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## Meta-Analysis of the Impact of Exercise on Postmenopausal Bone Loss

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## ABSTRACT

### META-ANALYSIS OF THE IMPACT OF EXERCISE ON POSTMENOPAUSAL BONE LOSS

By

PHUNG D. TRAN

APRIL 28<sup>TH</sup>, 2025

**INTRODUCTION:** Osteoporosis is a significant health concern for postmenopausal women, increasing the risk of fractures and reducing quality of life. Exercise is often recommended as a non-pharmacological strategy to prevent or manage bone loss.

**AIM:** The meta-analysis investigates the effects of various exercise interventions in randomized controlled trials by comparing outcomes between treatment and control groups. Specifically, it examines the impact of exercise on bone mineral density (BMD), differences in effect magnitude across exercise types, and the variability of these effects between studies.

**METHODS:** Databases including PubMed, CINAHL Plus with Full Text, and Embase are searched for eligible studies up to 2015. Eligible studies included those that compared exercise intervention groups with non-exercising control groups and reported BMD outcomes at the lumbar spine, femoral neck, total body, and total hip. A fixed effect size model is used to calculate pooled effect sizes, and subgroup analyses were conducted to assess differences based on exercise type and intensity. Heterogeneity across studies was evaluated using the *Q*-test for homogeneity.

**RESULTS:** The findings are consistent with previous reviews, showing a generally positive effect of exercise—with routines combining aerobic and resistance training yielding a statistically significant result. There is no significant differences between the types of exercise and all DEXA scan sites.

**DISCUSSION:** Resistance training appears particularly beneficial, contributing to modest BMD improvements without adverse health effects. The findings support the role of exercise, especially when tailored appropriately, in promoting bone health among postmenopausal women.

META-ANALYSIS OF THE IMPACT OF EXERCISE  
ON POSTMENOPAUSAL BONE LOSS

by

PHUNG D. TRAN

B.S., GEORGIA STATE UNIVERSITY

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MASTER OF PUBLIC HEALTH

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# Meta-Analysis of the Impact of Exercise on Postmenopausal Bone Loss

Phung Tran

Capstone Protocol

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## Introduction

Osteoporosis is a serious and life-altering disease, commonly diagnosed in clinical settings. The condition increases the risk of falls and fractures, creating a decrease in quality of life for one in two women and one in five men after the age of 50 (van Staa et al., 2001).

Exercise has been promoted as a way to prevent and manage osteoporosis for postmenopausal women. Current findings and guidelines are unclear on how to best exercise for the most optimal results. Recommendations include complete avoidance of high-impact activities, integrating both high and low-impact activities, or engaging in low-weight-bearing activities without any advice on the degree of impact.

The American College of Sports Medicine (ACSM) on physical activity and bone health recommends regular weight-bearing endurance activities for preserving bone health in later life. However, the ACSM positions that it is not currently possible to quantify whether weight-bearing exercises assist in preventing and managing postmenopausal-related bone loss in the short term and long term (Kohrt et al., 2004).

The study aims to investigate the effect sizes of exercise interventions in randomized controlled trials on postmenopausal women by comparing outcomes between treatment and control groups. Specifically, it seeks to address two key questions:

- What are the effects of exercise on bone mineral density (BMD) in the treatment groups compared to controls?
- Based on the meta-analysis, how much do the effects vary across studies for each area of interest for BMD when comparing treatment to control groups?

## Methods

The meta-analysis was carried out in line with Cochrane handbook recommendations (2008) and utilized the PICOS process to define the review criteria:

- Population: postmenopausal women.

*Rationale: Women are more likely to be affected and diagnosed with osteoporosis, so they need to be the focus of the study.*

- Intervention: exercise interventions aimed at preventing and/or managing osteoporosis.  
*Rationale: ACSM positions that exercises can potentially prevent or manage osteoporosis so there should be literature available.*
  - The included exercise interventions are based on ACSM Guidelines, which include aerobics, strength, flexibility, or a combination.
  - Some studies employ whole-body vibration (WBV) exercises which are subsequently excluded.
- Comparison: exercise versus control groups.  
*Rationale: The effects of exercise can be compared between groups that received instructions versus the control group receiving only patient education or continuing usual care unsupervised.*
- Outcome: measures of bone mineral density measurements at the interested DEXA scanned areas.  
*Rationale: The outcome of exercise interventions can be captured with the DEXA scans.*
- Study designs: randomized control trials containing of the included routines, i.e. aerobic exercise, combinations of impact and aerobic exercise, and resistance exercise for a minimum of 6 months.  
*Rationale: Different types of exercise interventions are needed to compare the effects vary across studies.*  
*Rationale: Exercise interventions require appropriate duration to observe an effect on BMD (Howe et al., 2011).*

## Eligibility Criteria

To be included in the review, the study must be written or translated to English, published in 2015 and later, have a primary focus on women over the age of 45, and report the initial and final bone mass density measurements that allow for the calculation of pre-post effect size. The study design must be randomized trials where the exercise intervention was provided for at least six months. Studies that target pharmaceutical effects on bone mass density, do not have final BMD measurements and do not include women as participants will be excluded.

## Literature Search

Three databases with a focus on medical and public health were used to find literature for this meta-analysis with the help of a librarian. The names of the databases and search terms are as follows:

- a. PubMed:
  - a. Search terms: (("postmenopause"[mh] OR postmenopaus\*[tiab]) AND (exercise[mh] OR "resistance training"[mh] OR exercise[tiab] OR activit\*[tiab]) AND ("bone density"[mh] OR "bone density"[tiab] OR "bone mass density"[tiab] OR "bone mineral density"[tiab])) NOT ("Pharmaceutical Preparations"[mh] OR medicat\*[tiab] OR drug[tiab] OR pharmac\*[tiab])
  - b. Number of studies: 68
- b. CINAHL Plus with Full Text:
  - a. Search terms: AB postmenopaus\* AND ( exercise or physical fitness or physical activity ) AND ( bone density or bone mineral density or bone strength or bone health or bmd ) NOT ( pharmac\* OR drug OR medicat\* OR supplement\* )
  - b. Number of studies: 89
- c. Embase:
  - a. Search terms: postmenopaus\* AND postmenopaus\*:ti,ab,kw AND 'bone density'/exp/mj AND 'bone density':ti,ab,kw AND 'exercise'/exp/mj AND exercise:ti,ab,kw AND 'randomized controlled trial'/de
  - b. Number of studies: 15

## Screening Process

Duplicates from both databases were merged in Zotero, a reference management software. One retraction found in the initial search was automatically excluded. The first part of the screening process involved reading the titles and abstracts of each study identified in the initial literature search. All of the studies' citations were exported from Zotero to upload to Rayyan.ai in an .ris file format. The following list of questions guided the title and abstract screening:

- Is the study published from 2015 and later?
- Does the title/abstract include women as the study subject?
- Are the participants aged 45 and up?

- Does the title/abstract mention a type of exercise intervention to study its effect on BMD?
- Is the paper a meta-analysis or a cross-sectional study?
- Does the study focus on a pharmaceutical effect on BMD?

Eligible studies that passed the title and abstract screening moved on to the next step in Rayyan.ai with uploaded full-text articles. The full-text screening was only done by the author of this paper due to time constraints. The following list of questions guided full-text screening:

- Were the women participants in the study randomized to a treatment or control group?
- Did the women take any supplements or receive hormonal therapy during the study? If so, did both treatment and control groups receive similar therapies outside of exercise?
- Did the control receive patient education or no treatment and not an alternate exercise group?
- Did the study report on the means and standard deviations of BMD of the subjects pre- and post-tests?
- Was the intervention provided for at least six months?

## Coding

The meta-analysis employed MetaReviewer.org for the full-text coding. The codes are included in Appendix A with the rationales as follows.

- Study information: the section codes whether or not the study of interest is peer-reviewed, determines the possibility of conflict of interest, the year of publication, and the funding the study received. The information can provide an observation of the quality of the study as well as any potential biases.
- Sample characteristics: all characteristics of the exercise and control groups are collected in this section. The code includes information about each group, the average age of the participants, and the country of origin of each eligible study.
- Condition characteristics: the type of exercise interventions and the control are described in this section. The control group can receive encouragement or patient education for physical activity but conduct business as usual. The exercise intervention groups can be coded for each exercise type and the person providing the intervention. The length of the intervention is important to determine the quality of the exercise group to ensure qualified effect sizes for BMD. In addition, each group's sample size is also coded.

- Measures: the section contains the type of bone mineral density measurements of each study. The meta-analysis includes measurements of the total body, lumbar spine (L1-L4), femoral neck, and total hip.
- Study quality: questions about any potential confounds and if the results showed any significant difference from baseline.

## Effect Size

The meta-analysis studies the pre and post-test results (BMD g/cm<sup>2</sup>) for both exercise and control groups for the eligible studies. The effect size in this study is the difference-in-difference effect size, comparing the pre-post change in the treatment group to the pre-post change in the control group. The sample sizes, means, and standard deviations of the pre and post-test results are taken to calculate standardized mean differences to account for the intermachine differences between the dual-energy x-ray absorptiometry (DEXA) machine used by all the eligible studies (Zemel et al., 2020). Because no pre-post correlation was reported in any study, the meta-analysis assumes a pre-post correlation of 0.7 for analysis. The effect size for the pre-post standardized mean difference between the two groups for each study is calculated from the standardized mean differences and standardized mean difference variances (Morris et al., 2008).

The effect sizes are DEXA results measured from the total body, lumbar spine (L1-L4), femoral neck, and total hip average. The effect sizes are chosen because the numbers are used to screen for osteoporosis in postmenopausal women per the American Association of Clinical Endocrinologists and American College of Endocrinology Clinical Practice guidelines (2016).

## Analysis Strategy

### **Meta-analysis model**

The meta-analysis intended to use a random effect model to examine the BMD outcomes given the variation in treatments across the studies. Even though each study included in the meta-analysis used the same machine for the pre- and post-results, the meta-analysis needs to take into consideration the variously calibrated DEXA machines in all the studies. A random effect model can account for the potential variability between the machines.

### **Heterogeneity**

Heterogeneity will be examined by testing the significance of the test of between-study heterogeneity, the *Q*-statistic. The analysis plan included an examination of potential correlations

of heterogeneity if sufficient studies were identified as eligible for the analysis, and if there was significant heterogeneity. Moderators were planned to be the types of intervention: resistance, aerobic and a combination of bone-loading activities with aerobic movements and interventions with resistance exercises. On the other hand, resistance interventions can potentially load the bones more, which can affect the bone mineral density.

### **Publication bias**

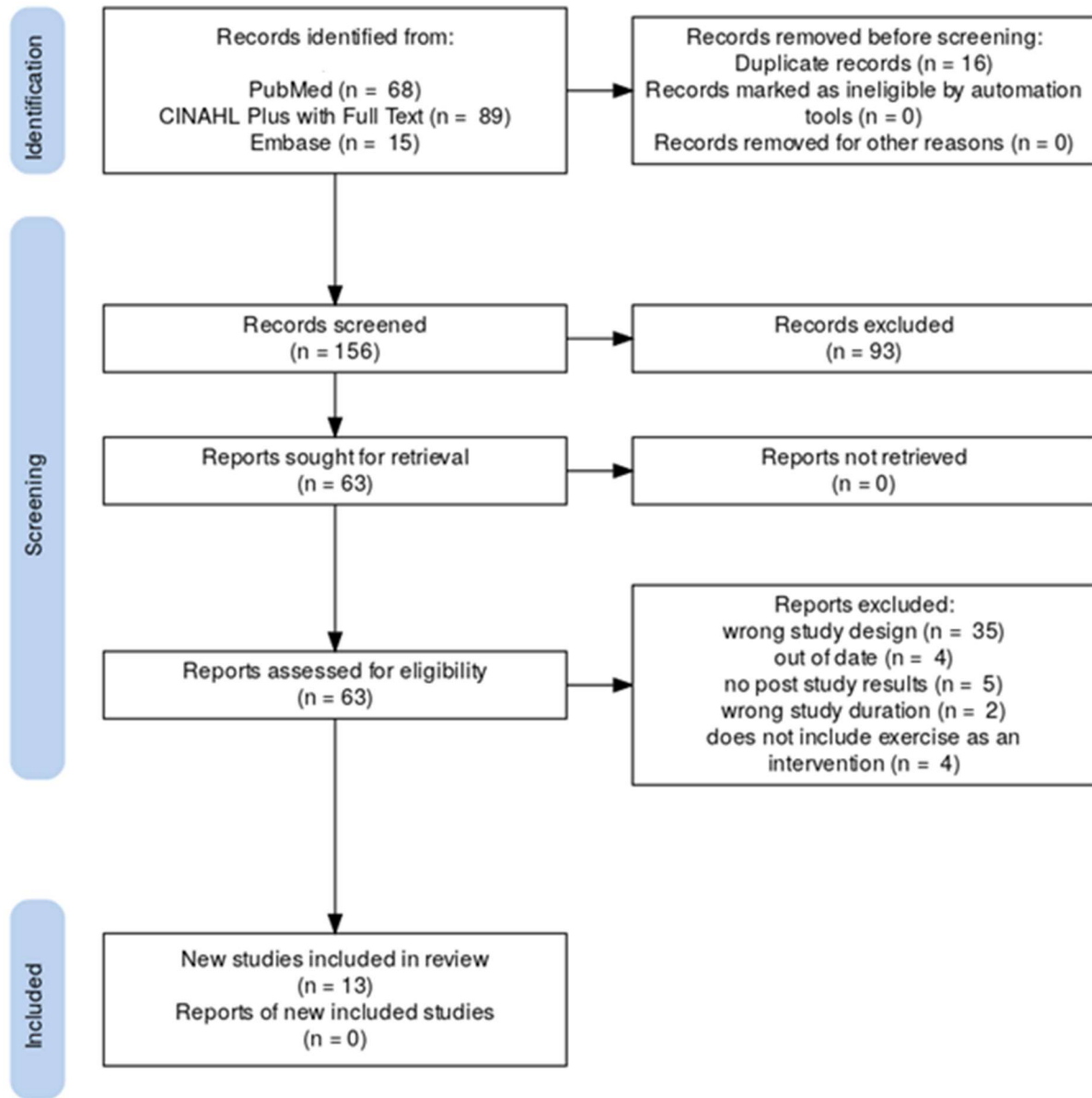
The analysis plan included the use of a contoured funnel plot for each effect size to examine the potential impact of publication bias. A contoured funnel plot for each effect size measurement from an eligible study was made. There is a need to include more research and unpublished literature to reduce publication bias.

## **Results**

### **Literature Search**

There are thirteen (13) studies identified during the literature search that report the BMD pre- and post-test results for postmenopausal female participants after going through a type of physical activity intervention.

Figure 1: PRISMA Flowchart



## Descriptive Results

Table 1: Eligible Study Characteristics

Study ID	Year of Publication	Mode of Exercise	Country of Origin	Sample Size of Exercise Group	Sample Size of Control Group
S01	2021	Aerobic	United States	26	28
S02	2016	Resistance	Canada	22	22
S03	2023	Combination	China	16	16

S04	2015	Resistance	Australia	24	26
S05	2020	Resistance	Turkey	16	18
S06	2023	Combination	Portugal	31	14
S07	2018	Combination	Brazil	17	17
S08	2015	Resistance	Norway	35	35
S09	2022	Resistance	United States	82	86
S10	2015	Resistance	United States	128	130
S11	2020	Resistance	Great Britain	17*	11
S12	2019	Aerobic	Taiwan	40	40
S13	2023	Resistance	Spain	27	11

\* The study includes more than one group receiving an exercise intervention

## Summary of Studies

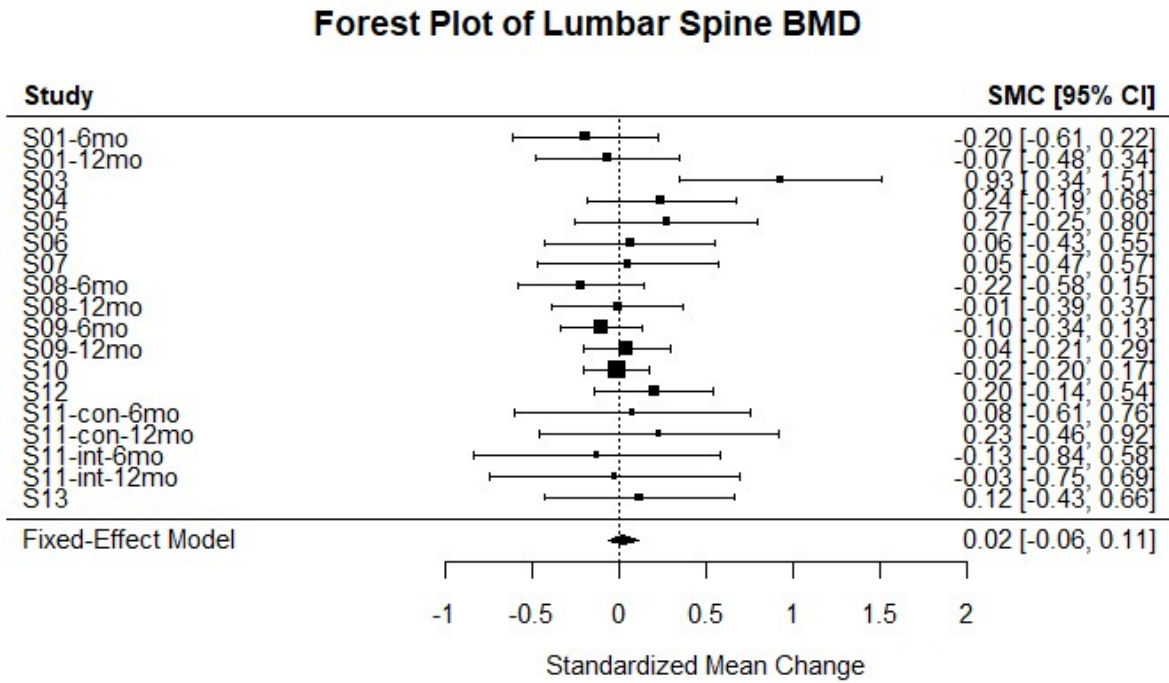
The studies included in this meta-analysis were conducted throughout the world, including but not limited to the United States, Brazil, Taiwan, and more as demonstrated in **Table 1**. All of the participants were female, and the majority of the participants followed through with the intervention and allowed for post-test data collection for analysis. The R code used to analyze the study is included in Appendix B.

## Distribution of Effect Sizes

The forest plots of the lumbar spine, femoral neck, total body, and total hip are represented below. The study employed difference-in-difference effect sizes.

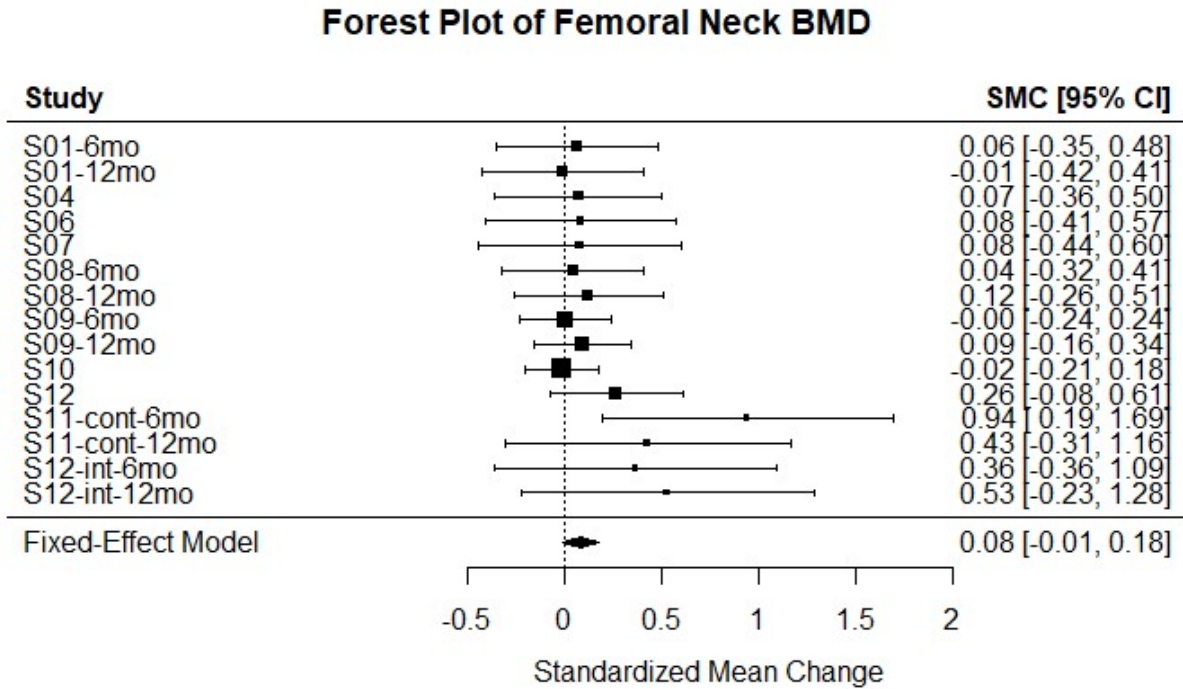
For the lumbar spine BMD, the estimate is 0.0238 ( $p=0.4510$ ) with a 95% confidence interval of -0.0647 and 0.1122 which is not significant. The  $Q$ -test of homogeneity is not significant with  $p$ -value = 0.4510 for  $Q(df = 17) = 17.0503$ . There is an outlier, but its weight is the smallest, thus, did not affect the standardized mean difference.

Figure 2: Forest plot of effect sizes of the lumbar spine BMD



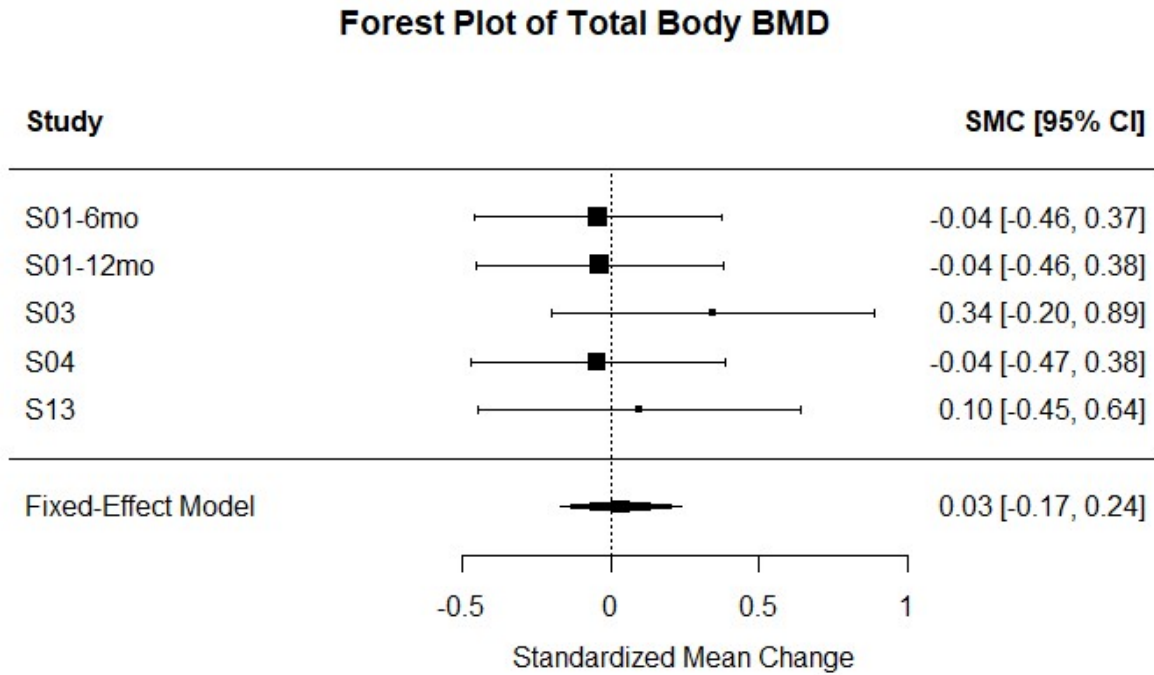
For the femoral neck BMD, the estimate is 0.0847 ( $p=0.0726$ ) which is not significant. The 95% confidence interval includes -0.0078 and 0.1772. The  $Q$ -test of homogeneity is not significant with  $Q(df = 14)$  of 10.6396 and  $p$ -value of 0.7141. The four outliers have the least weight and did not affect the standardized mean difference much.

Figure 3: Forest plot of the effect sizes of the femoral neck BMD



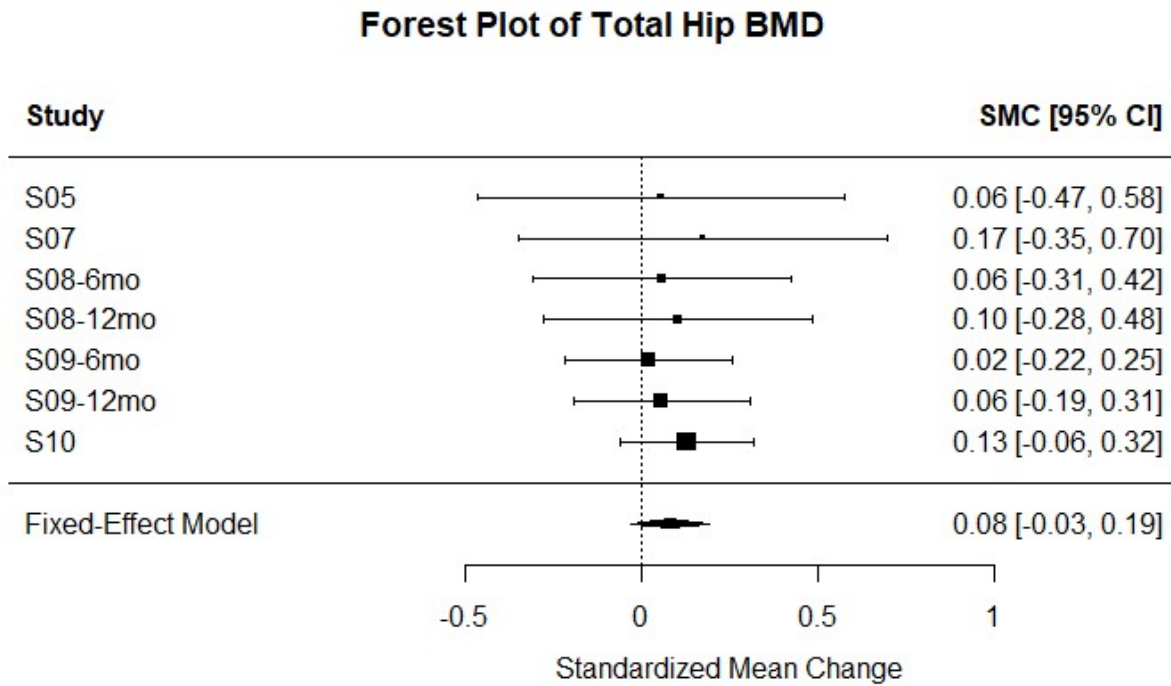
For the total body BMD, the estimate is 0.0329 ( $p = 0.7534$ ) which is not significant. The 95% confidence interval has -0.1726 as the lower bound and 0.2384 as the upper bound. The  $Q(df = 4)$  of 1.6745 is not significant because the p-value is 0.7954. There are only five effect sizes with the ones of heavier weights having a different direction than the smaller studies.

Figure 4: Forest plot of the effect sizes of the total body BMD



For the total hip BMD, the estimate is 0.0806 ( $p= 0.1493$ ) which is not significant. The 95% confidence interval has -0.0289 as the lower bound and 0.1900 as the upper bound. The  $Q$ -test result of 6 degrees of freedom is 0.6791 is not significant due to  $p$ -value being 0.9949.

Figure 5: Forest plot of the effect sizes of the total hip BMD



Moderation effect models for using the three types of exercise, aerobics, resistance, and combination for the outcomes of all interested DEXA scan sites are displayed below. The estimates are -0.0485, 0.0473, and 0.2354 for aerobic, resistance, and combination exercise groups respectively. Out of all three moderators, the combination group, which has a significant p-value of 0.0045 ( $\alpha = 0.05$ ), shows a statistically significant effect size. However, the mean effect sizes for each of the three groups are not significantly different from one another given the overlap in the confidence intervals.

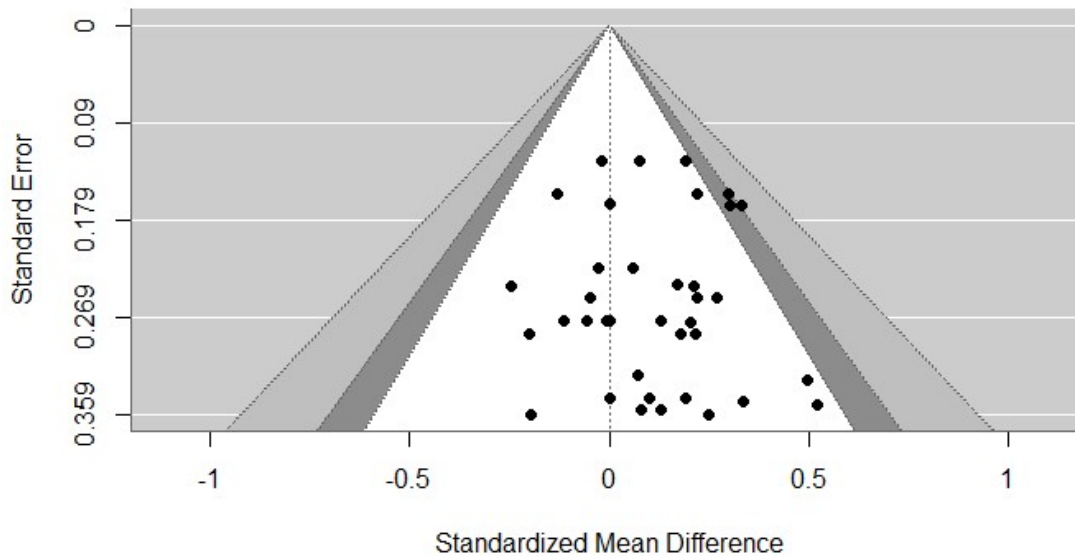
Table 2: Moderating factor model

	Estimate	Standard Error	p-value	Lower Bound Confidence Interval	Upper Bound Confidence Interval
Aerobic	-0.0485	0.0865	0.5749	-0.2180	0.1210
Resistance	0.2354	0.0305	0.1215	-0.0126	0.1072
Combination	0.0473	0.0828	0.0045	0.0731	0.3977

## Publication bias

Because they are all BMD measurements, it is appropriate to create a funnel plot to extrapolate publication bias. Three of the effect sizes fall out of the funnel but most of them are within the -0.5 to 0.5 residual value.

*Figure 6: Contoured funnel plot for all effect sizes*



## Discussion

The mean effect sizes of all BMD measurements show that there are no statistically significant differences between the exercise and control groups. There is a positive relationship between any type of exercise intervention with BMD, especially for the femoral neck and total hip areas. The findings are consistent with findings from the original meta-analysis (Howe et al., 2011).

Because all of the interested areas do not produce statistically significant BMD results, the study explores the relationship between exercise and BMD by moderating each type of exercise as a factor for the outcomes of all interested DEXA scan sites. A routine consisting of both aerobic and resistance exercises shows a statistically significant and positive correlation between exercise and BMD.

Because all effect sizes are BMD results measured using the DEXA machine, there is little if any heterogeneity among the effect sizes. However, there is a need to include more studies to conduct the meta-analysis. The meta-analysis only includes 13 studies, all of which reported post-test BMD results. While there are more up-to-date studies available, they only include the post-test BMD percentage change and/or T-values, thus creating a bias of choosing only specific kinds of studies with more restricted data. Moreover, a small number of studies preclude publication bias.

The meta-analysis has 2 primary limitations. The literature search only consisted of three databases and did not include gray literature. The limitation may have led to the omission of relevant unpublished studies and introduced publication bias as mentioned above. Second, the meta-analysis treated multiple effect sizes from several contributing studies as independent, which could potentially underestimate standard errors. Future analyses will account for the clustering of effect sizes within studies to address this issue more accurately.

## Conclusion

The findings of this meta-analysis are consistent with a previous Cochrane review on the same topic of exercise effects on bone mass density (Howe et al., 2011). There is a statistically significant positive relationship between routines that include aerobic and resistance exercise components.

Exercise, especially when combining aerobic and resistance training, can improve BMD slightly, which is beneficial for reducing instances of osteoporosis in postmenopausal women. More importantly, the study found that exercise does not have an adverse effect on postmenopausal women's health.

A more expanded meta-analysis will need to include more studies with different BMD post-test types of report. It might be beneficial to also conduct a Bayesian Meta-Regression on Standardized Mean Differences (to include more past data) to see if there is a significant relationship between the exercise intervention to the bone mineral density.

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## Appendix A: MetaReviewer code

### Study Information

Was at least one of the studies peer-reviewed?	Yes No Unclear
Is there a conflict of interest with this report?	COI identified by author COI identified by coder No COI identified
Was there funding received to support this study?	Yes No Unclear
Year of publication	Year published

### Sample Characteristics

Sample ID	Unique ID
What kind of sample is this?	Exercise Control
What is the country of origin for this sample?	Based on the country of the study
What is the number of participants in this sample?	The number of participants in the sample
What was the average age of participants in this sample?	The age of the participants
What was the standard deviation of the average age of participants in this sample?	The standard deviation of the age of the participants

### Condition Characteristics

Condition ID	Unique ID
What kind of condition is this?	Exercise Control
What is the unit of assignment?	Individual Group Unclear
What is the number of participants in this sample?	The number of participants in the sample
How were units assigned to groups?	Randomly Not randomly Unclear
How long did it take to implement the intervention?	The length of the intervention
Who delivered the intervention?	Trained exercise professional Physical therapists Self

### Measures

Measure ID	LumbarSpine FemoralNeck TotalHip TotalBody
Describe the measure	The measurement of bone mass density at a specific location
What construct does this measure assess?	criterion
Does this measure demonstrate construct validity?	Yes No Unclear
How were units assigned to groups?	Randomly Not randomly Unclear
How was this measure collected?	Same DEXA machine Different DEXA machine
Does this measure have evidence of reliability?	Yes, the study reports measure reliability Yes, the study uses an established or standardized measure No information or evidence of unsatisfactory reliability

### Study Quality

Was the primary outcome preregistered?	Yes No Unclear
Did the study have any observable confounds?	Yes No Unclear
If so, explain the confound	Confound explanation
If the study was randomized, was the randomization compromised?	Yes No Unclear

## Appendix B: R code

```
`` `{r}
library(dplyr)
library(metafor)
library(meta)
`` `

## Read in data
`` `{r}
totalbody <- read.csv("TotalBody.csv")
lumbarSpine <- read.csv("LumbarSpine.csv")
totalhip <- read.csv("TotalHip.csv")
femoralneck <- read.csv("FemoralNeck.csv")
`` `

## Pre-Post
`` `{r}
totalbody <- escalc(measure = "SMCR",
  m1i = ExercisePostMean, sd1i = ExercisePostSD,
  m2i = ExercisePreMean, sd2i = ExercisePreSD,
  ni = ExerciseN,
  ri = 0.7,
  data = totalbody,
  var.names = c("EXd", "EXv"))
totalbody <- escalc(measure = "SMCR",
  m1i = ControlPostMean, sd1i = ControlPostSD,
  m2i = ControlPreMean, sd2i = ControlPreSD,
  ni = ControlN,
  ri = 0.7,
  data = totalbody,
  var.names = c("CNTLd", "CNTLv"))
totalbody$SMDpp <- totalbody$EXd - totalbody$CNTLd # SMDpp
totalbody$SMDppvar <- totalbody$EXv + totalbody$CNTLv # SMDpp variance
preposttotal <- rma(yi = SMDpp, vi = SMDppvar, data = totalbody, method = "FE")
preposttotal
forest(preposttotal,,
  main = "Forest Plot of Total Body BMD",
  slab = totalbody$studyID)

lumbarSpine <- escalc(measure = "SMCR",
  m1i = ExercisePostMean, sd1i = ExercisePostSD,
  m2i = ExercisePreMean, sd2i = ExercisePreSD,
  ni = ExerciseN,
  ri = 0.7,
  data = lumbarSpine,
```

```

var.names = c("EXd", "EXv"))
lumbaraspine <- escalc(measure = "SMCR",
m1i = ControlPostMean, sd1i = ControlPostSD,
m2i = ControlPreMean, sd2i = ControlPreSD,
ni = ControlN,
ri = 0.7,
data = lumbaraspine,
var.names = c("CNTLd", "CNTLv"))
lumbaraspine$SMDpp <- lumbaraspine$EXd - lumbaraspine$CNTLd # SMDpp
lumbaraspine$SMDppvar <- lumbaraspine$EXv + lumbaraspine$CNTLv # SMDpp variance
prepostlumb <- rma(yi = SMDpp, vi = SMDppvar, data = lumbaraspine, method = "FE")
prepostlumb
forest(prepostlumb,
main = "Forest Plot of Lumbar Spine BMD",
slab = lumbaraspine$studyID)

```

```

femoralneck <- escalc(measure = "SMCR",
m1i = ExercisePostMean, sd1i = ExercisePostSD,
m2i = ExercisePreMean, sd2i = ExercisePreSD,
ni = ExerciseN,
ri = 0.7,
data = femoralneck,
var.names = c("EXd", "EXv"))
femoralneck <- escalc(measure = "SMCR",
m1i = ControlPostMean, sd1i = ControlPostSD,
m2i = ControlPreMean, sd2i = ControlPreSD,
ni = ControlN,
ri = 0.7,
data = femoralneck,
var.names = c("CNTLd", "CNTLv"))
femoralneck$SMDpp <- femoralneck$EXd - femoralneck$CNTLd # SMDpp
femoralneck$SMDppvar <- femoralneck$EXv + femoralneck$CNTLv # SMDpp variance
prepostfem <- rma(yi = SMDpp, vi = SMDppvar, data = femoralneck, method = "FE")
prepostfem
forest(prepostfem,
main = "Forest Plot of Femoral Neck BMD",
slab = femoralneck$studyID)

```

```

totalhip <- escalc(measure = "SMCR",
m1i = ExercisePostMean, sd1i = ExercisePostSD,
m2i = ExercisePreMean, sd2i = ExercisePreSD,
ni = ExerciseN,
ri = 0.7,
data = totalhip,
var.names = c("EXd", "EXv"))
totalhip <- escalc(measure = "SMCR",

```

```

m1i = ControlPostMean, sd1i = ControlPostSD,
m2i = ControlPreMean, sd2i = ControlPreSD,
ni = ControlN,
ri = 0.7,
data = totalhip,
var.names = c("CNTLd", "CNTLv"))
totalhip$SMDpp <- totalhip$EXd - totalhip$CNTLd # SMDpp
totalhip$SMDppvar <- totalhip$EXv + totalhip$CNTLv # SMDpp variance
preposthip <- rma(yi = SMDpp, vi = SMDppvar, data = totalhip, method = "FE")
preposthip
forest(preposthip,
main = "Forest Plot of Total Hip BMD",
slab = totalhip$studyID)
```

```

```

## Regression
```{r}

```

```

merged_data <- bind_rows(totalbody, lumbaraspine, femoralneck, totalhip)
merged_data <- escalc(measure = "SMD", # the measure is the type of effect size
m1i = ExercisePostMean, sd1i = ExercisePostSD, n1i = ExerciseN,
m2i = ControlPostMean, sd2i = ControlPostSD, n2i = ControlN,
data = merged_data,
var.names = c("smd", "varsmd"))
MR1 <- rma(yi = smd,
vi = varsmd,
mods = ~ -1 + factor(TrtEvent),
data = merged_data,
method = "REML")
summary(MR1)

```

```

funnel_data <- merged_data %>%
filter(ExerciseN >= 10)
funnel_data_re <- rma(yi = smd,
vi = varsmd,
data = funnel_data,
method = "REML"
)
funnel(funnel_data_re, # RE results
level=c(90, 95, 99), #significance levels
shade = c("white", "gray55", "gray75"),
refline = 0,
legend = F)
```

```