Author(s): Daly, Robin M.; Dalla Via, Jack; Fyfe, Jackson J.; Nikander, Riku; Kukuljan, Sonja

Title: Effects of exercise frequency and training volume on bone changes following a multi-component exercise intervention in middle aged and older men : secondary analysis of an 18-month randomized controlled trial

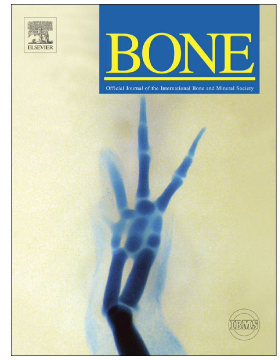
Year: 2021

Version: Accepted version (Final draft)

Please cite the original version:

Daly, R. M., Dalla Via, J., Fyfe, J. J., Nikander, R., & Kukuljan, S. (2021). Effects of exercise frequency and training volume on bone changes following a multi-component exercise intervention in middle aged and older men : secondary analysis of an 18-month randomized controlled trial. Bone, 148, Article 115944. https://doi.org/10.1016/j.bone.2021.115944

Journal Pre-proof



Effects of exercise frequency and training volume on bone changes following a multi-component exercise intervention in middle aged and older men: Secondary analysis of an 18-month randomized controlled trial

Robin M. Daly, Jack Dalla Via, Jackson J. Fyfe, Riku Nikander, Sonja Kukuljan

PII: S8756-3282(21)00106-X

DOI: https://doi.org/10.1016/j.bone.2021.115944

Reference: BON 115944

To appear in: *Bone*

Received date: 2 January 2021

Revised date: 1 March 2021

Accepted date: 30 March 2021

Please cite this article as: R.M. Daly, J.D. Via, J.J. Fyfe, et al., Effects of exercise frequency and training volume on bone changes following a multi-component exercise intervention in middle aged and older men: Secondary analysis of an 18-month randomized controlled trial, *Bone* (2021), https://doi.org/10.1016/j.bone.2021.115944

Effects of exercise frequency and training volume on bone changes following a multi-component exercise intervention in middle aged and older men: Secondary analysis of an 18-month randomized controlled trial

Robin M. Daly,[1] Jack Dalla Via,[1] Jackson J. Fyfe,[1] Riku Nikander,[2,3,4] Sonja Kukuljan, PhD [1]

[1] Institute for Physical Activity and Nutrition, Deakin University, Geelong, Australia

[2] Faculty of Sports Science, Gerontology Research Centre (Gerec), University of Jyväskylä, Finland

[3] Central Hospital of Central Finland, Jyväskylä, Finland

[4] GeroCenter Foundation for Aging Research & Development, Jyväskylä, Finland

Running Title: Dose-response effect of exercise on bone

Address for correspondence

Professor Robin M. Daly

Institute for Physical Activity and Nutrition

School of Exercise and Nutrition Sciences

Deakin University

221 Burwood Highway, Burwood

Melbourne, Victoria, AUSTRALIA 3125

Phone: +61 3 9244 6040

Email: rmdaly@deakin.edu.au

ORCID ID: 0000-0002-9897-1598

Emails:

rmdaly@deakin.edu.au

j.dallavia@deakin.edu.au

jackson.fyfe@deakin.edu.au

riku.p.nikander@jyu.fi

skukuljan@ffgl.com.au

Abstract

Progressive resistance training (PRT) combined with weight-bearing impact exercise are recommended to optimize bone health, but the optimal frequency and dose of training remains uncertain. This study, which is a secondary analysis of an 18-month intervention in men aged 50-79 years, examined the association between exercise frequency and the volume of training with changes in DXA and QCT-derived femoral neck (FN) and lumbar spine (LS) bone outcomes, respectively. Men were allocated to either thrice-weekly PRT plus impact exercise training (n=87) or a non-exercising (n=85) group. Average weekly exercise frequency (ExFreq) and training volume per session [PRT volume (weight lifted, kg), number of weight-bearing impacts (jumps completed) and total training volume] over the 18-months were calculated from the participants' exercise cards. Regression analysis showed that average weekly ExFreq and training volume per session were positively associated with the 18-month changes in FN BMD and LS trabecular volumetric BMD. Men completing on average 1 to <2 and ≥2 sessions/week had a 1.6 to 2.2% greater net gain in FN BMD relative to non-exercising men, while those completing ≥2 sessions/week had 3.9 to 5.2% net gain in LS trabecular vBMD compared to non-exercising men and those completing <1 session/week. Further analysis showed that the average number of impact loads per session, but not the average PRT weight-lifted, was positively associated with changes in BMD. Every 10 impact loads per session over 18 months was associated with a 0.3% and 1.3% increase in FN BMD and LS trabecular vBMD, respectively. In conclusion, this study indicates that exercise frequency and training volume were predictors of the changes in hip and spine BMD following a multi-component exercise program, and that the number of impact loads rather than PRT weight lifted per session was more important for eliciting positive skeletal responses in middle-aged and older men.

Keywords: Weight-bearing exercise; resistance training; dose-response; bone mineral density; older men

1. Introduction

Exercise is recommended to improve bone health and prevent osteoporosis and fractures, but not all forms are equally effective, with the skeletal responses being dependent upon the modality and dose of exercise prescribed, and adherence to the training. Several systematic reviews and meta-analyses of randomized controlled trials (RCT) in older adults have reported that multi-component exercise programs incorporating a combination of weight-bearing impact loading activities and progressive resistance training (PRT) are effective for maintaining or improving areal bone mineral density (aBMD) at clinically-relevant sites such as the hip and spine [1-4]. However, whether there is an optimal dose (frequency, volume, intensity or duration) of exercise needed to elicit positive skeletal responses in older adults remains uncertain.

In postmenopausal women and older men, there is evidence that relatively few weight-bearing impact loads (~10-100 jumps, 3-7 times per week) of moderate to high magnitude (>2-3 times body weight) or applied in novel/diverse directions can maintain or improve hip and spine aBMD [5-10]. For PRT, the most effective programs have been those which have included moderate- to high-intensity (70-85% of maximum strength) training performed at least twice weekly, incorporated the principle of progressive overload, and included specific exercises that targeted muscles attached to or near the hip and spine [11-14]. However, a meta-analysis of 53 trials in postmenopausal women reported mixed findings with regard to the effects of training intensity on changes in BMD [15]. At the lumbar spine, high intensity training, defined as PRT >80% of maximum for less than eight repetitions or impact activities >4 times body weight, was superior to low intensity training (PRT <65% of maximum for 16 or more repetitions or impact activities <2 times body weight) [15]. In contrast, low intensity and moderate intensity exercise (PRT 65-80% of maximum for 8-15 repetitions or impact activities 2-4 times body weight) were equally effective at the femoral neck, but only moderate intensity training was effective at the total hip [15]. Beyond training intensity, few human exercise intervention trials in older adults, particularly men, have examined whether there is a dose-response relationship in terms of the frequency of exercise training, or whether the actual training volume completed is associated with any subsequent changes in bone density, structure or strength. The findings from a 16-year non-randomized trial in early postmenopausal women that involved PRT with weight-bearing impact exercise training found that at least two exercise sessions per week was the minimum effective dose to positively influence BMD over the long-term relative to controls [16], but whether these findings can be generalized to other populations, including middle-aged and older men, is not known.

In an 18-month factorial design RCT in men aged 50 years and over, we previously reported that a multi-component exercise program incorporating moderate- to high-intensity PRT with weight-bearing impact exercises prescribed three days per week was effective for improving DXA femoral neck aBMD, cross-sectional area and section modulus, as an estimate of bone strength, and QCT lumbar spine trabecular volumetric BMD, but that providing additional calcium-vitamin D_3 fortified milk did not enhance the osteogenic response [17]. As part of this study, all exercises undertaken, the amount of weight lifted for each resistance training exercise, and the number of sets and repetitions completed for each resistance and impact exercise, were recorded for each session by all participants allocated to the exercise intervention. Therefore, in a secondary analysis the aims of this study were to examine whether there was an association between exercise training frequency (average sessions completed per week) and training volume per session [PRT volume (weight lifted, kg), number of impacts (jumps) completed and total training volume (sum of PRT volume and number of impacts)] with the 18-month exercise-induced changes in DXA and QCT-derived femoral neck and lumbar spine bone traits.

2. Materials and Methods

2.1 Study Design

This study is a retrospective analysis using data that was collected from the Geelong Exercise and Nutrition Training Study (GENTS), which was an 18-month factorial 2x2 RCT [17]. The primary aim of this study was to examine whether calcium-vitamin D_3 fortified milk could enhance the effects of a multi-component exercise program on areal BMD, bone structure and estimates of whole bone strength in middle aged and older men. As previously reported [17], 180 men were randomized to one of four groups: 1) exercise plus calcium-vitamin D fortified milk (n=45); 2) exercise alone (n=46); 3) calcium-vitamin D fortified milk alone (n=45); or 4) a control group (n=44), stratified according to age (<65 or ≥ 65 years) and dietary calcium intake (<800 or ≥ 800 mg/day). As reported elsewhere [17], there was no exercise by calcium-vitamin D interactive effects on any of the bone outcomes. Therefore, the current study focused on the positive effects of the exercise program on femoral neck and lumbar spine bone outcomes in which we calculated the exercise training frequency and training volume (PRT weight lifted, number of impact loads completed and the total training load) for the two exercise groups combined. The Deakin University Human Ethics Committee and Barwon Health Human Research Ethics Committee approved the study, and it was registered with the Australian and New Zealand Clinical Trials Registry (ACTRN12617001224314). All participants provided written informed consent prior to participation.

2.2 Participants and Screening

Middle aged and older men (age range 50-79 years) were recruited from within the local community in Geelong and surrounding areas, Victoria, Australia. As reported previously [17], men were excluded based on the following criteria: 1) use of calcium-vitamin D supplements within the past 12-months; 2) participation in resistance training in the past 12-months or high-impact weight bearing activities for greater than 30 minutes three times per week in the preceding 6-months; 3) BMI >35 kg/m^2; 4) a history of osteoporotic fracture or any medical condition or medication use known to affect bone metabolism; 5) lactose intolerance; 6) consumption of >4 standard alcoholic drinks per day; 7) current smokers; and 8) any chronic condition that might limit participation in the study.

A total of 451 men were initially screened via telephone, from which 296 were invited to have a DXA proximal femur aBMD scan to determine if their total hip or femoral neck T-score was between +0.4 and –2.4 SD (normal to below average BMD). A total 180 men met the inclusion criteria and were randomized to one of the four groups described above according to our statistician's computer generated randomisation of study numbers. All eligible men were required to obtain medical clearance from their local doctor to ensure that they were free of any contraindicated medical conditions to exercise. For this study, we included men allocated to the exercise training (exercise alone or exercise plus calcium-vitamin D) who had complete baseline and 18 months data (DXA femoral neck, n=87; QCT lumbar spine, n=85). As previously reported [17], four of the 91 men allocated to the exercise training withdrew from the study due to time (n=2) or illness (n=2). For the non-exercising controls (calcium-vitamin D alone and controls), 85 of the 89 men returned for the 18 months assessment (three withdrew due to time commitments and one withdrew as they were dissatisfied with their group allocation) and were included in this study (DXA femoral neck, n=85; QCT lumbar spine, n=79).

2.3 Intervention

Detailed information about the exercise intervention has been reported previously [17]. Briefly, participants randomized to the exercise program were assigned to one of four community leisure centres and asked to train on three non-consecutive days per week under the supervision of qualified exercise trainers. The training session were 60-75 minutes in duration and included PRT with core muscle stabilisation exercises, and a series of moderate to high impact weight-bearing activities. The 18-month periodised training program was divided into 12-weekly mesocycles, each with three, four-weekly microcycles in which the training was made progressively more challenging. During the first four weeks of the program, the exercise trainers supervised all exercise sessions to ensure correct lifting and landing techniques and to monitor the appropriate amount of exercise and rest intervals. Thereafter, participants received one supervised session per week to ensure ongoing personal support and attention to the training progressions. For the remaining two sessions, participants were able to seek assistance from local trained gymnasium staff when needed.

The PRT program was designed to be moderate-to-high in intensity and included a combination of free and machine weights. The key exercises used throughout the program focused on major muscle groups with attachments on or near the hip and spine. This included leg press, squats, lunges, hip abduction/adduction, latissimus dorsi pull down (or seated row), back extension and a combination of abdominal and core muscle stability exercises. Additional exercises that were rotated throughout the program to ensure the development of muscle was balanced included: leg extension, calf raises, bench press, military press, bicep curls, triceps extension and lumbo-pelvic and spine stabilisation exercises. During the first 12-week mesocycle (introductory phase), participants completed three sets of 15-20 repetitions at 50 to 60% of their one repetition maximum (1-RM) strength or a self reported rating of

11 to 12 ('fairly light') on the 20-point Borg Rating of Perceived Exertion (RPE) scale. Thereafter, the training volume was set at two sets of 8-12 repetitions at 60 to 85% of 1-RM or an RPE of 13 to 14 ('somewhat hard') progressing to 15 to 18 ('hard/very hard'). For the first 12-months, all training (exercises) was performed in a slow, controlled manner. For the final 6 months, the program progressed to high-velocity, power-based training in which the focus of the lower limb exercises was on performing the concentric (pushing) phase of each exercise as rapidly as possible. The weight-bearing impact exercises were specifically designed to load the lower extremities. For each 12-week mesocycle, 2-3 sets of 10-20 repetitions for three different impact exercises were interspersed between the resistance training exercises. The magnitude, rate, and distribution (direction) of loads (jumps) applied to the lower body were increased progressively throughout the program by increasing the height of jumps and/or by introducing more complex movement patterns. Some examples of the weight-bearing impact exercises included: marching, heel drops, squat/mini-tuck jumps, vertical leaps, side-to-side jumping/hopping, forward/lateral bench step-ups, forward/lateral jumps and drop jumps from a bench height of 15-30 cm. Any adverse events or injuries associated with the program were recorded by the exercise trainers and reported to the investigators.

2.4 Exercise Frequency and Training Volume

Exercise training frequency (average number of sessions completed per week over the 18 months) was derived from the participants exercise cards completed at each training session (and regularly checked by the exercise trainers) that were returned to the research staff every month. Total PRT volume for each participant was calculated from the weight lifted (in kg) multiplied by the number of repetitions performed for each exercise and then summed for each set completed across all the exercises throughout the 18-month intervention. The total number of impact loads undertaken for each participant was derived from the number of impacts (jumps) completed for each set across all exercises over 18-months. The results were then expressed as the average PRT volume (weight lifted) and average number of impacts completed per week or per session based on the number of weeks training (~80 weeks) or number of sessions prescribed (~240). To calculate the total training volume per session, it was not feasible to simply add the PRT volume with the number of impact loads per session due to the different units of measurement (kg versus number) and thus scaling. For instance, if summed, the PRT weight lifted contributed to the majority of the total training volume (e.g. 100 kg leg press x 10 repetitions x 3 sets = 3000 kg, compared to 20 vertical jumps x 3 sets = 60 impact loads). Therefore, to calculate each participant's total training volume per session, the average PRT volume and average number of impact loads per session were standardized by converting them into z-score, and then summed. This approach assumes that both PRT and impact loading were of equal importance in term of their potential influence on the changes in bone.

2.5 Measurements

Anthropometry and habitual physical activity

Height was assessed using a stadiometer, and weight was measured on a digital scale. Dietary calcium intakes were assessed using a 3-day food diary (2 weekdays and 1 weekend day) and analyzed using the Foodworks software program (Xyris Software, Brisbane, Queensland, Australia). Habitual weight-bearing activity outside of the exercise intervention (hours/week) was assessed using the Community Healthy Activities Model Program for Seniors (CHAMPS) activity questionnaire, developed and validated for use with older adults [18].

Bone mineral density, bone structure and strength and lean mass

The non-dominant proximal femur areal BMD (aBMD) and total body lean mass were assessed by DXA (Prodigy, GE Lunar Corp., Madison, WI, USA), with analysis software version 8.10.027. The Lunar Advanced Hip Analysis (AHA) program was used to calculate femoral neck cross-sectional area (CSA, cm^2) and section modulus (Z, cm^3) from the planar DXA scan as described previously [19]. The short term % coefficient and variation (%CV) and root-mean-squared (RMS) %CV for repeated measurements of femoral neck aBMD in 30 participants in our laboratory is 1.02% and 1.29%, respectively. Quantitative computed tomography (QCT) scans of the lumbar spine (L_1-L_3) were obtained using a Philips Mx8000 CT scanner (Philips Mx8000 Quad CT scanner, Philips Medical Systems, The Netherlands). The scan parameters were 120kVp and 50-100mAs. Four 2.5mm slices were obtained through the mid-portion of L_1-L_3, with the middle two slices at each site analyzed and averaged. All participants were scanned simultaneously with a fluid dipotassium hydrogen phosphate (K_2HPO_4) bone equivalent calibration phantom. L_1-L_3 trabecular volumetric BMD (vBMD, g/cm^3) were assessed using the Geanie 2.1 software program (BonAlyse Oy, Jyväskylä, Finland) using thresholds previously described [20].

2.6 Statistical Analysis

Statistical analyses were conducted using Stata Statistical Software, release 16.0 (Stata, College Station, TX). Baseline characteristics are reported as means with standard deviations (SD) or for non-normally distributed data, median with interquartile range (IQR). The 18-month change (absolute or percentage) results are reported as means with 95% confidence intervals (95% CI). To explore the association between exercise training frequency (per week) with the different weekly training loads [PRT volume (weight-lifted), number of impact loads and the total training volume], Pearson's correlations were used. Multiple linear regression was used to assess the association between exercise training frequency (average sessions per week) and the average total training volume per session (sum of the z-scores from the average PRT volume and impact loads per session) with the percentage changes in the DXA and QCT-derived bone traits. The results were analysed unadjusted (model 1), and adjusted for baseline bone traits, age, treatment with the calcium-vitamin D fortified milk (yes/no), baseline BMI and baseline weight-bearing exercise (model 2). Since the cumulative training volume (e.g, total training volume, weight-lifted and number of impacts) might be influenced by baseline lean mass, we replaced baseline BMI with baseline DXA total body lean mass as a covariate in the above regression analysis. However, all results remained unchanged (data not shown) and so models 1 and 2 are presented. To explore the potential dose-response effects of exercise training frequency relative to the non-exercise group (calcium-vitamin D fortified milk alone and controls), analysis of covariance (ANCOVA) adjusting for the same covariates as above were used. The 18-month percentage changes in DXA bone traits or QCT lumbar spine trabecular vBMD were entered as the dependent variables with the non-exercising controls (DXA n=82; QCT n=79) and those men in the exercise group that completed on average <1 (DXA, n=13; QCT n=13), 1 to <2 (DXA n=20; QCT n=20) and ≥2 (DXA n=54, QCT n=52) sessions per week entered as the group (fixed) factor. Post-hoc analysis with Bonferroni correction was used to compare changes between the groups. Paired t-tests were used to evaluate whether there were any significant changes in BMD from baseline in each group. Finally, both the average PRT volume (weight lifted) and average number of impact loads per session were entered into the regression model to evaluate their influence on the changes in each bone trait. To facilitate interpretation of the findings, the beta-coefficients (95% CI) were reported as the percentage change in each bone trait per 100 kg weight lifted for the PRT volume and per 10 impact loads (jumps) completed per session over the 18-months. There was no evidence of multicollinearity as assessed by the variance inflation factor (VIF) of each variable. For all analyses, $P<0.05$ was considered statistically significant.

3. Results

3.1 Baseline characteristics, adverse events and changes in weight and habitual exercise

The baseline characteristics of the participants are shown in Table 1, which highlights that the groups were comparable following randomisation. On average, the men were aged 61 years, with a mean dietary calcium intake of 1007 mg/d (57% had a calcium intake below the Australian Recommendation Dietary Intake of 1000 mg/d) and a mean BMI of 27 kg/m^2 (58% were classified as overweight and 21% as obese). As reported previously [17], there were no serious injuries or adverse events associated with the exercise program. After 18 months, there was no significant difference for the change in weight between the groups, despite a significant increase in the non-exercise group [0.8 kg (95% CI, 0.3, 1.4), P=0.005], there was no significant change in weight the exercise group [mean within group change, 0.3 kg (95% CI, -0.3, 0.9]. Habitual weight-bearing exercise undertaken outside the intervention did not change in either group over time [mean change, exercise -0.5 hours per week (95% CI, -1.2, 0.3); non-exercise 0.7 hours per week (95% CI -0.2, 1.5)].

Table 1: Selected baseline characteristics of the exercise and non-exercise group, and the exercise training frequency and training volumes of the men that completed the 18-month multi-component exercise program.

Characteristics	**Exercise**	**Non-Exercise**
n	87	85
Age, *years*	61.2 ± 7.3	61.0 ± 7.6
Height, *cm*	174.3 ± 6.4	174.8 ± 6.3
Weight, *kg*	84.2 ± 11.6	82.5 ± 9.8
BMI, *kg/m^2*	27.7 ± 3.5	27.0 ± 2.9
Total body lean mass, *kg*	57.8 ± 6.5	57.0 ± 5.6
Dietary calcium intake, *mg/d*	990 ± 418	1024 ± 389
Habitual weight-bearing activity, *h/week*	3.7 ± 3.6	3.3 ± 4.0
Exercise intervention		
Exercise training frequency, *sessions per week*	1.9 ± 0.3	-
Resistance training volume (weight-lifted), *kg per session*	2208 ± 1187	-
Weight-bearing impact loads (jumps), *number per session*	38 ± 21	-

All values are mean ± SD.

3.2 Training frequency and volume

Over the 18 month intervention, the mean number of exercise sessions completed per week was 1.9 [median (IQR): 2.2 (1.4, 2.5)], the mean PRT weight lifted per session was 2208 kg (95% CI, 1955, 2461), and the mean number of impact loads (jumps) completed per session was 38 (95% CI, 33, 42) (Table 1). As shown in Figure 1, the number of men that completed the training at each session tended to decrease progressively over the first 36-40 weeks and remain relatively stable thereafter. Histograms of the average exercise training frequency per week, the average weight-lifted and number of impact loads completed per session are shown in Figure 2. Bivariate correlations showed that exercise training frequency (average sessions per week) was positively associated with the weekly average total training volume (r=0.79, P<0.001), average PRT volume (r=0.79, P<0.001), and average number of impact loads completed (r=0.84, P<0.001). The average PRT volume per week was also positively associated with the average number of impact loads per week (r=0.74, P<0.001).

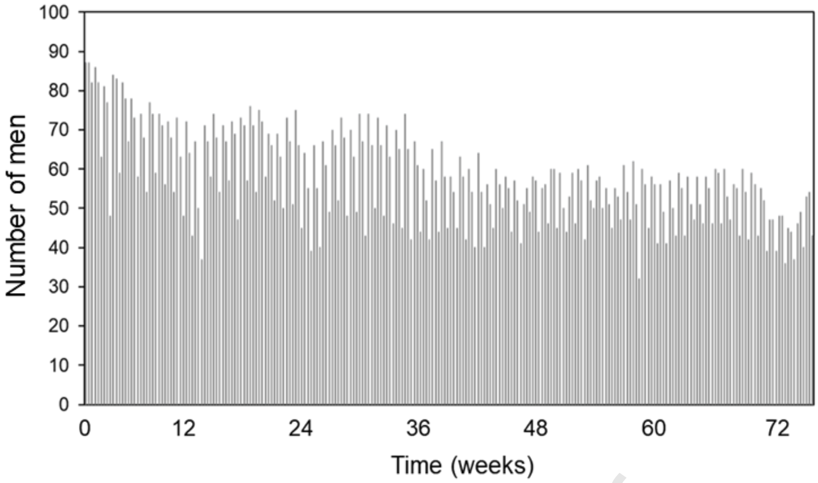


Figure 1: Number of men that completed the multi-component exercise program by session over the 18-month intervention.

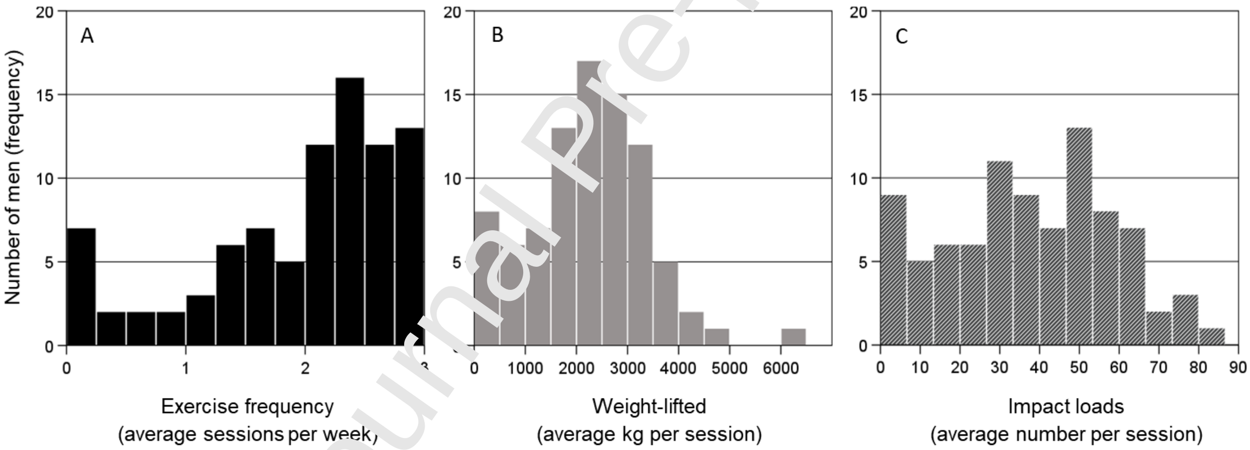


Figure 2: Histograms of the average exercise training frequency (panel A), average PRT weight lifted (PRT volume, kg) (panel B) and the average number of weight-bearing impact loads completed (panel C) per session over the 18-month exercise intervention in the 87 men that completed the study.

3.3 Association between exercise frequency and total training load with the bone traits

As reported previously [17], the exercise intervention resulted in significant net gains in DXA FN aBMD [1.9% (95% CI, 1.2, 2,5)], FN CSA [1.8% (95% CI, 0.8, 2.7)], FN section modulus [2.1% (95% CI, 0.5, 3.6)] and QCT lumbar spine trabecular vBMD [2.2% (95% CI, 0.2, 4.1)] relative to no-exercise. Regression analysis (unadjusted and adjusted for covariates in model 2) of the association between the average exercise training frequency over the 18 months with the percentage changes in BMD, structure and strength revealed that each additional training session per week was associated with a 0.7% and ~3.1% increase in FN aBMD and lumbar spine trabecular vBMD, respectively (Table 2). Similarly, each SD increase in the average total training volume per session was associated with a 0.3% and ~1.5% increase in FN aBMD and lumbar spine trabecular vBMD, respectively. All results remained unchanged if change in weight was included as a covariate instead of baseline BMI. Scatterplots of the associations between the average weekly exercise training frequency and the average total training volume per session with the changes in FN and lumbar spine BMD are shown in Supplementary Figure 1. There were no associations between the average exercise training frequency or the average total training volume per session with the changes in FN CSA or section modulus (Table 2).

Table 2: Multiple regression analysis showing the percentage change in femoral neck (FN) aBMD, cross-sectional area (CSA) and section modulus and lumbar spine (LS) trabecular vBMD with the average exercise training frequency and the average total training volume per session in middle-aged and older men that completed the 18-month multi-component exercise program.

	Training Frequency [1]		**Total Training Volume** [2]	
% Change	*B* (95% CI)	P-value	*B* (95% CI)	P-value
FN aBMD				
Unadjusted	***0.71 (0.14, 1.29)***	***0.016***	0.25 (-0.02, 0.51)	0.069
Adjusted	***0.70 (0.13, 1.29)***	***0.017***	***0.28 (0.01, 0.55)***	***0.041***
FN CSA				
Unadjusted	-0.15 (-1.02, 0.73)	0.737	-0.02 (-0.42, 0.37)	0.902
Adjusted	-0.11 (-0.99, 0.74)	0.811	0.04 (-0.36, 0.44)	0.852
FN section modulus				
Unadjusted	0.11 (-1.23, 1.44)	0.876	0.00 (-0.61, 0.61)	1.000
Adjusted	0.12 (-1.12, 1.37)	0.842	0.08 (-0.52, 0.68)	0.788
LS Trabecular vBMD				
Unadjusted	***3.04 (1.38, 4.70)***	***<0.001***	***1.57 (0.83, 2.31)***	***<0.001***
Adjusted	***3.05 (1.44, 4.66)***	***<0.001***	***1.46 (0.73, 2.19)***	***<0.001***

B (95% CI) represent unstandardized regression coefficients with 95% confidence interval (CI) for the percentage change in each of the bone traits by average exercise training frequency and the average total training volume both unadjusted and adjusted for baseline bone traits, age, treatment with the calcium-vitamin D fortified milk (yes/no), baseline BMI and habitual weight-bearing exercise. [1] Exercise training frequency represent the average number of training sessions completed per week over the 18-month intervention. [2] Total training volume represents the sum of the z-scores for the average total PRT volume (weight lifted) and the average number of impact loads completed per session over the 18-month intervention.

When average exercise frequency over the 18 months was categorised into one of three frequencies (<1, 1 to <2 and ≥2 sessions per week) and compared to the non-exercise group, those averaging 1 to <2 and ≥2 sessions per week had a statistically significant 1.6% (P<0.05) and 2.2% (P<0.001) greater net gain in FN aBMD compared to the no-exercise group (Figure 2). For lumbar spine trabecular vBMD, men completing ≥2 sessions per week experienced a significant 3.9% (P<0.01) and 5.2% (P<0.05) net gain over 18 months compared to the non-exercise group and men averaging <1 session per week, respectively (Figure 3).

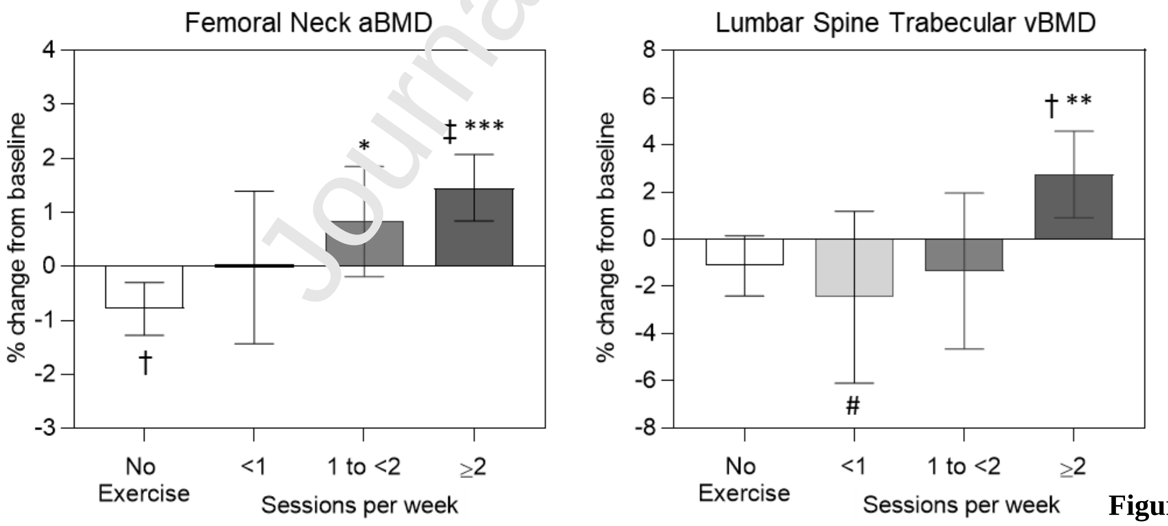


Figure 3: Mean (95% CI) percentage changes after 18-months in femoral neck (FN) aBMD and lumbar spine (LS) trabecular vBMD between non-exercising men and those in the exercise group that completed on average <1, 1 to <2 and ≥2 session per week. † P<0.01, ‡ P<0.001 versus baseline; * P<0.05, ** P<0.01, *** P<0.001 versus no exercise; # P<0.05 versus ≥2 sessions per week.

When both the average PRT volume (weight lifted) per session and the average number of impacts (jumps) completed per session were entered into a regression model, only the average number of impact loads was significantly associated with the 18-month percentage changes in FN aBMD and lumbar spine trabecular vBMD (Table 3). Every 10 impact loads (jumps) completed per session over 18 months was associated with a 0.3% and 1.3% increase in FN aBMD and lumbar spine trabecular vBMD (adjusted model), respectively, independent of the average PRT weight lifted per session. There was no evidence of any multicollinearity for either the FN aBMD (VIF=2.1-2.2) or lumbar spine trabecular vBMD (VIF=2.2-2.3) analysis and the results remained unchanged in change in weight was included as a covariate instead of baseline BMI.

Table 3: Multiple regression analysis showing the percentage change in femoral neck (FN) aBMD, cross-sectional area (CSA) and section modulus, and lumbar spine (LS) trabecular vBMD with the average PRT volume (weight-lifted, kg) per session and the average number of impact loads per session in middle-aged and older men that completed the 18-month multi-component exercise program.

	Resistance Training Volume		**Number of Impact Loads**	
% Change	*B* (95% CI) [1]	P-value	*B* (95% CI) [2]	P-value
FN aBMD				
Unadjusted	-0.02 (-0.08, 0.03)	0.444	***0.36 (0.03, 0.69)***	***0.030***
Adjusted	-0.01 (-0.07, 0.04)	0.644	***0.34 (0.00, 0.67)***	***0.047***
FN CSA				
Unadjusted	0.00 (-0.09, 0.09)	0.960	-0.01 (-0.49, 0.47)	0.969
Adjusted	0.02 (-0.07, 0.11)	0.640	-0.08 (-0.58, 0.42)	0.745
FN section modulus				
Unadjusted	0.04 (-0.09, 0.17)	0.555	-0.22 (-0.97, 0.52)	0.558
Adjusted	0.12 (-0.01, 0.25)	0.069	-0.50 (-1.20, 0.19)	0.154
LS Trabecular vBMD				
Unadjusted	0.06 (-0.10, 0.23)	0.432	***1.11 (0.19, 2.04)***	***0.019***
Adjusted	0.01 (-0.15, 0.17)	0.899	***1.30 (0.38, 2.22)***	***0.006***

β (95% CI) represent unstandardized regression coefficients with 95% confidence interval (CI) for the percentage change per 100 kg PRT weight-lifted [1] or per 10 impact loads (jumps) [2] completed each training session over the 18-month intervention both unadjusted and adjusted for baseline bone traits, age, treatment with the calcium-vitamin D fortified milk (yes/no), baseline BMI and habitual weight-bearing exercise.

4. Discussion

A key finding from this secondary analysis of our 18-month multi-component resistance and impact loading exercise intervention in middle-aged and older men was that exercise frequency related to the program was positively associated with changes in both FN aBMD and lumbar spine trabecular vBMD. Specifically, we found that for each additional training session per week over the 18 months there was a 0.7% and 3.1% increase in FN aBMD and lumbar spine trabecular vBMD, respectively. Similarly, the average total training volume per session, derived from sum of the PRT volume (weight lifted from all sets and repetitions completed) and the number of impact loads completed for all weight-bearing exercises, was also positively associated with the changes in BMD at both skeletal sites. Further analysis revealed that the average number of impact loads completed per session over the 18 months, and not the average PRT volume (weight lifted) per session, was significantly associated with the changes in both FN and lumbar spine trabecular BMD. Collectively, these findings indicate that both exercise frequency and the total training volume related to a multi-component resistance and impact loading program are important predictors of the changes in hip and spine BMD in middle-aged and older men, but that the number of impact loads per session (rather than the PRT volume) may be more important for eliciting a positive skeletal response at both skeletal sites.

Current clinical practice guidelines for osteoporosis recommend multi-component exercise programs incorporating high-intensity PRT performed at least twice per week in combination with moderate-to-high impact weight bearing activities performed 4-7 days per week [21]. However, previous exercise interventions of PRT or weight bearing impact training that were designed to examine the dose-response effects of exercise frequency (varying doses of 1, 2, 3, 4 or 7 sessions per week) on changes in bone have reported mixed findings [22-24]. This may be explained in part by the varied adherence to each exercise doses (range 65-90%) in the completed studies, such that participants trained on average less than that prescribed, making it difficult to determine if there was an optimal frequency.

In a secondary analysis of a 16-year, non-randomized trial of 55 early osteopenic postmenopausal women, Kemmler et al. [16] examined the dose-response relationship of actual exercise frequency (sessions completed per week) following a multi-component PRT plus weight bearing impact exercise program that involved two supervised and two home-based sessions per week. Over the 16 years, the individual exercise frequency rate per participant ranged from 1.3 to 3.0 sessions per week. Regression analysis revealed that exercise frequency was associated with the changes in both hip and lumbar spine aBMD, with at least two exercise sessions per week found to be the minimum effective dose to positively influence BMD at these sites relative to non-exercising controls [16]. However, in this study the exercise attenuated the losses in BMD relative to controls, that is, it did not result in a maintenance or increase relative to baseline. Another PRT plus weight-bearing impact exercise trial (prescription of three sessions per week) conducted over 4 years in postmenopausal women found that those completing >2 sessions per week (highest tertile) experienced the greatest improvements in hip and spine aBMD (mean increase ~0.8% and ~1.8%) relative to those in the lowest exercise frequency tertile (mean BMD losses ~1.0%) [25]. In our 18-month study, we found that FN aBMD and LS trabecular vBMD only increased significantly from baseline (mean 1.5% and 2.7%) in men in the ≥2 sessions per week group. However, when compared to the non-exercising controls who experienced mean losses of 0.8 to 1.2% in BMD, men who completed on average, 1 to <2 and ≥2 sessions per week, had a net 1.6% and 2.2% greater gain in FN aBMD, respectively, but only men who completed ≥2 sessions per week experienced a significantly greater net gain (3.9% net difference) in lumbar spine trabecular vBMD after 18 months. While these findings support previous work that at least two multi-component exercise sessions per week appears to be optimal to favourably improve hip and spine BMD, they also indicate that a lower frequency of training can have a positive effect at the hip.

In addition to exercise frequency, a recent systematic review reported that higher doses of physical activity and exercise programs undertaken for 60+ minutes, 2–3 times per week for 7+ months were generally associated with positive effects on bone [3]. Despite this, there are mixed findings from a limited number of RCTs that have specifically investigated whether there was a dose-response relationship between the actual volume of training completed [e.g. total weight lifted for PRT or the number or intensity (magnitude) of impact loads (jumps)] with changes in BMD [9, 26-28]. This is likely due to the heterogeneity in the dose of exercise prescribed (frequency, intensity and/or duration) across the different studies. In our study, we found that there was a positive association between the average total training volume (PRT volume plus number of impacts loads) per session with the 18-month changes in both FN and lumbar spine BMD. For each SD increase in training volume, there a 0.3% and 1.5% increase in FN aBMD and lumbar spine trabecular vBMD, respectively. It is possible that this association may simply reflect greater exercise frequency, since both exercise frequency and the average total training volume were correlated (r=0.72), with evidence of collinearity (VIF=4.1-4.2) in the multiple regression models. Thus, it was not feasible to enter both variables into the same model. However, when we converted exercise frequency into z-scores (data not shown), there was overlap in the confidence intervals for the beta-coefficients with the total training volume z-scores, which suggests that perhaps neither had a superior influence on the bone outcomes. Interestingly, secondary analysis from a 12-month PRT plus weight bearing intervention (prescription of three sessions per week) in 140 early postmenopausal women showed that the total weight lifted (in kg) from PRT was predictive of changes in trochanter aBMD, but not FN or lumbar spine aBMD [26]. The positive findings at the trochanter in this previous study may be due to the fact that muscle attachments are found on the trochanter (and not the FN), and that the lower limb exercises contributed to over 50% of the total weight lifted. The number of impact loads undertaken by the participants in this previous study was not recorded or included in the total training volume, which may be important as there is evidence that brief bouts of weight-bearing exercise can positively affect FN aBMD in older adults [5, 7, 10, 28-30].

Despite evidence to support the benefits of multi-component exercise programs incorporating PRT plus weight bearing impact exercise for bone health in older adults, we aimed to address the question of whether the actual dose of PRT (weight lifted) and/or the number of impact loads (jumps) completed per session (after adjusted for each in the same model) as part of our multi-component program were associated with any subsequent changes in BMD. Regression analysis identified that the number of impact loads completed per session, and not the average PRT volume (weight lifted), was significantly related to the changes in both FN aBMD and lumbar spine trabecular vBMD. Over the 18-month intervention, every 10 impact loads (jumps) completed per session was associated with a 0.3% and 1.3% increase in FN aBMD and lumbar spine trabecular vBMD, respectively, independent of the average PRT weight lifted per session. These findings support *in vivo* loading studies which have demonstrated that relatively few loading cycles were required to elicit an osteogenic response [31]. Similarly, human trials in middle-aged and older adults have shown that brief bouts of impact loading (10-50 jumps, 3-7 days per week) can significantly improve BMD, particularly at the proximal femur [5, 7, 10, 28-30]. However, a recent systematic review and meta-analysis in postmenopausal women found that interventions involving weight-bearing exercise alone (n=30 studies), PRT alone (n=18) or the combination (n=36) resulted in similar significant improvements in lumbar spine, femoral neck and total hip BMD [1]. It was also reported that the benefits of weight-bearing exercise were less pronounced at the lumbar spine compared to PRT, which appears to contrast with our findings. However, the authors noted that many of the weight-bearing interventions included low impact exercises (e.g. walking) which are likely to impart low axial loads on the spine [1]. In our study, the men completed a diverse range of moderate to high impact weight-bearing activities in which we had previously assessed that the peak vertical ground reaction forces (GRFs) would range from 1.5 to 9.7 times body weight (BW) [32].

We had previously reported that our multi-component exercise intervention resulted in significant net gains in both FN CSA [1.8% (95% CI, 0.8, 2.7)] and section modulus [2.1% (95% CI, 0.5, 3.6)], which provides a measure of bone's resistance to bending forces [17]. However, in the present study we did not detect any association between exercise frequency or training volume (either total, PRT alone or the number of impacts alone) with the exercise-induced changes in FN CSA and section modulus. It is difficult to explain these findings, but it may relate to the greater variability associated with these geometric properties which are derived from two-dimensional DXA images. Indeed, the SD for the exercise-induced changes in FN CSA and section modulus in our study were 1.4 to 2.2-fold greater than the SD for the change in FN aBMD.

The key strengths of this study are the relatively long-term (18-month) follow-up, high participant retention (96%) and the comprehensive exercise frequency and training volume data that was derived from the participants exercise cards, which were reviewed by the trainers after each session or weekly. However, there are several limitations which must be considered when interpreting our findings. Firstly, the average exercise frequency per week and the average training volume per session over the 18 months used in the analysis do not consider potential inter-individual differences in the pattern of adherence or training volume over time, which may influence the responses to the intervention. However, as shown in Figure 1 there was a relatively consistent pattern (steady decline) in the number of men that completed each training session over time, particularly up until weeks 36-40. Secondly, other PRT training components (e.g, relative intensity, repetition speed/tempo) and the magnitude, rate, and distribution of the impact loads for the various weight-bearing activities were not included in the training volume calculations. Previous research has shown that training intensity (percentage of maximum strength) is an important determinant of the skeletal response to PRT [12], and animal/*in vivo* loading studies have demonstrated that moderate to high magnitude loads which are applied rapidly and/or with unusual strain distributions, are particularly effective for stimulating an osteogenic response [31, 33-36]. However, since the relative PRT training intensity was similar throughout the study, it is unlikely that this would markedly influence the results. Thirdly, this study represents an unplanned postintervention analysis of our previous 18-month factorial design RCT, which could increase the risk of bias and the probability of a type I error. Finally, this study was limited to relatively healthy older men with normal to low BMD, and thus the results cannot be generalized to other populations (e.g. postmenopausal women or those with osteoporosis).

In summary, the findings from this study indicate that exercise frequency during an 18-month multi-component exercise program was positively related to the changes in hip and spine bone density in middle-aged and older men with normal to low BMD, with twice-weekly participation resulting in the greatest skeletal benefits. We also found that the average total training volume per session (sum of PRT weight lifted and the number of impact loads completed per session) was similarly associated with the changes in BMD. However, further analysis revealed that the average number of impact loads completed per session, rather than the average PRT weight lifted, was predictive of the changes in BMD at both sites. Every 10 impact loads (jumps) completed per session over 18 months was associated with a 0.3% to 1.3% increase in hip and spine BMD, independent of the PRT weight lifted per session. While these latter findings support the important role of weight-bearing impact activities for bone health in middle-aged and older men, it is still important that muscle strengthening exercises be included in all osteoporosis prevention or management exercise programs given the established links between muscle mass, strength and/or function with falls risk, hyperkyphosis and/or fragility fractures.

5. Acknowledgements

Funding source/grants: This study was financially supported by a grant from the Australian Research Council (ARC) Linkage Scheme (LP0347469). Professor Robin Daly was supported by a National Health and Medical Research Council (NHMRC) Career Development Award (ID 425849).

Competing financial interest statement: None of the other authors had a conflict of interest for this article.

Data availability: Data described in the manuscript will not be made available because approval was not sought or granted from the Deakin University Human Research Ethics Committee to freely make available the data.

6. References

[1] W. Kemmler, M. Shojaa, M. Kohl, S. von Stengel, Effects of Different Types of Exercise on Bone Mineral Density in Postmenopausal Women: A Systematic Review and Meta-analysis, Calcif Tissue Int 107(5) (2020) 409-439. https://doi.org/10.1007/s00223-020-00744-w

[2] M. Martyn-St James, S. Carroll, A meta-analysis of impact exercise on postmenopausal bone loss: the case for mixed loading exercise programmes, Br J Sports Med 43(12) (2009) 898-908. https://doi.org/10.1136/bjsm.2008.052704

[3] M.B. Pinheiro, J. Oliveira, A. Bauman, N. Fairhall, W. Kwok, C. Sherrington, Evidence on physical activity and osteoporosis prevention for people aged 65+ years: a systematic review to

inform the WHO guidelines on physical activity and sedentary behaviour, Int J Behav Nutr Phys Act 17(1) (2020) 150. https://doi.org/10.1186/s12966-020-01040-4

[4] R. Zhao, M. Zhang, Q. Zhang, The Effectiveness of Combined Exercise Interventions for Preventing Postmenopausal Bone Loss: A Systematic Review and Meta-analysis, J Orthop Sports Phys Ther 47(4) (2017) 241-251. https://doi.org/10.2519/jospt.2017.6969

[5] S.J. Allison, J.P. Folland, W.J. Rennie, G.D. Summers, K. Brooke-Wavell, High impact exercise increased femoral neck bone mineral density in older men: a randomised unilateral intervention, Bone 53(2) (2013) 321-8. https://doi.org/10.1016/j.bone.2012.12.045

[6] S.J. Allison, K.E. Poole, G.M. Treece, A.H. Gee, C. Tonkin, W.J. Rennie, J.P. Folland, G.D. Summers, K. Brooke-Wavell, The Influence of High-Impact Exercise on Cortical and Trabecular Bone Mineral Content and 3D Distribution Across the Proximal Femur in Older Men: A Randomized Controlled Unilateral Intervention, J Bone Miner Res 30(9) (2015) 1709-16. https://doi.org/10.1002/jbmr.2499

[7] K.A. Bolam, T.L. Skinner, D.G. Jenkins, D.A. Galvao, D.R. Taaffe, The Osteogenic Effect of Impact-Loading and Resistance Exercise on Bone Mineral Density in Middle-Aged and Older Men: A Pilot Study, Gerontology 62(1) (2015) 22-32. https://doi.org/10.1159/000435837

[8] P.S. Hinton, P. Nigh, J. Thyfault, Effectiveness of resistance training or jumping-exercise to increase bone mineral density in men with low bone mass: A 12-month randomized, clinical trial, Bone 79 (2015) 203-12. https://doi.org/10.1016/j.bone.2015.06.008

[9] W.M. Kohrt, A.A. Ehsani, S.J. Birge, Jr., Effects of exercise involving predominantly either joint-reaction or ground-reaction forces on bone mineral density in older women, J Bone Miner Res 12(8) (1997) 1253-61. https://doi.org/10.1359/jbmr.1997.12.8.1253

[10] L. Welsh, O.M. Rutherford, Hip bone mineral density is improved by high-impact aerobic exercise in postmenopausal women and men over 50 years, Eur J Appl Physiol Occup Physiol 74(6) (1996) 511-7.

[11] A.T. Harding, B.K. Weeks, C. Lambert, S.L. Watson, L.J. Weis, B.R. Beck, A Comparison of Bone-Targeted Exercise Strategies to Reduce Fracture Risk in Middle-Aged and Older Men with

Osteopenia and Osteoporosis: LIFTMOR-M Semi-Randomized Controlled Trial, J Bone Miner Res 35(8) (2020) 1404-1414. https://doi.org/10.1002/jbmr.4008

[12] D. Kerr, A. Morton, I. Dick, R. Prince, Exercise effects on bone mass in postmenopausal women are site-specific and load-dependent, J Bone Miner Res 11(2) (1996) 218-25. https://doi.org/10.1002/jbmr.5650110211

[13] G.F. Maddalozzo, C.M. Snow, High intensity resistance training: effects on bone in older men and women, Calcif Tissue Int 66(6) (2000) 399-404.

[14] R. Zhao, M. Zhao, Z. Xu, The effects of differing resistance training modes on the preservation of bone mineral density in postmenopausal women: a meta-analysis, Osteoporosis Int 26(5) (2015) 1605-18. https://doi.org/10.1007/s00198-015-3034-0

[15] M. Kistler-Fischbacher, B.K. Weeks, B.R. Beck, The effect of exercise intensity on bone in postmenopausal women (part 2): A meta-analysis, Bone 143 (2021) 115697. https://doi.org/10.1016/j.bone.2020.115697

[16] W. Kemmler, S. von Stengel, M. Kohl, Exercise frequency and bone mineral density development in exercising postmenopausal osteopenic women. Is there a critical dose of exercise for affecting bone? Results of the Erlangen Fitness and Osteoporosis Prevention Study, Bone 89 (2016) 1-6. https://doi.org/10.1016/j.bone.2016.04.019

[17] S. Kukuljan, C.A. Nowson, K.M. Sanders, G.C. Nicholson, M.J. Seibel, J. Salmon, R.M. Daly, Independent and combined effects of calcium-vitamin D3 and exercise on bone structure and strength in older men: an 18-month factorial design randomized controlled trial, J Clin Endocrinol Metab 96(4) (2011) 955-63. https://doi.org/10.1210/jc.2010-2284

[18] A.L. Stewart, K.M. Mills, A.C. King, W.L. Haskell, D. Gillis, P.L. Ritter, CHAMPS physical activity questionnaire for older adults: outcomes for interventions, Med Sci Sports Exer 33(7) (2001) 1126-41.

[19] N. Crabtree, M. Lunt, G. Holt, H. Kroger, H. Burger, S. Grazio, K.T. Khaw, R.S. Lorenc, J. Nijs, J. Stepan, J.A. Falch, T. Miazgowski, P. Raptou, H.A. Pols, J. Dequeker, S. Havelka, K. Hoszowski, I. Jajic, S. Czekalski, G. Lyritis, A.J. Silman, J. Reeve, Hip geometry, bone mineral distribution, and

bone strength in European men and women: the EPOS study, Bone 27(1) (2000) 151-9. https://doi.org/10.1016/s8756-3282(00)00300-8

[20] R.M. Daly, S. Bass, C. Nowson, Long-term effects of calcium-vitamin-D3-fortified milk on bone geometry and strength in older men, Bone 39(4) (2006) 946-53. https://doi.org/10.1016/j.bone.2006.04.003

[21] B.R. Beck, R.M. Daly, M.A. Singh, D.R. Taaffe, Exercise and Sports Science Australia (ESSA) position statement on exercise prescription for the prevention and management of osteoporosis, J Sci Med Sport 20(5) (2017) 438-445. https://doi.org/10.1016/j.jsams.2016.10.001

[22] M.C. Ashe, E. Gorman, K.M. Khan, P.M. Brasher, D.M. Cooper, H.A. McKay, T. Liu-Ambrose, Does frequency of resistance training affect tibial cortical bone density in older women? A randomized controlled trial, Osteoporosis Int 24(2) (2013) 623-32. https://doi.org/10.1007/s00198-012-2000-3

[23] C.A. Bailey, K. Brooke-Wavell, Optimum frequency of exercise for bone health: randomised controlled trial of a high-impact unilateral intervention, Bone 46(4) (2010) 1043-9. https://doi.org/10.1016/j.bone.2009.12.001

[24] D.A. Bemben, M.G. Bemben, Dose-response effect of 40 weeks of resistance training on bone mineral density in older adults, Osteoporosis Int 22(1) (2011) 179-86. https://doi.org/10.1007/s00198-010-1182-9

[25] E.C. Cussler, S.B. Going, L.B. Houtkooper, V.A. Stanford, R.M. Blew, H.G. Flint-Wagner, L.L. Metcalfe, J.E. Choi, T.G. Lohman, Exercise frequency and calcium intake predict 4-year bone changes in postmenopausal women, Osteoporosis Int 16(12) (2005) 2129-41. https://doi.org/10.1007/s00198-005-2014-1

[26] E.C. Cussler, T.G. Lohman, S.B. Going, L.B. Houtkooper, L.L. Metcalfe, H.G. Flint-Wagner, R.B. Harris, P.J. Teixeira, Weight lifted in strength training predicts bone change in postmenopausal women, Med Sci Sports Exerc 5(1) (2003) 10-7. https://doi.org/10.1249/01.MSS.0000043284.92353.9C

[27] A. Vainionpaa, R. Korpelainen, H. Sievanen, E. Vihriala, J. Leppaluoto, T. Jamsa, Effect of impact exercise and its intensity on bone geometry at weight-bearing tibia and femur, Bone 40(3) (2007) 604-11. https://doi.org/10.1016/j.bone.2006.10.005

[28] A. Vainionpaa, R. Korpelainen, E. Vihriala, A. Rinta-Paavola, J. Leppaluoto, T. Jamsa, Intensity of exercise is associated with bone density change in premenopausal women, Osteoporosis Int 17(3) (2006) 455-63. https://doi.org/10.1007/s00198-005-0005-x

[29] C.M. Snow, J.M. Shaw, K.M. Winters, K.A. Witzke, Long-term exercise using weighted vests prevents hip bone loss in postmenopausal women, J Gerontol A Biol Sci Med Sci 55(9) (2000) M489-91. https://doi.org/10.1093/gerona/55.9.m489

[30] E.J. Bassey, M.C. Rothwell, J.J. Littlewood, D.W. Pye, Pre- and postmenopausal women have different bone mineral density responses to the same high-impact exercise, J Bone Miner Res 13(12) (1998) 1805-13. https://doi.org/10.1359/jbmr.1998.13.12.1805

[31] Y. Umemura, T. Ishiko, T. Yamauchi, M. Kurono, S. Mashiko, Five jumps per day increase bone mass and breaking force in rats, J Bone Miner Res 12(9) (1997) 1480-5.

[32] S. Kukuljan, C.A. Nowson, S.L. Bass, K. Sanders, G.C. Nicholson, M.J. Seibel, J. Salmon, R.M. Daly, Effects of a multi-component exercise program and calcium-vitamin-D3-fortified milk on bone mineral density in older men: a randomised controlled trial, Osteoporosis Int 20(7) (2009) 1241-51. https://doi.org/10.1007/s00198-008-0776-y

[33] L.E. Lanyon, A.E. Goodship, C.J. Pye, J.H. MacFie, Mechanically adaptive bone remodelling, J Biomech 15(3) (1982) 141-54.

[34] L.E. Lanyon, C.T. Rubin, Static vs dynamic loads as an influence on bone remodelling, J Biomech 17(12) (1984) 897-905.

[35] C.T. Rubin, L.E. Lanyon, Regulation of bone formation by applied dynamic loads, J Bone Joint Surg Am 66(3) (1984) 397-402.

[36] C.T. Rubin, L.E. Lanyon, Regulation of bone mass by mechanical strain magnitude, Calcified tissue international 37(4) (1985) 411-7.

CRediT authorship contribution statement

Robin M Daly, conceptualization, methodology, validation, data curation, formal analysis, writing – original draft, supervision, funding acquisition; Jack Dalla Via, writing – review and editing, visualization; Jackson J. Fyfe, writing – review and editing, visualization; Riku Nikander, writing – review and editing, visualization; Sonja Kukuljan, methodology, validation, investigation, data curation, project administration; writing – review and editing.

Highlights

1. Exercise frequency in a multi-modal program was linked to BMD changes in older men
2. Twice-weekly exercise training was associated with the greatest skeletal benefits
3. Total training volume over 18-months was associated with changes in BMD
4. The number of impacts, rather than weight-lifted, was predictive of changes in BMD