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The effect of physical exercise on bone density in middle-aged and older men: A systematic review

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ABSTRACT

Although trials have shown that exercise has positive effects on bone mineral density (BMD), the majority of exercise trials have been conducted in older women. The aim of this study was to systematically review trials examining the effect of weight-bearing and resistance-based exercise modalities on the BMD of hip and lumbar spine of middle-aged and older men. Eight electronic databases were searched in August 2012. Randomised controlled or controlled trials that assessed the effect of weight-bearing and resistance-based exercise interventions on BMD measured by dual-energy x-ray absorptiometry (DXA), and reported effects in middle-aged and older men were included. Eight trials detailed in 9 papers were included. The interventions included walking (n=2), resistance training (n=3), walking + resistance training (n=1), resistance training + impact-loading activities (n=1), resistance training + Tai Chi (n=1). Five of the 8 trials achieved a score of less than 50% on the modified Delphi quality rating scale. Further, there was heterogeneity in the type, intensity, frequency and duration of the exercise regimens. Effects of exercise varied greatly among studies, with 6 interventions having a positive effect on BMD and 2 interventions having no significant effect. It appears that resistance training alone or in combination with impact-loading activities are most osteogenic for this population, whereas the walking trials had limited effect on BMD. Therefore, regular resistance training and impact-loading activities should be considered as a strategy to prevent osteoporosis in middle-aged and older men. High quality randomised controlled trials are needed to establish the optimal exercise prescription.

Keywords: Exercise · Men · Bone · Osteoporosis · Aging · Systematic review

INTRODUCTION

With the aging of the population, developing safe and effective strategies to prevent osteoporosis and consequent fractures is of great importance. The mechanisms that underpin bone mineral density (BMD) decline following peak bone mass are multifaceted and complex in nature. Although changes in sex hormones, nutrition and bone-loading are responsible for bone loss across the lifespan in males and females, important gender-specific differences exist [1, 2]. The decline in bone mass in men up to the age of 50 and in premenopausal women is approximately 0.3 to 1.1% per year [3], with an accelerated rate of bone loss in women for four to eight years following menopause [4] due to oestrogen withdrawal. During this period, women will lose approximately 15% in BMD or 1 standard deviation (SD), leading to a 1.5-to 3-fold increase in fracture risk [5, 6]. In contrast, the decline in bone mass for men is more gradual with an age-related loss of ~0.7% per year after age 50 [3]. Nonetheless, approximately one third of all osteoporotic fractures are accounted for by middle-aged and older men [7] and so understanding the role preventative strategies (for example exercise) may have in attenuating the bone loss experienced by men in this age group is of great importance.

Regular physical exercise has been recommended as a low-cost and safe non-pharmacological strategy to counter the loss of bone mass that accompanies aging. The principles of effective bone loading are somewhat unique compared to the exercise response of other body systems such as the muscular or cardiovascular systems. It has long been established that to improve bone density, bone tissue must be subjected to mechanical loading above that experienced in daily activities [8]. Mechanical loading should be dynamic, novel and involve high strain magnitudes and rates resulting in substantial overload [8, 9].

To date, the effects of exercise on the skeleton have been examined predominantly in pre- and post-menopausal women [10-17] due to the higher rates of osteoporosis in women than in men. Reviews of these exercise trials indicate that, in women, the combination of high-impact loading exercises and moderate to high intensity resistance training is the most beneficial to prevent age-related bone loss [13-15, 17, 18]. However, older women not only have different rates of bone loss compared to older men, but during menopause the skeleton's response to loading is dampened [19] due to the reduced sensitivity of bone cells [20]. Consequently, the response of bone to exercise is dissimilar between middle-aged men and women during the first few years following the onset of menopause [21].

As the burden of osteoporosis in men is becoming increasingly recognized [22], a small but growing number of exercise interventions have been trialled in men. Recent reviews of the effect of exercise on the BMD of male and female adults [23] and older adults [18] have focused on the effects on BMD in women. To our knowledge, only one review by Kelley and colleagues [24] has exclusively focused on the effect of exercise interventions on BMD in men. Of the eight interventions included in the review [24], only two used dual x-ray absorptiometry (DXA) to measure BMD of middle-aged or older male participants, while the remaining studies recruited exclusively younger participants or used other methods to assess BMD. The authors [24] concluded that exercise may help improve or maintain bone density, but that more trials were required to confirm the benefits in men. However, the review by Kelley et al. [24] was published over a decade ago and therefore an updated review of the effects of exercise on the bone health of middle-aged and older men is warranted.

Moreover, there is some discrepancy between the conclusions of bone and exercise reviews [17, 18, 23] and recent international practice guidelines for osteoporosis in men [22]. These new guidelines recommend activities such as walking as a preventative strategy for osteoporosis despite an apparent lack of supporting evidence from randomized controlled trials. Whilst walking is beneficial for an array of health outcomes, its prescription as a stand-alone osteoporosis prevention strategy is inconsistent with the current American College of Sports Medicine (ACSM) position stand on physical activity for bone health [25].

With an aging population and thus an increasing prevalence of osteoporosis in men, there is a growing urgency for health professionals to develop evidence-based exercise guidelines for men. Therefore, the aim of this systematic review was to examine both the findings and the study quality of exercise trials examining the effect of weight-bearing and resistance-based modalities on BMD of the hip and lumbar spine in middle-aged and older men.

METHODS

Literature search

We conducted searches in the databases PubMed, EMBASE (via EMBASE.com), CENTRAL (Cochrane Central Register of controlled trials), PEDro and SPORTDiscus in August 2012. Search terms included combinations of thesaurus terms (MeSH in PubMed, CENTRAL, EMtree in EMBASE) and free text terms. Free terms for exercise (‘resistance*training’, ‘strengthening’, ‘exercise’, ‘weight*lifting’, ‘weight*bearing’, ‘jump*’, ‘bounding’, ‘skipping’, ‘hopping’, ‘impact*loading’, ‘high*impact’, ‘running’, ‘stair*climbing’, ‘jogging’, ‘walk*’, ‘leap*’, ‘weight*training’, ‘resistance’, ‘strength’) were used in AND-combination with the search terms expressing the target population (‘men’, ‘adults’, ‘patients’, ‘participants’, ‘subjects’, ‘people’, middle*aged’, ‘aged’, ‘aged, 80 and over’) and search terms representing bone density (e.g. ‘bone*density’, ‘bone*strength’, ‘bone*mass’, ‘bone*mineral’, ‘bone*tissue’, ‘metabolic*bone*disease’). In PubMed, search results were limited by search terms indicating specific study designs (e.g. ‘trial’, ‘random’, ‘intervention’, ‘pilot*study’). The complete list of search terms is available on request.

Inclusion criteria

The inclusion criteria were: 1) design: randomized controlled trials (RCT) or controlled trials (CT); 2) population: middle-aged or older men (45 years and older). Studies in middle-aged and older men and studies including men and women in which results for men and women were reported separately were eligible for inclusion; 3) intervention: any exercise protocol involving resistance training only, impact loading exercise only, weight-bearing aerobic exercise only or a combination of these types of exercise; and 4) outcome: bone mineral density (BMD, g/cm^2) of the lumbar spine, Ward’s triangle, trochanter, proximal femur, femoral neck or total hip measured by DXA. Only full-text articles were included and no restrictions were placed on the language of the article. Titles and abstracts of articles identified through the search process were reviewed first by K.A.B to exclude articles out of scope. Subsequently, K.A.B., J.G.Z.v.U. and D.R.T. independently reviewed the full texts of all potentially relevant articles for eligibility. Disagreements were discussed and resolved. Articles that met the inclusion criteria were also examined to ensure that the same subjects were not included in more than one article based on data from the same study. Reference lists of eligible articles were manually checked for additional references.

Quality assessment and data extraction

Data on the study population, exercise programs, and outcome measures were extracted independently by two authors (K.A.B. and D.R.T.). On the basis of program descriptions in the individual studies, programs were qualified by an exercise physiologist as weight-bearing aerobic, strength training, impact-loading exercise or a combination thereof. Methodological quality of the included reviews was independently determined by 2 of the 3 authors (K.A.B. and D.R.T. or J.G.Z.v.U.) using the Delphi list developed by Verhagen et al. [26]. This list consists of 9 quality criteria assessing different methodological aspects. Two of the 9 criteria (i.e. blinding of the trainers and blinding of the participants) were not appropriate for the type of interventions we were reviewing and these items were excluded. Thus, quality of included studies was examined using a 7 item quality rating list [26, 27].

1. Was the method of randomization performed?

2. Was the treatment allocation concealed?

3a. Were the groups similar at baseline regarding the most prognostic indicators?

3b. If groups weren't similar at baseline, was this adjusted for in the analyses?

4. Were the eligibility criteria specified?

5. Was the outcome assessor blinded?

6. Were point estimates and measures of variability presented for BMD?

7. Did the analysis include an intention-to-treat analysis (ITT) (defined as all of participants randomised were included in analysis)?

All criteria were equally rated using a "yes" (1), "no" (0), or "unclear" (0) answer format and a quality score was generated as a percentage of the maximum score for each included study.

RESULTS

The systematic search resulted in 3106 records; details of the search process are shown in Figure 1. Abstracts of 3106 articles were initially reviewed. After removing articles out of scope the full text of 42 articles was independently checked for eligibility. Thirty-three articles were excluded. Checking the reference lists of eligible articles did not result in additional articles. Nine articles from eight studies met the inclusion criteria [28-36]. One intervention was described in 2 articles, but with different durations of intervention [30, 31] . Both articles are included and are considered as the 1 intervention.

Quality assessment

The results of the methodological quality assessment are presented in Table 1. Quality scores ranged from 29% to 100% with 3 of the 8 studies scoring over 50%. Although 6 of the included studies were RCT's, randomisation was not concealed in two of these RCTs. Methodological aspects that were not scored positively in most of the 8 included studies were reporting of point estimates (included in 1 study [30, 31]), blinding of the outcome assessor (included in 3 studies [28, 30, 31, 33]), and conducting an ITT analysis (included 4 studies [30-33, 36]). All of the studies scored well for group similarity at baseline [28-36] and 5 of the 8 specified eligibility criteria [28-32, 35].

Study population and exercise programs

Characteristics of the study participants and exercise programs are shown in Table 2. Participants in the studies were middle-aged and older men predominantly from non-clinical populations but one study included heart transplant patients on glucocorticoid treatment [36]. Sample sizes ranged from 11 to 147 men, with participants aged 50 to 79 years. The duration of the programs ranged from 3 months to 4 years (mean 13 months) with DXA assessments at the start and after completion of the exercise programs. In the heart transplantation study, Braith and colleagues [36] also measured the BMD of participants 2 months prior to commencing the exercise intervention to assess the impact of glucocorticoid therapy following transplantation. Changes in BMD over the initial 2 months prior to exercise are also reported in Table 2. Of the eight exercise programs 2 included walking only, 3 included resistance training only, 1 included walking and resistance training, 1 included resistance training and impact-loading activities, and 1 included resistance training and Tai Chi. The majority of the programs prescribed 3 exercise sessions a week (ranging from 2-5 each week). The prescribed intensities of the interventions varied greatly. Within the trials that included resistance exercises, intensity in all but 1 of the inventions used individualised intensities; percentage of 1-RM [30, 31] where RM or repetition maximum is the maximum amount that can be moved or lifted one time only, 8-RM [29] or 5-15-RM [35]. The exception was the study by Woo et al. [28], who did not report intensity but instead the participants were supplied with a medium strength elastic band (Theraband) for resistance. The 2 trials involving aerobic exercise required the participants to walk at a brisk pace corresponding to 40-60% of their maximal oxygen uptake (VO_2 max) [34] or their lactate threshold [33]. The jumping program in the trial by Kukuljan and colleges [30, 31] required the participants to perform impact-loading activities with ground reaction forces (GRFs) ranging from 1.5 to 9.7 times body weight.

Four of the 8 trials were supervised and in the majority of cases this was by exercise specialists/exercise physiologists. In addition to an exercise specialist, in the trial by Menkes and colleagues [35] registered nurses and physical therapists were the supervisors. Three of the studies did not report if the sessions were supervised [28, 32, 33] and 1 was unsupervised [34]. Machine and free weights were used in all of the resistance training protocols with the exception of the 1 trial that used elastic bands [28]. No equipment was used by the participants in the walking interventions while the impact loading intervention used boxes and benches [30, 31]. While all of the 8 studies included control groups, only 4 described the instructions given to these participants and these were poorly detailed [28, 29, 34, 36]. Braith et al. [36] compared their intervention with a post-operative walking program, Huuskonen et al. [34] advised the control group participants to make their personal choice whether to engage in physical activity or not, Whiteford and colleagues [29] provided their control group with education and advised them to walk 30 minutes 3 days per week, and Woo et al. [28] reported that the control group was not prescribed any exercise.

Reported findings

The effects of the interventions on BMD are shown in Table 2. BMD of the lumbar spine was reported in 7 of the 8 studies [28, 29, 31, 32, 34-36]. In addition, femoral neck BMD was reported in 5 [29, 31, 32, 35, 36], total hip BMD in 3 [28, 29, 31], trochanteric BMD in 3 [29, 31, 32], both Ward's triangle [32] and proximal femur BMD in 1 [34], while Paillard and colleagues [33] reported only that they measured hip BMD.

The greatest between group change in BMD was in the trial by Braith et al. [36] among heart transplant patients. The only study to include high-impact loading exercise or high-velocity power resistance training in their trial was Kukuljan et al. [31]. Although there were significant increases in BMD in most of the resistance training programs, the study by Kukujan et al. was the only trial to report a significant difference in BMD (femoral neck) between the exercise and control group following the intervention period. Both the exercise and control group lost BMD in the trials by Paillard et al. [33], Ryan et al. [32] and Whiteford et al. [29] with the exception of the increase in femoral neck BMD of the exercising group in the study by Ryan et al. [32]. Importantly, although not statistically significant, the exercise groups all lost less BMD than the control groups, in all but one of the studies [28].

Conversely, in the trial by Woo et al. [28] total hip BMD of those in the elastic band resistance group declined more than individuals in the control group, although lumbar spine BMD of the control and exercise groups increased. Between group differences for 2 of the studies [34, 35] could not be calculated because numerical data were not reported in these papers.

Dropout, attendance and adverse events

Four of the 8 studies reported no dropouts from the control or exercise groups [32, 33, 35, 36]. Of the trials that did report dropout the average rate was 3.3% [28, 29, 31, 34]. For the 4 studies [28-31, 35] who reported dropout by group, the overall dropout rates were 6.8% and 2.1% for the exercise and control groups, respectively. Reason for drop out included personal reasons [29, 34], death of participants [34], illness [29, 31], or work and personal commitments [29, 31]. Only 4 of the 8 studies reported attendance rates [28-31, 35]. Six of the 8 studies did not include or report any adverse events [28, 32-36]. In the 2 studies that did, Kukuljan and colleagues [30, 31] noted that although there were no serious or adverse events associated with their exercise regimen (exercise only and the exercise and milk groups), a number of medical complaints occurred. These included exacerbation of longstanding gout of the foot (n=1), aggravated knee or hip pain (n=2), lower back injury (n=2), aggravation of a long standing shoulder injury (n=2). In addition 3 men suffered an inguinal hernia. All of these men were able to continue with the program except for one man whose longstanding lower back injury caused him to withdraw from the trial. Similarly, Whiteford et al. [29] noted the following as reasons given for withdrawal from their resistance training program: bypass surgery (n=1), fracture of a thoracic vertebra (n=1), hip replacement (n=1), depression (n=1), hip problems (n=1), chronic illness (n=1), moved (n=3), and personal reasons (n=7). These reasons were not reported as adverse events associated with or as a result of participation in the resistance training program. Five men in the trial by Whiteford et al. [29] withdrew from the control group due to depression (n=1), moved away from the study location (n=3), or for personal reasons (n=1).

DISCUSSION

The purpose of this systematic review was to investigate the effects of exercise on hip or spine BMD in middle-aged and older men. Following a search of the literature, we identified 8 intervention studies reported in 9 journal articles that met the inclusion criteria. The results from this review support the findings of similar reviews in pre- and post-menopausal women, that resistance training and high-impact loading activities are more likely to induce positive effects on the BMD of weight-bearing skeletal sites than walking, which is relatively low-impact. Nevertheless, the optimal exercise prescription for middle-aged and older men cannot be determined from the results of the trials in this systematic review due to variations in reported BMD changes and in the design of the exercise programs, and the relatively poor methodological quality of a number of the trials.

Five of the 8 trials achieved a quality rating score of less than 50% on the modified Delphi rating scale, and therefore caution should be taken when interpreting the results of these studies due to their methodological quality. Further, essential information regarding methodological quality was missing in all included studies, even if the trial itself was methodologically sound, and for all but one of the studies it was necessary to request further information from the authors.

Of the studies scoring higher on the Delphi quality rating scale, only Kukuljan and colleagues [30, 31] scored positively on all methodological items. Their trial of resistance training and high-impact loading exercise was also the only trial to find significant between group effects at the femoral neck favouring the exercise group. However, this significant difference between the exercise and control group was not mirrored at the other measured sites (lumbar spine or total hip). Woo et al. [28] who scored the second highest quality rating reported that there was no significant differences between the groups at either the spine or hip site although only elastic bands were used as the resistance. Whiteford et al. [29] who scored 57%, also found no significant differences in BMD between the resistance training and the control groups following the intervention. All but 1 of the trials [34] that scored less than 50% reported that exercise had a positive effect on BMD. It is important to note that 2 of the 4 exercise interventions that reported significant within group improvements in BMD allowed participants to choose their group allocation. This non-random allocation may have been a further confounding factor within these studies and results from these 2 trials should be interpreted cautiously. Methodological aspects that should be improved in future studies include providing point estimates and measures of variability, blinding the outcome assessor, concealing the treatment allocation and including an intention to treat analysis. It is important to describe this well in future studies, so that readers can appropriately appraise the quality of the study.

In addition to methodological quality and reporting, the appropriateness of the design of exercise trials must be considered when drawing conclusions from the results. Only 4 of the 8 studies [28-31, 35] recorded and reported attendance rates of the exercise groups. Further, none of the 8 studies reported adherence, which should not be confused with attendance. A participant can attend an exercise session but might not adhere to the exercises as prescribed in terms of intensity, etc. The fact that this was not consistently reported in the studies included in this review is an important limitation, which could have resulted in an underestimation of the true effect of exercise on BMD if attendance and adherence rates were low. Consequently, we strongly suggest that both attendance and adherence rates be reported in future intervention studies examining the effect of exercise on BMD. In addition, improvements in bone density are relatively modest with exercise and occur over a prolonged period of time due to the length of the remodelling cycle [25]. A recent review of exercise regimens [18] showed that exercise regimens that were effective in improving the BMD of women were commonly 12 months or longer in duration. In the current review, only 4 of the 8 trials [28-31, 34] were 12 months or more in duration and therefore the results from trials of shorter duration may not accurately reflect the effect these exercise modalities may have on BMD and must be interpreted with caution.

It is also well established that the intensity and novelty of the load are two of the most important training characteristics that influence the effect of exercise on bone [37]. Bone adapts to habitual loads and without progressing the intensity of the mechanical loads with exercise, BMD will likely be maintained rather than improved [38]. Despite this, the intensity of the exercise programs was not progressed in 3 of the 8 trials [28, 33, 34]. Furthermore, the rate of progression in the 5 studies that did include progression was generally lacking in details. Given the importance of progression rather than customary loads to bone adaptation, researchers should aim to make intensity progression a focus when developing new protocols. Less is known about the optimal frequency of exercise for bone health. A recent randomised controlled trial in women by Bailey and colleagues [39] found that brief bouts of impact loading exercise were more beneficial when completed daily than 4 days a week. While both of these frequencies induced increases in bone density, those in the group that exercised 2 days a week saw no change in their BMD and the control group (no exercise) lost BMD. Five of the 8 protocols in this systematic review required participants to exercise 3 days each week. Therefore it may be the case that the frequencies of these studies were not optimal for improving bone health. However, compliance to exercise sessions is an important public health issue and in light of the already low levels of physical activity participation amongst the population, the challenges associated with asking individuals to exercise daily are significant. Trials that further our understanding of the dose-response relationship between exercise and bone are certainly required, particularly in men.

In comparison to the considerably larger number of exercise studies in middle-aged and older women, the existing comparable studies in men are generally shorter in duration and have fewer participants. Furthermore, a greater number of impact-loading exercise interventions have been conducted in women than in men. Although the results from the trials examined in this systematic review are similar to the existing literature in pre and post-menopausal women [18, 40, 41], further trials in middle-aged and older men are warranted.

Only 5 of the 8 studies included the participants' level of exercise participation in their exclusion criteria. Ryan et al. [32] and Menkes et al. [35] stated that regular exercise participation was part of their exclusion criteria but did not define the levels of participation that were acceptable. Woo et al. [28] stated that eligible subjects could not be participating in Tai Chi or resistance training at the time of entering the study, which does not capture past exercise participation. Similarly, Whiteford et al. [29] specified that the participants should not be participating in "brisk walking", however, like Woo et al. [28] their inclusion criteria did not capture the participants' level of exercise on entry into the study, nor did it exclude regular walkers exercising at lesser intensities. Given that bone adapts favourably to a novel stimuli, failing to assess and control for the participants' current level of exercise participation may explain different responses to a particular exercise modality. Further, only 3 of the 8 interventions reported the calcium levels of the participants [29-31, 34] and fewer still also reported vitamin D status [30, 31]. Given the important roles of calcium and vitamin D in bone metabolism [42], it would be prudent to suggest that data on calcium and vitamin D levels should be included in future exercise trials. The exclusion criteria developed by Kukuljan et al. [31] were highly specific and thus more clearly described the study population. Future studies should aim to include this level of detail when designing and reporting the details of trials.

Results of recent meta-analyses of different exercise modalities (aerobic, resistance training and impact-loading) on BMD in post-menopausal women [43-45] support the findings of the current review in that the effect of exercise on bone density of older adults appears to be modality and intensity-dependent. Specifically, it appears that resistance training alone or in combination with high-impact loading activities, has the potential to attenuate or reverse the decline of BMD in middle-aged and older men. Including resistance training would also result in improved physical function [46] and a reduction in falls risk due to increased muscle strength, therefore reducing the risk for fracture [47]. While men should engage in regular walking due to its positive effect on cardiovascular, metabolic and psychosocial health, the evidence from this review does not support the inclusion of walking alone in exercise recommendations for the targeted prevention of osteoporosis in middle-aged and older men. This finding is supported by the results of recent reviews that indicated that walking alone was not effective in increasing the bone density of older women [43, 44]. Nevertheless, a trial in peri-menopausal women indicated that bone density at the femoral neck was maintained following a program of brisk walking and jogging [45]. Further, brisk walking has been shown to have a positive effect on hip and spine BMD of post-menopausal women [46, 47]. Although it would seem prudent to suggest that men may also benefit from brisk walking, future trials are needed to confirm this recommendation. Consequently, recent guidelines for osteoporosis in men [22] that have recommended walking alone as an osteoporosis prevention strategy are not consistent with the current evidence base on the effect of exercise on BMD in men.

While there is a need to determine the optimal exercise prescription for "healthy" older adults, clinical populations at risk for bone health issues may have the most to gain from undertaking an appropriate osteogenic exercise program. One of the 8 trials in this review was conducted in heart transplant patients, receiving glucocorticoid treatment which has a deleterious effect on bone [48]. The extent to which exercise improved the bone density in this clinical group of patients was most likely due to the rapid rate of treatment-related bone loss immediately prior to the exercise intervention. Hence these noteworthy changes in BMD are clearly not replicated in healthy men of a comparable age. Despite this, these positive effects are in accordance with results of trials involving clinical populations similarly at risk of accelerated rates of bone loss such as men receiving androgen suppression therapy for prostate cancer [49] and women with breast cancer [50, 51] and thus would support the inclusion of exercise training as an adjuvant therapy for individuals at risk of experiencing treatment-related bone loss. Despite the great potential exercise may have in managing treatment-related side-effects, further trials are needed to determine the optimal exercise prescription for at risk clinical populations.

While resistance training alone or a combination of resistance training and high-impact loading activities appear to be safe and effective in preventing or reversing age-related bone loss in middle-aged and older men, the optimal frequency, session duration, intensity and exact exercise combination cannot be determined from the results of this systematic review. In comparison to the large number of exercise trials in women, osteoporosis prevention exercise trials in older men are sparse. Accordingly, the authors of the ACSM physical activity and bone health position stand [25] have based their recommendations for older adults predominantly from the results of trials in women. We propose that before the optimal exercise prescription to prevent osteoporosis in middle-aged and older men can be prescribed, methodologically robust, long-duration randomised controlled trials in this population are required. Given that gender-specific factors influence bone metabolism, where trials recruit men and women, analysis should be conducted by gender. Trials in this area are logistically challenging due to attrition, adherence and the high costs of undertaking relatively long-duration interventions, however, given the aging of the population and the proportion of men potentially at risk for osteoporosis, efforts to address the osteogenic exercise requirements for men are urgently required.

This systematic review has several limitations which are worthy of comment. First, our analysis includes only data from published studies and the possibility exists of missing relevant unpublished trials. Second, the relatively small number of participants in a number of these studies may limit the ability to detect a statistically significant difference between the intervention and control groups, and this should be considered when interpreting the results of these studies. As a result, it is strongly suggested that statistical power calculations be included in reports of future intervention studies. Third, many of the studies included in this review did not report the post-intervention scores or post-intervention data were not available. In addition to this, due to the heterogeneous nature of the included exercise protocols and the variation in BMD measurement sites, a meta-analysis was not performed. Lastly, it must be noted that using BMD as measured by DXA is a further limitation of this review due to concerns regarding the inherent inaccuracies of this method of measurement and its inability to provide information regarding important determinants of bone strength (size, shape and structure) [52]. Consequently, there is growing interest in using quantitative computed tomography (QCT) to assess bone strength and researchers should aim to use this method to assess the effects of exercise interventions on whole bone strength where possible. To the best of our knowledge only 1 exercise trial has used QCT to assess bone strength in middle-aged and older men [31]. While there is a possibility that some studies were missed in the literature search, it is more likely that the small number of trials in this systematic review reflects the strong focus on preventing osteoporosis in women rather than in men.

Safety aspects

Although resistance training and impact-loading activities appear to be safe methods of exercise training, older adults should be carefully screened and supervised prior to and during exercise participation to ensure safety and correct technique. Where appropriate, clinicians should refer patients to appropriate health professionals, such as exercise physiologists or physiotherapists, trained to prescribe exercise for individuals with chronic disease and associated co-morbidities.

CONCLUSION

Results from this systematic review indicate that resistance training alone or in combination with impact-loading activities is safe and may assist in the prevention of osteoporosis in middle-aged and older men. However, due to the variation among studies as well as in study quality, additional high-quality randomized controlled trials in this population are required in order to establish evidence-based guidelines for the optimal exercise prescription. Nevertheless, for those individuals willing and able to perform physical exercise, regular resistance training and impact-loading activities should be considered as an effective strategy to prevent osteoporosis in middle-aged and older men.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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Figure 1. Search process flow chart

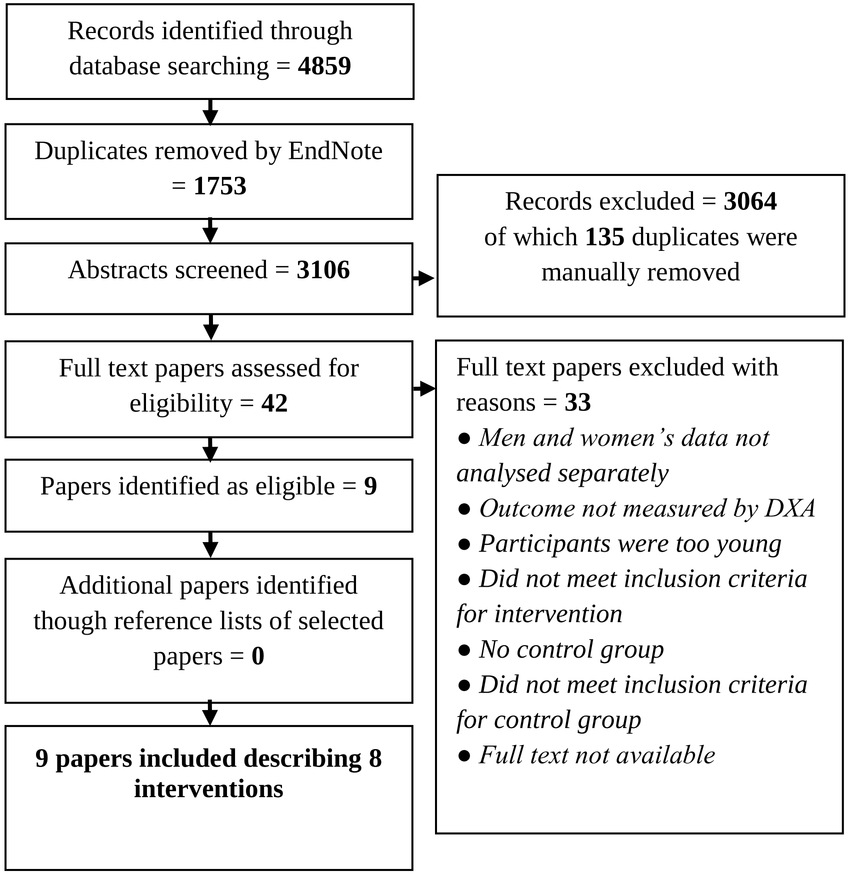

Table 1. Quality rating table

Author, Year	1 Randomization	1b Treatment Allocation concealed	2 Group similarity at baseline	3 Specified eligibility criteria?	4 Blinded outcome assessor	5 Point estimates and measures of variability	6 Intention to treat analysis	**Score**
1. Braith, et al. (1996)	Y	U	Y	N	U	N	Y	43%
2. Huuskonen, et al. (2001)	Y	Y	Y	N	U	N	N	43%
3a. Kukuljan, et al. (2009)** 3b. Kukuljan, et al. (2011) **	Y	Y	Y	Y	Y*	Y	Y	100%
4. Menkes et al, (1993)	N*	N	Y	Y	U	N	N	29%
5. Paillard, et al. (2004).	Y	U	Y	N	Y*	N	Y	43%
6. Ryan, et al. (1994)	N	N	Y	Y	U	N	Y	29%
7. Whiteford, et al. (2010).	Y	Y*	Y	Y	N*	N	N	57%
8. Woo, et al. (2007)	Y	Y	Y	Y	Y	N	N	78%
# papers scoring a point/total papers	6/8	4/6	8/8	5/8	3/8	1/8	4/8	

Y = yes, N = no, * = quality rated after requesting and obtaining additional information from the authors, U = unclear after requesting additional information from the authors, ** same trial, but different durations and papers, point estimates and measures of variability = between groups change and either standard deviation (SD), standard error (SE) or confidence intervals (CI).

Table 2. Study characteristics and outcomes

Study details Author (year) Country	**Study Design**	**Participants** (mean age ± SD, range (years))	**Exercise intervention** T: exercise type, equipment, exercises, ID: intervention duration, F: frequency, S&R: sets & reps, Int: intensity, SD: session duration, Sup: supervision, Att: attendance, Con: control	**Dropout number**	**Between groups change**	**Within groups change**
1. Braith, R. W., et al. (1996) [36] USA	RCT	Middle-aged men heart transplant patients on glucocorticoid treatment n = 16 Ex = 8 (56.0 ± 6.0) Con = 8 (52.0 ± 10)	**T:** 9 resistance training exercises, machines Lumbar extension (LE), chest press, knee extension, pullover, knee flexion, triceps extension, biceps flexion, shoulder press, abdominals + post-operative walking program (not described) **ID:** 6 months **F:** RT 2 days/wk, LE 1day/wk **S&R:** 1 set, 15 reps **Int:** 15RM **SD:** not reported **Sup:** yes, exercise specialists **Att:** not reported **Con:** post-operative walking program (not described)	Nil	**Pre- and post-intervention** LS 18.7% FN 6.9% **Pre-transplantation - post intervention** LS 17%† FN 5.5%†	**Pre and post transplantation** **Ex** LS -14.9%* FN -5.9%* **Con** LS -12.2% FN -4.5%* **Pre and post intervention** **Ex** LS ↑15.1% FN ↑4.1% **Con** LS -4.6%* FN -2.8% **Pre-transplantation and post intervention** **Ex** LS ↑0.2% FN -1.8%

						Con LS -16.8%* FN -7.3%
2. Huuskonen, J., et al. (2001) Finland	RCT	Middle-aged men n = 140 (53-62) Ex = 70 (58.2 ± 2.9) Con = 70 (58.1 ± 2.9)	**T:** Brisk walking, no equipment **ID:** 48 months **F:** 3days /wk → 5 days/wk **Int:** “brisk walking” → 40-60% of $\dot{V}O_2$max **SD:** 30-45 → 60 minutes **Sup:** not supervised **Att:** not reported **Con:** participants were advised to make their personal choice whether to engage in physical activity or not	4 died 4 dropped out (groups not reported)	LS ↔ Prox fem ↔	**Ex & Con** (numerical data not reported) LS ↔ Prox fem ↔
3a. Kukuljan, S., et al. (2009) Australia *Exercise + milk and milk alone groups not included in this review*	RCT	Middle-aged and older men n = 90 Ex = 46 (60.7 ± 7.1) Con = 44 (59.9 ± 7.4)	**T:** 6-8 RT exercises, machine and free weights, slow and controlled Squats or leg press, lunges, hip abduction and adduction, lat pull down or seated row, back extension, leg extension, calf raises, bench press, shoulder press, biceps curls triceps extension and lumbo-pelvic, spine and a combination of core muscle stabilization exercises + 3 IL exercises, benches and boxes (15, 30cm) Single and double foot multi-directional landings, bench stepping and jumping off boxes **ID:** 12 months **F:** 3 days/wk **S & R:** RT: 3 sets, 15-20 reps → 2 sets, 8-12 reps IL: 3 sets, 10-20 impacts → 90-180 impacts **Int:** RT: set 1, 2 & 3: 50-60%1RM → set 1: 60-65%1RM, set 2: 60-70% → set 1: 60-65%1RM,	Ex = 1 Con = 2	LS 1.5% FN 1.9% Tot hip 0.7% Tr 0.8%	**Ex** LS ↑2.1%* FN ↑1.7%* Tot hip ↑1.2%* Tr ↑1.6%* **Con** LS ↑0.6% FN -0.2% Tot hip ↑0.5% Tr ↑0.8%

			set 2: 80-85% IL GRF 1.5 to 9.7 x BW. Intensity increased by increasing height of jumps and/or adding more complex movement patterns **SD:** 60-75 minutes **Sup:** yes, qualified exercise trainers **Att:** 67% **Con:** not described			
3b. Kukuljan, S., et al. (2011) [31] Australia *Continuation-study 3a* *Exercise + milk and milk alone groups not included in this review*	RCT	Middle-aged and older men n = 90 Ex = 46 (60.7 ± 7.1) Con = 44 (59.9 ± 7.4)	*As 12 month study, with the exception of the following changes for month 13-18* **T:** high-velocity power based training (rapid concentric muscle contractions) **ID:** 18 months **Att:** 63%	Ex = 2 Con = 2	FN 1.9%† LS & Tot hip (unable to be calculated)	**Ex** LS ↑1.0% FN ↑1.1% Tot hip ↑0.3% **Con** LS ↑0.6% FN -0.8% Tot hip ↑0.2%
4. Menkes, A., et al. (1993) [35] USA	CT	Middle-aged and older men n = 18 Ex = 11 (59.0 ± 2.0 SE) Con = 7 (55.0 ± 1.0 SE)	**T:** 13 RT exercises, machines and free weights Upper body exercises (UB): Chest press, lat pull down, shoulder press, upper back row, seated triceps extension, seated dumbbell biceps curls Lower body exercises (LB): leg press, leg curl, leg extension, leg abduction, leg adduction, trunk extensions, modified sit-ups **ID:** 4 months **F:** 3 days/wk **S & R:** LB 2 sets, 15 reps; UB 1 set, 15 reps **Int:** 5RM-15RM **SD:** not reported **Sup:** registered nurse, physical therapist, exercise	Ex = 2 (Didn't want to complete BMD testing)	Numerical data not reported LS ↔ FN ↔	**Ex** LS ↑2.0%* FN ↑3.8%* **Con** (numerical data not reported) LS ↔ FN ↔

			specialists **Att:** 95% **Con:** "inactive controls" (not described)			
5. Paillard, T., et al. (2004) [33] France	RCT	Middle-aged and older men n = 21 (63-72) Ex = 11 (66 ± 2.0) Con = 10 (67 ± 2.0)	**T:** Brisk walking **ID:** 3 months **F:** 5 days/wk **Int:** individualized intensity corresponding to lactate threshold **SD:** 45-60 minutes **Sup:** not reported **Att:** not reported **Con:** not reported	Nil	Hip 2.1%	**Ex** Hip -1.2% **Con** Hip -3.3%
6. Ryan, A. S., et al. (1994) [32] USA	CT	Middle-aged and older men n = 37 Ex = 21 (61.1 ± 1.0 SE) Con = 16 (59.2 ± 2.0 SE)	**T:** 14 RT exercises, machines and free weights Leg press, chest press, leg curl, lat pull down, leg extension, shoulder press, leg adduction, leg abduction, upper back row, triceps press, lower back extension, upper abdominals, biceps curl, lower abdominals **ID:** 4 months **F:** 3 days/wk **S & R:** 1st set, 15 reps for all exercises 2nd set of 15 for leg press, leg curl and leg machine only **Int:** 5RM-15RM **SD:** not reported **Sup:** not reported **Att:** not reported **Con:** not reported	Nil	Ward's 1.4% Tr 1.5% LS, FN ↔ (unable to calculate, numerical data not reported)	**Ex** LS -0.1% FN ↑2.8%* Ward's -0. 2% Tr -0.1% **Con** LS, FN ↔ (numerical data not reported) Ward's -1.6% Tr -1.6%
7. Whiteford, J., et al. (2010) [29]	RCT	Middle-aged and older men	**T:** 8 RT exercises, machines and free weights Hip flexion, hip extension, hip abduction, hip adduction, calf raise, triceps pushdown, wrist	RT = 16 Con = 5	LS ↔ FN 0.3% Tr ↔	**RT** LS -0.1% FN -0.3%

Australia		n = 147 Ex = 73 (64.0 ± 6.0) Con = 74 (64.0 ± 6.0)	curl, reverse wrist curl, biceps curl, forearm pronation/ supination **ID:** 12 months **F:** 3 days/week **S & R:** 3 sets, 15 reps → 3 sets, 8 reps **Int:** 15RM → 8RM **SD:** 60 minutes **Sup:** qualified exercise physiologist **Att:** 71% RT group, active control not monitored **Con:** Participants were provided with education and advised to walk 30 mins/3 days per week		Tot hip ↔	Tr ↑2.2%* Tot hip ↑0.8%* **Con** LS -0.1% FN -0.6% Tr ↑2.2%* Tot hip ↑0.8%*
8. Woo, J., et al. (2007) [28] Hong Kong	RCT	Middle-aged and older men n = 90 (65-74) RT = 30 (68.7 ± 3.0) Tai Chi = 30 (68.2 ± 2.4) Con = 30 (68.07 ± 2.7)	**T:** 6 RT exercises, elastic bands Arm lifting, hip abduction, heel raise, hip flexion, hip extension, squatting dorsiflexion **ID:** 12 months **F:** 3 days/wk (RT and Tai Chi) **S & R:** 2 sets, 30 reps **Int:** medium strength elastic band (RT), not reported (Tai Chi) **SD:** not reported **Sup:** not reported **Att:** RT 76.3%, Tai Chi 81% **Tai Chi:** Yang style with 24 forms **Con:** "no exercise prescribed"	RT = 1 Con = 1	**Con v RT** LS 0.8% Tot hip 1.1%‡ **Con v Tai Chi** LS 0.9% Tot hip 0.3%‡	**RT** LS ↑1.3% Tot hip -1.2% **Tai Chi** LS ↑1.4 % Tot hip -0.5% **Con** LS ↑0.5% Tot hip -0.2%

Abbreviations: RCT, randomised controlled trial; CT, controlled trial; Ex, exercise group; Con, control; Reps, repetitions; wk, week; RM, repetitions maximum; RT, resistance training; →, progressing to; $\dot{V}O_2max$, maximal oxygen uptake; GRF, ground reaction force; UB, upper body; LB, lower body; IL, impact-loading; BW, body weight; BMD, bone mineral density (g/cm^2); LS, lumbar spine; FN, femoral neck; Tr, trochanter; Ward's, Ward's triangle; Tot hip, total hip; ↑, increase; ↔, no change reported; *, significant difference from baseline; †, significant difference between groups; ‡, greater BMD loss in exercise group than control group.