise	24	30-60 min x session; 3 x week	GC: Pre: 0.886 ± 0.091 Post: 0.892 ± 0.097	p = 0.89***
				EG: Pre: 0.918 ± 0.103 Post: 0.927 ± 0.098	p = 0.45**
(42)	EG: RT CG: no exercise	48	30 min x session; 3 x week	CG: Pre: 0.997 ± 0.02 Post: 0.979 ± 0.02	p = 0.01***
				EG: Pre: 1.007 ± 0.02 Post : 0.976 ± 0.02	p = 0.16**
(52)*	EG: Pilates CG: no exercise	12	NI x session; 2 x week	GC: Pre: 0.86 ± 0.01 Post: 0.90 ± 0.14	p = 0.38***
				GE: Pre: 0.90 ± 0.01 Post: 0.91 ± 0.12	p = 0.00001**
(43)	EG1: RT a 30% 1RM EG2: RT a 50% 1RM CG: no exercise	24	30 min x session; 3 x week	GC: Pre: 1.196 ± 0.1 Post: 1.187 ± 0.1	p = 0.80***
				EG1: Pre: 1.195 ± 0.1 Post: 1.189 ± 0.1	p = 0.97**
				EG2: Pre: 1.192 ± 0.1 Post: 1.182 ± 0.1	p = 0.90**
(53)	EG: Aerobic 60 – 80% HRR + RT CG: no exercise	24	NI x session; 3 x week	GC: Pre: 1.030 ± 0.068 Post: 1.027 ± 0.069	p = 0.88***
				EG: Pre: 1.016 ± 0.078 Post: 1.016 ± 0.077	p = 0.52**
(54)	EG: Aerobic 60% HRR CG: no exercise	12	60 min x session; 3 x week	GC: Pre: 1.030 ± 0.111 Post: 1.028 ± 0.109	p = 0.97***
				EG: Pre: 1.053 ± 0.078 Post: 1.057 ± 0.077	p = 0.59**

VT: Training Volume; EG: Experimental Group; CG: Control Group; BMD: Body Mineral Density; RT: Resistance Training; sd: standard deviation; HRR: Heart Rate Reserve; *study not included in the meta-analysis because it showed a significant difference in initial total BMD between CG vs EG; **significance level of initial total BMD between CG vs EG using the mean difference test between groups; ***significance level of the final total BMD of the CG.

cially if the participants are unhealthy and the duration of the exercise program extends far beyond what is necessary. However, even so, physical exercises were beneficial for this population because they functioned as a protective factor, preventing the loss of bone mass in the groups of participants who engaged in physical exercises (**table III**).

Another important point to be discussed was the fact that the study (37) was the only one to report a statistically significant, albeit very small, increase in total bone mineral density (SMD = 0.95 [0.25 to 1.65]^a and 1.72 [0.89 to 2.55]^b – **figure 1**), after a large amount (52 weeks in duration, 3 times per week) of physical exercise (**table III**). However, this is a very important finding, especially because the participants in this RCT were postmenopausal women, a situation favorable to bone loss (56).

The strengths of this meta-analysis are the low and significant heterogeneity, providing more validity to the found result; the number of studies directly reflecting the quantity of 237 participants in the exercise group and 209 participants in the control group, making the found result more precise; the absence of suspicion of publication bias; and the certainty of the moderate evidence found (**figure 1** and **table I**).

On the other hand, the main limitation of this meta-analysis was the high risk of bias presented by all 11 included studies, despite being randomized controlled trials. The common cause for high risk of bias was the lack of blinding of participants, those who administered the physical exercises, and those who assessed total bone mineral density (**figure 2**). Future RCTs intending to study the effect of physical exercises on total bone mineral density should reduce the risk of performance and detection bias by including blinding.

Despite the low clinical significance, the results of this meta-analysis may contribute scientifically to future studies on such an important subject as the gain of total bone mineral density in the elderly population, since engaging

in physical exercises has low cost and no side effects. The elderly population, estimated to represent 16% of the population by 2050 (57, 58), suffers greatly from falls and bone fractures (58).

CONCLUSIONS

Up to this point, the practice of physical exercise has shown low efficacy and moderate certainty of evidence for increasing total bone mineral density in the older population.

Future studies using physical exercises with longer intervention time (2 years or more) and with greater weekly frequency (> 4 × per week) could cause significant improvements in BMD.

FUNDINGS

None.

DATA AVAILABILITY

Data are available under reasonable request to the corresponding author.

CONTRIBUTIONS

DGL, RGSV: formal analysis, writing – original draft, final assessments, data curation, writing – review & editing. GCPSMS, ABMCM: sample selection, evaluation, interim reviews. CJB, EBS, BGL: writing – original draft, formal analysis.

CONFLICT OF INTERESTS

The authors declare that they have no conflict of interests.

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