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Resistance Training and Bone Mineral Density in Women

A Meta-Analysis of Controlled Trials

ABSTRACT

Kelley GA, Kelley KS, Tran ZV: Resistance training and bone mineral density in women: a meta-analysis of controlled trials. *Am J Phys Med Rehabil* 2001;80:65–77.

The purpose of this study was to use meta-analysis to examine the effects of resistance training on bone mineral density at the femur, lumbar spine, and radius in pre- and postmenopausal women. Resistance training had a positive effect on bone mineral density at the lumbar spine of all women and at the femur and radius sites for postmenopausal women. It was concluded that resistance training has a positive effect on bone mineral density in women.

Key Words: Exercise, Bone, Women, Meta-Analysis

Osteopenia and osteoporosis are major public health problems in the United States, affecting primarily lean, white, postmenopausal women.[1] Currently approximately 26.2 million white, postmenopausal women in the United States have either osteopenia or osteoporosis.[1] More specifically, osteopenia, defined as bone density that is 1 to 2.5 SD below the young adult reference range, affects an estimated 16.8 million (54%) of postmenopausal white women in the United States, whereas osteoporosis, defined as bone density >2.5 SD below the young adult reference range, affects another 9.4 million (30%) women.[1, 2] Low-bone density increases the risk for fractures, particularly at the hip, spine, and distal forearm. Currently, the estimated lifetime risk for fracture in 50-yr-old white women in the United States is 17.5% at the hip, 15.6% at the vertebrae, and 16.0% at the distal forearm.[1] In terms of the mortality rate, the survival rate at 5-yr follow-up relative to those of like age and gender is 0.83 for those who have experienced a hip fracture, 0.82 for vertebral fractures, and 1.00 for fractures of the forearm.[3] In the United States,

the estimated cost of fractures can be as high as $20 billion per year, with hip fractures accounting for more than a third of the total cost.[4] Furthermore, because of increased life expectancy, the number of women with low-bone density and subsequent fractures is expected to increase substantially in future years.

Physical activity has been suggested as a nonpharmacologic intervention for maximizing bone density during the younger years and preventing the bone loss during the later years.[5] Recent meta-analyses[6, 7] demonstrated the positive effects of aerobic exercise on both lumbar spine and hip bone mineral density (BMD) in postmenopausal women. Another potentially valuable type of physical activity is resistance training. Resistance training is a low-cost, nonpharmacologic intervention that is available to most of the public. Besides the positive effects on the bone, resistance exercise increases lean-body mass, decreases body fat, and increases muscular strength in both adult men and women.

Unfortunately, traditional narrative reviews on the effects of progressive resistance exercise on BMD have led to conflicting results. For example, seven reviews[8–14] have suggested that progressive resistance exercise *may* have a positive effect on BMD, although nine reviews[15–23] have suggested that progressive resistance exercise *does* have a positive effect. These discrepancies are not surprising given the fact that intervention studies[24–52] examining the effects of resistance exercise on BMD in adults have led to less than overwhelmingly positive results. For example, for the BMD sites assessed in previously mentioned studies, only 20% were reported as statistically significant. One of the possible reasons for the lack of statistically significant findings may be the result of the low statistical power leading to an increased risk of type 2 errors in some studies. Meta-analysis is a quantitative approach in which individual studies addressing a common problem are statistically aggregated.[53, 54] It is especially useful with a small number of subjects in the studies.[54]

As part of a larger study, we[55] previously showed a weight-training-induced improvement of approximately 1% in BMD at all sites combined in postmenopausal women. However, a detailed examination of the effects of progressive resistance exercise on BMD was not conducted. This is also the case with another meta-analysis[56] that combined BMD results from both progressive resistance and aerobic exercise studies. To date, we are unaware of any meta-analysis that has provided a detailed examination of the effects of resistance training on BMD in women. Given the healthcare consequences of low BMD, especially among women, it is important to gain a better understanding of the effects of resistance training on BMD. Thus, the purpose of this study was to use the meta-analytic approach to examine the effects of resistance training on BMD in women.

METHODS

Data Sources

We performed computerized literature searches of articles indexed between January 1966 and December 1998 using MEDLINE, Current Contents, Sport Discus, and Dissertation Abstracts International databases. The following keywords were used either alone or in combinations for computer searches: bone, bone density, bone mineral density, exercise, physical activity, women, females, physical fitness, fitness, weight training, resistance exercise, resistance training, osteoporosis, and osteopenia. The titles and abstracts of studies identified in the computerized searches were examined to exclude irrelevant studies. We retrieved the full text of the remaining articles and we read each paper to determine whether it contained information on the topic of interest. Because computer searches have been shown to yield less than two-thirds of relevant articles,[57] the reference lists from both original and review articles were also reviewed to locate studies that had not been previously identified and which seemed to contain information on the topic of interest. In addition, we also hand searched selected journals. Furthermore, three experts on exercise and BMD (Drs. Charlotte Sanborn, David Nichols, and Christine Snow) reviewed our reference list and coding sheet for thoroughness and completeness.

Study Selection

Inclusion criteria for this study were as follows: (1) randomized or nonrandomized trials that included a comparative nonexercise control group or control period; (2) resistance training, defined as any external resistance added while performing exercises, as the only intervention; (3) adult female humans (mean study age, $\geq$18 yr) as subjects; (4) journal articles, dissertations, and master's theses published in the English-language literature; (5) studies published and indexed between January 1966 and December 1998; (6) BMD (relative value of bone mineral per measured bone area) assessed at the femur, lumbar spine, or radius; (7) training studies lasting a minimum of 16 wk. Only information that met the above criteria was included in our analysis. Thus, for example, if BMD was also assessed in women performing aerobic exercise, we did not include this information because it did not meet our inclusion criteria. We limited our analysis to the femur, lumbar spine, and radius because they are the most often studied and these areas are the most vulnerable to fracture. Because dissertations may eventually become full-length journal articles, we cross-refer-

enced between the two to avoid duplication. We did not include abstracts and conference papers from national meetings because of the paucity of data provided as well as the inability to obtain complete data from the authors. Studies published in foreign language journals were also not included because of the potential error in the translation and interpretation of findings. Studies that met our inclusion criteria were also examined to ensure that the same subjects were not included in more than one study.[58] For studies that met our inclusion criteria but did not provide appropriate information on changes in BMD,[59, 60] we personally tried to contact the authors to retrieve such information.

Data Extraction

Coding sheets that could hold 242 items were developed and used in this investigation. In addition, coding instructions that described how to code each item on the coding sheet were developed and used. To avoid coding bias, all data were extracted independently by two authors. The authors then met and reviewed every item for accuracy and consistency. Disagreements were resolved by consensus. Blinding of coders to study information in relation to the identity and institutional affiliation of the study authors, as well as study results, were not performed because, according to a recent work,[61] these procedures have neither a clinically nor statistically significant effect on the results. The major categories of variables coded included study characteristics, physical characteristics of subjects, and primary and secondary outcomes.

Statistical Analysis

Primary Outcomes. The primary outcomes in this study were changes in BMD at the femur, lumbar spine, and radius. Because of the various ways in which the authors reported data on changes in BMD and because we also wanted to maximize the number of studies and outcomes that could be included in our analysis, we used the standardized difference approach as our effect size (ES) measure.[62] This was calculated by subtracting the change outcome in the exercise group from the change outcome in the control group, and then dividing this difference by the pooled standard deviation of the exercise and control groups.[62] The ES was then corrected for small-sample bias.[62] For studies that included multiple outcomes because of more than one group (for example, an exercise group that trained at a higher intensity *vs.* one that trained at a lower intensity), net changes in bone mineral density were treated as independent data points.[63] In general, an ES of 0.20 was considered a small effect, 0.50 a moderate effect, and 0.80 a large effect.[64] An ES of 0.20, for example, means that the exercise group differed from the control group by two-tenths of a standard deviation in favor of the exercise group. Because of the small-sample size in this study, especially for subgroup analyses, bootstrap resampling (5,000 iterations) was used to generate 95% BCIs around mean ES changes for BMD.[65] The bootstrap technique is a computer-intensive, nonparametric method of estimating the reliability of the original sample estimate, in this case, ES changes in BMD. By randomly drawing from the available sample, with replacement, samples the same size as the original are generated. Each time an observation is selected for a new sample, each of the elements of the original sample has an equal chance of being selected. This is similar to replicating each member of a sample 5,000 times (iterations). The main advantage of this approach is that the estimate desired is not based on some theoretical distribution, but rather, on the sample itself. This approach frees one from the constraints of the central limit theorem. The number of iterations chosen was based on previous research demonstrating that improvement of estimation accuracy was limited beyond 5,000 iterations.[66] If the 95% confidence interval included zero (0.00), it was concluded that there was no statistically significant effect of exercise on BMD.

Heterogeneity of ES changes in BMD was examined using the Q statistic.[62] A random-effects model was used when changes were significantly heterogeneous ($P < 0.05$), whereas a fixed-effects model was used in the absence of significant heterogeneity.[53] For studies that included multiple outcomes because of more than one group, net changes were treated initially as independent data points. However, to examine the influence (sensitivity) of each study on the overall results, analyses were performed with each study deleted from the model.

Publication bias (the tendency for journals to publish studies that yield statistically significant results and/or authors to only submit studies that yield statistically significant results) was examined using Kendall's tau statistic (τ).[67] A statistically significant result ($P < 0.05$) was considered to be suggestive of publication bias.

Study quality was assessed using a three-item questionnaire designed to assess bias, specifically, randomization, blinding, and withdrawals/dropouts.[68] The number of points possible ranged from a low of 0 to a high of 5. All questions were designed to elicit yes (1 point) or no (0 point) responses. The questionnaire took less than 10 min per study. The questionnaire has been shown to be both valid (face validity) and reliable (researcher interrater agreement, $r = 0.77$, 95% confidence interval = 0.60–0.86).[68]

Subgroup Analyses. For categorical variables, subgroup analyses for primary outcomes were performed using analysis of variance-like procedures for meta-analysis.[62] These procedures provide statistics for both

TABLE 1
Study characteristics

Study	Design/Subjects	Resistance Training Intervention	BMD Assessment
Bouxsein[24]	RCT that included 20 premenopausal women ~20 yr old assigned to either a resistance training (n = 12) or control (n = 8) group	35 wk of training consisting of 14 exercises performed 3 times per week for 3 sets of 8–12 repetitions at 65–85% of 1 RM	DEXA (Hologic) at the lumbar spine (L2-4), femoral neck, trochanter, and Ward's triangle
Chilibeck et al.[25]	CT consisting of 30 premenopausal women assigned to either a resistance training (n = 20; age = 20.3 ± 1.0 yr) or control (n = 10; age = 20.2 ± 0.4 yr) group	20 wk of training consisting of 7 exercises performed 3 times per week for 5 sets of 6–12 repetitions at 70–80% of 1 RM	DEXA (Hologic) at the arms, ribs, thoracic spine, lumbar spine, pelvis, legs, whole body, femoral neck, trochanter, intertrochanter, Ward's triangle, and total hip
Delaney[26]	RCT that included 88 premenopausal women ~28 to 39 yr of age assigned to either a resistance training (n = 46) or control (n = 42) group	20 wk of training consisting of 12 exercises performed 3 times per week for 3 sets of 8–12 repetitions at 70% of 1 RM	DEXA (Lunar) of the lumbar spine (L2-4) and total body; SPA (Lunar) at the radius
Dornemann et al.[27]	RCT consisting of 26 premenopausal women assigned to either a resistance training (n = 12; age = 43 ± 3 yr) or control (n = 14; age = 45 ± 3 yr) group	24 wk of training consisting of 7 exercises performed 3 times per week for 1–5 sets of 4–15 repetitions	DEXA (Hologic) at the lumbar spine, femoral neck, and distal radius
Gleeson et al.[28]	CT that included 72 premenopausal women assigned to either a resistance training (n = 34; age = 33.4 ± 6.3 yr) or control (n = 38; age = 32.7 ± 5.6 yr) group	52 wk of training consisting of 8 exercises performed 3 times per week for 2 sets of 20 repetitions at 60% of 1 RM	DPA (Lunar) at the lumbar spine; SPA (Osteon) at the os calcis
Hartard et al.[29]	CT that included 31 postmenopausal women with osteopenia assigned to either a resistance training (n = 16; age = 63.6 ± 6.2 yr) or control (n = 15; age = 67.4 ± 9.7 yr) group	24 wk of training performed 2 times per week for 1–2 sets of 8–12 repetitions at 70% of 1 RM	DEXA (Norland) at the lumbar spine (L2-4) and femoral neck
Heinonen et al.[30]	CT that included 32 premenopausal women assigned to either a resistance training (n = 13; age = 23.8 ± 5.0 yr) or control (n = 19; age = 25.7 ± 5.2 yr) group	52 wk of training consisting of 2 exercises performed 5 times per week for 5 sets of 10 repetitions at 80% of 1 RM	DEXA (Norland) at the proximal humerus, humeral shaft, radial shaft, ulnar, distal forearm, and calcaneus
Heinonen et al.[31]	RCT that included 53 perimenopausal women 52–53 yrs of age assigned to either a resistance training (n = 26) or control (n = 27) group	78 wk of calisthenics consisting of 8 exercises performed 4 times per week for 3 sets of 16 repetitions with the addition of ankle and wrist bands (1–2 kg)	DEXA (Norland) at the lumbar spine (L2-4), femoral neck, calcaneus, and distal radius
Kerr et al.[32]	RCT that included 42 postmenopausal women 40–70 yr of age assigned to either a muscular strength (n = 23) or muscular endurance (n = 19) group (nonexercising limb served as control)	52 wk of training consisting of 11 exercises performed 3 times per week for 3 sets of 8 repetitions (strength group) or 3 sets of 20 repetitions (endurance group)	DEXA (Hologic) at the femur (trochanter, intertrochanter, femoral neck, Ward's triangle) and radius (ultra distal, mid, and 1/3)
Little[33]	CT that included 10 postmenopausal women assigned to either a resistance training (n = 6; age = 59.5 ± 2.3 yr) or control (n = 4; age = 60.8 ± 1.4 yr) group	32 wk of training consisting of 9 exercises performed 3 times per week for 1 set of 8–12 repetitions at 60–80% of 1 RM	DPA (Lunar) at the lumbar spine (L2-4) and femoral neck; SPA (Lunar) at the distal radius
Lohman et al.[34]	RCT that included 56 premenopausal women assigned to either a resistance training (n = 22; age = 34.2 ± 2.6 yr) or control (n = 34; age = 34.4 ± 3.8 yr) group	78 wk of training consisting of 12 exercises 3 times per week for 3 sets of 8–12 repetitions at 70–80% of 1 RM	DEXA (Lunar) at the lumbar spine (L2-4), femoral neck, trochanter, Ward's triangle, and radius
Mayoux-Benhamou et al.[35]	RCT that included 33 postmenopausal women assigned to either a psoas training (n = 21; age = 58.2 ± 3.4 yr) or control (n = 12; age = 58.9 ± 1.3 yr) group	156 wk of daily psoas training consisting of 2–3 sets of 60 daily hip flexions with 5 kg on the knee	QCT (Elscint) at the lumbar spine (L1-4)

TABLE 1
Continued

Study	Design/Subjects	Resistance Training Intervention	BMD Assessment
Nelson et al.[36]	RCT that included 39 postmenopausal women assigned to either a resistance training (n = 20; age = 61.1 ± 3.7 yr) or control (n = 19; age = 57.3 ± 6.3 yr) group	52 wk of training consisting of 5 exercises performed 2 times per week for 3 sets of 8 repetitions at 80% of 1 RM	DEXA (Lunar) at the lumbar spine (L2-4) and femoral neck
Nichols et al.[37]	RCT that included 17 postmenopausal women at least 60 yr of age assigned to either an exercise (n = 9) or control (n = 7) group	52 wk of training consisting of 8 exercises performed 3 times per week for 3 sets of 10–12 repetitions at 80% of 1 RM	DEXA (Lunar) at the lumbar spine (L2-4), femoral neck, and trochanter
Notelovitz et al.[38]	RCT that included 20 surgically menopausal women assigned to either an estrogen + resistance training (n = 9; age = 43.3 ± 9.6 exercise yr) or estrogen + no exercise (n = 11; age = 46.2 ± 6.8 yr) group	52 wk of training consisting of up to 11 exercises performed 3 times per week for 8 repetitions per exercise	DPA (Lunar) at the spine as well as total body; SPA (Lunar) at the radius
Payne[39]	CT that included 48 premenopausal women assigned to either a resistance training (n = 28; age = 24.6 ± 9.2 yr) or control (n = 20; age = 22.8 ± 6.1 yr) group	18 wk of training consisting of 9 exercises performed 3 times per week for 1–6 sets of 6–10 repetitions per exercise	DEXA (Lunar) at the lumbar spine (L2-4), femoral neck, Ward's triangle, trochanter, and total body
Preisinger et al.[40]	RCT that included 58 postmenopausal women assigned to either an exercise (n = 27; age = 62.6 ± 5.9 yr) or control (n = 31; age = 59 ± 8 yr) group	208 wk of training consisting of 3 exercises performed 3 times per week for 3 repetitions	SPA (Osteodensitometer) at the mid and distal forearm
Protiva[41]	CT that included postmenopausal women 74–94 yr of age observed during a 6-mo control period (n = 13) and then assigned to 9 mo of resistance training (10 of the 13 completed the training along with an additional five subjects)	36 wk of training that included 8 exercises performed 3 times per week for 1–2 sets of 6–12 repetitions while wearing a weighted vest	DEXA (Hologic) at the femoral neck, trochanter, hip, and whole body
Pruitt et al.[42]	CT that included 26 postmenopausal women assigned to either a resistance exercise (n = 17; age = 53.6 ± 4.1 yr) or control (n = 9; age = 55.6 ± 2.9 yr) group	36 wk of training that included 11 exercises performed 3 times per week for one set of 10–15 repetitions at 50–60% of 1 RM	DPA (Lunar) at the lumbar spine (L2-4) and femoral neck
Pruitt et al.[43]	RCT that included 26 postmenopausal women assigned to either high-intensity resistance training (n = 8; age = 67 ± 0.5 yr), low-intensity resistance training (n = 7; age = 67.6 ± 1.4 yr) or control (n = 11; age = 69.6 ± 4.2 yr) group	52 wk of training that included 10 exercises performed 3 times per week for either 2 sets of 7 repetitions at 80% of 1 RM (high-intensity) or 3 sets of 14 repetitions at 40% of 1 RM (low-intensity)	DEXA (Hologic) at the lumbar spine (L2-4) and total hip (femoral neck, trochanter, and Ward's triangle)
Rockwell et al.[44]	CT that included 17 premenopausal women assigned to either a resistance training (n = 10; age = 36.2 ± 3.9 yr) or control (n = 7; age = 40.4 ± 11.5 yr) group	36 wk of training that included 8 exercises performed 2 times per week for 2 sets of 12 repetitions at 70% of 1 RM	DEXA (Lunar) at the lumbar spine and femoral neck
Shaw and Snow[45]	CT that included 40 postmenopausal women assigned to either a resistance training (n = 18; age = 64.2 ± 5.8 yr) or control (n = 22; age = 62.5 ± 6.6 yr) group	36 wk of training that included 6 exercises performed 3 times per week for 3–5 sets of 10–15 repetitions while wearing a weighted vest. Subjects also performed jumping exercises with a weighted vest.	DEXA (Hologic) at the lumbar spine (L2-4) and femoral neck
Sinaki et al.[46]	RCT that included 67 premenopausal women 30–40 yr of age assigned to either a resistance training (n = 32) or control (n = 35) group	156 wk of training that included exercises performed 3 times per week for 3 sets of 10 repetitions	DEXA (Hologic) at the lumbar spine (L2-4), trochanter, femoral neck, and Ward's triangle

TABLE 1
Continued

Study	Design/Subjects	Resistance Training Intervention	BMD Assessment
Sinaki et al.[47]	RCT that included 65 postmenopausal women assigned to either a resistance training (n = 34; age = 55.6 ± 4.5 yr) or control (n = 31; age = 56.5 ± 4.5 yr) group	104 wk of back extension exercise performed 5 times per week for 1 set of 10 repetitions at 30% of maximal isometric back muscle strength	DPA at the lumbar spine (L2-4)
Smidt et al.[48]	RCT that included 49 postmenopausal women assigned to either a resistance training (n = 22; age = 56.6 ± 6.6 yr) or control (n = 27; age = 55.4 ± 8.0 yr) group	52 wk of training that included 3 exercises performed 3–4 times per week for 3 sets of 10 repetitions at 70% of 1 RM	DPA at the lumbar spine (L2-4), femoral neck, Ward's triangle, and trochanter
Snow-Harter et al.[49]	RCT that included 20 premenopausal women approximately 20 yr old assigned to either a resistance training (n = 12) or control (n = 8) group	32 wk of training that included 14 exercises performed 3 days per week for 3 sets of 8–12 repetitions at 65–85% of 1 RM	DEXA (Hologic) at the lumbar spine (L2-4), femoral neck, trochanter, and Ward's triangle
Taafe et al.[50]	RCT that included 25 postmenopausal women assigned to either a high-intensity resistance training (n = 7; age = 67.0 ± 0.5 yr), low-intensity resistance training (n = 7; age = 67.6 ± 1.3 yr), or control (n = 11; age = 69.6 ± 4.3 yr) group	52 wk of training that included 3 exercises performed 3 days per week for either 3 sets of 14 repetitions at 40% of 1 RM (low-intensity) or 2 sets of 7 repetitions at 80% of 1 RM (high-intensity)	DEXA (Hologic) at the femur and middle third of the femur
Thorvaldson[51]	RCT that included 50 postmenopausal women assigned to either a resistance training (n = 12; age = 54.6 ± 2.1 yr) or control (n = 21; age = 54.6 ± 2.1 yr) group	24 wk of training that included 6 exercises performed 3–5 days per week for 3 sets of 10 repetitions	DEXA (Hologic) at the lumbar spine (L1-4) and femoral neck; QCT at the distal radius
Vuori et al.[52]	CT that included 24 premenopausal women assigned to either a resistance exercise (n = 12; age = 21.0 ± 2.5 yr) or control (n = 12; age = 22.0 ± 3.0 yr) group	52 wk of training that included leg press exercise performed 5 times per week for 5 sets of 10 repetitions at 80% of 1 RM	DEXA (Norland) at the lumbar spine, femoral neck, distal femur, patella, proximal tibia, and calcaneus

RCT, randomized controlled trial; CT, controlled trial; subjects; ages reported as mean ± SD; number of subjects listed includes only those who completed the study; BMD, bone mineral density; 1 RM, one repetition maximum; DEXA, dual-energy x-ray absorptiometry; DPA, dual photon absorptiometry; SPA, single photon absorptiometry; QCT, quantitative computed tomography.

within (Q_w) and between (Q_b) group differences. If statistically significant within-group (Q_w) heterogeneity existed ($P < 0.05$), a random-effects model was used. If no statistically significant within-group (Q_w) heterogeneity existed, a fixed-effects model was used. ES changes in BMD were examined initially when the data were partitioned according to study design (randomized vs. nonrandomized), country in which the study was conducted (United States vs. other), study quality (0–2 vs. 3–5), menopausal status (pre vs. post), calcium supplementation, changes in dietary intake during the study, drugs that could affect BMD, and physical activity habits of subjects. For the femur site, we also examined changes in BMD with data partitioned according to the femoral neck, trochanter, intertrochanter, and Ward's triangle. We were unable to examine specific sites at the lumbar spine and radius because of insufficient data. Bootstrap resampling (5,000 iterations) was used to generate 95% confidence intervals around ES changes for all subgroups. Randomization tests (5,000 iterations) were used to generate probability values for between-group differences.[69] Randomization tests using 5,000 iterations can detect a probability as low as 0.002.[69]

Regression Analysis. For continuous variables, potential associations with ES changes in BMD were conducted using meta-regression procedures, calculated with each ES weighted by the reciprocal of its variance, according to procedures described by Hedges and Olkin.[62] This model yields a test of the significance of each predictor (Q_R) as well as a test of model specification (Q_E) which assesses whether systematic variation remains unexplained in the regression model. Thus, a statistically significant Q_R value means that the variables included in the regression are significantly related to the variable of interest, whereas a nonsignificant Q_E value means that the model is well specified. Continuous variables that were examined included percentage

of dropout (number of subjects who did not complete the study), age, height, initial as well as changes in body weight, body mass index, percentage of body fat and lean-body mass, changes in muscular strength, initial BMD, calcium intake, years postmenopausal, length and intensity of training, number of exercises performed, and compliance, defined as the percentage of exercise sessions attended by the subjects.

Secondary Outcomes. Secondary outcomes (changes in body weight, body mass index, percentage of body fat, and lean-body mass) were calculated as the difference (exercise minus control) of the changes (initial minus final) in these mean values. The original metric was used for all secondary outcomes. For those studies in which variance estimation was necessary, these were accomplished using the same procedures as those for estimating variances for BMD.[63] Fixed and random effects models were used following the same procedures as those previously described for BMD. Percentage of changes in muscular strength (one repetition maximum) were reported separately for exercise and control groups.

Unless otherwise noted, all results are reported as mean ± SD. The α level for statistical significance was set at $P < 0.05$. Values between 0.05 and 0.10 were considered as a trend toward statistical significance. Bonferroni adjustments were not made because of the increased risk of a type 2 error.

RESULTS

Study Characteristics

Thirty-one studies met the criteria for inclusion.[24–52, 59, 60] However, we were unable to include two studies[59, 60] because of the inability to obtain data necessary for the calculation of an ES. Thus, we had a 6% loss that met our inclusion criteria. One study[70] was excluded because it included some of the same subjects from another study that we included.[40] A general description of the 29 included studies is shown in Table 1 and the physical characteristics of the exercise and control group subjects are described in Table 2. The per person time to code each study once ranged from 0.58 to 4.67 hr (1.26 ± 0.79 hr). Study quality ranged from 1 to 4 (2 ± 1). The 29 included studies represented 94 ES (femur = 53, lumbar spine = 24, radius = 17) from 61 groups (32 exercise, 29 control). Twenty-three studies were published in journals,[25, 27–32, 34–38, 40, 42–50, 52] five were dissertations,[24, 26, 33, 39, 41] and one was a master's thesis.[51] Twenty studies were conducted in the United States,[24, 26–28, 33, 34, 36–39, 41–50] three in Finland,[30, 31, 52] two each in Austria[29, 40] and Canada,[25, 51] and one each in Australia[32] and France.[35] Percentage of dropout, defined as the number of subjects who did not complete the study, ranged from 0 to 63% in the exercise groups (28 ± 17%) and 0 to 69% in the control groups (17 ± 18%). Thus, pre and post measures of BMD were available for 572 subjects who served as exercisers and 551 subjects who served as controls. The minimum and maximum number of subjects in the exercise groups was 6 and 46 (18 ± 10), respectively, whereas the minimum and maximum number of subjects in the control groups was 7 and 42 (19 ± 10), respectively. For the 14 studies that reported information on race, 12 reported that all of the subjects were white,[26, 28, 33–36, 40, 43, 45–48] one study reported that the subjects were white and black,[42] and another reported that the subjects were white and Asian.[51] For the 18 studies that reported information on calcium supplementation during the study, eight studies reported that some subjects were taking supplements,[33, 36–38, 43, 46, 48, 51] seven reported that all of the subjects were taking supple ments,[24, 26–28, 34, 44, 49] and three reported that none of the subjects were taking supplements.[35, 39, 47] For the 23 studies that reported on whether subjects were taking any type of pharmacologic interventions that could affect BMD, 14 reported that none were taking any pharmacologic interventions,[26, 27, 32–37, 40, 42, 44, 46, 47, 51] eight reported that some were,[25, 28, 30, 31, 39, 43, 45, 48] and one study reported that all were.[38] Ten studies reported that none of the subjects smoked cigarettes,[25, 31, 33, 36, 39, 40, 44–47] whereas four reported that some subjects smoked.[28, 35, 48, 51] Two studies reported that some of the subjects consumed alcohol.[25, 48] Ten studies reported that none of the subjects had been previously active,[25, 26, 29, 31, 33, 34, 36, 39, 40, 43] eight reported that some were,[24, 28, 32, 35, 44, 48–50] and five reported that all were.[30, 37, 46, 51, 52] Five studies reported that none of the subjects had suffered previous fractures,[29, 39, 43, 46, 47] whereas three reported that some had.[33, 36, 40] Compliance, defined as the percentage of resistance training sessions that the exercise groups attended, ranged from 44% to 96% (79 ± 13%). Reliability for BMD assessment (coefficient of variation) ranged from approximately 0.6% to 4% at the femur, 0.6% to 5.0% at the lumbar spine, and 0.5% to 5% at the radius.

Primary Outomes

Initial BMD values for exercise and controls are shown in Table 3, whereas ES changes in BMD are shown in Table 4. BMD values were available for a total of 743 subjects at the femur (392 exercise, 351 control), 870 at the lumbar spine (450 exercise, 420 control), and 441 at the radius (219 exercise, 222 control). Because there was no statistically significant heterogeneity at any of the sites observed, a fixed-effects model was used for overall results at all three sites.

TABLE 2
Initial physical characteristics of subjects

Variable	*n*	Exercise (Mean ± SD)	*n*	Control (Mean ± SD)
Age (yr)	32	49.0 ± 17.9	29	47.7 ± 17.8
Height (cm)	27	163.2 ± 2.3	24	163.3 ± 2.8
Weight (kg)	30	63.5 ± 3.7	27	64.4 ± 3.3
BMI (kg/m^2)	28	23.9 ± 1.6	25	24.3 ± 1.5
Fat (%)	13	31.6 ± 5.8	12	31.7 ± 5.8
Lean mass (kg)	12	42.4 ± 3.3	11	42.4 ± 3.7
Postmenopausal (yr)	13	8.6 ± 4.7	12	8.5 ± 4.0
Calcium (mg)	16	926 ± 227	14	825 ± 114

n, number of groups reporting data; BMI, body mass index.

Proximal Femur. Small and statistically insignificant changes in BMD were observed at the femur site. These changes were equivalent to a 0.33% increase in the exercise groups and a 0.05% decrease in the control groups. No evidence of publication bias was observed ($r = 0.12$, $P = 0.26$). With each study deleted from the model once, ES changes in BMD at the femur ranged from a low of 0.02 ± 0.37 (95% Bootstrap Confidence Interval [BCI], −0.07–0.11) to a high of 0.09 ± 0.36 (95% BCI, 0.03–0.17). Approximately 90% of the 53 ESs were reported by the authors of the original studies as not being statistically significant.

Lumbar Spine. Small but statistically significant ES changes in BMD were found at the lumbar spine. These changes were equivalent to a 0.19% decrease in the exercise groups and a 1.45% decrease in the control groups. No evidence of publication bias was observed ($r = -0.08$, $P = 0.62$). With each study deleted from the model once, ES changes in BMD ranged from a low of 0.19 ± 0.37 (95% BCI, 0.09–0.33) to a high of 0.27 ± 0.36 (95% BCI, 0.14–0.41). Approximately 67% of the 24 ESs were reported by the authors of the original studies as not being statistically significant.

Radius. Small and statistically significant ES changes in BMD were observed at the radius. ES changes were equivalent to a 1.22% increase in BMD for the exercise groups and a 0.95% decrease in the control groups. No evidence of publication bias was observed ($r = 0.17$, $P = 0.38$). With each study deleted from the model once, ES changes in BMD at the radius ranged from a low of 0.19 ± 0.36 (95% BCI, 0.03–0.45) to a high of 0.33 ± 0.34 (95% BCI, 0.16–0.52). Approximately 65% of the 17 ESs were reported by the authors of the original studies as not being statistically significant.

Subgroup Analysis

Subgroup analyses for those variables in which there were statistically significant differences or trends for statistically significant differences between groups are shown in Table 5.

Femur. There was a trend for greater ES changes in BMD at the femur when studies were of higher vs. lower quality. Higher-quality studies yielded ES changes that were equivalent to a 1.03% increase in BMD in the exercise groups and a 0.16% increase in the control groups. Lower-quality studies yielded ES changes that were equivalent to a 0.21% increase in the exercise groups and a 0.09% decrease in the control groups. There was also a trend for greater ES changes in BMD at the femur when subjects were postmenopausal vs. premenopausal. For postmenopausal women,

TABLE 3
Initial BMD values

Variable	Studies (*n*)	Exercise Subjects (Mean ± SD)	Exercise Values (*n*)	Exercise (g/cm^2) (Mean ± SD)	Control Subjects (Mean ± SD)	Control Values (*n*)	Control (g/cm^2) (Mean ± SD)
Femur	22	18 ± 8	53	0.852 ± 0.197	16 ± 9	46	0.832 ± 0.178
Lumbar spine	23	20 ± 10	24	1.075 ± 0.115	18 ± 11	23	1.071 ± 0.121
Radius	10	22 ± 14	17	0.497 ± 0.153	22 ± 11	14	0.513 ± 0.160

BMD, bone mineral density; BMD data based on number of exercise and control values.

TABLE 4
BMD results

Variable	Studies (*n*)	Subjects (Mean ± SD)	ES (*n*)	ES (Mean ± SD)	BCI (95%)	Q (*P*)
Femur	22	34 ± 16	53	0.07 ± 0.36	−0.02to0.15	43.81 (0.78)
Lumbar spine	23	38 ± 20	24	0.24 ± 0.36	0.11to0.38[a]	20.68 (0.60)
Radius	10	44 ± 24	17	0.30 ± 0.33	0.13to0.48[a]	23.69 (0.10)

[a] Statistically significant.
BMD, bone mineral density; ES, effect size; BCI, Bootstrap Confidence Interval, Q (*P*), heterogeneity (probability for alpha).

ES changes in BMD were equivalent to a 0.40% increase in the exercise groups and a 0.21% decrease in the controls. For premenopausal women, ES changes were equivalent to a 0.26% increase in the exercise groups and a 0.13% increase in the control groups. No statistically significant between-group differences were found when data were partitioned according to study design, country in which the study was conducted, calcium supplementation, previous physical activity habits, type of BMD assessment, and different sites at which BMD was assessed. Insufficient data were available to examine differences in BMD at the femur when data were partitioned according to diet as well as drugs that could affect BMD.

Lumbar Spine. No statistically significant between-group differences were observed for ES changes at the lumbar spine when data were partitioned according to source of study, country in which the study was conducted, study design, menopausal status of subjects, calcium supplementation, previous physical activity, and type of BMD assessment. Insufficient data were available to examine between-group differences in BMD when data were partitioned according to study quality, drugs that could affect BMD, diet, and sites at which the lumbar spine BMD was assessed.

Radius. There was a trend for greater ES changes in BMD at the radius when studies were of higher vs. lower quality. Higher-quality studies yielded ES changes that were equivalent to a 0.82% increase in BMD in the exercise groups and a 1.87% decrease in the control groups. Lower-quality studies yielded ES changes that were equivalent to a 1.75% increase in BMD in the exercise groups and a 0.23% increase in the control groups. ES changes at the radius were also greater in postmenopausal vs. premenopausal women. For postmenopausal women, ES changes were equivalent to a 1.71% increase in BMD in the exercise groups and a 1.39% decrease in the control groups. For premenopausal women, ES changes were equivalent to a 0.17% increase in the exercisers and a 0.01% increase in the controls. No statistically significant differences

TABLE 5
Subgroup analyses

Variable	Studies (*n*)	Subjects (*n*)	ES (*n*)	ES (Mean ± SD)	BCI (95%)	Q_b (*P*)
Femur						
Study quality						
0–2	21	682	45	0.03 ± 0.37	−0.07–0.10	3.05 (0.08)[a]
3–5	1	61	8	0.24 ± 0.37	0.03–0.44	
Menopausal status						
Premenopausal	9	309	28	−0.01 ± 0.36	−0.16–0.09	2.34 (0.09)[a]
Postmenopausal	12	381	24	0.15 ± 0.38	0.03–0.28	
Radius						
Study quality						
0–2	7	296	8	−0.01 ± 0.38	−0.09–0.05	14.11 (0.001)[b]
3–5	3	145	9	0.56 ± 0.36	0.38–0.75	
Menopausal status						
Premenopausal	4	202	5	−0.02 ± 0.42	−0.13–0.05	9.99 (0.004)[b]
Postmenopausal	5	186	11	0.52 ± 0.36	0.33–0.71	

ES, effect size; BCI, Bootstrap Confidence Interval; Q_b, difference between groups.
[a] Trend for statistical significance when P ranges from ≥ 0.05 to ≤ 0.10; [b] Statistically significant when $P < 0.05$.
ES outcomes based on number of ESs.

were observed when data were partitioned according to source of study, country in which the study was conducted, study design, previous physical activity habits, and type of BMD assessment. Insufficient data were available to examine between-group differences in BMD when data were partitioned according to calcium supplementation, drugs that could affect BMD, diet, and different sites at which BMD of the radius was assessed.

Regression Analyses

Femur. The only significant predictor for ES changes in BMD at the femur was changes in the percentage of fat ($Q_R = 6.67$, $P = 0.03$; $Q_E = 14.32$, $P = 0.35$). Larger ES changes in BMD at the femur were observed among subjects with smaller changes in the percentage of fat. No other statistically significant associations were observed.

Lumbar Spine

No significant predictors were observed for ES changes in BMD at the lumbar spine.

Radius. The only significant predictor for ES changes in BMD at the radius was initial lean-body mass ($Q_R = 6.76$, $P = 0.009$; $Q_E = 9.26$, $P = 0.41$). Smaller ES changes in BMD at the radius were observed among subjects with higher initial levels of lean-body mass. Insufficient data were available to examine the relationship between ES changes in BMD and changes in the percentage of body fat and lean-body mass.

Secondary Outcomes

Statistically significant decreases were observed for the percentage of body fat ($-2 \pm 2\%$; 95% BCI, -3 to -1%), whereas there was a statistically significant increase in lean-body mass (2 ± 1 kg; 95% BCI, 1–2 kg). No statistically significant changes were observed for body weight or body mass index. There was a 40% increase in muscular strength in the exercise groups and a 6% increase in the control groups.

DISCUSSION

Implications for Practice

The overall results of this study suggest that across all groups of women included in this analysis, resistance training helps to preserve lumbar spine BMD. Resistance training also seems to increase and preserve BMD at the femur and radius sites in postmenopausal women. Furthermore, with the exception of changes in BMD at the proximal femur, these results were consistent after deletion of each study once from our models.

An interesting finding of this study is the fact that the largest effect on BMD occurred at the radius site in postmenopausal women. One possible reason for this may be the fact that most subjects included in these studies were able to ambulate. Consequently, they may have had greater daily loading placed on the lumbar spine and femur vs. the radius before participation in the studies. Therefore, there may have been an opportunity for resistance training to have a greater effect on BMD at the radius vs. the lumbar spine and femur. However, it may also be that the resistance training programs placed greater relative loads on the radius vs. the lumbar spine and femur sites. The larger changes observed in BMD at the femur when changes in the percentage of fat were smaller as well as the smaller changes at the radius when initial lean-body mass was higher are supportive of the fact that in general, women who weigh more place greater stress on their bones. Thus, heavier women may not experience the same improvements in BMD as leaner women.

Although it seems that postmenopausal women may have the most to gain from a program of resistance training, this form of intervention should almost always be encouraged across all age groups, especially because of other benefits that can be derived from participation in such activities. For example, in this investigation, we saw statistically significant improvements in body composition (decreases in the percentage of body fat and increases in lean-body mass). However, we believe that it is unrealistic to think that any optimal training program (resistance, exercises, sets, repetitions, length of rest intervals, total workload) will ever be developed for maximizing BMD. The best that can occur is some minimal levels to achieve the desired changes. However, even these recommendations are imprecise. For example, despite the various training protocols used in the studies included in this meta-analysis, the deletion of each study once from the analysis had little effect on the overall results. Thus, the best recommendation we can make at this time is to adhere to the general principles of specificity and overload when prescribing resistance training programs aimed at maintaining and/or improving BMD.[5]

Although it is encouraging that resistance training seems to have positive effects on BMD at the lumbar spine, femur, and radius, the clinical importance of such small effects is not known, especially as it relates to fracture risk. We are not aware of any randomized trial(s) that have proven that resistance training reduces the risk of fracture. However, it may be that other factors contribute to increases in bone strength and subsequent reductions in fracture risk. For example, a recent animal study[71] found that mechanical loading improves bone strength by reshaping the bone structure with no apparent increase in BMD. Thus, resistance training may have a similar effect in humans.

Because most of the studies included in this meta-analysis examined the efficacy (does the treatment

work?) of resistance training for enhancing BMD in women, the effectiveness (does the treatment work in the real world?) of such an intervention could be questioned. This may be especially important given the fact that in the United States only 16% of people between the ages of 18 and 64 yr report regular participation in progressive resistance exercise.[72] It may be that other forms of therapy (calcium and/or vitamin D supplementation, hormone replacement therapy, selective estrogen receptor modulators, bisphosphonates) not only have a greater impact on BMD, but they also reduce the risk of fracture. For example, a recent meta-analysis[73] examined over a 3-yr period the effects of 10 mg of alendronate on BMD in osteoporotic women between the ages of 42 and 85 yr. The authors reported increases in BMD of 8.8% at the spine, 7.8% at the trochanter, and 5.9% at the femoral neck. The estimated cumulative incidence of nonvertebral fractures after 3 yr was 12.6% in the placebo group and 9.0% in the alendronate-treated group. It was concluded that administration of alendronate reduces the risk of nonvertebral fractures in osteoporotic postmenopausal women. Given the former, resistance training in conjunction with other types of nonpharmacologic and/or pharmacologic therapy may be most appropriate, especially for those women with osteoporosis.

Implications for Research

One of the surprising findings of this study was the fact that changes in BMD were greater in studies of higher quality. It is generally believed that studies of higher quality yield less positive results than studies of lower quality. For example, a recent study,[74] using the same quality rating scale as ours, examined the impact of study quality on outcomes in placebo-controlled trials of homeopathy. These authors[74] concluded that studies of higher methodologic quality produced less positive results. However, it may be possible that trials with good designs reduce random variability and allow the intervention to produce a larger ES. This may have been the case with our investigation.

The fact that we included both randomized and nonrandomized controlled trials in our study could be questioned. It is generally felt that randomized trials yield results that are more conservative when compared with nonrandomized trials. However, because we did not find a statistically significant difference between any of our outcomes when the data were partitioned by study design, we felt it was appropriate to include both in our analysis.

Although it is important to conduct many statistical tests when performing a meta-analysis, some of our statistically significant results may have been the result of chance vs. any real effect. However, we believe that a greater risk existed of committing a type 2 error if Bonferroni adjustments were made to our data. Thus, our data were analyzed without any type of Bonferroni adjustments.

Although some may feel that the inclusion of dissertations and master's theses which have not been published as journal articles is inappropriate because they lack the same "rigor," we believe that it is critical, given appropriate resources, to include such because of the reported publication bias that has been shown to exist in the literature.[75, 76] For example, Stern and Simes[76] found that approximately 96% of selected psychology journals and 85% of selected medical journals published studies that yielded a statistically significant result. The inclusion of unpublished data represents a feeling that is shared by the majority of meta-analysts and methodologists, as a study by Cook and colleagues[77] has shown that approximately 80% feel that unpublished material such as dissertations and master's theses should definitely or probably be included in scientific overviews.

Despite the knowledge that studies can be more objectively evaluated using the meta-analytic vs. traditional, narrative approach, potential problems still exist. In general, the very nature of meta-analysis dictates that the meta-analysis itself inherits those limitations that exist in the literature. Therefore, the meta-analyst must point out these limitations and provide directions for future research. One of the common problems in meta-analysis is the issue of missing data for outcomes other than the primary ones of interest. For example, the fact that insufficient data were available to perform subgroup analysis on BMD at different lumbar and radius sites could have impacted our results. Although the inability to compare BMD at different lumbar and radius sites was more a function of a lack of sample size vs. the absence of reporting such information, additional studies directed at these sites would seem appropriate. In addition, we would suggest that future studies dealing with the effects of resistance training on BMD in women do a better job of assessing and reporting on the dietary habits of their subjects as well as the types of pharmacologic interventions that these subjects may be taking. Furthermore, because few studies included an assessment of the alcohol and calcium intake of the subjects, greater attention to these in the future seem warranted. It is also recommended that future studies include an evaluation of their data using both an analysis-by-protocol as well as an intention-to-treat approach. As a result, one may examine both the efficacy and effectiveness of resistance training for enhancing BMD in women. This will help provide clinicians with more meaningful information regarding the use of resistance training for enhancing BMD in women. Additional information regarding appropriate study design when examining the effects of exercise on BMD may be found in the excellent review of Snow

et al.[78] Finally, it would seem plausible to suggest that a need exists for a large randomized trial that examines the effect of resistance training on both BMD and fracture risk. However, a trial of this nature may never be successfully conducted.

In conclusion, the results of this meta-analysis suggest that resistance training has a positive effect on the BMD of all women at the lumbar spine, and in postmenopausal women at the femur and radius.

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