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Cöster, Marcus E.; Rosengren, Björn E.; Karlsson, Caroline; Dencker, Magnus; Karlsson, Magnus K.

Published in:
Bone

DOI:
10.1016/j.bone.2016.09.021

2016

Document Version:
Peer reviewed version (aka post-print)

Effects of an 8-Year Childhood Physical Activity Intervention on Musculoskeletal Gains and Fracture Risk

Marcus E. Cöster, M.D.[1], Björn E. Rosengren, M.D., Ph.D.[1], Caroline Karlsson M.D., Ph.D.[1], Magnus Dencker M.D., Ph.D.[2], Magnus K. Karlsson, M.D., Ph.D.[1]

[1]Clinical and Molecular Osteoporosis Research Unit, Department of Orthopedics and Clinical Sciences and [2]Department of Physiology and Clinical Sciences, Lund University, Skåne University Hospital, SE-205 02 Malmö, Sweden

Correspondence: Marcus Cöster, Department of Orthopedics, Skåne University Hospital, SE-205 02 Malmö, Sweden. Tel: +46 40 331000; Fax: +46 40 336200; Email: marcus.coster@med.lu.se

Abstract

Background: Physical activity (PA) in childhood is associated with musculoskeletal benefits while the effect on fracture risk is yet to be determined. The aim of this study was to evaluate whether extension of a PA intervention leads to improvement in musculoskeletal traits with an accompanied reduced fracture risk. We hypothesized that the PA program would have beneficial effects in both sexes, but more so in girls since they tend to be less physically active than boys during this time frame.

Methods: In one elementary school we increased physical education (PE) from 60 to 200 minutes per school week and followed 65 girls and 93 boys from a mean age of 7 years until a mean age of 15 years. Thirty-nine girls and 37 boys in three other schools continued with 60 minutes of PE per week during the same years and served as controls. We measured bone mineral content (BMC), areal bone mineral density (aBMD), and bone area annually with dual energy X-ray absorptiometry, and leg muscle strength with a computerized dynamometer. In 3 534 children within the same PE program (1 339 in the intervention and 2 195 in the control group) we registered incident fractures during the 8-year study period and estimated annual sex-specific fracture incidence rate ratios (IRRs).

Results: Girls in the intervention group annually gained more total body less head aBMD, spine aBMD ($p<0.01$), femoral neck BMC ($p<0.05$), lumbar vertebrae size ($p<0.05$), and knee flexion strength ($p<0.05$) than girls in the control cohort. In boys we found no group differences. There was an inverse correlation between number of years with extra PE and the annual IRR of sustaining fractures in both girls ($r = –0.90$ (95% CI –0.98 to –0.51); $p<0.001$) and boys ($r = –0.74$ (95% CI –0.94 to –0.02); $p<0.05$).

Conclusion: In this 8-year pediatric school-based moderate exercise intervention program there is an inverse correlation in both sexes between annual IRR and each additional year of extra PA. A sub-cohort of girls in the intervention group had greater gains in bone mass, bone size, and muscle strength, which could possibly explain the inverse correlation between years within the PA program and fracture risk, while in boys the reason for the inverse correlation remains unknown. It should be noted that differences in unreported factors such as skeletal maturity status, diet, and spare time PA could confound our inferences. That is, true causality cannot be stated.

Key words: Bone mineral density, Children, Growth, Muscle Strength, Physical activity

1 Background

As nearly half of all boys and one third of all girls sustain at least one fracture during growth[1-3], strategies to reduce fracture risk are important. Bone mass, bone structure, neuromuscular function, and muscle strength are traits that in adults are known to affect fracture and/or fall risks[4-6]. Previous physical activity (PA) intervention studies have found that these traits can be improved in children and that pediatric fracture risk then may be reduced[7-10]. Also, studies suggest that there might be a sex difference in the response to PA[11, 12], which highlights the importance of sex-specific evaluations.

In previous Pediatric Osteoporosis Prevention (POP) studies we have reported that the school-based PA intervention program enhances the gain in bone mass and muscle strength in children of both sexes in a short-term perspective[13, 14]. However, with extension of the program, the benefits seemed to gradually attenuate so that after seven years (when the children were in puberty) no residual effects were seen in boys and only some benefits remained in girls[11]. The sex difference may partly be explained by the fact that since girls mature before boys they may reduce their PA levels earlier than boys[15-17]. In girls the intervention will thus contribute relatively more to the total amount of PA and therefore have a larger impact than in boys. These recent findings urge further extension of the study to determine whether, as they get older, all musculoskeletal benefits will disappear in girls too.

The aim of this study was to sex-specifically evaluate the effects of the extension of the previously reported exercise intervention program[11] on the gain in bone mass, bone size, muscle strength, and fracture risk. Since there seem to be sex differences in PA levels during growth[15-17] we hypothesized that the extension would continue to have greater effects in girls than in boys, but that fracture risk reduction would still be evident in both sexes with each additional year of extra PA. Furthermore, we hypothesized that the fracture risk reduction could be a result of gains in bone mass and muscle strength, but that other PA-improved endpoint variables not evaluated by this paper also could have effects.

2 Material and Methods

2.1 Study design

The Malmo Pediatric Osteoporosis Prevention (POP) study is a prospective controlled intervention study in children that examines the effects of increased school-based PA on various health-related outcomes including musculoskeletal function and fracture risk. The study design has been described in detail in previous publications[18, 19]. To summarize, we asked four elementary schools within the same area in the city of Malmo, Sweden, to participate. One of the schools served as intervention school while the remaining three served as control schools. In the intervention school we increased the amount of physical education (PE) from 60 minutes per school week to 200 minutes per school week given in lessons of 40 minutes per school day. During weekends and holidays (15 weeks per year) there was no PE. The control schools continued with the Swedish standard of one to two lessons of 60 minutes of PE per school week. The ethics committee of Lund University approved the study and we obtained informed written consent from parents of all participating children before study start.

The study was conducted according to the Declaration of Helsinki and registered as clinical trial with registration identification ClinicalTrials.gov.NCT00633828.

2.2 Subjects

We invited all children, six to eight years old, with school start from 1998 to 2000 in the intervention school and school start from 1999 to 2000 in the control schools to participate in the study arm where musculoskeletal measurements were performed. In the intervention group 94 of the 105 invited girls and 123 of the 132 invited boys accepted participation while in the control group 64 of the 157 invited girls and 68 of the 170 invited boys accepted participation. We performed bone and muscle measurements before study start and annually during the study. To be included in the current study the children were not allowed to have diseases or use medications that affect bone or muscle development, they had to have a baseline measurement and at least one of the three last annual measurements. With these inclusion criteria we excluded two girls and four boys in the intervention group because of diseases or medications that might affect musculoskeletal development, and 27 girls and 26 boys because of lack of baseline data (they accepted participation in the study but then did not partake) or follow-up data. The corresponding numbers for the control group are as follows: we excluded one girl because of medications that might affect musculoskeletal development and 24 girls and 31 boys because of lack of follow-up data. As a result we achieved 65 girls and 93 boys in the intervention group and 39 girls and 37 boys in the control group with prospective bone mass and muscle strength measurements.

2.3 Dropouts

Our dropout analyses, which compare the baseline measurements between those children who only attended the baseline measurements and those who also attended the follow-up, showed no group differences (data not shown). Furthermore, the dropout analyses that analyzed anthropometric data from the compulsory 1st grade school health examinations found no difference between the children who participated at the baseline exam and those who declined participation already at baseline[20].

2.4 Lifestyle and skeletal traits

We measured anthropometrics using standard equipment and analyzed lifestyle factors through a self-completed questionnaire. This questionnaire included questions of participation in organized PA during leisure time; to be accepted as organized these activities had to be structured and supervised by coaches. Thus, games and playing activities were not included. Total duration of PA for each individual was then estimated as the duration of PE in school and the duration of organized PA during leisure time. We made this estimation separately for winter and summer and then used the mean values as an estimate of the total duration of PA during the year. At study start our research nurses assessed pubertal maturation as Tanner stage while at follow-up the children assessed Tanner stage through self-assessment. To assist in maturation assessment at baseline our research nurses were provided with pictures of genitals (boys), breasts (girls), and pubic hair (both) from the different Tanner stages. We then asked them to decide which Tanner stage they found the children belonged to. At follow-up the children were provided with the same pictures and were asked to decide which Tanner stage they were in. We measured areal bone mineral density (aBMD, g/cm^2), bone mineral content (BMC, g), femoral neck area (cm^2), and first to fourth lumbar vertebrae (L1–L4) area

(cm^2) by dual X-ray absorptiometry (DXA, DPX-L® version 1.3z, Lunar Corporation, Madison, WI, USA) and calcaneal speed of sound (SOS, m/s) and broadband ultrasound attenuation (BUA, dB/MHz) by quantitative ultrasound (QUS, Lunar Achilles model 1061®, Lunar Corporation, Madison, WI, USA). All methods have been described in detail in previous publications[13, 18]. Our research technicians performed all measurements and calibrated the DXA apparatus regularly with a phantom. There was no long-term drift in the equipment. The coefficient of variation (CV%), evaluated by duplicate measurements in 13 healthy children, was 2.4–2.6% for aBMD, 1.4–5.2% for BMC, 0.2% for SOS, and 6.7% for BUA.

2.5 Muscle strength

In this cohort we also measured muscle strength as concentric isokinetic Peak Torque (PT) for right knee extension (ext) and flexion (flex) by a computerized dynamometer (Biodex System III Pro®). The method has been described in detail in previous publications[21, 22]. We used the highest peak torque value of five repeated movements (extension and flexion) in the knee joint at 60 and at 180 °/sec (PT_{ext60}; PT_{flex60}; PT_{ext180}; $PT_{flex180}$). The CV% was 6.6% for PT_{ext60}, 12.1% for PT_{flex60}, 12.3% for PT_{ext180}, and 9.1% for $PT_{flex180}$, assessed after repeated measurements in 21 healthy children aged 7 to 15 years.

2.6 Fractures

In a larger cohort of children within the same intervention program we registered incidence fractures. This cohort consisted of 3 534 children who began 1st grade between 1998 and 2012 in the four participating schools, 1 339 children in the intervention and 2 195 children in the control schools and included those children participating in musculoskeletal measurements. Fractures were only evaluated through register data and children were thus not individually asked to participate. The children with school start 1998 to 2005 were followed for eight years, while those with school start in 2006 and later were followed until 2013. Children who moved out of our region or changed school between intervention and control schools (n=183) were followed until this event. Fractures were registered through repeated evaluations of the regional computerized radiographic database that has records of all radiographs within the region. Any fractures occurring outside of the region were registered at follow-ups at our hospital. This method has previously been used extensively at our research center[23, 24], a method that enabled us to evaluate every child that entered the study. Of the entire cohort of 3 534 children, only the 234 children from whom musculoskeletal traits were measured provided background lifestyle or anthropometric data.

2.7 Statistics

We used IBM SPSS Statistics® version 20 for the statistical analyses. Data are presented as absolute numbers, means ± standard deviations (SD), or means with 95% confidence intervals (95% CI). We estimated annual changes by linear regression for each individual in each trait by using all available measurements and then used the mean value for the slopes in each group for group comparisons. We estimated group differences by student's t-test between means, Fisher's exact test, or Mann-Whitney U-test. When comparing musculoskeletal gains during the study we used analysis of covariance (ANCOVA) with adjustments for the baseline value of the respective evaluated trait and Tanner stage at follow-up. Tanner stage was used as a dummy variable in these analyses. We calculated sex-specific annual incidence

rate ratios (IRR) by dividing the incidence in the intervention group by the incidence in the control group and then used Spearman's test for correlations to evaluate whether there were any associations between each year of intervention and the IRR for each year. We regarded $p<0.05$ as a statistically significant difference.

3 Results

3.1 Background and activity data

Baseline and follow-up anthropometrics and lifestyle data are shown in Table 1. Before the intervention started, the mean weekly duration of PA was similar in the intervention and the control groups for both sexes (in girls 1.7 ± 1.7 hours versus (vs.) 2.1 ± 1.6 hours ($p=0.214$), in boys 3.1 ± 3.6 hours vs. 3.5 ± 3.2 hours ($p=0.631$). After initiation of the intervention the mean duration of PA was higher in the intervention group than in the control group for both sexes (in girls 5.0 ± 1.7 hours vs. 3.1 ± 1.6 hours ($p<0.001$), in boys 6.4 ± 3.6 hours vs. 4.5 ± 3.2 hours ($p=0.005$). The corresponding data at follow-up were in girls 7.9 ± 3.0 hours vs. 4.7 ± 2.5 hours ($p<0.001$) and in boys 9.5 ± 4.6 hours vs. 6.4 ± 3.8 hours ($p<0.001$).

3.2 Body composition and skeletal traits

Body composition and bone traits were similar before study start in the intervention and control groups in both girls and boys (Table 2). During the study period girls in the intervention group annually gained more fat mass, total body less head aBMD, spine aBMD, femoral neck BMC, L1–L4 area, and BUA than the girls in the control group (Table 3). The annual relative mean differences were 23% for fat mass, 10% for total body less head aBMD, 16% for spine aBMD, 16% for femoral neck BMC, 7% for L1–L4 area, and 100% for BUA. These gains resulted in greater total body fat mass, total body less head aBMD, femoral neck aBMD, spine aBMD, and BUA at follow-up in the intervention girls than in the control girls (Table 4). The mean differences are shown in table 4, corresponding to relative mean differences of 23% for fat mass, 4% for total body less head aBMD, 6% for femoral neck aBMD, 5% for spine aBMD, and 10% for BUA. No group differences were found in boys (Table 3 and 4).

3.3 Muscle strength

Both girls and boys in the control group had greater peak torque flexion at study start than their intervention counterparts, and the intervention boys also had greater peak torque extension at 60 °/sec (Table 2). The intervention girls annually gained more in peak torque flexion at 60 °/sec than control girls during the study period (Table 3) (relative mean difference of 14%), but in spite of this they did not reach higher strength at follow-up (Table 4). No group differences were found in boys (Tables 4 and 5).

3.4 Fractures

During the study period we identified 506 fractures among the 3 534 children in the larger cohort, 173 in girls and 333 in boys. There was an inverse correlation between number of years of intervention and annual IRR of sustaining fractures in both girls ($r = –0.90$ (95% CI –0.98, –0.51); $p<0.001$) and boys ($r = –0.74$ (95% CI –0.94, –0.02); $p<0.05$).

4 Discussion

This study indicates that an 8-year population-based PA intervention in childhood and adolescence, in girls was associated with accrual of bone mass, gain in bone size, and gain in muscle strength, while no such associations were found in boys. Also, there was an inverse correlation between each additional year of extra PA and a reduced fracture risk in both girls and boys.

The previous 7-year POP study report infers that short-term musculoskeletal benefits from PA interventions may be attenuated or totally disappear in puberty[11]. However, even though other aspects than the PA intervention could have affected the results, one additional year of intervention resulted in almost a 0.4 SD higher femoral neck aBMD in girls than control girls at follow-up, which ought to translate to a 25% lower fracture risk[25]. Intervention girls also developed a larger skeleton, at least in the lumbar spine, which might be of importance since vertebral bone size in elderly women independently has been inversely correlated with spine fractures[26]. Furthermore, they also had a greater gain in muscle strength that indicates improved neuromuscular function, which may reduce fall and fracture risks even further[27, 28].

We have previously reported that our PA intervention program is associated with a borderline lower fracture risk after seven years[10], but it is not known whether there are any sex differences. Since the PA-induced musculoskeletal benefits after seven years only seemed to be retained in girls this is a possible scenario[11], which is further supported by the results in this 8-year study. However, in contrast to this hypothesis we can now show data suggesting that the fracture risk diminishes in both girls and boys with each additional year of extra PA. In the girls, this could at least partly be explained by beneficial gains in both skeletal traits and muscle strength, while the reasons behind the fracture reduction in boys remain to be identified. We must however underline that fracture data were collected in 3 534 children and the musculoskeletal evaluation was undertaken only in a sub-sample of these children (n = 234). It is of course possible, but not likely, that the sample of children undergoing musculoskeletal measurements is not representative for all the participating children. The following discussion is based on the assumption that children in the larger cohort have had the same beneficial musculoskeletal gains as the children in the sub-cohort undergoing musculoskeletal examinations even though we did not examine all 3 534 children.

Our results support previous short-term pediatric exercise studies that have reported improvement in musculoskeletal development[7-9]. The current study increases our knowledge showing long-term retained benefits, but only in girls. A possible explanation could be that girls in general, as in our study, are less active in their leisure time than boys and the extra school-based PE thereby results in a proportionally greater increase in PA in girls than boys. This could become even more prominent during puberty, as girls during this period reduce their PA more than boys[15]. Thus, the relatively high participation rate in PA for boys in both groups in our study could either mask effects from the intervention program or suggest that the extended amount of PA is not enough to induce musculoskeletal effects. We therefore speculate that one approach to reach musculoskeletal benefits in boys would be to increase the duration or the intensity of the intervention.

Another finding in this report was that girls in the intervention group gained more weight and fat mass than control girls. The reasons for this finding remain unclear, but one possible explanation could be that women have increased appetite after exercise, which does not seem to apply to men to the same magnitude[29, 30]. This feature has been suggested to be a result of effects induced by PA on hunger-regulating hormones[31]. If the same appetite effect is present also in children it could perhaps explain our findings. However, as previous dose-response analyses found no correlation between total amounts of PA and gain in fat mass[21], the higher gain in fat mass could also be independent of the increased PA. Regardless of the explanation for the higher weight and fat mass gain, this finding is interesting. Previous studies in adults have implied that bone mass is positively associated with body weight[32-34], but there are questions regarding this association. For example, in women high weight due to lean mass has been suggested to be more positively associated with bone mass gains than high weight due to fat mass[35]. So it is unclear whether the girls in the intervention group gained more bone mass due to the weight gain, which only was achieved due to greater fat mass gains and not lean mass gains, or whether the greater gain in bone mass was independent of this finding.

A final observation from our data is that although we could not find any statistically significant differences in the duration of PA in either sex before the commencement of the study, the children in the control group reported an average of 24 minutes' more participation in PA compared to the children in the intervention group. This difference could perhaps lead to a difference in bone and muscle adaptation to PA, possibly explaining the reported group differences in muscle strength at baseline. However, this is only speculation.

Study strengths include the population-based study design, the general school-based PA on a level facilitating participation by all children, the fact that the study is the longest of its kind, the inclusion of several different surrogate endpoint variables, and the inclusion of the clinically relevant endpoint incident fractures. A major limitation is the absence of individual randomization of the children, which was neither feasible nor accepted by teachers or parents. Other study limitations include lack of information on non-organized PA during leisure time, lack of registration of participation rate and activity level during the reported organized activities, and the fact that we only have maturation in stages based on self-assessment of secondary sex characteristics. It would have been preferable to have a continuous measurement of maturity, enabling assessment of the pubertal growth spurt and the maturational development. Such a measurement would facilitate even better estimates of the connection between our PA program and body composition and musculoskeletal changes. Furthermore, the use of a composite of secondary sex characteristics as a determinant of maturation is a limitation and makes reliable gender comparisons most difficult[36]. We did not collect any information regarding diet or skeletal maturity and thus could not include these variables as covariates. It would also have been advantageous to have a larger sample enabling robust sex-specific comparisons of fracture risk for each study year and not, as in this study, only being able to evaluate sex-specific correlations for the entire period. Finally, we must emphasize that true causality between the PE intervention and beneficial gain in musculoskeletal traits could not be stated. If the program resulted in extended non-organized PA outside of school or in other health-related effects such as improved diet, this could also have a causal effect on the endpoint variables and thus influence our inferences.

5 Conclusions

In conclusion, an 8-year school-based pediatric exercise intervention program during growth is associated with enhanced bone mass, bone size, and muscle strength in girls (but not in boys). Furthermore, in both sexes each additional year of extra PA seems to be inversely correlated with fracture risk.

6 Acknowledgments

We thank all teachers and children who participated in the POP study. Financial support was received from the Centre for Athletic Research, the Herman Järnhardt Foundation, Skåne Regional Foundations, and ALF Foundations. The authors declare conflicts of interest: none.

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8 Tables

Table 1. Participant characteristics at baseline and follow-up. Data are presented as means ± standard deviations or as number of children with proportions within brackets. Statistically significant group differences are bolded. A chronic medical condition is defined as a persistent health condition or illness diagnosed by a physician.

	Girls			**Boys**		
	Intervention group	**Control group**	**p-value**	**Intervention group**	**Control group**	**p-value**
	n = 65	*n = 39*		*n = 93*	*n = 37*	
At baseline						
Age	7.5 ± 0.5	7.8 ± 0.7	**0.003**	7.6 ± 0.6	7.9 ± 0.7	**0.001**
Height (cm)	127.0 ± 5.6	128.4 ± 7.6	0.34	128.3 ± 6.7	130.3 ± 6.1	0.11
Weight (kg)	27.3 ± 5.4	26.8 ± 5.4	0.66	27.6 ± 5.5	28.2 ± 4.7	0.56
BMI (kg/m^2)	16.8 ± 2.7	16.1 ± 1.9	0.13	16.6 ± 2.4	16.5 ± 1.9	0.78
Tanner stage (1/2/3/4/5)	65/0/0/0/0	39/0/0/0/0	NA	93/0/0/0/0	37/0/0/0/0	NA
Excluding dairy products	0	1 (3%)	0.36	0	4 (11%)	**0.005**
Chronic medical condition	6 (10%)	2 (6%)	0.71	12 (13%)	3 (8%)	0.55
Current medication	8 (13%)	2 (6%)	0.49	16 (18%)	3 (8%)	0.27
At follow-up						
Age	15.1 ± 0.5	15.0 ± 0.8	0.78	15.0 ± 0.6	15.1 ± 0.7	0.57
Height (cm)	166.7 ± 5.5	165.2 ± 7.1	0.22	173.9 ± 8.4	175.0 ± 7.8	0.51
Weight (kg)	59.4 ± 10.3	54.7 ± 10.1	**0.03**	63.0 ± 13.5	63.0 ± 11.1	0.92
BMI (kg/m^2)	21.4 ± 3.4	20.0 ± 2.8	**0.03**	20.7 ± 3.6	20.6 ± 3.3	0.83
Tanner Stage (1/2/3/4/5)	0/0/5/26/34	0/0/3/19/17	0.44	0/1/6/23/63	0/0/1/10/26	0.67
Smoking	6 (9%)	6 (15%)	0.36	3 (3%)	1 (3%)	1.00
Alcohol consumer	11 (17%)	5 (13%)	0.78	18 (19%)	4 (11%)	0.31

NA = Not applicable.

Table 2. Baseline data of body composition (BC), areal bone mineral density (aBMD), bone mineral content (BMC), bone size (BS), quantitative ultrasound (QUS), and Peak Torque (PT). Data are presented as means ± standard deviation and mean differences with 95% confidence intervals within brackets. Statistically significant group differences are bolded.

	Girls				**Boys**			
	Intervention	**Control**	**Mean difference**	**p-value**	**Intervention**	**Control**	**Mean difference**	**p-value**
	n = 65	*n = 39*			*n = 93*	*n = 37*		
BC (kg)								
Lean mass	19.6 ± 2.4	19.9 ± 2.6	-0.3 (-1.3, 0.7)	0.57	21.4 ± 2.8	22.1 ± 2.7	-0.7 (-1.8, 0.4)	0.20
Fat mass	5.2 ± 3.2	5.0 ± 3.4	0.2 (-1.1, 1.5)	0.77	3.9 ± 3.4	3.8 ± 2.2	0.1 (-1.1, 1.3)	0.85
aBMD (g/cm^2)								
Total Body Less Head	0.68 ± 0.05	0.68 ± 0.05	-0.00 (-0.02, 0.02)	0.82	0.69 ± 0.05	0.70 ± 0.05	-0.01 (-0.03, 0.01)	0.39
Femoral Neck	0.71 ± 0.10	0.70 ± 0.09	0.01 (-0.03, 0.05)	0.70	0.78 ± 0.11	0.79 ± 0.12	-0.01 (-0.05, 0.03)	0.66
Total Spine	0.68 ± 0.06	0.69 ± 0.07	-0.01 (-0.04, 0.01)	0.32	0.68 ± 0.07	0.70 ± 0.06	-0.02 (-0.04, 0.01)	0.13
BMC (g)								
Total Body Less Head	609 ± 132	612 ± 145	-4 (-59, 52)	0.90	650 ± 151	681 ± 140	-31 (-88, 26)	0.28
Femoral Neck	2.5 ± 0.6	2.6 ± 0.6	-0.0 (-0.3, 0.2)	0.73	2.8 ± 0.6	2.9 ± 0.5	-0.0 (-0.3, 0.2)	0.81
Total Spine	82.6 ± 19.3	77.7 ± 17.4	4.8 (-2.8, 12.4)	0.21	85.5 ± 21.6	86.7 ± 17.3	-1.1 (-8.3, 6.1)	0.75
BS (cm^2)								
Femoral Neck	3.5 ± 0.4	3.6 ± 0.5	-0.1 (-0.3, 0.1)	0.34	3.6 ± 0.4	3.6 ± 0.3	-0.0 (-0.2, 0.1)	0.87
L1 - L4	27.5 ± 3.2	27.9 ± 3.6	-0.4 (-1.8, 0.9)	0.51	29.1 ± 3.5	29.9 ± 3.4	-0.8 (-2.2, 0.5)	0.22
QUS								
SOS (m/s)	1528 ± 23	1530 ± 17	-2 (-12, 8)	0.66	1533 ± 23	1533 ± 21	1 (-10, 11)	0.87
BUA (dB/MHz)	94 ± 10	96 ± 6	-2 (-6, 2)	0.28	95 ± 11	97 ± 9	-2 (-7, 3)	0.41
PT (Nm)								
PT_{ext60}	40.2 ± 9.8	43.1 ± 9.7	-2.9 (-6.8, 1.0)	0.14	41.6 ± 9.7	46.4 ± 11.7	-4.8 (-8.8, -0.8)	**0.02**
PT_{flex60}	20.3 ± 5.0	23.5 ± 5.6	-3.2 (-5.3, -1.1)	**0.003**	22.0 ± 6.9	25.1 ± 7.0	-3.1 (-5.8, -0.4)	**0.03**
PT_{ext180}	32.0 ± 7.3	34.8 ± 6.8	-2.8 (-5.6, 0.1)	0.06	34.4 ± 8.0	37.1 ± 9.0	-2.6 (-5.8, 0.6)	0.11
$PT_{flex180}$	18.2 ± 5.6	21.3 ± 4.6	-3.1 (-5.2, -1.0)	**0.004**	20.0 ± 5.6	23.5 ± 6.2	-3.5 (-5.7, -1.3)	**0.002**

Table 3. Annual changes in body composition (BC), areal bone mineral density (aBMD), bone mineral content (BMC), bone size (BS), quantitative ultrasound (QUS), and Peak Torque (PT). Data are presented as means with 95% confidence intervals. Statistically significant group differences are bolded.

	Girls				**Boys**			
	Intervention	**Control**	**Mean difference***	**p-value***	**Intervention**	**Control**	**Mean difference***	**p-value***
	n = 65	*n = 39*			*n = 93*	*n = 37*		
BC (kg)								
Lean mass	2.6 (2.5, 2.7)	2.7 (2.5, 2.8)	-0.0 (-0.2, 0.1)	0.91	3.7 (3.5, 3.8)	4.0 (3.7, 4.2)	-0.2 (-0.4, 0.1)	0.16
Fat mass	1.7 (1.5, 1.9)	1.3 (1.1, 1.5)	0.3 (0.0, 0.6)	**0.03**	1.0 (0.8, 1.2)	0.8 (0.6, 1.1)	0.1 (-0.2, 0.4)	0.42
aBMD (g/cm^2)								
Total Body	0.046	0.042	0.004		0.044	0.047	-0.002	
Less Head	(0.044, 0.048)	(0.040, 0.045)	(0.001, 0.007)	**0.02**	(0.042, 0.046)	(0.043, 0.050)	(-0.005, 0.002)	0.37
Femoral Neck	0.044	0.038	0.006		0.033	0.034	0.000	
	(0.040, 0.048)	(0.033, 0.043)	(-0.000, 0.012)	0.05	(0.030, 0.036)	(0.027, 0.040)	(-0.006, 0.006)	0.97
Total Spine	0.049	0.043	0.007		0.039	0.038	0.001	
	(0.046, 0.053)	(0.040, 0.046)	(0.003, 0.011)	**0.001**	(0.036, 0.041	(0.034, 0.042)	(-0.003, 0.006)	0.58
BMC (g)								
Total Body Less Head	189 (180, 199)	178 (165, 191)	11 (-0, 23)	0.06	206 (194, 217)	220 (203, 236)	-5 (-21, 10)	0.48
Femoral Neck	0.36 (0.33, 0.38)	0.31 (0.27, 0.34)	0.05 (0.01, 0.09)	**0.03**	0.36 (0.33, 0.38)	0.37 (0.33, 0.41)	-0.01 (-0.05, 0.04)	0.78
Total Spine	25.4 (24.1, 26.8)	24.2 (22.3, 26.0)	0.3 (-1.3, 1.9)	0.68	22.9 (21.3, 24,4)	24.1 (21.8, 26.4)	-0.9 (-2.9, 1.2)	0.40
BS (cm^2)								
Femoral Neck	0.19 (0.17, 0.21)	0.17 (0.15, 0.19)	0.01 (-0.01, 0.04)	0.30	0.23 (0.21, 0.24)	0.24 (0.21, 0.26)	-0.01 (-0.03, 0.02)	0.58
L1 - L4	3.1 (3.0, 3.2)	3.0 (2.8, 3.1)	0.2 (0.0, 0.3)	**0.04**	3.3 (3.2, 3.5)	3.6 (3.3, 3.8)	-0.1 (-0.4, 0.1)	0.31
QUS								
SOS (m/s)	10 (9, 12)	10 (8, 12)	2 (-0, 4)	0.07	7 (6, 8)	8 (6, 11)	-1 (-3, 1)	0.39
BUA (dB/MHz)	4 (3, 4)	2 (1, 2)	2 (1, 3)	**<0.001**	3 (2, 4)	3 (2, 4)	-0 (-1, 1)	0.95
PT (Nm)								

PT_{ext60}	10.5 (9.8, 11.1)	10.4 (9.4, 11.3)	0.1 (-1.0, 1.2)	0.88	14.1 (13.2, 15.0)	15.2 (13.7, 16.7)	-0.6 (-2.2, 1.0)	0.49
PT_{flex60}	6.0 (5.6, 6.4)	5.6 (5.0, 6.2)	0.8 (0.1, 1.4)	**0.02**	8.1 (7.6, 8.6)	8.8 (8.1, 9.6)	-0.4 (-1.3, 0.5)	0.35
PT_{ext180}	7.2 (6.8, 7.6)	7.2 (6.7, 7.8)	0.1 (-0.6, 0.8)	0.77	10.2 (9.7, 10.8)	10.7 (10.1, 11.4)	-0.2 (-1.0, 0.7)	0.70
$PT_{flex180}$	4.1 (3.8, 4.3)	3.8 (3.3, 4.3)	0.3 (-0.3, 0.8)	0.33	5.9 (5.5, 6.2)	6.1 (5.7, 6.6)	-0.1 (-0.7, 0.5)	0.77

*Adjusted for the baseline value of respective trait and Tanner stage at follow-up.

Table 4.

Follow-up data of body composition (BC), areal bone mineral density (aBMD), bone mineral content (BMC), bone size (BS), quantitative ultrasound (QUS), peripheral quantitative computed tomography (pQCT), and Peak Torque (PT). Data are presented as means ± standard deviation and means with 95% confidence intervals within brackets. Also, mean percent gain ± standard deviation from baseline to follow-up is presented for each variable. Statistically significant group differences are bolded.

	Girls				**Boys**			
	Intervention	**Control**	**Mean difference#**	**p-value#**	**Intervention**	**Control**	**Mean difference#**	**p-value#**
	n = 65	*n = 39*			*n = 93*	*n = 37*		
BC (kg)								
Lean mass	38.4 ± 3.8	37.8 ± 4.3	0.6 (–1.0, 2.2)	0.44	48.8 ± 7.8	50.4 ± 6.5	–1.1 (–3.5, 1.3)	0.36
(mean gain, %)	(97 ± 17%)	(91 ± 20%)			(129 ± 26%)	(130 ± 23%)		
Fat mass	17.7 ± 7.9	14.2 ± 7.0	3.2 (0.3, 6.1)	**0.03**	11.3 ± 8.1	10.0 ± 6.2	1.1 (–1.4, 3.7)	0.39
(mean gain, %)	(288 ± 145%)	(228 ± 122%)			(242 ± 157%)	(183 ± 156%)		
aBMD (g/cm^2)								
Total Body Less Head	1.02 ± 0.08	0.98 ± 0.09	0.04 (0.00, 0.07)	**0.03**	1.03 ± 0.11	1.05 ± 0.10	–0.01 (–0.05,	0.48
(mean gain, %)	(49 ± 8%)	(43 ± 8%)			(49 ± 12%)	(50 ± 11%)	0.02)	
Femoral Neck	1.04 ± 0.13	0.98 ± 0.14	0.06 (0.00, 0.11)	**0.04**	1.03 ± 0.14	1.07 ± 0.15	–0.02 (–0.07,	0.45
(mean gain, %)	(47 ± 19%)	(39 ± 16%)			(34 ± 17%)	(36 ± 19%)	0.03)	
Total Spine	1.05 ± 0.12	0.99 ± 0.11	0.05 (0.01, 0.10)	**0.03**	0.98 ± 0.13	1.00 ± 0.12	–0.01 (–0.05,	0.75
(mean gain, %)	(54 ± 12%)	(43 ± 10%)			(44 ± 13%)	(42 ± 13%)	0.04)	
BMC (g)								
Total Body Less Head	1986 ± 365	1840 ± 384	135 (–10, 280)	0.07	2210 ± 513	2292 ± 473	–55 (–219, 110)	0.51
(mean gain, %)	(232 ± 49%)	(205 ± 44%)			(245 ± 61%)	(241 ± 55%)		
Femoral Neck	5.2 ± 0.9	4.8 ± 1.1	0.3 (–0.1, 0.7)	0.09	5.6 ± 1.1	5.8 ± 1.0	–0.1 (–0.5, 0.3)	0.58
(mean gain, %)	(109 ± 44%)	(89 ± 34%)			(102 ± 41%)	(105 ± 34%)		
Total Spine	266.3 ± 50.6	245.5 ± 50.8	18.9 (–0.3, 38.1)	0.05	261.0 ± 68.6	267.5 ± 65.1	–2.7 (–24.9, 19.5)	0.81
(mean gain, %)	(230 ± 56%)	(221 ± 54%)			(210 ± 63%)	(210 ± 51%)		

BS (cm^2)								
Femoral Neck	5.0 ± 0.4	4.9 ± 0.6	0.1 (–0.1, 0.3)	0.46	5.4 ± 0.5	5.4 ± 0.6	–0.0 (–0.2, 0.1)	0.70
(mean gain, %)	(42 ± 19%)	(36 ± 16%)			(50 ± 18%)	(50 ± 17%)		
L1–L4	50.0 ± 5.2	48.3 ± 5.5	1.5 (–0.4, 3.4)	0.12	54.5 ± 7.8	55.5 ± 7.1	–0.5 (–3.1, 2.1)	0.71
(mean gain, %)	(83 ± 13%)	(74 ± 15%)			(88 ± 18%)	(86 ± 16%)		
QUS								
SOS (m/s)	1604 ± 40	1595 ± 36	10 (–6, 26)	0.24	1589 ± 33	1596 ± 39	–7 (–20, 7)	0.32
(mean gain, %)	(5 ± 3%)	(4 ± 2%)			(4 ± 2%)	(4 ± 2%)		
BUA (dB/MHz)	120 ± 21	108 ± 12	11 (4, 19)	**0.003**	117 ± 17	120 ± 18	–3 (–10, 4)	0.35
(mean gain, %)	(27 ± 21%)	(12 ± 12%)			(23 ± 18%)	(23 ± 18%)		
PT (Nm)								
PT_{ext60}	116.2 ± 22.3	116.0 ± 25.1	–0.7 (–10.3, 8.9)	0.89	148.3 ± 40.5	154.3 ± 39.0	–3.7 (–17.5, 10.0)	0.59
(mean gain, %)	(199 ± 67%)	(178 ± 66%)			(266 ± 100%)	(241 ± 86%)		
PT_{flex60}	63.9 ± 13.6	61.8 ± 15.3	1.8 (–4.1, 7.7)	0.55	84.5 ± 23.7	90.1 ± 19.2	–4.0 (–11.4, 3.5)	0.30
(mean gain, %)	(225 ± 76%)	(169 ± 62%)			(311 ± 143%)	(274 ± 93%)		
PT_{ext180}	84.3 ± 14.0	83.6 ± 15.8	0.5 (–5.6, 6.6)	0.87	112.2 ± 25.9	112.1 ± 19.3	1.7 (–6.3, 9.7)	0.68
(mean gain, %)	(174 ± 69%)	(146 ± 44%)			(233 ± 73%)	(210 ± 56%)		
$PT_{flex180}$	49.3 ± 9.4	46.9 ± 11.3	2.2 (–2.1, 6.4)	0.31	67.4 ± 16.3	67.5 ± 13.4	1.1 (–4.0, 6.1)	0.68
(mean gain, %)	(202 ± 145%)	(127 ± 50%)			(252 ± 100%)	(198 ± 69%)		

#Adjusted for age and Tanner stage at follow-up.