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Original Article

Impact of a multimodal exercise program on tibial bone health in adolescents with Development Coordination Disorder: an examination of feasibility and potential efficacy

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Abstract

Objectives: Developmental coordination disorder (DCD) compromises bone health purportedly due to lower levels of physical activity. The potential of an exercise intervention to improve bone health parameters in adolescents with DCD has not previously been studied. This study thus aimed to determine the impact of a multimodal exercise intervention on bone health in this population at-risk of secondary osteoporosis. **Methods**: Twenty-eight adolescents (17 male, 11 female) aged between 12-17 years (M_{age}=14.1) with DCD participated in a twice weekly, 13-week generalised multimodal exercise intervention. Peripheral quantitative computed tomography scans of the tibia (4% and 66%) were performed over a six month period. Generalised estimating equations were used to examine the impact of fitness measures on bone parameters over time. **Results**: An overall improvement trend was observed for bone health, with significant increases at the 66% tibial site for bone mass (4.12% increase, d_{cohen}=0.23, p=0.010) and cortical area (5.42% increase, η^2 =12.09, p=0.014). Lower body fitness measures were significantly associated with improvements in bone health parameters, tempered by the degree of motor impairment. **Conclusion**: A multimodal exercise intervention may be effective in improving bone health of adolescents with DCD. Given the impact of motor impairments, gains may be greater over an extended period of study.

Keywords: Bone Health, Developmental Coordination Disorder, Developmental Disorder, Exercise, Physical Activity

Introduction

Developmental Coordination Disorder (DCD) is a neurodevelopmental disorder typified by the slow acquisition and poor performance of motor skills across an individual's lifespan[1]. Persons with DCD tend to have low levels of physical activity[2-4] which has been purportedly linked to detrimental bone health[5], including bone health impairments[6-10] and increased rates of fracture[6,11] placing them at risk of osteoporotic fractures later in life. Furthermore, suboptimal bone health is not just a consequence of reduced overall physical activity in paediatric DCD populations, but also from a lack of diversity in activities engaged[7], such that paediatric DCD populations appear to benefit most from physical activity that is diverse and intense[12]. As diverse mechanical loading modalities, methods, and intensity are known to be an essential part of all osteogenic activities[13] it is likely that a similar association between incidental physical activity and prescribed exercise with bone-specific outcomes also applies to adolescent and adult DCD populations, however this has not as yet been established. Furthermore, while physical activity (i.e. incidental and/or nonspecific activities requiring bodily movement) appears to improve bone health in DCD populations, exercise (i.e. purposeful, prescriptive, programmed and progressive

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activities targeting physiological outcomes) is likely to produce even greater benefits[13].

No studies, to our knowledge, have investigated the relationship between physical activity or exercise and bone health in adolescents with DCD. Weight bearing activity is known to have a particularly strong osteogenic effect during the early to mid-puberty time frame due to the velocity of bone growth and endocrine changes seen at this age[14,15] with significant improvements noted in bone health from a broad range of exercise interventions within adolescent populations[16-20]. Exercise interventions are known to be particularly effective in populations who are relatively inactive[21], with a substantial benefit anticipated for the typically inactive DCD population[2-4]. The benefits of exercise interventions in this age group, however, are heavily influenced by the types of activities or exercise modalities used[16,17,22]. Given the difficulties of motor skill acquisition and performance inefficiency inherent with DCD[1,23] it is likely there will be specific challenges concerning the implementation of prescribed exercise interventions in DCD populations. Thus, it is not yet known whether adolescents with DCD can engage in exercise interventions to a degree that would induce improvements in muscle and bone parameters. Indeed, to have an osteogenic effect, physical activity and/or exercise is required to be frequent, with a variety of different loading types, and be progressive through increasing magnitudes and rates of loading[13]. However, as individuals with DCD have a slower rate of mastering movements and a lower level of engagement in physical activity[24] such effects may be impeded. Accordingly, this study examined whether participating in a multimodal exercise intervention designed to address the general needs of adolescents with DCD, shown to improve the physical fitness[25] and self-perception of physical abilities among adolescents with DCD[26], would also have the capacity to produce improvements in bone health parameters.

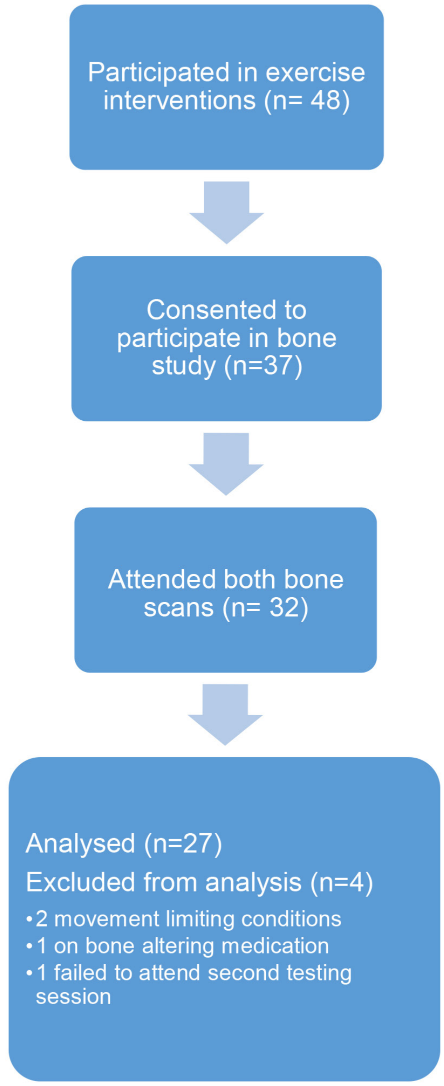

Figure 1. Inclusion of participants for bone health analysis.

Materials and methods

Experimental Design

A longitudinal, single-cohort study design was used to explore the feasibility and preliminary efficacy of a 13-week exercise program in adolescents with DCD to improve tibial bone health outcomes. All participants attended two testing sessions, six months apart, for anthropometry and lower-limb muscle bone morphology, with the first session taking place immediately prior to the commencement of the exercise program. Participants attended the local tertiary paediatric hospital to have their anthropometry (height, weight and tibial length) and lower limb muscle-bone morphology measures taken. Lower limb fitness assessments and motor performance tests were performed at The University of Notre Dame Australia's exercise clinic on the first and last session of the exercise intervention. Bone measurements were performed approximately three months following the completion of the exercise program to allow time for bone adaptation. Participants were also required to attend the exercise clinic two days per week throughout the program to complete their supervised exercise sessions.

Participants

Participants were recruited from the Adolescent Movement Program (AMPitup: www.movegrowengage.com.au/ampitup/), a research program providing an exercise intervention for adolescents with movement difficulties[4,25,26]. The program is aimed at adolescents aged 12 to 18 years with a reported history of movement difficulties below what would be expected for their age that has impacted upon their activities of daily living as per the diagnostic criteria for DCD[1]. Participants in the study are recruited through referral from allied health professionals (e.g. Occupational Therapists, Physiotherapists) or through word of mouth.

All participants in the Adolescent Movement Program were offered the opportunity to participate in this bone health study. Participants whose movement difficulties did not occur early in the developmental period or were due to an intellectual or physical disability were excluded from this analysis in keeping with the diagnostic criteria for DCD[1]. As indicated in Figure 1, two participants were excluded for this reason, with another participant being excluded due to use of bone affecting medication for epilepsy. The study had ethics approval from the Human Research Ethics Committee of the University of Notre Dame Australia (Reference 011004F, 09004F, 09050F, 09039F) and written informed consent was provided by participants and their caregivers prior to participation. The study and its procedures conformed to the World Medical Associations' Declaration of Helsinki for Medical Research Involving Human Subjects.

Intervention

A multimodal exercise intervention was undertaken as part of the AMPitup program. Participants received individualised exercise training over thirteen weeks consisting of two 90-minute sessions per week after school, overseen by an accredited exercise physiologist (AEP; Exercise and Sport Science Australia) and clinically experienced academics. Each participant received one to one coaching from physiotherapy and exercise sport science undergraduate students, together with exercise physiology postgraduate students. The use of one to one coaching has been found to increase the participants engagement in the intervention[26] and also allows for individualised feedback on technique. Each participant had two assigned trainers through-out the intervention, one for each exercise session of the week, to encourage variability in exercise routines. The AMPitup program is general and broad in focus, thus activities are not explicitly targeting osteogenesis. All exercise sessions include a combination of aerobic training (cardiorespiratory fitness), resistance training (muscle and strength development) and other activities aimed at improving motor skills and balance. Stretching and flexibility activities, core strength, and postural exercises, were also included dependent on the participant's individual fitness interests, goals and needs. Fitness games and group activities were often included to improve participant's engagement and enjoyment of physical activity. A full list of activities used are included in Table 1. The volume and intensity of exercises were prescribed as recommended by Faigenbaum and colleagues[27], and Falk and Klentrou[28], relative to the participant's physical abilities and fitness. Progression in sets, repetitions and weight occurred after proper technique was achieved as determined by the trainer[29].

Measures

Musculoskeletal Morphology

Tibial scans were performed using peripheral Quantitative Computed Tomography (pQCT; Stratec XCT-3000, Stratec

Table 1. List of activities performed by participants.

Cardiovascular exercises	Core strength and flexibility	Motor and postural skills
• Arm ergometer • Bike • Boxing • Cross-trainer • Hula hooping • Mountain climbers • Rower • Running • Stair run • Step aerobics combinations • Walk	• Abdominal crunch • Ball rollouts • Dead bugs • Farmers walk • Fitball knee tucks • Glute bridge • Heel slide • Hover • Leg lifts • Oblique leg slide • Oblique twist • Pilates Machine • Plank • Rotary torso • Stretches • Wheelbarrow	• Balance on beam • Balance on bosu • Balance on one leg • Catching • Fitball balance on all fours • Heel-toe walk • Kicking • Obstacle course • Star excursion balance • Throwing over object • Throwing into bucket/bin/net • Throwing while balancing • Throwing while standing on one leg
Resistance training (for lower body)	**Resistance training (general)**	**Plyometrics**
• Bear crawls • Burpees • Calf raises • Chair sit to stand • Climbing frame • Heel press • Heel raises • Leg curl • Leg extension • Leg press • Leg raises • Lunges • Reverse leg curls • Side kicks • Squats • Travelling lunges • Tricep dip • Tricep extension	• Arnold dumbbell press • Arm raises • Arm extension • Bridge • Back extension • Bent over barbell row • Bicep curl • Bicep extension • Cable pull down • Chest press • Chin ups • Deadlifts • Dead row • Dumbbell snatches • High pull • Kettlebell swings • Lateral pulldown • Lateral shoulder raise • Medicine ball passes • Medicine ball slam • Medicine ball twist • Overhead press • Pectoral fly • Pelvic lift • Pull up • Push press • Rope climbing • Seated cable row • Shoulder press • Shoulder shrug • Supine rows	• Body weight jump squat • Bounding • Box jumps • Broad jumps • Hopping • Hopscotch • Horizontal jumps • Hurdles • Jump over board • Lateral jump • Side to side hops/ jumps • Skipping • Star jumps • Toe taps • Vertical jump **Group and partner games** • Baseball • Basketball • British bulldog • Circuit of park equipment • Dodgeball • Four square • Frisbee • Kick to kick • Piggy in the middle • Soccer • Tennis • Two square

GmbH; slice thickness 2.3 mm, pixel size 0.4 × 0.4 mm) at proximal (66% of tibial length, T66) and distal (4% of tibial length, T4) sites of the tibia, of the non-dominant side as reported by the participant. Participants sat on a height-adjustable chair with their lower limb fully extended through the acrylic cylinder and central gantry of the pQCT machine and secured to the foothold attachment under the supervision of a trained bone densitometry hospital technician. A 30-mm scout scan was produced at the base of the malleolus in order to identify the talocrural joint, as an internal reference point from which the scan commenced to measure cross-sectional slices at 4% (T4) and 66% (T66) of tibial length. Scans per participant spanned approximately five minutes and were performed approximately six months (20.4 (8.4) weeks) after baseline testing; approximately three months following the completion of the 13-week exercise program. Following scan completion, total tibial mass (g/cm) and cross-sectional area (mm^2) were assessed at both sites. In addition, total density (mg/cm^3) and trabecular density (mg/cm^3) were assessed at the T4 site, and cortical density(mg/cm^3), cortical area (mm^2), stress strain index (SSI, mm^3), fracture load on the X and Y axis (N), muscle and fat cross-sectional area were assessed at T66. SSI and fracture load were used as surrogates for bone strength. To account for the absence of a concurrently assessed control group, Z-scores were calculated using height and sex-specific means and standard deviations from the Stratec reference database (Version 6.20, Stratec, Stratec GmbH)[30] using the formula:

$$z=\frac{(x-\mu)}{\sigma}$$

where x is the individual value, μ is the sex and height specific mean and σ is the associated standard deviation.

Anthropometry

Stature was recorded to the nearest 0.1 cm using a wall-mounted stadiometer (Mentone Educational Centre), with body weight recorded to the nearest 0.1 kg using an electronic scale (Homedics). Tibial length of the non-dominant leg was assessed using a retractable measuring tape, defined as the tibial plateau at the knee joint (proximal end) to the medial malleolus (distal end), recorded to the nearest 0.1 cm. Body mass index (BMI) was subsequently calculated using weight (kg) / height $(m)^2$.

Pubertal Status

Pubertal status was assessed using the Pubertal Developmental Scale, a non-invasive self-report scale which covers five aspects of pubertal development including sex specific questions[31]. Items are scored on a scale of one to five, with five indicating a mature stage. The scale can be converted to correspond to five categories of pubertal development (Peterson et al 1998 in Bond et al[32]). Validity has been established against physical exams and self-report measures of puberty[31], with a Kappa concordance of 0.5 with self-reported Tanner stage[32]. Reliability has been established in rural and urban populations[33].

Motor Performance

Motor performance was assessed using the McCarron Assessment of Neuromuscular Development (MAND)[34] as part of the screening process for the AMPitup program. The MAND is a ten-item test designed for the assessment of gross and fine motor skills in adolescents and young adults. Scores from the ten items are scaled and summed to produce a Neuromuscular Developmental Index (NDI), with a mean of 100 and standard deviation of 15. Lower NDI scores indicate poorer performance of motor skills and as such a greater degree of motor impairment. A NDI of more than one standard deviation below the mean (85) was required in order to be eligible for participation in the intervention, however participants with a NDI above 85 were included if a substantial history of motor difficulties impacting on their daily life was reported. The MAND has a test-retest of 0.99 after one month and concurrent validity to a number of different motor skill tests[34].

Lower Limb Fitness Measures

Lower limb fitness was measured using three assessments: the standing broad jump, vertical jump and a 1 repetition maximum (1RM) leg press. All measures are reliable forms of evaluation of lower limb fitness validated under similar conditions to their use in this study. The standing broad jump has an intraclass correlation coefficients (ICC) from test-retest of 0.98 in an adolescent population[35], while the vertical jump, as measured by the Vertec system, has an 0.91 ICC in college aged females (M_{age}=19.5, SD=1.3), and 0.94 in college aged males (M_{age}=19.7, SD=1.5)[36]. The 1 RM leg press has an test-retest ICC of 0.95 in college aged athletes (M_{age}=18.9, SD =1.2)[37] and 0.99 in untrained adults[38]. The measures were taken for each participant at the first and last session of the thirteen-week exercise intervention. The standing broad jump was measured as the horizontal distance achieved by the participant jumping forwards from a standing stationary position, by drawing a line behind their heels following the landing point. Each participant had three attempts with the best achieved jump being recorded in inches (in)[34]. The vertical jump was measured as the maximum vertical height achieved in a standing jump (Vertec, Sports Imports, Hilliard) by determining the difference in the number of vanes between the participant's standing reach and jump reach at peak height. Vanes are spaced 1.27 cm apart with vertical jump height in centimetres calculated as the number of vanes multiplied by 1.27. Each participant was provided with multiple attempts with short rests of about a minute until a plateau in performance was observed, with the best achieved jump retained for analysis[25]. Leg strength was assessed using 1RM leg press, recording the maximum weight that could be lifted through a full range of motion in kilograms (kg). Failure was defined as an incomplete range of motion through execution, or an inability to lift the weight in two attempts[39]. Due to technical specifications of the leg press machine, increase of weight was in 5 kg increments. Fitness procedures were performed in the same set pattern for all participants with the 1RM leg press being performed last.

Table 2. Descriptive characteristics of the total sample, males and females.

Characteristic	Total Sample (n=28)		Male (n=17)		Female (n=11)	
	M	*SD*	*M*	*SD*	*M*	*SD*
Age (years)	14.06	1.28	13.98	0.92	14.18	1.75
Height (cm)	163.81	10.55	163.86	9.97	163.74	11.89
Weight (kg)	61.40	14.94	61.11	16.15	61.85	13.59
Puberty score	6.41	1.78	6.35	2.03	6.50	1.35
NDI	66.29	17.90	68.12	17.94	63.45	18.34

Table 3. Intervention group difference.

	Intervention-Naive (n=17)		Intervention – Experienced (n=11)					
	M	*SD*	*M*	*SD*	d_{cohen}	*d* 95% Confidence Interval	T test	P- value
Age (years)	13.38	0.53	15.11	1.40	12.13[b]		-3.62[a]	*<0.001
Height (cm)	161.27	11.39	167.73	8.07	0.25	-0.28 to 0.78	1.63	0.116
Weight (kg)	57.88	13.66	66.84	15.82	12.10[b]		1.53[a]	0.134
T4								
Mass (g/cm)	2.87	0.52	3.54	0.61	1.18	0.61 to 1.75	-3.14	*0.004
Total area (mm^2)	1100.74	164.81	1211.21	199.90	0.60	0.07 to 1.14	-1.59	0.123
Total density (mg/cm^3)	261.19	29.28	293.55	24.20	4.93	3.88 to 5.98	-3.05	*0.005
Trabecular density (mg/cm^3)	224.86	35.50	249.75	22.18	0.84	0.29 to 1.39	-2.07	*0.048
Trabecular density Z-score	0.38	1.58	0.25	1.05	-0.10	-0.62 to 0.43	-1.28	0.212
T66								
Mass (g/cm)	2.88	0.52	3.57	0.49	1.37	0.78 to 1.95	-3.56	*0.001
Total area (mm^2)	616.58	161.00	612.00	122.12	12.11[b]		-0.21[a]	0.853
Cortical density (mg/cm^3)	1022.87	49.65	1061.69	44.79	12.12[b]		-2.19[a]	*0.029
Cortical area (mm^2)	207.11	58.15	278.50	36.68	12.13[b]		-3.65[a]	*<0.001
SSI (mm^3)	1639.67	323.05	1910.04	374.69	0.77	0.23 to 1.32	-2.03	0.050
Fracture load X3N	4112.75	883.31	5038.25	1188.45	0.88	0.34 to 1.43	-2.36	*0.026
Fracture load Y3N	3215.80	765.04	3540.28	727.05	0.44	-0.10 to 0.97	-1.12	0.274
Cortical density Z-score	-0.33	1.44	0.45	0.87	0.66	0.12 to 1.19	-1.79	0.084
Cortical area Z-score	-1.72	1.72	-0.25	1.11	1.02	0.46 to 1.57	-2.75	*0.011
SSI Z-score	-0.71	1.00	-0.52	0.95	0.20	-0.33 to 0.72	-0.50	0.619
Fitness parameters								
1 RM leg press (kg)	59.33	20.17	96.00	32.86	1.35	0.77 to 1.93	-3.01	*0.008
Vertical jump (cm)	33.39	11.59	34.52	7.78	0.11	-0.41 to 0.64	-0.28	0.779
Standing broad jump (in)	41.71	15.50	47.00	15.13	0.35	-0.18 to 0.87	-0.89	0.381

a=Mann-Whitney U test standardized test statistic, b=eta squared

Table 4. Pre-post group difference on fitness measures.

	Baseline		Post-intervention					
Fitness measure	*M*	*SD*	*M*	*SD*	d_{cohen}	*d* 95% Confidence Interval	T-test statistic	P-value
1 RM leg press (kg)	68.50	28.14	83.00	26.77	0.53	-0.01 to 1.06	-3.68	*0.002
Standing broad jump (in)	43.79	15.30	46.14	15.10	0.16	-0.37 to 0.68	-2.74	*0.011
Vertical jump (cm)	33.84	10.11	35.61	12.60	0.16	-0.37 to 0.68	-1.21	0.235

Statistical analysis

All statistical calculations, except effect sizes, were completed using SPSS[40]. Effect sizes were calculated using Psychometrica online calculator[41]. Normality of data distribution was explored using a Shapiro-Wilk test. Full statistical analysis was performed for bone measurements in both the raw data and Z-scores. Baseline and post intervention differences in bone parameters and fitness assessments were explored using paired sample t-tests for parametric variables or Wilcoxon signed rank tests for non-parametric variables. Effect sizes were calculated using Cohen's d for parametric variables and eta squared for non-parametric variables. Sex differences for bone parameters, fitness measures, and descriptive characteristics were determined via independent t-tests for parametric variables and Mann Whitney U tests for non-parametric variables. Generalised estimating equations (GEE) were used to identify determinants of bone parameters. Sex, puberty score, age, height, and weight were included in the GEE model as they were considered likely influencers of improvements in bone health in this age group. Physical fitness measures were included in order to evaluate the impact of the intervention. Separate GEE models were performed including age^2 to assess for the effects of growth but did not substantially alter the results (Supplementary Tables), and due to sample size the more simple model was retained and reported. As participants who had prior fitness intervention exposure were included in the sample, a sensitivity analysis was conducted to determine any differences in baseline bone parameters and fitness measures as well as differences in changes over the course of the intervention. The impact of age between the intervention groups was explored using a two-way between groups analysis of variance. Alpha of <0.05 was considered statistically significant. Sample size was not formally calculated as participation in the bone health study was offered to all participants of AMPItUp. The program is limited to a maximum of 25 participants per semester for accommodation purposes[26].

Results

Baseline

The sample comprised 28 participants, 17 male and 11 female, ranging in age between 12.57 and 17.59 years with a mean age of 14.06 (SD=1.28) years. The mean pubertal score was 6.41 (SD=1.78) with conversion of pubertal scores to categories indicating that the majority (92.9%) were in a mid or post-pubertal stage. Fourteen participants were mid-pubertal, 12 were post-pubertal and two were pre-pubertal. Four participants (14.8%) changed pubertal category over the course of the intervention, two moved from pre-pubertal to mid-pubertal and two moved from mid-pubertal to post-pubertal. There were no statistically significant differences between sexes for age, puberty score, height, weight, BMI or NDI. Baseline descriptive characteristics of the sample are presented in Table 2. Eleven participants had taken part in the 13-week intervention program at least once prior to bone parameter measurements being taken. Prior participants had completed between one and five programs, with a mean prior attendance of 2.18 (SD=1.11) programs.

Baseline measurements of bone parameters indicated a deficit in bone health with Z-scores indicating the deficit was also present when compared to sex and heighted matched norms (Table 3). The 11 participants who had previously taken part in the fitness intervention (intervention-experienced participants) had higher baseline parameters on all measurements of bone health than those who had never previously taken part (intervention-naïve participants). The differences between groups based on prior intervention engagement were statistically significant for all bone health parameters except total area (T4 and T66), fracture load on the Y-axis (Y3N), trabecular density and the Z-scores for SSI and cortical density. Fitness parameters, however, were not significantly different between groups based on prior participation status, apart from the 1RM leg press which was significantly higher in the intervention-experienced group (61.81% increase, d_{cohen}=1.35, t=-3.01, p=0.008). All baseline measurements for both groups are presented in Tables 3 and 4.

As the intervention-experienced participants were significantly older (15.11 years compared to 13.38 years respectively) (η^2=12.13, t=-3.62, p<0.001), a two-way between groups analysis of variance was conducted in order to explore the impact of prior intervention and age. The interaction effect between age and intervention status was not statistically significant for any variable. There was a statistically significant main effect for age only for fracture load F(5,20)=3.26, p=0.026, η_p^2 =0.45. A statistically significant main effect for intervention was found only for T4 trabecular density score, F(1,15)=5.34, p=0.025, partial eta squared=0.26.

Table 5. Pre-post group difference on pQCT bone health parameters.

	Baseline		Post-intervention					
	M	*SD*	*M*	*SD*	d_{cohen}	*d* 95% Confidence Interval	T-test statistic	P-value
Age (years)	14.06	1.28	14.45	1.25	12.07[b]		4.62[a]	*<0.001
Height (cm)	163.81	10.55	165.89	10.05	0.20	-0.32 to 0.73	-0.75	0.454
Weight (kg)	61.40	14.94	63.75	14.78	12.10[b]		0.64[a]	0.523
Fat/Muscle area ratio	60.75	42.29	35.16	2.08	-0.86	-1.40 to -0.31	0.90	0.534
Bone/Muscle area ratio	40.72	52.86	35.11	42.19	-0.12	-0.64 to 0.41	1.07	0.363
T4								
Mass (g/cm)	3.14	0.64	3.17	0.58	0.05	-0.48 to 0.57	-0.46	0.647
Total area (mm^2)	1144.14	184.16	1159.49	178.54	0.09	-0.44 to 0.61	-0.69	0.497
Total density (mg/cm^3)	273.89	31.37	273.79	34.48	0.00	-0.53 to 0.52	0.03	0.976
Trabecular density Z- score	-0.13	1.41	-0.65	2.16	-0.29	-0.81 to 0.24	1.07	0.290
T66								
Mass (g/cm)	3.15	0.61	3.28	0.53	0.23	-0.30 to 0.75	-2.75	*0.010
Cortical area (mm^2)	235.15	61.35	247.89	47.49	12.09[b]		2.45[a]	*0.014
Total area (mm^2)	614.78	144.53	595.00	103.56	12.10[b]		0.48[a]	0.633
Cortical density (mg/cm^3)	1038.12	50.76	1049.26	38.45	0.25	-0.28 to 0.77	-0.93	0.359
SSI (mm^3)	1745.89	363.21	1745.31	478.77	0.00	-0.53 to 0.52	0.01	0.992
Fracture load X3N	4476.34	1094.24	4609.13	1312.96	0.11	-0.41 to 0.63	-1.31	0.202
Fracture load Y3N	3343.28	754.31	3230.69	853.56	-0.14	-0.66 to 0.39	0.93	0.363
Cortical area Z-score	-1.14	1.66	-0.96	1.18	0.13	-0.40 to 0.65	-0.47	0.638
Cortical density Z-score	-0.03	1.29	0.18	0.86	0.19	-0.33 to 0.72	-0.69	0.495
SSI Z-score	-0.64	0.97	-0.81	1.13	-0.16	-0.69 to 0.36	0.61	0.546
Cortical area to total area ratio	21.43	5.99	22.55	5.09	0.20	-0.32 to 0.73	-1.86	0.071

a=Related samples Wilcoxon signed rank test, b=eta squared.

Intervention

Participants attended between 15 through to 25 out of a possible 26 sessions during the 13-week intervention, with a median attendance of 22 sessions (95% CI 20.58 -22.63). All fitness measures improved on average over the course of the intervention; 1RM leg press increased by 21.1% (d_{cohen}=0.53, p=0.002), standing broad jump by 5.36% (d_{cohen}=0.16, p=0.011), and vertical jump by 5.23% (d_{cohen}=0.16, p=0.235) (Table 4).

An improvement trend in bone health measurements was observed over the course of the 13 week intervention, with a statistically significant increase present for T66 measurements for bone mass (4.12% increase, d_{cohen}=0.23, t=-2.75, p=0.010) and cortical area (5.42% increase, η^2=12.09, t=2.45, p=0.014). A sensitivity analysis to limit analyses to only intervention-naïve participants indicated similar results for bone health parameters, except for the change in T66 mass which was no longer statistically significant (p=0.065). Non-statistically significant improvements were seen in the Z-scores for cortical area and cortical density. All pQCT measurements, prior and post-intervention, are shown in Table 5.

GEE modelling indicated that the improvement in T4 total area became statistically significant when the effect of sex, puberty score, age, height, weight, degree of motor impairment, and improvement in lower fitness measures was accounted for (β=-54.02, p=0.017). A statistically significant influence was found in the model for sex (β=116.94, p=0.007), height (β=6.29, p=0.014), and NDI score (β=2.29, p=0.044), with vertical jump measurements not statistically significant (β=6.69, p=0.060). The model was such that T4 total area increased as height and vertical jump performance increased, improvements were greater for those with a lower degree of motor impairment as measured by NDI, and for males compared to females. Vertical jump also had a statistically significant impact in the model for T66 cortical area (β=2.01, p=0.043) and T66 cortical area Z score (β=0.02, p=0.037). The only other fitness measure that had a statistically significant impact on any model was 1RM leg press in the model for T66 cortical density (β=0.56, p=0.015), and cortical density Z score (β=0.02, p=0.037) as well as a negative impact on fracture load on the Y axis (β=-13.51, p=0.033). The degree of motor impairment as indicated by NDI was a statistically significant influencer in

Table 6. GEE modelling showing relationships between changes in bone health and potential mediators.

	β Estimate	SE	β 95% Confidence interval	p-value
T4 Total area				
Pre/post[a]	-54.02	22.68	-98.47 to -9.57	*0.017
Sex[b]	116.94	43.42	31.84 to 202.04	*0.007
Puberty score	-23.64	15.15	-53.34 to 6.06	0.119
Age	20.28	39.61	-57.36 to 97.91	0.609
Height	6.29	2.56	1.29 to 11.31	*0.014
Weight	-1.23	2.26	-5.66 to 3.21	0.587
1 RM leg press	-1.09	0.83	-2.72 to 0.53	0.188
Vertical jump	6.69	3.57	-0.29 to 13.69	0.060
Standing broad jump	-4.14	3.87	-11.72 to 3.44	0.285
NDI	2.29	1.14	0.06 to 4.53	*0.044
T66 Mass				
Pre/post[a]	-0.02	0.08	-0.18 to 0.14	0.783
Sex[b]	-0.40	0.17	-0.74 to -0.07	*0.019
Puberty score	0.00	0.06	-0.13 to 0.12	0.949
Age	0.58	0.17	0.25 to 0.91	*<0.001
Height	-0.01	0.01	- 0.03 to 0.01	0.281
Weight	0.01	0.01	-0.01 to 0.03	0.357
1 RM leg press	-0.01	0.004	-0.01 to 0.00	0.137
Vertical jump	0.01	0.01	-0.01 to 0.03	0.373
Standing broad jump	-0.01	0.01	-0.03 to 0.01	0.302
NDI	0.01	0.01	0.00 to 0.02	*0.044
T66 Cortical area				
Pre/post[a]	-3.38	9.50	-21.99 to 15.24	0.722
Sex[b]	-27.19	16.82	-60.17 to 5.78	0.106
Puberty score	-2.48	7.70	-17.57 to 12.62	0.748
Age	34.23	15.72	3.41 to 65.04	*0.029
Height	0.60	1.16	-1.68 to 2.88	0.607
Weight	0.66	0.92	-1.14 to 2.46	0.473
1 RM leg press	-0.21	0.36	-0.91 to 0.49	0.557
Vertical jump	2.01	0.99	0.06 to 3.95	*0.043
Standing broad jump	-0.71	0.77	-2.24 to 0.81	0.359
NDI	0.53	0.59	-0.62 to 1.69	0.366
T4 Trabecular density Z score				
Pre/Post[a]	0.72	0.81	-0.87 to 2.32	0.374
Puberty score	-0.28	0.22	-0.70 to 0.14	0.190
Age	-0.83	0.40	-1.61 to -0.04	*0.039
Weight	0.05	0.02	0.01 to 0.09	*0.016
1 RM leg press	0.03	0.02	-0.01 to 0.06	0.105
Vertical jump	0.07	0.06	-0.06 to 0.19	0.304
Standing broad jump	0.00	0.03	-0.06 to 0.06	0.997
NDI	-0.04	0.02	-0.08 to 0.00	*0.049
T66 Cortical density Z score				
Pre/post[a]	-0.06	0.27	-0.58 to 0.47	0.835
Puberty score	0.02	0.14	-0.26 to 0.31	0.869
Age	-0.06	0.26	-0.46 to 0.57	0.831
Weight	-0.02	0.02	-0.06 to 0.02	0.335
1 RM leg press	0.02	0.01	0.001 to 0.03	*0.037
Vertical jump	0.03	0.04	-0.04 to 0.10	0.382
Standing broad jump	0.01	0.02	-0.03 to 0.06	0.635
NDI	-0.02	0.01	-0.04 to 0.01	0.246

Table 6. *(Cont. from previous page).*

	β Estimate	SE	β 95% Confidence interval	p-value
T66 Cortical area Z score				
Pre/Post[a]	-0.16	0.31	-0.77 to 0.45	0.613
Puberty score	-0.08	0.26	-0.58 to 0.43	0.764
Age	0.16	0.52	-0.86 to 1.18	0.758
Weight	0.02	0.03	-0.04 to 0.08	0.597
1 RM leg press	0.01	0.01	-0.02 to 0.03	0.655
Vertical jump	0.07	0.04	-0.01 to 0.14	0.081
Standing broad jump	-0.02	0.03	-0.07 to 0.03	0.467
NDI	0.01	0.02	-0.03 to 0.05	0.736
T66 SSI Z score				
Pre/Post[a]	0.28	0.22	-1.04 to 0.35	0.203
Puberty score	0.04	0.17	0.30 to 0.38	0.824
Age	-0.35	0.35	-1.04 to 0.35	0.327
Weight	0.02	0.02	-0.02 to 0.06	0.270
1 RM leg press	0.00	0.01	-0.02 to 0.02	0.804
Vertical jump	0.03	0.03	-0.03 to 0.09	0.290
Standing broad jump	0.00	0.02	-0.05 to 0.05	0.998
NDI	0.00	0.02	-0.03 to 0.03	0.909
a Where pre-intervention is the comparison group and β=1; b Where male is the comparison group and β=1; SE=standard error.				

Table 7. GEE modelling showing relationships between changes in bone health and potential mediators for intervention-naive participants only.

	β Estimate	SE	β 95% Confidence interval	p-value
T66 Mass				
Pre/post[a]	-0.07	2.73	-9.61 to 1.09	0.119
Sex[b]	-0.42	0.15	-0.72 to -0.12	*0.005
Puberty score	-0.04	0.07	-0.18 to 0.10	0.579
Age	0.67	0.29	0.09 to 1.24	*0.022
Height	-0.02	0.01	- 0.03 to 0.002	0.090
Weight	0.02	0.01	0.002 to 0.03	*0.022
1 RM leg press	-0.01	0.01	-0.02 to 0.00	0.130
Vertical jump	0.01	0.01	-0.02 to 0.03	0.588
Standing broad jump	0.00	0.01	-0.02 to 0.02	0.864
NDI	0.01	0.05	0.00 to 0.02	0.079
T66 Total area				
Pre/Post[a]	168.54	67.93	35.40 to 301.69	*0.013
Sex[b]	70.55	36.58	-1.15 to 142.25	0.054
Puberty score	-14.01	23.37	-59.82 to 31.81	0.549
Age	136.09	53.60	31.04 to 241.14	*0.011
Height	-0.77	1.31	-3.34 to 1.80	0.555
Weight	-0.51	1.87	-4.18 to 3.16	0.785
1 RM leg press	2.70	1.07	0.61 to 4.79	*0.011
Vertical jump	-9.43	2.30	-15.31 to -3.56	*0.002
Standing broad jump	-0.94	1.45	-3.78 to 1.90	0.516
NDI	3.39	0.80	1.82 to 4.95	*<0.001
T66 Cortical area				
Pre/post[a]	-27.02	19.80	-65.84 to 15.96	0.799
Sex[b]	-26.41	14.30	-54.43 to 1.62	0.065

Table 7. *(Cont. from previous page).*

	β Estimate	SE	β 95% Confidence interval	p-value
Puberty score	-2.39	9.36	-20.73 to 15.96	0.799
Age	16.62	32.85	-47.76 to 81.00	0.613
Height	0.38	0.99	-1.56 to 2.32	0.699
Weight	1.79	0.71	0.39 to 3.18	*0.012
1 RM leg press	-0.61	0.56	-1.70 to 0.48	0.274
Vertical jump	2.80	1.03	0.79 to 4.81	*0.006
Standing broad jump	0.12	0.80	-1.37 to 1.62	0.874
NDI	0.57	0.50	-0.93 to 1.04	0.910
T66 SSI				
Pre/Post[a]	164.65	79.93	22.72 to 307.59	*0.024
Sex[b]	63.19	144.82	-220.65 to 347.02	0.663
Puberty score	32.82	46.83	-58.97 to 124.60	0.483
Age	27.16	239.47	-442.20 to 496.51	0.910
Height	9.96	8.20	-6.12 to 26.04	0.225
Weight	4.79	5.01	-5.02 to 14.60	0.339
1RM leg press	2.76	3.40	-3.91 to 9.42	0.418
Vertical jump	-1.28	10.36	-21.59 to 19.03	0.902
Standing broad jump	2.19	9.27	-15.97 to 20.35	0.813
NDI	5.08	4.18	-3.11 to 13.27	0.224
T66 Fracture load X3N				
Pre/post[a]	369.08	164.29	47.09 to 691.08	*0.025
Sex[b]	-270.67	312.20	-882.57 to 341.23	0.386
Puberty score	-81.70	96.43	-270.70 to 107.31	0.397
Age	409.16	521.97	-613.88 to 1432.20	0.433
Height	10.60	17.24	-23.19 to 44.39	0.539
Weight	17.84	10.38	-2.51 to 38.19	0.086
1 RM leg press	7.99	7.54	-6.79 to 22.77	0.289
Vertical jump	5.14	17.79	-29.72 to 39.99	0.773
Standing broad jump	13.72	16.98	-19.56 to 47.01	0.419
NDI	8.40	9.24	-9.71 to 26.50	0.363
T66 Fracture load Y3N				
Pre/post[a]	590.86	258.79	83.65 to 1098.07	*0.022
Sex[b]	-224.60	292.11	-347.94 to 797.13	0.442
Puberty score	123.73	124.84	-120.95 to 368.41	0.322
Age	409.16	521.97	-613.88 to 1432.20	0.433
Height	12.97	17.80	-21.92 to 47.85	0.466
Weight	0.52	13.19	-25.33 to 26.38	0.968
1 RM leg press	-0.32	6.63	-13.32 to 12.68	0.962
Vertical jump	-20.33	26.03	-71.35 to 30.68	0.435
Standing broad jump	6.06	18.08	-29.38 to 41.49	0.738
NDI	14.31	10.53	-6.33 to 34.94	0.174
T4 Trabecular density Z score				
Pre/Post[a]	0.92	1.25	-1.54 to 3.38	0.463
Puberty score	-0.38	0.30	-0.96 to 0.20	0.201
Age	-1.01	0.75	-2.48 to 0.47	0.181
Weight	0.08	0.03	0.04 to 0.13	*<0.001
1 RM leg press	0.04	0.03	-0.02 to 0.09	0.171
Vertical jump	0.09	0.07	-0.03 to 0.22	0.151
Standing broad jump	-0.01	0.04	-0.09 to 0.06	0.781
NDI	-0.05	0.02	-0.09 to -0.01	*0.010

Table 7. *(Cont. from previous page).*

	β Estimate	SE	β 95% Confidence interval	p-value
T66 Cortical density Z score				
Pre/post[a]	-0.48	0.53	-1.52 to 0.56	0.366
Puberty score	0.11	0.23	-0.33 to 0.56	0.616
Age	-0.41	0.61	-1.60 to 0.79	0.506
Weight	-0.01	0.02	-0.05 to 0.03	0.476
1 RM leg press	0.01	0.01	-0.01 to 0.03	0.339
Vertical jump	0.06	0.04	-0.03 to 0.14	0.174
Standing broad jump	0.02	0.02	-0.03 to 0.06	0.500
NDI	-0.03	0.01	-0.05 to -0.001	*0.038
T66 Cortical area Z score				
Pre/Post[a]	-1.02	0.75	-2.48 to 0.44	0.172
Puberty score	0.29	0.31	-0.33 to 0.90	0.360
Age	1.21	0.86	-2.91 to 0.48	0.161
Weight	0.02	0.03	-0.04 to 0.07	0.609
1 RM leg press	0.00	0.02	-0.05 to 0.04	0.865
Vertical jump	0.07	0.03	0.01 to 0.13	*0.034
Standing broad jump	0.00	0.03	-0.06 to 0.05	0.934
NDI	0.01	0.02	-0.03 to 0.05	0.735
T66 SSI Z score				
Pre/Post[a]	0.39	0.21	-0.02 to 0.80	0.061
Puberty score	0.28	0.11	0.05 to 0.50	*0.015
Age	-0.66	0.35	-1.35 to 0.02	0.057
Weight	-0.01	0.02	-0.04 to 0.02	0.541
1 RM leg press	0.01	0.01	-0.01 to 0.03	0.188
Vertical jump	-0.01	0.02	-0.06 to 0.03	0.547
Standing broad jump	0.00	0.02	-0.05 to 0.04	0.961
NDI	0.02	0.01	-0.01 to 0.05	0.148

a Where pre-intervention is the comparison group and β=1; b Where male is the comparison group and β=1.

some of the models (T4 total area, total density, trabecular density, and trabecular density Z score; T66 mass) with the direction of influence varying between models. A positive association was found such that bone gains increased as NDI score increased (motor impairment decreased) in T4 total area (β=2.29, p=0.044) and T66 mass (β=0.01, p=0.044) and a negative association such that bone gains decreased as NDI score decreased (motor impairment increased) in T4 total density (β=-0.64, p=0.044), T4 trabecular density (β=-0.69, p=.028) and T4 trabecular density Z score (β=-0.04, p=0.049). Growth as indicated by age, height and weight were found to be statistically significant influences in only some of the models (T4 trabecular density, T4 trabecular density Z-score, T66 mass and T66 cortical area; T4 total area; T4 total density, T4 trabecular density and T4 trabecular density Z-score) as was sex (T4 total area, T66 mass, T66 cortical density and fracture load X3N respectively). The increase in bone mass for both T66 mass and cortical area ceased to be statistically significant after controlling for confounders. GEE models for parameters found to have a statistically significant effect in pre and post modelling, as well as models for Z-scores, are presented in Table 6 with results for all GEE models presented as appendices one, two and three.

A sensitivity analysis of only intervention-naïve participants found that the changes in T66 total area (β=168.54, p=0.013), SSI (β=164.65, p=0.024), and fracture load X3N and Y3N (β=369.08, p=0.025; β=590.86, p=0.022) became statistically significant when the effect of other variables was controlled for statistically. The models for these parameters as well as T66 mass, T66 cortical area, and all Z scores are presented in Table 7, GEE models for other variables are presented in appendix three. Fitness measures in this group were implicated in more models than when intervention-experienced participants were included. Vertical jump was implicated in T4 mass (β=0.03, p=0.002), T4 total area (β=9.46, p=0.015), T4 trabecular density (β=1.77, p=0.030), T66 total area (β=-9.43, p=0.002), T66 cortical area (β=2.80, p=0.006), T66 cortical area Z-score (β=0.07, p=0.034) and an effect nearing significance in T66 cortical density (β=2.89, p=.067); 1RM leg press in T4 total area (β=-2.28, p=0.038) and T66 total area (β=2.70, p=0.011); and standing broad jump showed a statistically significant influence in T4 total density (β=1.04, p=0.033). NDI, however, had a primarily negative effect in modelling for this sample with bone gains decreasing as motor impairment decreased in models for T4 total density (β=-0.91, p<0.001), T4 trabecular density (β=-1.04, p=0.001), T66 cortical density (β=-1.03, p=0.023), T4 trabecular density Z-score (β=-0.05, p=0.010) and T66 cortical density Z-score (β=-0.03, p=0.038) while a positive effect was seen only for T66 total area (β=3.39, p<0.001).

To compensate for the non-linear effect of age on growth, models were also run using age^2 as a growth estimate. While recognising that the models are likely underpowered, models which included age^2 as an estimate of growth found a statistically significant influence for growth, as indicated by age^2, age, height or weight, for the following measures T4 mass, T4 total area, T4 total density, T4 trabecular density, T4 trabecular density Z-score, T66 mass, T66 SSI, T66 cortical area, and T66 fracture load X3N. Models including age^2 also showed a stronger role for fitness measures which were additionally implicated in T4 mass, T4 total area, T4 total density, T4 trabecular density, and cortical density Z scores (appendix 2). It was not possible to run models including age^2 in the intervention naïve group only due to the smaller sample size .

Discussion

This study explored whether a prescribed multimodal exercise intervention established to improve physical abilities among adolescents with DCD[25,26] could also improve measures of bone health. Positively, AMPitup Program improved fitness parameters over the 13-week intervention, with improvements in bone parameters subsequently observed in bone scans conducted during the follow-up assessment period (approximately 3 months post-intervention). Prior research on fitness improvements in AMPitup have found that fitness gains tend to return to baseline over the break between interventions and thus can be attributed to the intervention rather than due to growth[25]. Statistical modelling also indicated that improvements in bone health parameters were related to improvements in fitness measures and gains were above what could be attributed to growth. Considering the short intervention time and sample size, these findings indicate that participation in a generalised multimodal exercise intervention may be effective in improving bone health of adolescents with DCD.

Bone parameters indicated an impairment at baseline and improvement over the course of the intervention, with the group overall moving towards a healthier bone phenotype. The size of the gains demonstrated in this study appear similar to what has been shown in other exercise interventions in comparable age groups, which have shown increases of between 1 to 8% in bone strength at the loaded sites[15,22]. The pattern of changes in bone parameters were primarily in bone mass and cortical area as would be anticipated for changes during an exercise intervention in a peri pubertal population[14,15,42,43], since loading in this age group results in reshaping of bone cross-sectionally along with a redistribution of bone minerals to the cortical area[15,42,43].

GEE modelling indicated that improvements in physical fitness contributed to changes in bone parameters beyond the effects of growth as indicated by age, height, weight, age^2 and pubertal stage, with vertical jump and 1RM leg press being implicated in several models. Fitness measures had a stronger role in models of only intervention-naïve participants, which likely reflects a low level of baseline physical activity in this population. Individuals who have lower baseline physical activity levels tend to show more substantial bone changes in response to an exercise intervention[21]. A low baseline of physical activity may also explain the finding in many models that bone gains increased as motor impairment increased (lower NDI). Physical activity has been found previously to decrease as motor impairment increases[44] and as such it is probable that those with greater motor impairment had lower baseline levels of physical activity. Some bone measures however, had an inverse finding with bone gains found to increase as degree of motor impairment decreased (higher NDI). This may reflect the impact of motor impairment on exercise performance with improvements in fitness being more limited in those that have more motor impairment which is then reflected in bone gains.

The role of motor impairment upon bone gains is also implicated by the smaller scale of change in muscle strength than would be anticipated based on other similar exercise interventions[19,20,22]. Although this could reflect on the osteogenic potential of the program, it may also indicate that the impact of exercise interventions on bone parameters is somewhat less effective in this population. It was noted in this study that exercise progression, including increasing loading, was slow for many participants with some participants remaining at the same level of loading throughout the intervention. Other studies have found that gains in fitness are more limited in individuals with DCD when compared to individuals without DCD[45] and have indicated the need for a longer learning period[24]. As increased loading and variety are required to stimulate osteogenic change[13], a slower exercise progression will limit the osteogenic potential of the exercise program. A longer time frame therefore may be needed by individuals with DCD to learn and effectively execute the exercise tasks before the osteogenic effects can be accurately observed and assessed.

This study had the advantage of including intervention experienced participants and sensitivity analysis supported the need for a longer intervention period by showing continued improvement in those participants. This would seem to indicate that once necessary motor skills are acquired for the exercise program modalities, participants are then able to achieve the increased loading and variety required to stimulate osteogenic change[13]. The study was strengthened by the use of a program specifically designed for individuals with DCD and already established to improve strength in an adolescent population with DCD[25], however it is likely that the 13 week program in this study was insufficient to allow for skill mastery. A longer study period would also allow more time for bone adaptation, however the five to seven-month epoch between the scans should have been sufficient to allow bone remodelling to occur[46]. The study was conspicuously limited by the absence of a control group, however the use of sex and height-matched Z-scores derived from the Stratec reference values[30] and statistical modelling to control for variables related to growth provided the advantage of being able to indicate that the effect of the exercise interventions on changes in bone outcomes were possibly above what would be anticipated from growth. Future research should include a control group to determine the impact of DCD specific impairments upon exercise intervention. The impact of the exercise program upon other exercise benefits such as improved muscle function and balance was beyond the reach of this study, however these are likely to magnify the benefits of the found small gains in bone mass[15,47]. Combined benefits, including improvements in muscle function and balance, as well as clinical benefits such as fracture rates are a potential avenue for future research along with confirmation of improvements in bone parameters.

The outcomes of this study are promising in relation to the ability of the intervention to be effective in improving muscle and bone parameters in adolescents with DCD. The changes detected in this study are small but reasonable given the timing of the study and the motor difficulties of the individuals with DCD. Further research should be undertaken over a longer period to determine whether bone improvements can be achieved and sustained to promote maximal bone mass accrual closer to the normal range during this critical developmental period. This is important for the prevention of future bone-health related adverse outcomes, particularly as this group reports a higher falls rate.

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Authorship contribution

Author #1 is responsible for statistical analysis of the data and prepared the first draft of the paper. Authors #2, #3, #4 and #7 contributed to the bone analysis. Authors #5 and #6 designed and contributed to the exercise intervention. All authors revised the paper critically for intellectual content and approved the final version. All authors agree to be accountable for the work and to ensure that any questions relating to the accuracy and integrity of the paper are investigated and resolved.

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Appendix A. GEE modelling showing relationships between changes in bone health and potential mediators.

	β	SE	β 95% Confidence interval	p
T4 Mass				
Pre/Post[a]	-0.09	0.10	-0.29 to 0.10	0.348
Sex[b]	0.23	0.16	-0.08 to 0.54	0.146
Puberty score	-0.11	0.07	-0.25 to 0.03	0.108
Age	-0.02	0.13	-0.27 to 0.23	0.870
Height	0.01	0.09	0.00 to 0.03	0.122
Weight	0.02	0.01	0.00 to 0.04	0.056
1 RM leg press	0.00	0.004	-0.01 to 0.01	0.844
Vertical jump	0.02	0.01	0.00 to 0.05	0.074
Standing broad jump	0.00	0.01	-0.02 to 0.02	0.694
NDI	0.00	0.004	-0.01 to 0.01	0.701
T4 Total area				
Pre/Post[a]	-54.02	22.68	-98.47 to -9.57	*0.017
Sex[b]	116.94	43.42	31.84 to 202.04	*0.007
Puberty score	-23.64	15.15	-53.34 to 6.06	0.119
Age	20.28	39.61	-57.36 to 97.91	0.609
Height	6.29	2.56	1.29 to 11.31	*0.014
Weight	-1.23	2.26	-5.66 to 3.21	0.587
1 RM leg press	-1.09	0.83	-2.72 to 0.53	0.188
Vertical jump	6.69	3.57	-0.29 to 13.69	0.060
Standing broad jump	-4.14	3.87	-11.72 to 3.44	0.285
NDI	2.29	1.14	0.06 to 4.53	*0.044
T4 Total density				
Pre/Post[a]	4.23	6.13	-7.79 to 16.25	0.490
Sex[b]	-10.05	6.83	-23.44 to 3.34	0.141
Puberty score	-2.46	3.17	-8.64 to 3.81	0.447
Age	-7.56	5.76	-18.86 to 3.74	0.190
Height	-0.15	0.48	-1.11 to 0.80	0.754
Weight	1.88	0.45	1.00 to 2.77	*<0.001
1 RM leg press	0.23	0.22	-0.19 to 0.65	0.287
Vertical jump	0.33	0.27	-0.99 to 1.66	0.624
Standing broad jump	0.79	0.45	-0.08 to 1.66	0.076
NDI	-0.64	0.32	-1.25 to -0.02	*0.044
T4 Trabecular density				
Pre/Post[a]	5.67	8.61	-11.21 to 22.55	0.510
Sex[b]	6.59	8.53	-10.12 to 23.31	0.439
Puberty score	-4.83	3.69	-12.06 to 2.39	0.190
Age	-15.53	7.18	-29.60 to -1.47	*0.030
Height	0.61	0.54	-0.44 to 1.66	0.256
Weight	1.46	0.50	0.47 to 2.44	*0.004
1 RM leg press	0.45	0.25	-0.05 to 0.95	0.079
Vertical jump	0.89	0.94	-0.95 to 2.75	0.341
Standing broad jump	-0.06	0.69	-1.42 to 1.29	0.929
NDI	-0.69	0.32	-1.32 to -0.08	*0.028
T4 Trabecular density Z score				
Pre/Post[a]	0.72	0.81	-0.87 to 2.32	0.374
Puberty score	-0.28	0.22	-0.70 to 0.14	0.190
Age	-0.83	0.40	-1.61 to -0.04	*0.039
Weight	0.05	0.02	0.01 to 0.09	*0.016
1 RM leg press	0.03	0.02	-0.01 to 0.06	0.105

Appendix A. *(Cont. from previous page).*

	β	SE	β 95% Confidence interval	p
Vertical jump	0.07	0.06	-0.06 to 0.19	0.304
Standing broad jump	0.00	0.03	-0.06 to 0.06	0.997
NDI	-0.04	0.02	-0.08 to 0.00	*0.049
T66 Mass				
Pre/Post[a]	-0.02	0.08	-0.18 to 0.14	0.783
Sex[b]	-0.40	0.17	-0.74 to -0.07	*0.019
Puberty score	0.00	0.06	-0.13 to 0.12	0.949
Age	0.58	0.17	0.25 to 0.91	*<0.001
Height	-0.01	0.01	-0.03 to 0.01	0.281
Weight	0.01	0.01	-0.01 to 0.03	0.357
1 RM leg press	-0.01	0.004	-0.01 to 0.00	0.137
Vertical jump	0.01	0.01	-0.01 to 0.03	0.373
Standing broad jump	-0.01	0.01	-0.03 to 0.01	0.302
NDI	0.01	0.01	0.00 to 0.02	*0.044
T66 SSI				
Pre/Post[a]	111.08	70.30	-26.71 to 248.88	0.114
Sex[b]	-180.33	135.79	-446.48 to 85.82	0.184
Puberty score	10.32	46.17	-80.17 to 100.80	0.823
Age	135.27	115.95	-91.99 to 365.53	0.243
Height	0.86	9.47	-17.71 to 19.43	0.928
Weight	9.57	6.34	-2.86 to 21.99	0.131
1RM leg press	-3.28	3.02	-9.19 to 2.63	0.277
Vertical jump	10.15	11.75	-12.87 to 33.19	0.387
Standing broad jump	0.85	8.39	-15.59 to 17.28	0.920
NDI	2.76	3.65	-4.39 to 9.90	0.450
T66 SSI Z score				
Pre/Post[a]	-0.28	0.22	-1.04 to 0.35	0.203
Puberty score	0.04	0.17	0.30 to 0.38	0.824
Age	-0.35	0.35	-1.04 to 0.35	0.327
Weight	0.02	0.02	-0.02 to 0.06	0.270
1RM leg press	0.00	0.01	-0.02 to 0.02	0.804
Vertical jump	0.03	0.03	-0.03 to 0.09	0.290
Standing broad jump	0.00	0.02	-0.05 to 0.05	0.998
NDI	0.00	0.02	-0.03 to 0.03	0.909
T66 Total area				
Pre/Post[a]	37.08	33.62	-28.81 to 102.98	0.270
Sex[b]	7.82	48.15	-86.56 to 102.19	0.871
Puberty score	-7.82	18.14	-42.58 to 28.52	0.698
Age	51.29	38.33	-23.82 to 126.41	0.181
Height	-3.04	2.15	-7.25 to 1.16	0.156
Weight	3.24	2.93	-2.50 to 8.97	0.269
1RM leg press	-0.84	0.85	-2.51 to 0.82	0.321
Vertical jump	-1.85	3.22	-8.16 to 4.46	0.566
Standing broad jump	-0.34	2.32	-4.88 to 4.21	0.885
NDI	1.48	1.69	-1.84 to 4.79	0.382
T66 Cortical density				
Pre/Post[a]	-2.68	10.20	-22.67 to 17.32	0.793
Sex[b]	-39.82	10.61	-60.62 to -19.02	*<0.001
Puberty score	-1.91	4.55	-10.82 to 7.00	0.674
Age	13.32	8.34	-3.04 to 29.67	0.110

Appendix A. *(Cont. from previous page).*

	β	SE	β 95% Confidence interval	p
Height	-0.30	0.49	-1.27 to 0.67	0.544
Weight	0.09	0.67	-1.22 to 1.40	0.893
1 RM leg press	0.56	0.23	0.11 to 1.01	*0.015
Vertical jump	1.71	1.26	-0.76 to 4.18	0.175
Standing broad jump	-0.10	0.67	-1.41 to 1.22	0.888
NDI	-0.55	0.49	-1.52 to 0.42	0.267
T66 Cortical density Z score				
Pre/Post[a]	-0.06	0.27	-0.58 to 0.47	0.835
Puberty score	0.02	0.14	-0.26 to 0.31	0.869
Age	-0.06	0.26	-0.46 to 0.57	0.831
Weight	-0.02	0.02	-0.06 to 0.02	0.335
1 RM leg press	0.02	0.01	0.001 to 0.03	*0.037
Vertical jump	0.03	0.04	-0.04 to 0.10	0.382
Standing broad jump	0.01	0.02	-0.03 to 0.06	0.635
NDI	-0.02	0.01	-0.04 to 0.01	0.246
T66 Cortical area				
Pre/Post[a]	-3.38	9.50	-21.99 to 15.24	0.722
Sex[b]	-27.19	16.82	-60.17 to 5.78	0.106
Puberty score	-2.48	7.70	-17.57 to 12.62	0.748
Age	34.23	15.72	3.41 to 65.04	*0.029
Height	0.60	1.16	-1.68 to 2.88	0.607
Weight	0.66	0.92	-1.14 to 2.46	0.473
1RM leg press	-0.21	0.36	-0.91 to 0.49	0.557
Vertical jump	2.01	0.99	0.06 to 3.95	*0.043
Standing broad jump	-0.71	0.77	-2.24 to 0.81	0.359
NDI	0.53	0.59	-0.62 to 1.69	0.366
T66 Cortical area Z-score				
Pre/Post[a]	-0.16	0.31	-0.77 to 0.45	0.613
Puberty Score	-0.08	0.26	-0.58 to 0.43	0.764
Age	0.16	0.52	-0.86 to 1.18	0.758
Weight	0.02	0.03	-0.04 to 0.08	0.597
1 RM leg press	0.01	0.01	-0.02 to 0.03	0.655
Vertical jump	0.07	0.04	-0.01 to 0.14	0.081
Standing broad jump	-0.02	0.03	-0.07 to 0.03	0.467
NDI	0.01	0.02	-0.03 to 0.05	0.736
T66 Fracture load X3N				
Pre/Post[a]	132.07	154.73	-171.20 to 435.34	0.393
Sex[b]	-766.77	338.21	-1429.64 to -103.91	*0.023
Puberty score	-73.44	118.54	-305.77 to 158.89	0.536
Age	606.97	316.71	-13.78 to 1227.72	0.055
Height	-4.25	22.52	-48.39 to 39.89	0.850
Weight	26.64	15.23	-3.21 to 56.48	0.080
1RM leg press	-7.92	6.75	-21.15 to 5.30	0.240
Vertical jump	33.00	22.55	-11.19 to 77.20	0.143
Standing broad jump	6.58	15.49	-23.78 to 36.94	0.671
NDI	4.96	8.76	-12.21 to 22.14	0.571
T66 Fracture load Y3N				
Pre/Post[a]	240.39	176.35	-105.25 to 586.03	0.173
Sex[b]	-150.89	243.10	-627.37 to 325.58	0.535
Puberty score	113.34	96.31	-75.42 to 302.11	0.239

Appendix A. *(Cont. from previous page).*

	β	SE	β 95% Confidence interval	p
Age	320.16	200.73	-73.26 to 713.58	0.111
Height	-1.02	16.40	-33.17 to 31.13	0.950
Weight	14.01	10.79	-7.14 to 35.17	0.194
1 RM leg press	-13.51	6.34	-25.94 to -1.08	*0.033
Vertical jump	4.21	23.18	-41.23 to 49.66	0.856
Standing broad jump	3.49	16.42	-28.69 to 35.67	0.832
NDI	10.53	8.64	-6.41 to 27.46	0.223

a Where pre-intervention is the comparison group and β=1; b Where male is the comparison group and β=1.

Appendix B. GEE modelling showing relationships between changes in bone health and potential mediators with age^2 included.

	β	SE	β 95% Confidence interval	p
T4 Mass				
Pre/Post[a]	0.04	0.09	-0.14 to 0.22	0.636
Sex[b]	0.15	0.14	-0.13 to 0.42	0.291
Puberty score	-0.20	0.06	-0.33 to -0.07	*0.002
Age	5.54	1.33	2.94 to 8.14	*<0.001
Age^2	-0.19	0.05	-0.28 to -0.10	*<0.001
Height	0.00	0.01	-0.01 to 0.02	0.726
Weight	0.03	0.01	0.01 to 0.05	*0.003
1 RM leg press	0.00	0.002	0.00 to 0.01	0.250
Vertical jump	0.03	0.01	0.00 to 0.05	*0.018
Standing broad jump	0.00	0.01	-0.02 to 0.02	0.933
NDI	0.00	0.004	-0.01 to 0.004	0.414
T4 Total area				
Pre/Post[a]	-24.39	21.88	-67.28 to 18.50	0.265
Sex[b]	98.91	38.27	23.90 to 173.91	*0.010
Puberty score	-42.11	12.66	-66.92 to -17.30	*0.001
Age	1212.31	225.24	770.85 to 1653.76	*<0.005
Age^2	-40.32	7.01	-54.06 to -26.59	*<0.005
Height	3.89	2.62	-1.25 to 9.02	0.138
Weight	0.58	2.04	-3.42 to 4.58	0.776
1 RM leg press	-0.66	0.74	-2.10 to 0.79	0.372
Vertical jump	6.96	3.30	0.48 to 13.43	*0.035
Standing broad jump	-3.42	3.55	-10.38 to 3.55	0.336
NDI	2.02	1.04	-0.02 to 4.06	0.052
T4 Total density				
Pre/Post[a]	8.76	6.30	-3.58 to 21.10	0.164
Sex[b]	-12.81	6.46	-25.46 to -0.15	*0.047
Puberty score	-5.24	3.08	-11.28 to 0.81	0.089
Age	174.66	89.32	-0.42 to 349.73	0.051
Age^2	-6.16	3.07	-12.18 to -0.15	*0.045
Height	-0.52	0.41	-1.32 to 0.28	0.201
Weight	2.17	0.46	1.26 to 3.07	*<0.001
1 RM leg press	0.30	0.19	-0.07 to 0.66	0.110
Vertical jump	0.37	0.59	-0.78 to 1.53	0.527
Standing broad jump	0.90	0.43	0.06 to 1.74	*0.036
NDI	-0.68	0.31	-1.30 to -0.06	*0.031
T4 Trabecular density				
Pre/Post[a]	10.55	8.86	-6.82 to 27.91	0.234
Sex[b]	3.63	8.96	-13.94 to 21.19	0.686
Puberty score	-7.87	4.11	-15.94 to 0.19	0.056
Age	180.77	111.25	-37.28 to 398.82	0.104
Age^2	-6.64	3.73	-13.96 to 0.68	0.075
Height	0.21	0.57	-0.91 to 1.33	0.709
Weight	1.76	0.53	0.72 to 2.79	*0.001
1 RM leg press	0.52	0.21	0.11 to 0.94	*0.014
Vertical jump	0.94	0.82	-0.67 to 2.55	0.253
Standing broad jump	0.06	0.66	-1.23 to 1.35	0.930
NDI	-0.74	0.32	-1.37 to -0.11	*0.021
T4 Trabecular density Z score				
Pre/Post[a]	0.91	0.82	-0.70 to 2.52	0.268

Appendix B. *(Cont. from previous page).*

	β	SE	β 95% Confidence interval	p
Puberty score	-0.40	0.24	-0.86 to 0.07	0.094
Age	6.66	4.08	-1.33 to 14.66	0.102
Age^2	-0.26	0.14	-0.53 to 0.01	0.060
Weight	0.06	0.02	0.02 to 0.10	*0.003
1 RM leg press	0.03	0.02	0.00 to 0.07	0.057
Vertical jump	0.07	0.06	-0.0 to 0.19	0.288
Standing broad jump	0.01	0.03	-0.05 to 0.07	0.822
NDI	-0.04	0.02	-0.08 to 0.00	*0.034
T66 Mass				
Pre/Post[a]	0.10	0.08	-0.07 to 0.26	0.243
Sex[b]	-0.48	0.13	-0.72 to -0.22	*<0.001
Puberty score	-0.08	0.06	-0.20 to 0.04	0.184
Age	5.45	0.89	3.70 to 7.19	*<0.001
Age^2	-0.17	0.03	-0.22 to -0.11	*<0.001
Height	-0.02	0.01	-0.04 to 0.01	*0.007
Weight	0.02	0.01	0.00 to 0.03	*0.048
1 RM leg press	0.00	0.003	-0.01 to 0.003	0.243
Vertical jump	0.01	0.01	-0.01 to 0.03	0.355
Standing broad jump	-0.01	0.01	-0.02 to 0.01	0.507
NDI	0.01	0.004	0.00 to 0.02	*0.036
T66 SSI				
Pre/Post[a]	170.88	66.81	39.94 to 301.83	*0.011
Sex[b]	-216.73	124.13	-460.02 to 26.57	0.081
Puberty score	-29.96	48.34	-121.71 to 67.79	0.577
Age	2541.25	982.46	615.66 to 4466.84	*0.010
Age^2	-81.38	31.96	-144.02 to -18.75	*0.011
Height	-4.01	9.44	-22.51 to 14.49	0.671
Weight	13.22	6.41	0.66 to 25.78	*0.039
1 RM leg press	-2.41	3.21	-8.70 to 3.88	0.454
Vertical jump	10.68	12.43	-13.69 to 35.05	0.390
Standing broad jump	2.31	8.47	-14.30 to 18.92	0.786
NDI	2.20	3.77	-5.19 to 9.59	0.559
T66 SSI Z score				
Pre/Post[a]	0.27	0.23	-0.19 to 0.72	0.255
Puberty score	0.05	0.21	-0.36 to 0.46	0.814
Age	-1.03	4.53	-9.91 to 7.85	0.820
Age^2	0.02	0.15	-0.28 to 0.32	0.877
Weight	0.02	0.02	-0.02 to 0.06	0.341
1 RM leg press	0.00	0.01	-0.02 to 0.02	0.837
Vertical jump	0.03	0.03	-0.03 to 0.09	0.292
Standing broad jump	0.00	0.02	-0.05 to 0.04	0.976
NDI	0.00	0.02	-0.03 to 0.04	0.899
T66 Total area				
Pre/Post[a]	47.28	36.08	-23.44 to 118.00	0.190
Sex[b]	1.61	46.52	-89.56 to 92.78	0.972
Puberty score	-13.39	18.20	-49.05 to 22.28	0.462
Age	461.60	306.75	-139.62 to 1062.82	0.132
Age^2	-13.88	10.39	-34.23 to 6.48	0.181
Height	-3.88	2.16	-8.10 to 0.35	0.072
Weight	3.86	3.07	-2.15 to 9.87	0.208

Appendix B. *(Cont. from previous page).*

	β	SE	β 95% Confidence interval	p
1 RM leg press	-0.70	0.84	-2.34 to 0.95	0.409
Vertical jump	-1.76	3.30	-8.23 to 4.71	0.594
Standing broad jump	-0.09	2.38	-4.75 to 4.58	0.971
NDI	1.39	1.66	-1.88 to 4.65	0.405
T66 Cortical density				
Pre/Post[a]	0.77	11.02	-20.83 to 22.37	0.944
Sex[b]	-41.92	9.50	-60.54 to -23.29	*<0.001
Puberty score	-4.06	4.84	-13.55 to 5.43	0.401
Age	152.09	79.73	-4.17 to 308.35	0.056
Age^2	-4.69	2.74	-10.06 to 0.67	0.086
Height	-0.58	0.42	-1.41 to 0.25	0.171
Weight	0.30	0.67	-1.02 to 1.62	0.655
1 RM leg press	0.61	0.23	0.15 to 1.07	*0.010
Vertical jump	1.74	1.22	-0.65 to 4.12	0.153
Standing broad jump	-0.01	0.67	-1.32 to 1.30	0.987
NDI	-0.58	0.48	-1.51 to 0.35	0.222
T66 Cortical density Z score				
Pre/Post[a]	-0.04	0.29	-0.61 to 0.53	0.893
Puberty score	0.01	0.16	-0.29 to 0.32	0.930
Age	0.72	2.45	-4.08 to 5.51	0.770
Age^2	-0.02	0.08	-0.18 to 0.14	0.784
Weight	-0.02	0.02	-0.06 to 0.02	0.364
1 RM leg press	0.02	0.01	0.001 to 0.03	*0.034
Vertical jump	0.03	0.04	-0.04 to 0.10	0.380
Standing broad jump	0.01	0.02	-0.03 to 0.06	0.621
NDI	-0.02	0.01	-0.04 to 0.01	0.232
T66 Cortical area				
Pre/Post[a]	8.46	8.95	-9.07 to 26.00	0.344
Sex[b]	-34.40	12.77	-59.43 to -9.37	*0.007
Puberty score	-9.86	6.79	-23.17 to 3.45	0.147
Age	510.67	123.36	268.90 to 752.45	*<0.001
Age^2	-16.12	4.23	-24.41 to -7.82	*<0.001
Height	-0.37	0.80	-1.94 to 1.21	0.648
Weight	1.38	0.82	-0.23 to 2.99	0.093
1 RM leg press	-0.04	0.32	-0.66 to 0.59	0.911
Vertical jump	2.11	0.99	0.17 to 4.05	*0.033
Standing broad jump	-0.42	0.79	-1.98 to 1.13	0.593
NDI	0.42	0.56	-0.68 to 1.53	0.450
T66 Cortical area Z-score				
Pre/Post[a]	-0.01	0.32	-0.64 to 0.61	0.969
Puberty Score	-0.17	0.28	-0.71 to 0.38	0.549
Age	5.97	6.14	-6.07 to 18.01	0.331
Age^2	-0.20	0.21	-0.61 to 0.21	0.340
Weight	0.02	0.03	-0.05 to 0.09	0.515
1 RM leg press	0.01	0.01	-0.02 to 0.03	0.463
Vertical jump	0.07	0.04	0.00 to 0.14	0.065
Standing broad jump	-0.02	0.03	-0.07 to 0.04	0.595
NDI	0.00	0.02	-0.04 to 0.05	0.833
T66 Fracture load X3N				
Pre/Post[a]	372.85	131.02	116.04 to 629.65	*0.004

Appendix B. *(Cont. from previous page).*

	β	SE	β 95% Confidence interval	p
Sex[b]	-913.33	266.30	-1435.27 to -391.39	*0.001
Puberty score	-223.51	107.92	-435.04 to -11.99	*0.038
Age	1204.22	2129.87	6119.76 to 14468.68	*<0.001
Age^2	-327.68	68.88	-462.67 to -192.68	*<0.001
Height	-23.86	19.92	-62.90 to 15.19	0.231
Weight	41.35	14.03	13.86 to 68.84	*0.003
1 RM leg press	-4.40	6.93	-17.98 to 9.18	0.525
Vertical jump	35.11	25.48	-14.83 to 85.05	0.168
Standing broad jump	12.45	16.27	-19.44 to 44.34	0.444
NDI	2.73	7.84	-12.63 to 18.09	0.728
T66 Fracture load Y3N				
Pre/Post[a]	304.03	184.08	-56.77 to 664.83	0.099
Sex[b]	-189.64	239.69	-659.42 to 280.15	0.429
Puberty score	73.68	105.01	-132.13 to 279.49	0.483
Age	2880.67	22225.56	-1481.34 to 7242.68	0.196
Age^2	-86.61	75.07	-233.75 to 60.53	0.249
Height	-6.20	16.06	-37.69 to 25.28	0.699
Weight	17.90	12.12	-5.86 to 41.66	0.140
1 RM leg press	-12.58	6.47	-25.26 to 0.11	0.052
Vertical jump	4.77	24.19	-42.64 to 52.18	0.844
Standing broad jump	5.04	16.55	-27.39 to 37.47	0.761
NDI	9.94	8.70	-7.12 to 26.99	0.254
a Where pre-intervention is the comparison group and β=1; b Where male is the comparison group and β=1.				

Appendix C. GEE modelling showing relationships between changes in bone health and potential mediators for intervention-naive participants only.

	β	SE	β 95% Confidence interval	p
T4 Mass				
Pre/Post[a]	-0.08	0.17	-0.41 to 0.36	0.653
Sex[b]	-0.07	0.01	-0.27 to 0.12	0.461
Puberty score	-0.23	0.09	-0.41 to 0.05	*0.011
Age	0.29	0.20	-0.10 to 0.68	0.141
Height	0.00	0.01	-0.02 to 0.01	0.683
Weight	0.04	0.01	0.02 to 0.06	*<0.001
1 RM leg press	0.00	0.004	-0.01 to 0.01	0.571
Vertical jump	0.03	0.01	0.01 to 0.06	*0.002
Standing broad jump	0.00	0.08	-0.02 to 0.02	0.941
NDI	-0.01	0.004	-0.01 to 0.00	0.060
T4 Total area				
Pre/Post[a]	-62.18	43.93	-148.29 to 23.92	0.157
Sex[b]	57.40	39.04	-19.12 to 133.93	0.141
Puberty score	-39.77	17.27	-73.63 to -5.91	*0.021
Age	72.35	68.03	-60.99 to 205.69	0.288
Height	2.96	2.90	-2.73 to 8.66	0.308
Weight	2.74	2.48	-2.12 to 7.60	0.269
1 RM leg press	-2.28	1.10	-4.43 to -0.12	*0.038
Vertical jump	9.46	3.87	1.87 to 17.04	*0.015
Standing broad jump	-3.35	3.70	-10.69 to 3.91	0.366
NDI	1.40	1.32	-1.18 to 3.98	0.289
T4 Total density				
Pre/Post[a]	-0.28	6.56	-13.13 to 12.57	0.966
Sex[b]	-21.66	7.53	-36.42 to -6.91	*0.004
Puberty score	-6.79	4.56	-15.73 to 2.15	0.137
Age	-4.64	17.02	-37.99 to 28.72	0.785
Height	-0.73	0.58	-1.86 to 0.41	0.211
Weight	2.88	0.41	2.08 to 3.68	*<0.001
1 RM leg press	0.07	0.28	-0.48 to 0.61	0.811
Vertical jump	0.76	0.56	-0.35 to 1.87	0.178
Standing broad jump	1.04	0.49	0.09 to 1.99	*0.033
NDI	-0.91	0.22	-1.33 to -0.48	*<0.001
T4 Trabecular density				
Pre/Post[a]	6.58	13.67	-20.21 to 33.37	0.630
Sex[b]	-11.91	11.39	-34.25 to 10.42	0.296
Puberty score	-11.64	5.93	-23.26 to -0.03	*0.050
Age	0.20	19.83	-38.67 to 39.07	0.992
Height	-0.32	0.70	-1.70 to 1.06	0.648
Weight	2.62	0.55	1.54 to 3.70	*<0.001
1 RM leg press	0.34	0.37	-0.39 to 1.07	0.360
Vertical jump	1.77	0.82	0.17 to 3.37	*0.030
Standing broad jump	-0.09	0.74	-1.55 to 1.36	0.900
NDI	-1.04	0.31	-1.65 to -0.42	*0.001
T4 Trabecular density Z score				
Pre/Post[a]	0.92	1.25	-1.54 to 3.38	0.463
Puberty score	-0.38	0.30	-0.96 to 0.20	0.201
Age	-1.01	0.75	-2.48 to 0.47	0.181
Weight	0.08	0.03	0.04 to 0.13	*<0.001

Appendix C. *(Cont. from previous page).*

	β	SE	β 95% Confidence interval	p
1 RM leg press	0.04	0.03	-0.02 to 0.09	0.171
Vertical jump	0.09	0.07	-0.03 to 0.22	0.151
Standing broad jump	-0.01	0.04	-0.09 to 0.06	0.781
NDI	-0.05	0.02	-0.09 to -0.01	*0.010
T66 Mass				
Pre/Post[a]	-0.07	2.73	-9.61 to 1.09	0.119
Sex[b]	-0.42	0.15	-0.72 to -0.12	*0.005
Puberty score	-0.04	0.07	-0.18 to 0.10	0.579
Age	0.67	0.29	0.09 to 1.24	*0.022
Height	-0.02	0.01	- 0.03 to 0.00	0.090
Weight	0.02	0.01	0.002 to 0.03	*0.022
1 RM leg press	-0.01	0.01	-0.02 to 0.00	0.130
Vertical jump	0.01	0.01	-0.02 to 0.03	0.588
Standing broad jump	0.00	0.01	-0.02 to 0.02	0.864
NDI	0.01	0.05	0.00 to 0.02	0.079
T66 SSI				
Pre/Post[a]	164.65	79.93	22.72 to 307.59	*0.024
Sex[b]	63.19	144.82	-220.65 to 347.02	0.663
Puberty score	32.82	46.83	-58.97 to 124.60	0.483
Age	27.16	239.47	-442.20 to 496.51	0.910
Height	9.96	8.20	-6.12 to 26.04	0.225
Weight	4.79	5.01	-5.02 to 14.60	0.339
1 RM leg press	2.76	3.40	-3.91 to 9.42	0.418
Vertical jump	-1.28	10.36	-21.59 to 19.03	0.902
Standing broad jump	2.19	9.27	-15.97 to 20.35	0.813
NDI	5.08	4.18	-3.11 to 13.27	0.224
T66 SSI Z score				
Pre/Post[a]	0.39	0.21	-0.02 to 0.80	0.061
Puberty score	0.28	0.11	0.05 to 0.50	*0.015
Age	-0.66	0.35	-1.35 to 0.02	0.057
Weight	-0.01	0.02	-0.04 to 0.02	0.541
1 RM leg press	0.01	0.01	-0.01 to 0.03	0.188
Vertical jump	-0.01	0.02	-0.06 to 0.03	0.547
Standing broad jump	0.00	0.02	-0.05 to 0.04	0.961
NDI	0.02	0.01	-0.01 to 0.05	0.148
T66 Total area				
Pre/Post[a]	168.54	67.93	35.40 to 301.69	*0.013
Sex[b]	70.55	36.58	-1.15 to 142.25	0.054
Puberty score	-14.01	23.37	-59.82 to 31.81	0.549
Age	136.09	53.60	31.04 to 241.14	*0.011
Height	-0.77	1.31	-3.34 to 1.80	0.555
Weight	-0.51	1.87	-4.18 to 3.16	0.785
1 RM leg press	2.70	1.07	0.61 to 4.79	*0.011
Vertical jump	-9.43	2.30	-15.31 to -3.56	*0.002
Standing broad jump	-0.94	1.45	-3.78 to 1.90	0.516
NDI	3.39	0.80	1.82 to 4.95	*<0.001
T66 Cortical density				
Pre/Post[a]	-15.60	19.94	-54.69 to 23.48	0.434
Sex[b]	-48.27	12.69	-73.14 to -23.40	*<0.001
Puberty score	-3.83	7.65	-18.83 to 11.18	0.617

Appendix C. *(Cont. from previous page).*

	β	SE	β 95% Confidence interval	p
Age	15.79	23.52	-30.31 to 61.89	0.502
Height	-0.81	0.61	-2.00 to 0.38	0.183
Weight	0.67	0.70	-0.71 to 2.05	0.342
1 RM leg press	0.24	0.27	-0.28 to 0.77	0.360
Vertical jump	2.89	1.57	-0.20 to 5.97	0.067
Standing broad jump	0.20	0.65	-1.06 to 1.47	0.753
NDI	-1.03	0.45	-1.92 to -0.14	*0.023
T66 Cortical density Z score				
Pre/Post[a]	-0.48	0.53	-1.52 to 0.56	0.366
Puberty score	0.11	0.23	-0.33 to 0.56	0.616
Age	-0.41	0.61	-1.60 to 0.79	0.506
Weight	-0.01	0.02	-0.05 to 0.03	0.476
1RM leg press	0.01	0.01	-0.01 to 0.03	0.339
Vertical jump	0.06	0.04	-0.03 to 0.14	0.174
Standing broad jump	0.02	0.02	-0.03 to 0.06	0.500
NDI	-0.03	0.01	-0.05 to -0.001	*0.038
T66 Cortical area				
Pre/Post[a]	-27.02	19.80	-65.84 to 15.96	0.799
Sex[b]	-26.41	14.30	-54.43 to 1.62	0.065
Puberty score	-2.39	9.36	-20.73 to 15.96	0.799
Age	16.62	32.85	-47.76 to 81.00	0.613
Height	0.38	0.99	-1.56 to 2.32	0.699
Weight	1.79	0.71	0.39 to 3.18	*0.012
1 RM leg press	-0.61	0.56	-1.70 to 0.48	0.274
Vertical jump	2.80	1.03	0.79 to 4.81	*0.006
Standing broad jump	0.12	0.80	-1.37 to 1.62	0.874
NDI	0.57	0.50	-0.93 to 1.04	0.910
T66 Cortical area Z score				
Pre/Post[a]	-1.02	0.75	-2.48 to 0.44	0.172
Puberty score	0.29	0.31	-0.33 to 0.90	0.360
Age	-1.21	0.86	-2.91 to 0.48	0.161
Weight	0.02	0.03	-0.04 to 0.07	0.609
1 RM leg press	0.00	0.02	-0.05 to 0.04	0.865
Vertical jump	0.07	0.03	0.01 to 0.13	*0.034
Standing broad jump	0.00	0.03	-0.06 to 0.05	0.934
NDI	0.01	0.02	-0.03 to 0.05	0.735
T66 Fracture load X3N				
Pre/Post[a]	369.08	164.29	47.09 to 691.08	*0.025
Sex[b]	-270.67	312.20	-882.57 to 341.23	0.386
Puberty score	-81.70	96.43	-270.70 to 107.31	0.397
Age	690.74	513.25	-315.22 to 1696.69	0.178
Height	10.60	17.24	-23.19 to 44.39	0.539
Weight	17.84	10.38	-2.51 to 38.19	0.086
1 RM leg press	7.99	7.54	-6.79 to 22.77	0.289
Vertical jump	5.14	17.79	-29.72 to 39.99	0.773
Standing broad jump	13.72	16.98	-19.56 to 47.01	0.419
NDI	8.40	9.24	-9.71 to 26.50	0.363
T66 Fracture load Y3N				
Pre/Post[a]	590.86	258.79	83.65 to 1098.07	*0.022
Sex[b]	-224.60	292.11	-347.94 to 797.13	0.442

Appendix C. *(Cont. from previous page).*

	β	SE	β 95% Confidence interval	p
Puberty score	123.73	124.84	-120.95 to 368.41	0.322
Age	409.16	521.97	-613.88 to 1432.20	0.433
Height	12.97	17.80	-21.92 to 47.85	0.466
Weight	0.52	13.19	-25.33 to 26.38	0.968
1 RM leg press	-0.32	6.63	-13.32 to 12.68	0.962
Vertical jump	-20.33	26.03	-71.35 to 30.68	0.435
Standing broad jump	6.06	18.08	-29.38 to 41.49	0.738
NDI	14.31	10.53	-6.33 to 34.94	0.174

a Where pre-intervention is the comparison group and β=1; b Where male is the comparison group and β=1.