CLINICAL TRIAL

JBMR®

High-Intensity Resistance and Impact Training Improves Bone Mineral Density and Physical Function in Postmenopausal Women With Osteopenia and Osteoporosis: The LIFTMOR Randomized Controlled Trial

Steven L Watson,[1,2] Benjamin K Weeks,[1,2] Lisa J Weis,[3] Amy T Harding,[1,2] Sean A Horan,[1,2] and Belinda R Beck[1,2,3]

[1]School of Allied Health Sciences, Griffith University, Gold Coast, Queensland, Australia
[2]Menzies Health Institute Queensland, Gold Coast, Queensland, Australia
[3]The Bone Clinic, Brisbane, Queensland, Australia

ABSTRACT

Optimal osteogenic mechanical loading requires the application of high-magnitude strains at high rates. High-intensity resistance and impact training (HiRIT) applies such loads but is not traditionally recommended for individuals with osteoporosis because of a perceived high risk of fracture. The purpose of the LIFTMOR trial was to determine the efficacy and to monitor adverse events of HiRIT to reduce parameters of risk for fracture in postmenopausal women with low bone mass. Postmenopausal women with low bone mass (*T*-score < -1.0, screened for conditions and medications that influence bone and physical function) were recruited and randomized to either 8 months of twice-weekly, 30-minute, supervised HiRIT (5 sets of 5 repetitions, >85% 1 repetition maximum) or a home-based, low-intensity exercise program (CON). Pre- and post-intervention testing included lumbar spine and proximal femur bone mineral density (BMD) and measures of functional performance (timed up-and-go, functional reach, 5 times sit-to-stand, back and leg strength). A total of 101 women (aged 65 ± 5 years, 161.8 ± 5.9 cm, 63.1 ± 10.4 kg) participated in the trial. HiRIT ($n = 49$) effects were superior to CON ($n = 52$) for lumbar spine (LS) BMD ($2.9 \pm 2.8\%$ versus $-1.2 \pm 2.8\%$, $p < 0.001$), femoral neck (FN) BMD ($0.3 \pm 2.6\%$ versus $-1.9 \pm 2.6\%$, $p = 0.004$), FN cortical thickness ($13.6 \pm 16.6\%$ versus $6.3 \pm 16.6\%$, $p = 0.014$), height (0.2 ± 0.5 cm versus -0.2 ± 0.5 cm, $p = 0.004$), and all functional performance measures ($p < 0.001$). Compliance was high (HiRIT $92 \pm 11\%$; CON $85 \pm 24\%$) in both groups, with only one adverse event reported (HiRIT: minor lower back spasm, 2/70 missed training sessions). Our novel, brief HiRIT program enhances indices of bone strength and functional performance in postmenopausal women with low bone mass. Contrary to current opinion, HiRIT was efficacious and induced no adverse events under highly supervised conditions for our sample of otherwise healthy postmenopausal women with low to very low bone mass. © 2017 American Society for Bone and Mineral Research.

KEY WORDS: CLINICAL TRIALS; DXA; EXERCISE; FRACTURE PREVENTION; OSTEOPOROSIS

Introduction

Exercise has been proposed as a potential strategy to manage osteoporosis;[1] however, the magnitude of benefit of exercise intervention is traditionally perceived as modest at best.[1–3] It is known that bone responds preferentially to mechanical loads that induce high-magnitude strains[4] at high rates[5] or frequencies[6] and that weight-bearing loading is vital.[7] High-intensity, progressive resistance and impact weight-bearing training (HiRIT) can be employed to generate such loads but have not been routinely prescribed by health care professionals in the absence of evidence to support its efficacy and safety. Instead, osteoporosis exercise guidelines typically recommend only moderate-intensity exercises (70% to 80% 1 repetition maximum [RM], 8 to 15 repetitions) for individual muscle groups that are unlikely to generate the requisite skeletal strain to stimulate an osteogenic response.[8] It is, therefore, unsurprising that previous exercise programs have produced modest, if any, improvements in indices of bone strength.[2]

By contrast, large multi-joint compound exercises such as the squat and deadlift that are conducted in weight-bearing positions and involve extensive muscle recruitment have the potential to apply large loads at clinically relevant bone sites such as the spine and hip.[9,10] Few studies have investigated the

Received in original form January 8, 2017; revised form August 24, 2017; accepted August 27, 2017.
Address correspondence to: Belinda R Beck, PhD, School of Allied Health Sciences, Gold Coast Campus, Griffith University, QLD 4222, Australia. E-mail: b.beck@griffith.edu.au
Journal of Bone and Mineral Research, Vol. 33, No. 2, February 2018, pp 211–220
DOI: 10.1002/jbmr.3284

effects of heavy-lifting programs or large multi-joint compound movements on osteoporosis. A small 12-week intervention of high-intensity (85% to 90% 1 repetition maximum) machine-based squats for postmenopausal women with low bone mass was found to be safe but did not enhance bone mineral density at the femoral neck (FN) or lumbar spine (LS).[11] This finding must be interpreted with caution however, in light of the inadequate duration of the trial to detect changes in bone mass, as well as the very small sample size. A 12-month study of squats and deadlifts at moderate intensity modified LS and FN bone mineral density (BMD) by 0.4% and −1.2%, respectively, in early postmenopausal women.[12] Thus a knowledge gap of whether an adequate duration program of high-intensity weight-bearing loading is efficacious and safe for the bones of people with osteoporosis remained.

The primary aim of the Lifting Intervention for Training Muscle and Osteoporosis Rehabilitation (LIFTMOR) trial was to determine the efficacy of brief, bone-targeted HiRIT for improving FN and LS BMD in postmenopausal women with low to very low bone mass. The secondary aims were to determine if HiRIT improves bone geometry, improves physical function, and is safe in postmenopausal women with low bone mass. We hypothesized that 1) HiRIT training would induce greater improvements in bone and physical function than a low-intensity exercise control program, and 2) HiRIT would not cause more injuries than a low-intensity exercise control program for postmenopausal women with low to very low bone mass.

Materials and Methods

Study design

The LIFTMOR study was a single-blind, randomized, controlled, exercise intervention trial. Eligible participants were randomized to 8 months of 30-minute, twice-weekly, supervised HiRIT, or unsupervised low-intensity home-based exercise (CON), with an allocation ratio of 1:1 (Fig. 1). The 8-month trial period was selected as the requisite duration for bone adaptation and mineralization to be sufficiently detectable on dual-energy X-ray absorptiometry (DXA). Although the duration of a bone remodeling cycle is approximately 4 months, there is a degree of lag before new bone can be detected radiologically as the osteoid mineralizes.[13] Although BMD changes have previously been observed from DXA after only 6 months of intense physical intervention,[14] we chose to extend the intervention period a further 2 months to maximize the opportunity to detect a treatment effect in our primary BMD outcome measures. Stratified randomization was based on existence or absence of established (12 months' exposure or lack of exposure) osteoporosis medication. At the completion of baseline testing, participants were stratified randomized, based on current presence or absence of osteoporotic medication, utilizing sequentially numbered opaque envelopes. The randomization sequence was produced by an external investigator via a random number generator (Microsoft Excel, Microsoft, Redmond, WA, USA) to generate either a 0 or 1, corresponding with CON or HiRIT, respectively. Once a potential participant was deemed eligible for participation, random group allocation was performed by a study investigator (SW) asking the participant to open the next sequentially numbered opaque envelope stratified on osteoporosis medication use. The trial was registered on the Australian and New Zealand Clinical Trials Registry (anzctr.org.au; CTR number: ACTRN12616000475448) and ethical approval was granted by the Griffith University Human Research Ethics Committee (approval number: AHS/07/14/HREC). After trial registration, a minor change was made to the inclusion criteria with the minimum age of eligibility reduced to 58 years from the originally stipulated "60 years of age." The current manuscript reports a subset of data collected in the LIFTMOR trial. Remaining data are to be published in a subsequent manuscript. A full list of primary and secondary outcomes can be found at the Australian and New Zealand Clinical Trials Registry. Written informed consent was obtained from every study participant.

Participants

Postmenopausal women older than 58 years with low bone mass (T-score < -1.0 at the hip and/or spine) were recruited from the community via posters, radio, newspaper, television, and word-of-mouth from May 2014 to November 2015 and all had completed the intervention by August 2016. Potential participants were screened for eligibility and excluded if they had any of the following: lower limb joint injury or surgery; recent fracture (within the last 12 months) or localized back pain; less than 5 years postmenopause; malignancy; uncontrolled cardiovascular disease; cognitive impairment; recent X-ray or radiation treatment; contraindications for participating in heavy physical activity; conditions known to influence bone health (eg, thyrotoxicosis or hyperparathyroidism, Paget's disease, renal disease, diabetes, or immobility); taking drugs (other than osteoporosis medications) known to influence bone (eg, prolonged use of corticosteroids, thyroxine, thiazides, or antiretroviral agents), or unable to attend the supervised training program if so assigned (Fig. 1).

Intervention exercise program

Participants allocated to the intervention group participated in an 8-month, twice-weekly, 30-minute, supervised HiRIT program at Griffith University, Gold Coast, Australia, or The Bone Clinic, Brisbane, Australia. To ensure safe transition to high-intensity exercise, the first month of the intervention comprised body weight and low-load exercise variants, with a focus on progressively learning the movement patterns of the HiRIT exercises. All participants were able to perform the 4 fundamental exercises of the intervention within 2 months. Resistance exercises (deadlift, overhead press, and back squat) were performed for the remainder of the intervention period in 5 sets of 5 repetitions, maintaining an intensity of >80% to 85% 1 RM. Participants performed up to 2 sets of deadlifts at 50% to 70% of 1 RM to serve as a warm-up, as required. Impact loading was applied via jumping chin-ups with drop landings. Participants were instructed to grasp an overhead bar with their shoulders and elbows flexed to 90 degrees, and their hands shoulder width apart with an underhand grip. The participant then jumped as high as possible while simultaneously pulling themselves as high as possible with their arms. At the peak of the jump, the participant dropped to the floor, focusing on landing as heavily as comfortably possible. Each exercise session was performed in small groups with a maximum of 8 participants per instructor, who was an exercise scientist and physiotherapist.

Control exercise program

The goal of a positive control group (CON) was to maximize participant retention. Participants allocated to CON undertook

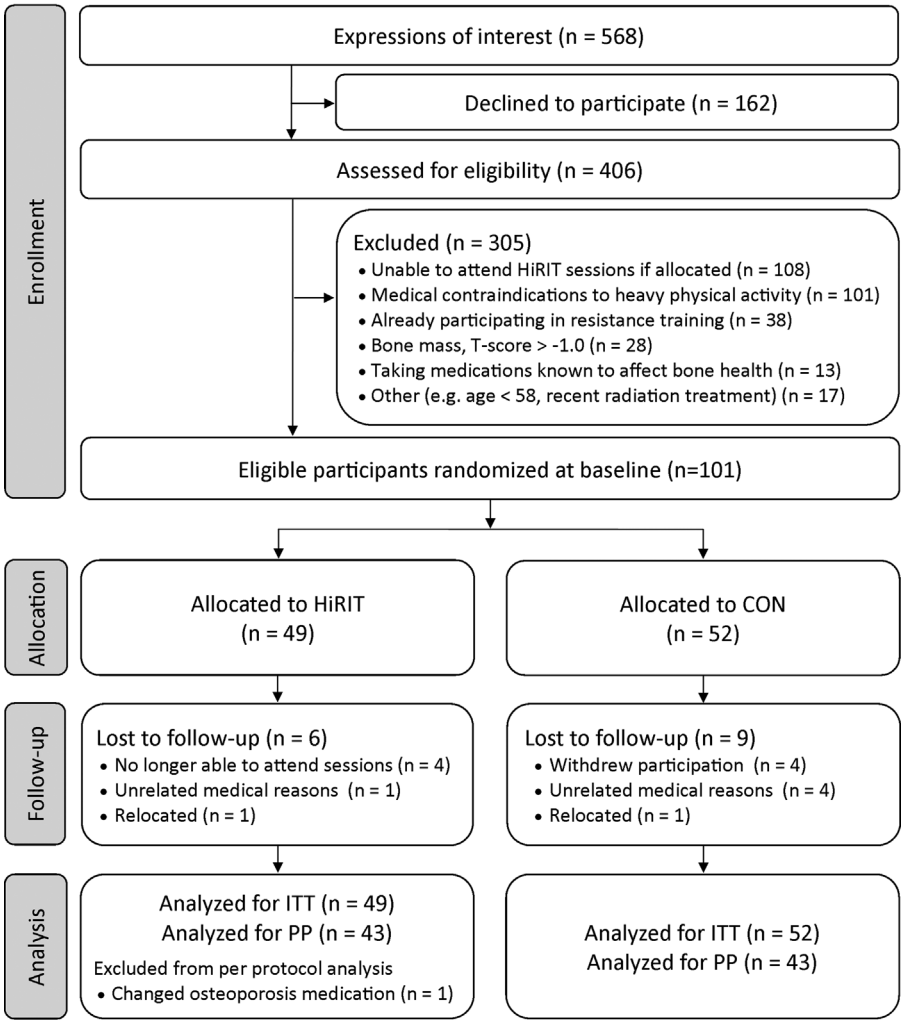

Fig. 1. CONSORT diagram of participant flow. ITT = intention to treat; PP = per protocol.

an 8-month, twice-weekly, 30-minute, home-based, low-intensity (10 to 15 repetitions at <60% 1 RM) exercise program designed to improve balance and mobility but provide minimal stimulus to bone. The CON program consisted of walking for warm-up (10 minutes) and cool down (5 minutes), low-load resistance training (lunges, calf raises, standing forward raise, and shrugs) and stretches (side-to-side neck stretch, static calf stretch, shoulder stretch, and side-to-side lumbar spine stretch). The intensity of resistance exercises was progressed from body weight to a maximum of 3 kg hand weights for the final month of the program.

Data collection

Participants were required to attend a 2-hour testing session at the Griffith University Gold Coast campus at baseline (T0) and follow-up (T1). Outcomes included anthropometrics, regional measures of bone, dietary calcium, physical activity, and functional performance. All measures were performed by a single unblinded investigator; however, to limit observer-expectancy bias, BMD outcome measures were verified by a blinded investigator.

Anthropometrics

Height and body mass were measured using a wall-mounted stadiometer (Seca 216, Ecomed Trading Pty Ltd, Seven Hills, Australia) and mechanical balance scales (Seca 700, Ecomed Trading Pty Ltd), respectively. Body mass index (BMI) was calculated per the accepted formula (BMI = weight/height^2, kg/m^2).

Lifestyle characteristics

Bone-relevant lifetime (tBPAQ) and current (cBPAQ) physical activity participation scores were derived from the Bone-Specific Physical Activity Questionnaire (BPAQ),[15] using a custom-designed Microsoft Visual Basic executable program (www.fithdysign.com/BPAQ/). Participants were instructed to record all physical activity undertaken during their lifetime (for a season or more on a weekly basis), and all activities engaged in over the past 12 months, to determine tBPAQ and cBPAQ, respectively.

Daily calcium intake was estimated using an Australian calcium-specific questionnaire (AusCal).[16] Participants recorded consumption frequency and serving size of common calcium-containing foods and supplements, and data were

analyzed using recognized dietary software (Foodworks 2007 Version 7, Xyris, Brisbane, Australia) to determine average daily calcium intake in milligrams.

Bone measures

Skeletally non-dominant FN and LS BMD (g/cm^2) were obtained using DXA. During the trial period, a change in DXA model was necessary, such that the first 50 participants (Norland XR-800, Norland Medical Systems, Inc., Trumbull, CT, USA) and the final 51 (Medix DR, Medilink, France) were measured on different devices. Each individual participant, however, was measured on the same DXA at baseline and follow-up. Short-term measurement reliability for FN and LS DXA scans was 1.1% and 0.4%, and 1.7% and 1.0% for the Norland and Medix DR devices, respectively.

Non-dominant proximal femur DXA scans for the final 51 participants (HiRIT, $n = 25$; CON $n = 26$) that were conducted on the Medix DR were additionally analyzed using 3D Hip software (DMS Group, Mauguio, France), to derive FN trabecular and cortical volume, trabecular and cortical bone mineral content (BMC), trabecular and cortical volumetric BMD, and FN cortical thickness. 3D parameters were determined according to manufacturer guidelines. Markers were placed on the standard 2D image using the cursor at the distal edge of the lesser trochanter and the superior and inferior junctions of the FN and head of the femur. The 3D Hip software then automatically reconstructed the femur based on both shape and BMD distribution of the standard 2D image. Reconstructions were performed by comparing individual 2D DXA scans to a reference set of proximal femur QCT scans for similarities to determine the reference scan of best fit. Once a reference scan was identified, the surface mesh of the reference scan was transformed to maximize similarities to the 2D DXA image. Finally, 2D BMD was transformed to match the shape model based on bone surface points to maintain BMD spacial distribution.[17]

Quantitative ultrasound (QUS) (Lunar Achilles TM Insight, GE Lunar, Madison, WI, USA) was used to assess both skeletally dominant and non-dominant heels to obtain calcaneal broadband ultrasound attenuation (BUA) (db/MHz), speed of sound (SOS) (m/s), and stiffness index (SI) (unitless).

Physical performance

Physical performance was determined from functional, muscle strength, and neuromuscular performance measures. All were performed in the same sequence at T0 and T1, and by the same investigator, with standardized instructions to maximize uniformity between participants. Maximal isometric muscle force was determined for both lower limb and back extensor muscles. Lower limb extensor strength (LES) was determined using an isometric dynamometer (TTM Muscular Meter, Tokyo, Japan).[18] Back extensor strength (BES) was measured using the Manual Muscle Testing System dynamometer (Lafayette Instrument Company, Lafayette, IN, USA).[19] Three trials were performed for both strength tests, and the highest force in kg across the 3 trials was used for analysis. Functional performance was determined using the timed up-and-go test (TUGT),[20] 5 times sit-to-stand test (FTSTS),[21] and functional reach test (FRT).[22] Three trials were performed for each functional performance test, with the best performance used for analysis.

Lower limb neuromuscular performance was determined from the maximal vertical jump test on a force plate (AMTI, Watertown, MA, USA). Ground reaction forces were captured at 1000 Hz using Vicon Nexus software version 1.8 (Vicon, Oxford Metrics, Oxford, UK). The participant performed 4 maximal vertical jump trials without arm swing, with a 30-second rest interval between trials as previously described.[19] Vertical ground reaction forces were analyzed from the point of stationary standing to the point of landing to determine impulse using custom-written software in Matlab version 7.8.0 (The MathWorks, Natick, MA, USA). All impulse measures were normalized to body mass and expressed as relative impulse (N·s/kg). The trial with the greatest relative impulse was used for analysis.

Safety and compliance

Participant safety and compliance was determined at training sessions and from individual training diaries. One hundred percent compliance was deemed to be the completion of 70 sessions over a period of 8 calendar months. Before each HiRIT exercise session, participants were asked to record any injuries, falls, changes to their diet, medications, well-being or physical activity participation and to rate their muscle soreness (10-point visual analogue scale). Investigators contacted CON participants weekly, either by telephone or e-mail, to obtain the same information and to remind participants to complete their training diaries.

Statistical analysis

Statistical analysis was undertaken using SPSS statistical software (Version 21; IBM Inc., Chicago, IL, USA). Descriptive statistics were generated for participant characteristics, biometrics, and all dependent variables. Both per protocol and intention-to-treat (mean values imputed) analyses were conducted. One-way ANOVA was used to examine differences between HiRIT and CON at baseline, whereas repeated measures ANCOVA was used to determine main effects for dependent variables. Initial values, age, and compliance were applied as covariates for all analyses, with the addition of physical activity participation and dietary calcium as covariates for bone analyses. All statistical outcomes were examined against a p value of 0.05 to determine statistical significance. To adjust for multiple comparisons, Fisher's LSD method was applied.

An *a priori* sample size calculation was conducted based on effect size data reported in a similar machine-based resistance training (80% 1 RM) trial of postmenopausal women.[23] One hundred participants were required to achieve a minimum of 80% statistical power to detect between-group differences of $2.7 \pm 4.5\%$ for FN BMD and $3.5 \pm 3.6\%$ for LS BMD, accounting for a dropout rate of 20%.

Results

Participant characteristics at baseline

A total of 406 postmenopausal women consented to participate in the LIFTMOR trial, of whom 101 met the inclusion criteria, completed initial testing, and were randomized to either HiRIT ($n = 49$) or CON ($n = 52$). The LS and FN T-scores of the participants included in the trial ranged from 0.0 to –3.9, with 44 (43.6%) (CON 21, HiRIT 23) participants being classified as osteoporotic and the remaining 57 being osteopenic at one or other of the sites. Twenty-seven participants (28%) reported an osteoporotic fracture within the last 10 years, 11 (41%) of which were a consequence of a fall. Participant 5-year risk of hip or

other osteoporotic fracture was 4 ± 6% and 8 ± 10%, respectively, and 12 ± 8.4% and 23 ± 14% for 10-year fracture risk, from the Garvan fracture risk calculator (https://www.garvan.org.au/promotions/bone-fracture-risk/calculator/). Of those excluded, the common reasons were: unable to attend session locations or times ($n = 108$), medical contraindications to heavy physical training ($n = 101$) (which included current musculoskeletal injury/condition [$n = 63$], uncontrolled cardiovascular disease [$n = 11$], undergoing treatment for cancer [$n = 10$], neurological condition that limited exercise capacity or exposed the individual to risk of injury [$n = 6$], ongoing surgical management for chronic medical condition [$n = 5$], and undisclosed medical reasons [$n = 6$]), and already undertaking resistance training ($n = 38$) (Fig. 1). CON ($n = 10$) and HiPRT ($n = 10$) had a similar distribution of participants on osteoporosis medication. The only significant between-group difference at baseline was for the TUGT, on which HiRIT performed more slowly (Table 1).

Eight-month change in anthropometrics and lifestyle characteristics

The HiRIT group exhibited an increase in height (0.2 ± 0.5 cm versus −0.2 ± 0.5 cm, $p = 0.004$; 95% confidence interval [CI] 0.0% to 0.3% versus 0.0% to −0.3%) compared with the CON group (ITT). Similar to the ITT analyses, per protocol analyses indicated preferential improvements in height for HiRIT compared to CON (Table 2). There were no significant between-group differences in change for weight, cBPAQ, or daily calcium intake.

Table 1. Baseline Participant Characteristics ($n = 101$)

Parameter	CON ($n = 52$)	HiRIT ($n = 49$)	p Value
Age (years)	65 ± 5	65 ± 5	0.993
Weight (kg)	62.2 ± 9.5	63.9 ± 11.3	0.415
Height (cm)	161.9 ± 6.4	161.6 ± 5.4	0.810
BMI (kg/m^2)	23.7 ± 3.2	24.5 ± 4.6	0.302
Osteoporosis medication			
Bisphosphonate	5	6	
Denosumab	3	4	
HT	2	0	
LS BMD (g/cm^2)	0.820 ± 0.107	0.821 ± 0.106	0.950
LS *T*-score	−2.1 ± 0.8	−2.1 ± 0.8	0.914
FN BMD (g/cm^2)	0.681 ± 0.62	0.698 ± 0.082	0.258
FN *T*-score	−2.1 ± 0.5	−1.9 ± 0.7	0.208
BUA (dB/MHz)	97.1 ± 11.3	100.5 ± 19.1	0.268
SOS (m/s)	1536.0 ± 26.6	1538.6 ± 25.6	0.606
SI	74.8 ± 13.3	76.2 ± 12.9	0.590
BES (kg)	32.2 ± 9.5	31.6 ± 11.1	0.784
LES (kg)	60.3 ± 14.7	60.3 ± 17.6	1.000
TUGT (sec)	5.9 ± 0.6	6.3 ± 0.7	0.008[a]
FTSTS (sec)	9.9 ± 1.5	9.9 ± 1.2	0.939
FRT (cm)	41.1 ± 4.7	40.0 ± 5.9	0.291
Vertical jump (N·s/kg)	1.30 ± 0.32	1.28 ± 0.25	0.228
tBPAQ	16.5 ± 17.5	12.4 ± 11.3	0.172
cBPAQ	0.74 ± 1.24	0.71 ± 1.24	0.907
Dietary calcium (mg)	1006 ± 596	892 ± 457	0.286

BMI = body mass index; HT = hormone therapy; LS = lumbar spine; BMD = bone mineral density; FN = femoral neck; BUA = broadband ultrasound attenuation; SI = stiffness index; SOS = speed of sound; LES = leg extensor strength; BES = back extensor strength; TUGT = timed up-and-go test; FTSTS = five times sit-to-stand; FRT = functional reach test; cBPAQ = current bone-specific physical activity questionnaire score; tBPAQ = total bone-specific physical activity questionnaire score.
[a]Between-group difference ($p < 0.05$).

Eight-month change in body composition

Eight-month change in bone outcomes are presented in Table 3 (per protocol). Percent change in LS BMD ranged from −3.4% to 12.4% for HiRIT, with only 8/43 (18.6%) participants having a reduction in LS BMD at follow-up compared with −6.9% to 5.8%, and 31/43 (72.1%) of participants having a reduction in LS BMD for CON. Participants in the HiRIT group exhibited FN BMD percent changes ranging from −6.0% to +6.8%, with 15/52 (28.8%) experiencing a reduction at follow-up compared with −8.5% to 3.9%, and 27/43 (62.8%) of participants having a reduction in FN BMD for CON. Unadjusted ITT analyses produced similar findings, with the HiRIT effect being superior to CON for LS BMD (2.9 ± 3.0% versus −1.2 ± 2.3%, $p < 0.001$; 95% CI 2.1% to 3.6% versus −1.9% to −0.4%) and FN BMD (0.1 ± 2.7% versus −1.8 ± 2.6%, $p = 0.001$; 95% CI −0.7% to 0.8% versus −2.5 to −1.0%), with non-significant change in QUS SOS (0.3 ± 1.0% versus 0.2 ± 1.1%, $p = 0.951$; 95% CI −0.0% to 0.6% versus −0.1% to −0.5%). When adjusting for covariates, SOS was significantly higher for HiRIT than CON (0.3 ± 1.0% versus 0.2 ± 1.0%, $p = 0.009$; 95% CI 0.0% to 0.6% versus −0.1% to −0.5%). Similar to the unadjusted analyses, HiRIT effect was superior to CON for LS BMD (2.9 ± 2.8% versus −1.2 ± 2.8%, $p < 0.001$; 95% CI 2.1% to 3.7% versus −1.9% to −0.4%), and FN BMD (0.3 ± 2.6% versus −1.9 ± 2.6%, $p = 0.004$; 95% CI −0.5% to 1.0% versus −2.7% to −1.2%). There were no significant between-group differences in change between HiRIT and CON for QUS SI or BUA (Fig. 2*A*). Subgroup analyses were undertaken to determine differences in response between those on and off osteoporosis medication. No between-group differences were observed between participants taking or not taking osteoporosis medications for either LS (CON: −0.2 ± 3.4% versus −1.4 ± 2.2%, $p = 0.192$; HiRIT: 2.4 ± 3.1% versus 3.0 ± 3.4%, $p = 0.631$) or FN BMD (CON: −1.9 ± 3.4% versus −1.7 ± 2.8%, $p = 0.835$; HiRIT: 1.5 ± 2.2% versus −0.3 ± 3.0%, $p = 0.119$) in either the CON or HiRIT groups.

Eight-month change in proximal hip geometry parameters are presented in Table 4. The HiRIT group was superior to CON for FN cortical BMC (7.7 ± 21.3% versus 6.2 ± 21.3%, $p = 0.028$; 95% CI −1.7% to 17.0% versus −2.6% to 15.2%) and FN cortical thickness (13.6 ± 16.6% versus 6.3 ± 16.6%, $p = 0.027$; 95% CI 6.2% to 20.9% versus −0.8% to 13.3%) (ITT). Furthermore, there was a within-group increase in FN cortical volume for HiRIT (9.8 ± 16.7%, $p = 0.024$). No other between-group differences were observed for parameters of FN geometry.

Eight-month change in physical performance

Eight-month change in physical performance measures is presented in Table 5 (per protocol). In ITT analyses, HiRIT improved LES (35.2 ± 19.8% versus 8.1 ± 20.7%, $p < 0.001$; 95% CI 29.1% to 41.2% versus 2.1% to 14.1%), BES (36.0 ± 22.4% versus 11.0 ± 22.4%, $p < 0.001$; 95% CI 29.3% to 42.8% versus 4.5% to 17.5%), TUGT (4.4 ± 6.0% versus −1.7 ± 6.0%, $p < 0.001$; 95% CI 2.7% to 6.0% versus −3.3% to −0.3%), FTSTS (11.6 ± 7.5% versus 1.7 ± 7.5%, $p < 0.001$; 95% CI 9.5% to 13.7% versus −0.3% to 3.9%), FRT (5.4 ± 7.2 % versus 0.1 ± 7.2%, $p < 0.001$; 95% CI 3.4% to 7.5% versus −1.8% to 2.1%) and VJ (6.2 ± 14.5% versus 2.5 ± 14.6%, $p < 0.001$) compared with CON (Fig. 2*B*).

Table 2. Baseline and 8-Month Measures (± SD) With Adjusted Change in Anthropometrics and Lifestyle Characteristics After an 8-Month Exercise Intervention in Postmenopausal Women With Low Bone Mass (Per Protocol Data, $n = 86$)

	CON ($n = 43$)			HiRIT ($n = 43$)			
Parameter	Baseline	Follow-up	% Change	Baseline	Follow-up	% Change	*p* Value
Weight (kg)	62.4 ± 9.2	62.2 ± 9.4	0.0 ± 2.3	63.5 ± 10.0	63.5 ± 10.1	−0.1 ± 2.2	0.860
Height (cm)	162.0 ± 6.0	161.8 ± 6.0	−0.2 ± 0.6	161.4 ± 5.5	161.6 ± 5.5[a]	0.2 ± 0.6	0.006[b]
BMI (kg/m^2)	23.7 ± 3.1	23.7 ± 3.0	−0.0 ± 0.9	24.5 ± 4.4	24.4 ± 4.3	−0.1 ± 0.9	0.863
cBPAQ	0.61 ± 0.97	0.62 ± 1.0	0.01 ± 0.51	0.61 ± 0.75	0.54 ± 0.80	−0.08 ± 0.85	0.579
Daily calcium intake (mg)	1026 ± 636	972 ± 615	−53 ± 369	972 ± 615	897 ± 438	10 ± 282	0.364

BMI = body mass index; cBPAQ = current bone-specific physical activity questionnaire score.
[a]Within-group difference ($p < 0.05$).
[b]Between-group difference based on adjusted percent change ($p < 0.05$).

Safety and compliance

Of the 101 participants who commenced the trial, 6 and 9 participants were lost to follow-up for HiRIT and CON, respectively. The main reason for dropout was the inability to attend training times because of work ($n = 3$) or family ($n = 2$) commitments for the HiRIT group and unrelated medical conditions ($n = 4$) and lack of interest ($n = 3$) for the CON group (Fig. 1). One participant in the HiRIT was excluded from the analysis after follow-up testing due to revealing a previously undisclosed change in bone medication during the trial period. Compliance was slightly higher for HiRIT (92 ± 11%) compared with CON (85 ± 24%), but the difference was not statistically significant ($p = 0.112$). A single adverse event occurred in the HiRIT group during the more than 2600 training sessions. At week 28, the participant experienced a mild low-back muscle strain on a final repetition of the last deadlift set. She missed the following 2 training sessions (1 week) before being able to recommence training with nil concerns thereafter and was able to complete the intervention as prescribed. Falls data were also collected throughout the trial, with 7 participants (CON, $n = 2$; HiRIT, $n = 5$) experiencing a fall over the trial period, none of which resulted in an injury to the participant and all took place outside of trial exercise sessions.

Discussion

The aim of the LIFTMOR trial was to determine the efficacy and to monitor adverse events of an 8-month, brief, supervised HiRIT program for bone and functional outcomes for postmenopausal women with low to very low bone mass. HiRIT was superior to CON for bone mass, FN geometry, and physical function compared with a low-intensity home exercise program serving as a positive control. Importantly, no fractures or major adverse events were observed, suggesting HiRIT may be safe for postmenopausal women with low to very low bone mass, despite previous safety concerns.

Myriad exercise trials to improve bone health of postmenopausal women have been conducted with varying results. The majority of resistance training studies have implemented moderate-intensity programs (8 to 12 repetitions at 67% to 80% 1 RM) that have induced only modest benefits to BMD at the hip or spine, with a mean treatment effect of 0.3% at both sites.[2] A 12-month randomized controlled trial in early postmenopausal women utilizing large compound exercises similar to the LIFTMOR trial has previously been conducted but only at a moderate-loading intensity. The latter study reported 12-month changes of 0.4% and −1.2% for LS and FN BMD, respectively.[12] To our knowledge, there has been no trial of adequate size and/or duration (≥8 months) to determine the efficacy of high-intensity loading to improve bone mass in postmenopausal women with low to very low bone mass; thus, our findings are novel. Our observed improvements in BMD surpass previous reports from reputable exercise interventions, an observation that could be considered intuitive in light of the well-known positive relationship between load magnitude and bone adaptation.[24,25] The limiting feature of high-intensity resistance training in this demographic has traditionally been the perceived increased risk of fracturing fragile bone with heavy loading. We believe this overly conservative approach has contributed to an unnecessary stagnation in the field. The evidence from the LIFTMOR trial that high-intensity loading can indeed be tolerated by postmenopausal women with low to

Table 3. Baseline and 8-Month Measures (± SD) With Adjusted Percent Change in DXA and QUS-Derived Measures of Bone After an 8-Month Exercise Intervention in Postmenopausal Women With Low Bone Mass (Per Protocol Data, $n = 86$)

	CON ($n = 43$)			HiRIT ($n = 43$)			
Parameter	Baseline	Follow-up	% Change	Baseline	Follow-up	% Change	*p* Value
LS BMD (g/cm^2)	0.816 ± 0.097	0.807 ± 0.098[a]	−1.2 ± 3.1	0.823 ± 0.108	0.846 ± 0.116[a]	2.9 ± 3.1	<0.001[b]
FN BMD (g/cm^2)	0.682 ± 0.059	0.670 ± 0.059[a]	−2.0 ± 3.0	0.699 ± 0.086	0.700 ± 0.084	0.3 ± 3.0	0.025[b]
BUA (dB/MHz)	97.7 ± 11.8	98.4 ± 11.3	0.8 ± 7.6	98.0 ± 10.6	99.0 ± 13.2	1.0 ± 7.6	0.534
SI	74.9 ± 13.5	76.1 ± 12.5	2.0 ± 6.8	75.7 ± 12.7	77.7 ± 13.6	2.7 ± 6.8	0.200
SOS (m/s)	1535 ± 26	1538 ± 28	0.2 ± 1.1	1538 ± 25	1542 ± 27.5	0.3 ± 1.1	0.006[b]

LS = lumbar spine; BMD = bone mineral density; FN = femoral neck; WB = whole body; BUA = broadband ultrasound attenuation; SI = stiffness index; SOS = speed of sound.
[a]Within-group difference ($p < 0.05$).
[b]Between-group difference based on adjusted percent change ($p < 0.05$).

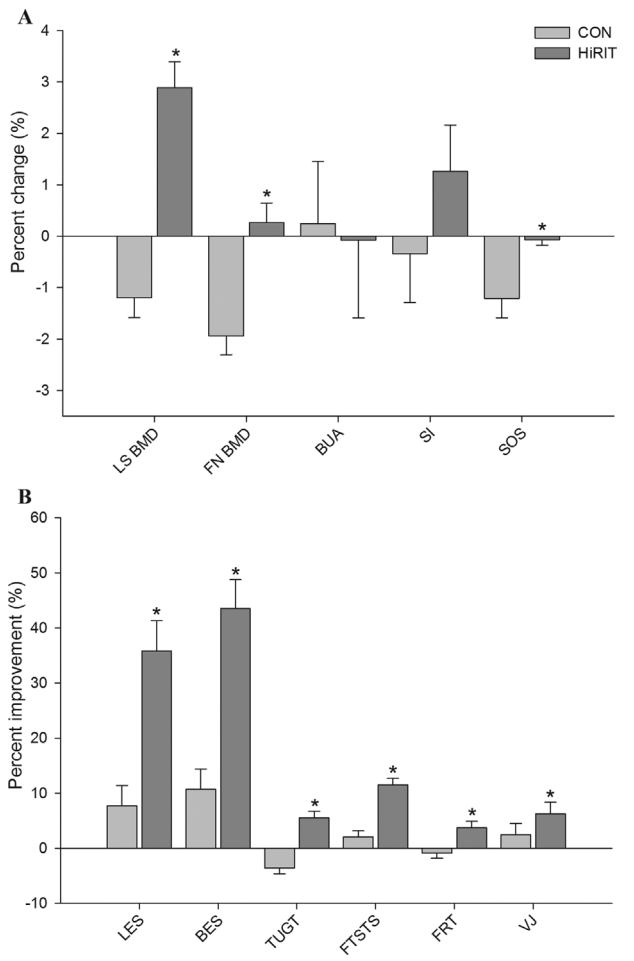

Fig. 2. Eight-month change (± SE) in (*A*) bone and (*B*) physical performance for HiRIT and CON after an 8-month exercise intervention in postmenopausal women with low bone mass ($n = 101$). LS = lumbar spine; BMD = bone mineral density; FN = femoral neck; BUA = broadband ultrasound attenuation; SI = stiffness index; SOS = speed of sound; LES = leg extensor strength; BES = back extensor strength; TUGT = timed up-and-go test; FTSTS = five times sit-to-stand; FRT = functional reach test; VJ = vertical jump. *Indicates between-group difference ($p < 0.05$).

very low bone mass justifies a quantum change in attitude in this regard. The graduated introduction of loading, close ongoing supervision, and focus on correct technique were key to the evident safety of the protocol and the ability of the LIFTMOR participants to tolerate the program. We do not recommend individuals with low bone mass undertake the LIFTMOR protocol in an unsupervised environment, even after notable training, because it is not possible to self-monitor technique.

The use of the Medix DR DXA and 3D Hip software that has been validated against QCT[17] provided the novel opportunity to examine the response of parameters of proximal femur geometry that are known to be associated with structural strength.[26–28] Although the FN BMD response to HiRIT was modest (reflecting essentially a maintenance effect), we observed superior results for FN BMC, cortical thickness, and volume in the HiRIT group compared with CON. Although trabecular changes were not observed, the increase in cortical mass is particularly important because cortical bone is the predominant contributor to FN compressive strength (>90%).[26] That is, cortical thickness is strongly associated with femoral neck failure loads,[27] highlighting the relevance of optimizing cortical elements of bone geometry to protect against hip fractures.

Exercise is recognized to be an effective and feasible treatment modality to prevent falls.[29] Falls prevention exercise programs are generally multimodal, including balance and functional and resistance training, and can effect a 61% reduction in falls resulting in fracture.[29] Although the current intervention did not have sufficient power to examine falls, improvements were nevertheless observed in characteristics that reduce the risk of falling, namely muscle strength and functional and neuromuscular performance. The improvements observed in lower limb strength are similar to those reported previously after resistance training, in the realm of 25% to 35%,[12,30] and parallel the increase in all functional and neuromuscular performance measures (TUGT, FRT, VJ, and FTSTS). Similar functional performance improvements have been observed in previous studies.[31–34] TUG, FTSTS, and functional reach scores have previously been shown to be related to balance and incident falls.[22,35,36] Improvements in those functional performance scores therefore suggest HiRIT may not only reduce the risk of fracture by enhancing parameters of bone strength but by preventing falls in postmenopausal women with low bone mass.

Because safety concerns around high-intensity loading for women with low bone mass have previously discouraged others from recommending (or even testing) it as a therapy for osteoporosis, adverse events were an important outcome measure in the LIFTMOR trial. A modicum of evidence had previously been reported for the safety of HiRIT in postmenopausal women with low bone mass, albeit limited by small sample size and short duration.[11] Our study similarly provides preliminary evidence for the feasibility and safety of a HiRIT exercise program for otherwise healthy postmenopausal women with low to very low bone mass, as no serious or chronic injuries related to the intervention were sustained. Further research is required to confirm safety of HiRIT exercise for individuals with comorbidities. The single minor low-back muscle strain limited training for 1 week, after which time training load was progressively increased over 2 weeks such that the remainder of the program could be completed as prescribed without any further concern. Although we observed no serious adverse events in the LIFTMOR trial, we were not adequately powered to assess safety as an outcome. Furthermore, our sample was relatively healthy, as volunteers with underlying musculoskeletal or serious cardiovascular comorbidities were excluded. We therefore recommend circumspection when applying our findings beyond the sample demographic and appropriate screening for contraindications to high-intensity resistance and impact training. The 92% compliance rate of the HiRIT group in the current study compares favorably to that of previous resistance training studies that range from 59% to 92% for 6 to 12 months of training.[12,23,37–39] Adherence was also high for both groups, with dropout rates of 12% and 17% for HiRIT and CON, respectively. The main reason for dropout was the inability to attend supervised sessions as a consequence of work or family commitments (Fig. 1). Lack of time is a common barrier to exercise, with adherence being as low as 50% in the first 6 months of some exercise programs.[12,40] The high compliance and adherence rates observed in the LIFTMOR trial

Table 4. Baseline and 8-Month Measures (± SD) With Adjusted Percent Change in Skeletally Non-dominant Proximal Femur Geometry Derived From 3D DXA After an 8-Month Exercise Intervention in Postmenopausal Women With Low Bone Mass (Per Protocol Data, $n = 44$)

	CON ($n = 23$)			HiRIT ($n = 21$)			
Parameter	Baseline	Follow-up	% Change	Baseline	Follow-up	% Change	p Value
FN trabecular volume (cm^3)	11.18 ± 1.80	10.82 ± 1.63	−0.8 ± 11.9	10.91 ± 1.60	10.65 ± 1.88	−2.9 ± 12.0	0.963
FN cortical volume (cm^3)	1.59 ± 0.31	1.68 ± 0.30	5.1 ± 16.7	1.59 ± 0.30	1.71 ± 0.35[a]	9.8 ± 16.7	0.492
FN total volume (cm^3)	12.77 ± 1.93	12.51 ± 1.80	−0.2 ± 10.8	12.51 ± 1.66	12.36 ± 2.00	−1.4 ± 10.7	0.987
FN trabecular BMC (g)	2.01 ± 0.49	1.88 ± 0.43	−2.9 ± 29.5	2.10 ± 0.55	2.02 ± 0.57	−0.3 ± 29.6	0.159
FN cortical BMC (g)	1.10 ± 0.23	1.15 ± 0.20	6.2 ± 21.3	1.10 ± 0.27	1.15 ± 0.25	7.7 ± 21.3	0.028[b]
FN total BMC (g)	3.11 ± 0.61	3.03 ± 0.54	−0.2 ± 23.6	3.20 ± 0.76	3.17 ± 0.74	1.7 ± 23.7	0.077
FN trabecular vBMD (g/cm^3)	0.181 ± 0.038	0.176 ± 0.041	−2.5 ± 28.8	0.194 ± 0.500	0.196 ± 0.074	2.4 ± 28.9	0.798
FN cortical vBMD (g/cm^3)	0.697 ± 0.121	0.689 ± 0.107	0.8 ± 15.0	0.698 ± 0.162	0.692 ± 0.189	−1.9 ± 15.1	0.310
FN total vBMD (g/cm^3)	0.244 ± 0.037	0.244 ± 0.044	−0.3 ± 24.3	0.258 ± 0.6	0.265 ± 0.093	3.7 ± 24.3	0.830
FN cortical thickness (mm)	0.90 ± 0.16	0.97 ± 0.16	6.3 ± 16.6	0.92 ± 0.19	1.00 ± 0.18[a]	13.6 ± 16.6	0.027[b]

FN = femoral neck; BMC = bone mineral content; vBMD = volumetric bone mineral density; TH = total hip.
[a]Within-group difference ($p < 0.05$).
[b]Between-group difference based on adjusted percent change ($p < 0.05$).

suggest that HiRIT is feasible and sufficiently appealing to postmenopausal women to be successfully implemented more broadly.

Although not originally a primary outcome measure, we observed that HiRIT improved stature compared with CON. The observed improvement in stature after HiRIT is likely to be a consequence of increased BES, as BES is inversely associated with magnitude of kyphosis.[41] Our results add support to the findings of other exercise intervention studies that have demonstrated improvements in BES by 21% and corresponding kyphosis reductions of 5° to 6° in postmenopausal hyperkyphotic women.[42] Notably, improvements in BES and kyphosis have been associated with a decreased incidence of vertebral fracture[43] and are therefore highly clinically significant.

Several study limitations warrant acknowledgement. First, a change of DXA device was necessary during the trial period. To reduce the impact of this change, every participant was scanned at baseline and follow-up on the same DXA scanner. Furthermore, statistical comparisons of the magnitude of treatment effects detected by the Norland and the Medix revealed no differences (data not reported). Second, we were unable to examine bone biomarkers, serum 25OHD, or circulating hormones and are therefore unable to account for the effects of those factors or their interactions on the study outcomes. Although unable to control for serum 25OHD, ensuring all participants were at least 5 years postmenopause reduced the influence of fluctuations in estrogen during the study period. Third, our data represent a composite of study participants on and off osteoporosis medications. To control for this highly influential variable, we stratified randomization on the basis of medication. Ultimately, 10 participants were randomized to each group, and no within-group differences in treatment effect were observed for our primary outcomes of FN or LS BMD from exploratory analyses of the medication-based subgroups. It is also important to note that preliminary findings were published.[19] The unblinding of data has the potential to result in observer-expectancy bias. To minimize the effect of a lack of the assessor blinding to group allocation at follow-up and the potential for observer-expectancy bias, BMD analyses were independently verified by an investigator who was blind to group allocation. Finally, although the use of 3D Hip software may provide insight into changes in geometry of the proximal femur, the software is very new and the association of geometric parameters to hip fracture is unknown.

In conclusion, the LIFTMOR trial is the first to show that a brief, supervised, twice-weekly HiRIT exercise intervention was efficacious and superior to previous programs for enhancing bone at clinically relevant sites, as well as stature and functional performance of relevance to falls in postmenopausal women with low to very low bone mass. Further, that no fractures or

Table 5. Baseline and 8-Month Measures (± SD) With Adjusted Percent Improvement in Functional Performance After an 8-Month Exercise Intervention in Postmenopausal Women With Low Bone Mass (Per Protocol Data, $n = 86$)

	CON ($n = 43$)			HiRIT ($n = 43$)			
Parameter	Baseline	Follow-up	% Change	Baseline	Follow-up	% Change	p Value
Leg extensor strength (kg)	59.2 ±14.7	61.4 ± 13.7	5.1 ± 23.1	62.5 ± 16.3	80.7 ± 13.9[a]	37.1 ± 20.3	<0.001[b]
Back extensor strength (kg)	32.5 ± 9.3	34.2 ± 10.3	10.9 ± 25.1	32.8 ± 10.3	42.6 ± 8.7[a]	36.3 ± 24.1	<0.001[b]
Timed up-and-go (sec)	5.9 ± 0.6	6.1 ± 0.6[a]	−2.2 ± 6.3	6.2 ± 0.7	5.8 ± 0.5[a]	4.3 ± 6.0	<0.001[b]
Five times sit-to-stand (sec)	9.8 ± 1.4	9.6 ± 1.2	1.7 ± 8.1	9.8 ± 1.2	8.6 ± 1.1[a]	11.6 ± 7.9	<0.001[b]
Functional reach test (cm)	40.9 ± 4.9	40.8 ± 4.7	0.1 ± 8.0	40.3 ± 5.5	42.4 ± 5.3[a]	5.5 ± 7.6	<0.001[b]
Vertical jump (N·s/kg)	1.34 ± 0.24	1.35 ± 0.26	3.6 ± 16.0	1.24 ± 0.26	1.31 ± 0.28	5.1 ± 16.0	<0.001[b]

[a]Within-group difference ($p < 0.05$).
[b]Between-group difference based on adjusted percent change ($p < 0.05$).

other serious injuries were sustained by any participant in our study suggests that HiRIT does not pose a significant risk for postmenopausal women with low bone mass when closely supervised, despite a common misconception to the contrary. In light of the very positive bone, function, safety, and feasibility outcomes of the LIFTMOR trial, we believe HiRIT to be a highly appealing therapeutic option for the management of osteoporosis in postmenopausal women with low to very low bone mass.

Disclosures

BRB and LJW are Directors of The Bone Clinic, Brisbane, QLD. All other authors state that they have no conflicts of interest.

Acknowledgments

The authors acknowledge Sports Medicine Australia for its support for exercise equipment and Griffith University for Postgraduate Research Scholarship support of SLW.

Authors' roles: Study design: SLW, BKW, SAH, and BRB. Study conduct: SLW, BKW, LJW, ATH, SAH, and BRB. Data collection: SLW, LJW, and ATH. Data analysis: SLW, BKW, ATH, and BRB. Data interpretation: SLW, BKW, ATH, and BRB. Drafting manuscript: SLW, BKW, ATH, SAH, and BRB. Revising manuscript content: SLW, BKW, ATH, SAH, and BRB. Approving final version of manuscript: SLW, BKW, LJW, ATH, SAH, and BRB. SLW, BKW, and BRB take responsibility for the integrity of the data analysis.

References

1. Howe TE, Shea B, Dawson LJ, et al. Exercise for preventing and treating osteoporosis in postmenopausal women. Cochrane Database Syst Rev. 2011(7):CD000333.
2. Zhao R, Zhao M, Xu Z. The effects of differing resistance training modes on the preservation of bone mineral density in postmenopausal women: a meta-analysis. Osteoporos Int. 2015;26(5):1605–18.
3. Forwood MR, Burr DB. Physical activity and bone mass: exercises in futility? Bone Miner. 1993;21(2):89–112.
4. Rubin CT, Lanyon LE. Regulation of bone mass by mechanical strain magnitude. Calcif Tiss Int. 1985;37(4):411–7.
5. O'Connor JA, Lanyon LE, MacFie H. The influence of strain rate on adaptive bone remodelling. J Biomech. 1982;15(10):767–81.
6. Rubin CT, McLeod KJ. Promotion of bony ingrowth by frequency-specific, low-amplitude mechanical strain. Clin Orthop Relat Res. 1994(298):165–74.
7. Kohrt WM, Snead DB, Slatopolsky E, Birge SJ Jr. Additive effects of weight-bearing exercise and estrogen on bone mineral density in older women. J Bone Miner Res. 1995;10(9):1303–11.
8. Giangregorio LM, Papaioannou A, Macintyre NJ, et al. Too fit to fracture: exercise recommendations for individuals with osteoporosis or osteoporotic vertebral fracture. Osteoporos Int. 2014;25(3):821–35.
9. Granhed H, Jonson R, Hansson T. The loads on the lumbar spine during extreme weight lifting. Spine. 1987;12(2):146–9.
10. Cappozzo A, Felici F, Figura F, Gazzani F. Lumbar spine loading during half-squat exercises. Med Sci Sports Exerc. 1985;17(5):613–20.
11. Mosti MP, Kaehler N, Stunes AK, Hoff J, Syversen U. Maximal strength training in postmenopausal women with osteoporosis or osteopenia. J Strength Cond Res. 2013;27(10):2879–86.
12. Maddalozzo GF, Widrick JJ, Cardinal BJ, Winters-Stone KM, Hoffman MA, Snow CM. The effects of hormone replacement therapy and resistance training on spine bone mineral density in early postmenopausal women. Bone. 2007;40(5):1244–51.
13. Clarke B. Normal bone anatomy and physiology. Clin J Am Soc Nephrol. 2008;3(Suppl 3):S131–S9.
14. Eleftheriou KI, Rawal JS, Kehoe A, et al. The Lichfield bone study: the skeletal response to exercise in healthy young men. J Appl Physiol (1985). 2012;112(4):615–26.
15. Weeks BK, Beck BR. The BPAQ: a bone-specific physical activity assessment instrument. Osteoporos Int. 2008;19(11):1567–77.
16. Beck BR, Weeks BK, Norling T. A novel Australian calcium specific diet questionnaire: validity and reliability. Osteoporos Int. 2011;22(Suppl 4):s561–6.
17. Whitmarsh T, Humbert L, De Craene M, Del Rio Barquero LM, Frangi AF. Reconstructing the 3D shape and bone mineral density distribution of the proximal femur from dual-energy X-ray absorptiometry. IEEE Trans Med Imaging. 2011;30(12):2101–14.
18. Scott D, Blizzard L, Fell J, Jones G. Statin therapy, muscle function and falls risk in community-dwelling older adults. QJM. 2009;102(9):625–33.
19. Watson SL, Weeks BK, Weis LJ, Horan SA, Beck BR. Heavy resistance training is safe and improves bone, function, and stature in postmenopausal women with low to very low bone mass: novel early findings from the LIFTMOR trial. Osteoporos Int. 2015;26(12):2889–94.
20. Podsiadlo D, Richardson S. The timed "up & go": a test of basic functional mobility for frail elderly persons. J Am Geriatr Soc. 1991;39(2):142–8.
21. Guralnik JM, Simonsick EM, Ferrucci L, et al. A short physical performance battery assessing lower extremity function: association with self-reported disability and prediction of mortality and nursing home admission. J Gerontol. 1994;49(2):M85–94.
22. Duncan PW, Weiner DK, Chandler J, Studenski S. Functional reach: a new clinical measure of balance. J Gerontol. 1990;45(6):M192–7.
23. Nelson ME, Fiatarone MA, Morganti CM, Trice I, Greenberg RA, Evans WJ. Effects of high-intensity strength training on multiple risk factors for osteoporotic fractures. A randomized controlled trial. JAMA. 1994;272(24):1909–14.
24. Cussler EC, Lohman TG, Going SB, et al. Weight lifted in strength training predicts bone change in postmenopausal women. Med Sci Sports Exerc. 2003;35(1):10–7.
25. Kerr D, Morton A, Dick I, Prince R. Exercise effects on bone mass in postmenopausal women are site-specific and load-dependent. J Bone Miner Res. 1996;11(2):218–25.
26. Holzer G, von Skrbensky G, Holzer LA, Pichl W. Hip fractures and the contribution of cortical versus trabecular bone to femoral neck strength. J Bone Miner Res. 2009;24(3):468–74.
27. Bousson V, Le Bras A, Roqueplan F, et al. Volumetric quantitative computed tomography of the proximal femur: relationships linking geometric and densitometric variables to bone strength. Role for compact bone. Osteoporos Int. 2006;17(6):855–64.
28. Ammann P, Rizzoli R. Bone strength and its determinants. Osteoporos Int. 2003;14(Suppl 3):S13–8.
29. El-Khoury F, Cassou B, Charles M-A, Dargent-Molina P. The effect of fall prevention exercise programmes on fall induced injuries in community dwelling older adults: systematic review and meta-analysis of randomised controlled trials. BMJ. 2013;347.
30. Rhodes EC, Martin AD, Taunton JE, Donnelly M, Warren J, Elliot J. Effects of one year of resistance training on the relation between muscular strength and bone density in elderly women. Br J Sports Med. 2000;34(1):18–22.
31. Henwood TR, Taaffe DR. Improved physical performance in older adults undertaking a short-term programme of high-velocity resistance training. Gerontology. 2005;51(2):108–15.
32. Hess JA, Woollacott M. Effect of high-intensity strength-training on functional measures of balance ability in balance-impaired older adults. J Manipulative Physiol Ther. 2005;28(8):582–90.
33. Farinatti PTV, Geraldes AAR, Bottaro MF, Lima MVIC, Albuquerque RB, Fleck SJ. Effects of different resistance training frequencies on the muscle strength and functional performance of active women older than 60 years. J Strength Cond Res. 2013;27(8):2225–34.
34. Sousa N, Sampaio J. Effects of progressive strength training on the performance of the functional reach test and the timed get-up-and-go

test in an elderly population from the rural north of Portugal. Am J Hum Biol. 2005;17(6):746–51.

35. Shumway-Cook A, Brauer S, Woollacott M. Predicting the probability for falls in community-dwelling older adults using the timed up & go test. Physical therapy. 2000;80(9):896–903.
36. Buatois S, Miljkovic D, Manckoundia P, et al. Five times sit to stand test is a predictor of recurrent falls in healthy community-living subjects aged 65 and older. J Am Geriatr Soc. 2008;56(8):1575–7.
37. Kerr D, Ackland T, Maslen B, Morton A, Prince R. Resistance training over 2 years increases bone mass in calcium-replete postmenopausal women. J Bone Miner Res. 2001;16(1):175–81.
38. Marques EA, Wanderley F, Machado L, et al. Effects of resistance and aerobic exercise on physical function, bone mineral density, OPG and RANKL in older women. Exp Gerontol. 2011;46(7):524–32.
39. Gianoudis J, Bailey CA, Ebeling PR, et al. Effects of a targeted multimodal exercise program incorporating high-speed power training on falls and fracture risk factors in older adults: a community-based randomized controlled trial. J Bone Miner Res. 2014;29(1):182–91.
40. Rodrigues IB, Armstrong JJ, Adachi JD, MacDermid JC. Facilitators and barriers to exercise adherence in patients with osteopenia and osteoporosis: a systematic review. Osteoporos Int. 2017;28(3):735–45.
41. Sinaki M, Itoi E, Rogers JW, Bergstralh EJ, Wahner HW. Correlation of back extensor strength with thoracic kyphosis and lumbar lordosis in estrogen-deficient women. Am J Phys Med Rehabil. 1996;75(5):370–4.
42. Katzman WB, Sellmeyer DE, Stewart AL, Wanek L, Hamel KA. Changes in flexed posture, musculoskeletal impairments, and physical performance after group exercise in community-dwelling older women. Arch Phys Med Rehabil. 2007;88(2):192–9.
43. Sinaki M, Itoi E, Wahner HW, et al. Stronger back muscles reduce the incidence of vertebral fractures: a prospective 10 year follow-up of postmenopausal women. Bone. 2002;30(6):836–41.