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Early Physical Activity Provides Sustained Bone Health Benefits Later in Childhood

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Abstract

Purpose—This study examined the potential effect of early childhood moderate and vigorous physical activity (MVPA) on later bone health.

Methods—Three hundred and thirty-three children, participating in the Iowa Bone Development Study, were studied at ages 5, 8, and 11. MVPA (min/d) was measured using an accelerometry-based physical activity monitor. Bone mineral content (BMC, g) of the whole body, lumbar spine, and hip was measured using dual energy x-ray absorptiometry (DXA). Mixed regression models were used to test whether age 5 MVPA had an effect on BMC at ages 8 and 11, after adjustment for concurrent height, weight, age, maturity, and MVPA. The analysis was repeated to control for age 5 bone outcomes. Mixed model least-squares means at the person level of covariates for age group were used to compare the BMC at age 8 and 11 of children in the highest and lowest quartiles of age 5 MVPA.

Results—For boys and girls, age 5 MVPA predicted BMC adjusted for concurrent height, weight, age, maturity, and MVPA at ages 8 and 11 ($p < 0.05$). When the analysis was repeated to also control for age 5 BMC, the effect of age 5 MVPA was significant for boys but not girls. Boys and girls in the highest age 5 MVPA quartile had 4 to 14% more BMC at age 8 and 11 than those in the lowest age 5 MVPA quartile ($p < 0.05$).

Conclusion—These results provide support for the benefits of early MVPA on sustained bone health during childhood especially for boys. Results indicate the importance of increasing MVPA as a strategy to improve BMC later in childhood.

Keywords

accelerometry; bone mineral content. children; DXA; longitudinal; skeletal

INTRODUCTION

Physical activity during childhood has been shown to have immediate bone health benefits. Results from cross-sectional, longitudinal, and randomized intervention studies indicate higher bone mineral content (BMC) in active children when compared to less active peers (1,9;16, 17). If higher BMC is maintained into early adulthood, an increase in peak bone mass would be expected; and peak bone mass is thought to be a critical factor in the reduction in fracture risk during middle and late adulthood (11). However, at this time it is not clear if the benefit in BMC accrual associated with early physical activity is sustained if physical activity is reduced during adolescence. This is an important public health issue given the known decrease in physical activity associated with aging, particularly its precipitous drop during adolescence and continued decline during adulthood (7,27).

Several carefully controlled animal studies indicate that targeted mechanical loading of bone in young animals results in lifetime structural changes (21,25,31). Retrospective studies of athletes (gymnasts, tennis players, and ballet dancers) suggest sustained benefits of early activity to the mature skeleton, including greater BMC (2,13,14). Other studies, however, suggest that the cessation of sport participation is associated with a reduction in BMC (19, 30). Recently, Gunter and colleagues (6) showed sustained effects from a short-term intervention study of peri-pubertal non-athletes ($n = 57$, ages 7 to 8 at baseline). In this study, children completing high-impact jumping exercises had 3.6% greater hip BMC than controls at the completion of the 7-month intervention and 1.4% greater hip BMC after approximately 7 years with no additional intervention.

Although studies of athletes and children engaged in targeted interventions provide unique and important information on the potential impact of exercise on BMC accrual, the mechanical loads incurred during these activities may not be conducive to public health recommendations; therefore, population-based studies are needed to set realistic recommendations for the amounts and types of physical activity needed to ensure bone health benefits. Ideally, population-based studies should be prospective to avoid the known limitations of retrospective studies including bias in the measurement of the physical activity exposure. Using a prospective longitudinal study design, Baxter-Jones and colleagues (3) recently reported that physically active children and adolescents ($n = 154$, ages 8 to 15 at baseline) had 8 to 10% more hip BMC in young adulthood (ages 23 to 30) when compared to less active peers, even after controlling for their adult physical activity levels. This study provides intriguing evidence of the long-term benefits of childhood physical activity on adolescent and adult BMC and supports conjecture that the promotion of physical activity in children could help to prevent osteoporosis later in life. In this report, we extend the work of Baxter-Jones et al. (3) by examining the effect of an early physical activity exposure (age 5) on BMC at age 8 and 11 in a cohort of normal healthy children ($n = 333$). We hypothesized that greater levels of early childhood physical activity would provide a sustained benefit in BMC evident 3 to 6 years later.

METHODS

Participants

Participants were part of the Iowa Bone Development Study, which is a longitudinal study of bone health during childhood and has been described elsewhere (8). Four hundred thirty-three cohort children participated in physical activity and BMC measurements at approximately 5 years of age (baseline), 495 at approximately 8 years of age, and 406 at approximately 11 years of age. Children with data from all three visits ($n = 333$, 185 boys and 148 girls) were included in the analyses. Mean age was 5.3 ± 0.4 yr at baseline, 8.8 ± 0.6 at 3-year follow-up, and 11.2 ± 0.3 yr at 6-year follow-up. Mean baseline heights and weights did not differ significantly ($p > 0.05$) between children with physical activity and BMC data at all three visits and those

without full data. However, there was a small mean baseline age difference between children with data at all three visits and those without (5.3 yr vs. 5.2 yr; $p < 0.05$). The parents of the children provided written informed consent and the children provided assent. The University of Iowa Institutional Review Board approved this study.

Physical Activity

Physical activity (movement counts) was measured using the ActiGraph uniaxial physical activity monitor (model number 7164, Pensacola, FL). Procedures for physical activity measurement using the ActiGraph and validation of this monitor have been described elsewhere (4,10,28). Children were asked to wear the monitors all day during waking hours for 4 consecutive days at ages 5 and 8. The number of wear days was increased at age 11 to 5 days to account for increased day-to-day variability in accelerometry-measured physical activity in older children when compared to younger children (10). To reduce seasonal effects, physical activity was only monitored during the autumn (September through November). Monitors were distributed to include at least one weekend day at age 5, 8, and 11. Children were included in the analysis of data if they wore the accelerometer at least 8 hours/day for at least 3 days and within 15 months of the dual energy x-ray absorptiometry (DXA) scan. One-minute epochs were used to sum movement count values and a summary variable of daily minutes spent in moderate and vigorous physical activity (MVPA) was calculated. The cut-point threshold of 3000 accelerometer movement counts per minute ($\text{ct} \cdot \text{min}^{-1}$) was used to define MVPA. This cut-point has been associated with MVPA at normal walking speeds in children (5).

Bone Mineral Content

At ages 5 and 8, whole body, anterior-posterior (AP) lumbar spine, and left hip scans were obtained using a Hologic QDR 2000 DXA (Hologic, Inc., Bedford, MA) with software version 7.20B. The fan-beam mode was used for spine and whole body scans and the pencil beam mode was used for the hip scan. At age 11, the Hologic QDR 4500 DXA (Delphi upgrade) with software version 12.3 and fan-beam mode was used for all scan acquisitions. All scans (ages 5, 8, and 11) were re-analyzed using Hologic software version 12.6. BMC (g) was derived from the scan images. Previous research suggests that skull size confounds whole body bone data in young children (26); therefore, all whole body results presented in this study represent BMC excluding the skull. Software-specific Global Regions of Interest (ROI) were used to designate the general boundaries of the hip and spine images. A review of the bone within the ROI box was confirmed by the operator and edited to ensure appropriate bone-edge detection. Quality control scans were performed daily using the Hologic spine phantom. To minimize operator-related variability, all measurements were conducted by one of three experienced technicians. The precision error for BMC measurements is low in our laboratory (coefficient of variation of $< 1\%$ for quality control scans performed daily using the Hologic phantom). Translational equations from 4500 DXA measures to 2000 DXA measures for age 11 records were used to adjust for the differences between the two DXA machines. To develop these translational equations a separate study was conducted where 60 of the children (32 boys, 28 girls) ages 9.9 to 12.4 (mean 11.4, SD 0.4) were scanned on each machine in random order during one clinic visit. The actual observations were closely aligned around the translational equation regression line and the coefficient for determination (R^2) for the 4500 DXA data regressed on to the 2000 DXA data was 0.99 (unpublished observations).

Anthropometry and Somatic Maturity

Research-trained nurses measured the child's height (cm) using a Harpenden stadiometer (Holtain, UK) and body mass (kg) using a Healthometer physician's scale (Continental, Bridgeview, IL) at each visit (age 5, 8, and 11 yr). At age 11, sitting height was measured and

used to estimate maturity offset (year from peak height velocity) using predictive equations established by Mirwald and colleagues (20). This approach includes age, gender, weight, height, sitting height, and leg length as predictors of years from peak height velocity (or somatic maturity). The Mirwald method has been validated in white Canadian children and adolescents ($R^2=0.91-0.92$, $SEE=0.49-0.50$) (20). We dichotomized the maturity offset variable as 0 (prior to peak height velocity or pre-mature) or 1 ($\geq$ peak height velocity or mature).

Statistical Analysis

Gender-specific descriptive analyses including Student's t-tests were conducted of measures obtained at age 5, 8, and 11. Mixed regression models for correlated data were used to examine whether physical activity at age 5 predicted BMC at ages 8 and 11 with adjustment for concurrent (at age 8 or 11) height, weight, age, somatic maturity, and MVPA. The residual observations within children were correlated through the within-person variance-covariance matrix and the appropriate matrix structure was determined based on Akaike's Information Criterion (AIC) for goodness of fit. An unstructured variance-covariance matrix was selected to allow for the higher variance of age 11 measures, together with the within-person covariance. Residual and studentized residual graphs were used to confirm the models' assumptions and fit (not shown). The analysis was repeated to also control for BMC (whole body, spine, or hip) at age 5.

To investigate the effect of high versus low age 5 physical activity, the high (most active) and the low (least active) quartile groups based on age 5 MVPA were identified for the whole sample and the analysis was stratified by gender. The highest quartile group consisted of 37 girls and 47 boys; whereas, lowest quartile group consisted of 25 boys and 59 girls. Mixed model least-squares means at the person level of covariates for age group were used to compare the BMC at age 8 and 11 of children in the highest and lowest quartiles of age 5 MVPA. The covariates included concurrent height, weight, age, somatic maturity, and MVPA. Least-squares BMC means for children at age 5 were calculated in a separate cross-sectional model. The approach was then repeated to include BMC at age 5 as a covariate in the age 8 and 11 group analyses. The level of significance was set at 0.05 for all analyses which were conducted using SAS (version 9.1.3).

RESULTS

Participant Characteristics

The characteristics of children at the time of each examination (age 5, 8, and 11), including age, height, weight, BMC, and MVPA are summarized in Table 1. Throughout the study, boys on average engaged in more MVPA than did girls ($p < 0.05$) and this difference increased as the children aged. Gender-related differences were also noted in BMC. At ages 5 and 8, the boys had greater spine BMC, and at age 8 the boys had greater hip BMC than girls. At age 11, the girls had greater spine BMC than boys.

Effect of Early Physical Activity on Later BMC

Gender-specific regression models for BMC are presented in the left half of Tables 2 and 3 in Panel A. After adjustment for concurrent (age 8 or 11) age, height, weight, somatic maturity, and MVPA, age 5 MVPA was a significant predictor of age 8 and 11 BMC in both boys and girls at the whole body, spine, and hip ($p < 0.05$) (Table 2 and 3, Panel A). The age 5 MVPA β (slopes) indicated that the contribution of age 5 MVPA to age 8 and 11 BMC was consistently greater in boys than girls. In all models for girls and in the whole body and spine models for boys, concurrent (age 8 or 11) MVPA was not significantly ($p > 0.05$) associated with BMC at age 8 and 11 when age 5 MVPA was included in the models. For boys, concurrent MVPA

remained significantly associated with hip BMC at age 8 and 11 ($p = 0.004$) after age 5 MVPA entered the model.

To examine the relationship between age 5 MVPA and BMC at age 8 and 11, independent of the age 5 MVPA contribution to age 5 BMC (which presumably contributed to age 8 and 11 BMC), regression models were fitted that included age 5 BMC (see right sides of Tables 2 and 3, Panel B) in addition to concurrent (age 8 or 11) age, height, weight, somatic maturity, and MVPA. This is a conservative approach that would be expected to attenuate the associations since the immediate benefit of age 5 MVPA on age 5 BMC is controlled. Therefore, what is tested is the potential impact beyond the age 5 time period. Age 5 MVPA remained a significant predictor of age 8 and 11 whole body BMC, spine BMC, and hip BMC in boys, but not girls. In these models with the exception of hip BMC in boys, concurrent (age 8 or age 11) MVPA was not significantly associated with BMC ($p > 0.05$).

Differences in BMC at Age 8 and 11 between the Least and Most Active Age 5 Children

A summary of characteristics of the children who were in the lowest (least active) and highest (most active) MVPA quartiles at age 5 is presented in Table 4. At age 5 there was no difference in age, weight, or height between the boys in the lowest and highest MVPA quartiles. At age 5, girls in the lowest MVPA quartile were heavier than girls in the highest MVPA quartile ($p < 0.05$). However, the absolute difference in weight between girls in the lowest and highest age 5 MVPA quartile was 1.16 kg, which was less than the absolute difference in weight between boys in the lowest and highest age 5 MVPA quartile. These data suggest that the statistically significance difference in weight in girls was due to our larger sample of girls (when compared to boys).

Least-squares BMC means for the lowest and the highest quartiles of age 5 MVPA are presented in Table 5. After adjustment for concurrent age, height, weight, and MVPA, boys and girls in the highest age 5 MVPA quartile had significantly greater BMC at age 8 and 11 than those in the lowest quartile ($p < 0.05$). On average, boys in the highest age 5 MVPA quartile had 8, 14, and 11% more BMC at the whole body, spine, and hip (respectively) at age 8 than boys in the lowest age 5 MVPA quartile. Girls in the highest age 5 MVPA quartile had 6, 8, and 8% more BMC at the whole body, spine, and hip (respectively) at age 8 than girls in the lowest age 5 MVPA quartile. At age 11, the difference between the highest and lowest quartile of age 5 MVPA in boys decreased to 5% for the whole body, 7% for the spine, and 7% for the hip. The age 11 BMC difference in girls was 4% for the whole body, 6% for the spine, and 5% for the hip. After controlling for age 5 BMC, BMC differences at age 8 and age 11 for girls were not significant ($p > 0.05$) (see table 6). However for boys, BMC differences at age 8 and age 11 remained significant at the spine and hip. On average, the BMC difference in boys for the spine was 7% at age 8 and 5% at age 11. For the hip, the BMC difference in boys was 6% at age 8 and 4% at age 11.

DISCUSSION

Little is known about habitual physical activity and BMC accrual in children younger than 8 yr (3). This is partially due to the challenges of measuring “everyday” physical activity in young children. To the best of our knowledge, the Iowa Bone Development Study is the first study to investigate longitudinal associations between objectively-measured physical activity and BMC in young children (8). Of the currently available objective instruments for the assessment of children’s physical activity, accelerometry-based physical activity monitors, such as the ActiGraphs used in our study, appear to be the most appropriate choice when bone outcomes are of interest. These monitors detect acceleration (m/s^2) which is proportional to the muscular and impact load forces acting on the skeletal system (22). In addition, they provide

an absolute measure that is, for the most part, independent of fitness, adiposity, and size; factors that are likely to change during the course of a longitudinal study.

In general, pediatric researchers have focused on children in middle and late childhood with the assumption that the time period just prior to puberty represents a “window of opportunity” when the skeleton is most sensitive to mechanical loading (12,23). Results from our work suggest widening the “window of opportunity” concept to include an earlier time period (age 5). Intervening early to increase physical activity may have the added advantage of improving compliance, since most young children are amenable, and even eager, to engage in age-appropriate physical activities and they have the discretionary time to do so.

To illustrate the implications of our findings, we calculated the average change in hip BMC expected with a 30 minute increase in MVPA at age 5. Thirty minutes was selected given the mean MVPA at age 5 in our cohort was approximately 28 min and current U.S. federal guideline for children is 60 minutes of daily age-appropriate moderate and vigorous activity (29). The mixed regression results for girls (presented in Table 2-Panel A) suggest that, if all other factors were held constant, 30 minutes of additional MVPA at age 5 years would result, on average, in an additional 0.5 g of hip BMC later in childhood. In our girls’ cohort, 0.5 g was 4.5% of the mean hip BMC at age 8 and 3.0% at age 11. Using this same approach, mixed regression results for boys (Table 3-Panel A) suggest 30 minutes of additional MVPA at age 5 years would result, on average, in an additional 0.8 g of hip BMC later in childhood. The additional hip BMC (0.8 g) was 6.7% of the mean hip BMC of our boys’ cohort at age 8 and 4.4% at age 11. Increases of this magnitude are similar to what is expected with targeted loading interventions (6,16,17) and likely to provide a meaningful increase in peak bone mass later in childhood (12).

We have consistently noted stronger associations between physical activity and BMC in boys (when compared to girls) in our cohort (8,9). McKay and colleagues (18) have also reported stronger relationships between physical activity and BMC in boys than girls. These findings are consistent with McDonald and colleagues suggestion of a sex-specific sensitivity of bone to mechanical loading that favors males (15). However, we also suspect that the stronger relationship observed in boys in our study was at least partially a result of the greater activity at age 5 in boys when compared to girls. On average, the boys in our study were 28% more active than girls at age 5. Our quartile analysis indicated that even within the most active group of age 5 children, the boys were 12% more active than the girls. More activity would result in more mechanical loading of the skeleton and presumably greater benefits.

Limitations of the present study include the use of a convenience sample of mostly Iowa children with low minority representation and relatively high socio-economic status. It is possible that the more active children at age 5 were different from their peers in ways that we did not consider or for which we were unable to control, e.g., dietary intake and genetic factors. Our study results should be confirmed via long-term follow-up of randomized, controlled trials using a more heterogeneous sample. In addition, accelerometry-based physical activity monitoring is considered the preferred method for measuring children’s physical activity in epidemiologic studies. However, our accelerometry method has limitations including our use of a one-minute epoch. This approach may have under-measured MVPA (30). Furthermore, there is no agreed upon age-related cut-point value for ActiGraph accelerometry measures for longitudinal studies. However, our approach is consistent with a 6-year follow-up study used to examine changes in physical activity and metabolic outcomes (7), as well as recent laboratory work suggesting that (accelerometry-derived) movement count values are stable in relationship to oxygen consumption during middle childhood (5).

This report provides evidence of a sustained benefit on BMC associated with early physical activity at the whole body, spine, and hip. Our findings support the hypothesis that there is a pathway between early physical activity and later BMC that is independent of the effect of accumulated physical activity. An important implication of our work is that children who are less physically active at an early age may lose out on the opportunity to obtain the highest peak BMC possible later in life when they are likely to be less active. If the residual benefit observed in this study persists through adolescence, early childhood may prove to be an important developmental period for the promotion of physical activity to optimize peak bone mass during young adulthood and, perhaps, the prevention of osteoporosis during later years.

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Table 1

Characteristics of the participants (n = 185 girls and 148 boys)

	Age 5		Age 8		Age 11	
	Girls	Boys	Girls	Boys	Girls	Boys
	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD
Ht (cm)	111.1 ± 5.5	112.0 ± 5.5	132.5 ± 6.8*	134.1 ± 7.4	149.1 ± 7.7	148.9 ± 7.7
Wt (kg)	20.0 ± 3.8	20.3 ± 3.4	31.7 ± 8.7	32.2 ± 8.5	44.6 ± 12.2	44.1 ± 12.4
Age at DXA (yr)	5.3 ± 0.4	5.2 ± 0.4	8.7 ± 0.6	8.7 ± 0.6	11.2 ± 0.3	11.2 ± 0.3
Whole Body BMC (g)	247.5 ± 80.6	246.2 ± 75.8	560.3 ± 165.8	581.5 ± 252.9	951.3 ± 267.1.	918.0 ± 253.0
Spine BMC (g)	14.0 ± 2.6*	14.6 ± 2.6	21.8 ± 4.4*	22.9 ± 4.5	31.9 ± 8.4*	29.6 ± 5.8
Hip BMC (g)	5.9 ± 1.3	6.1 ± 1.4	11.2 ± 2.6*	11.9 ± 3.0	17.7 ± 4.2	18.0 ± 4.4
MVPA (min/d)	24.2 ± 13.4*	31.1 ± 16.3	25.2 ± 13.1*	40.6 ± 21.4	22.6 ± 13.6*	42.3 ± 22.7

Note: No children were classified as mature at age 5 or age 8. At age 11, 19% of girls and no boys were classified as mature.

* $p < 0.05$ Student's t-test of girls vs. boys. BMC = bone mineral content, MVPA = moderate and vigorous physical activity.

Table 2

Mixed regression model analysis of BMC for girls (n = 185) at ages 8 and 11 as predicted by MVPA at age 5 years

Panel A without Age 5 BMC in the Model				Panel B with Age 5 BMC in the Model			
Effect	β	SE	p-value	Effect	β	SE	p-value
WB BMC							
Intercept	-487.80	272.91	0.076	Intercept	48.23	240.47	0.841
Age (yr)	-165.02	52.57	0.002	Age (yr)	-202.06	46.70	<.001
Age ² (yr ²)	9.36	2.74	0.001	Age ² (yr ²)	13.14	2.47	<.001
Maturity (0,1)	84.83	19.57	<.001	Maturity (0,1)	119.49	20.60	<.001
Ht (cm)	10.48	0.91	<.0001	Ht (cm)	6.10	0.80	<.001
Wt (kg)	11.39	0.67	<.001	Wt (kg)	8.84	0.63	<.001
Concurrent MVPA (10 min/d)	0.97	2.83	0.732	Concurrent MVPA (10 min/d)	3.55	2.40	0.142
Age 5 MVPA (10 min/d)	7.40	3.51	0.037	Age 5 MVPA (10 min/d)	1.52	2.84	0.594
Spine BMC							
Intercept	-8.49	11.14	0.447	Intercept	0.69	0.07	<.001
Age (yr)	-6.24	2.10	0.003	Age (yr)	9.60	9.16	0.296
Age ² (yr ²)	0.32	0.11	0.003	Age ² (yr ²)	-6.79	1.79	0.002
Maturity (0,1)	5.24	0.71	<.001	Maturity (0,1)	0.44	0.09	<.001
Ht (cm)	0.41	0.04	<.001	Ht (cm)	6.28	0.77	<.001
Wt (kg)	0.13	0.03	<.001	Wt (kg)	0.15	0.03	<.001
Concurrent MVPA (10 min/d)	0.02	0.12	0.871	Concurrent MVPA (10 min/d)	0.09	0.02	<.001
Age 5 MVPA (10 min/d)	0.39	0.17	0.022	Age 5 MVPA (10 min/d)	0.14	0.09	0.133
Hip BMC							
Intercept	-15.75	4.88	0.002	Intercept	0.06	0.11	0.594
Age (yr)	-2.02	0.91	0.029	Age 5 Spine BMC (g)	1.03	0.07	<.001
Age ² (yr ²)	0.12	0.05	0.01	Intercept	-7.32	4.54	0.108
Maturity (0,1)	1.91	0.30	<.001	Age (yr)	-2.53	0.86	0.004
Ht (cm)	0.24	0.02	<.001	Age ² (yr ²)	0.18	0.04	<.001
Wt (kg)	0.10	0.02	<.001	Maturity (0,1)	2.38	0.32	<.001
Concurrent MVPA (10 min/d)	0.08	0.05	0.117	Ht (cm)	0.15	0.02	<.001
Age 5 MVPA (10 min/d)	0.18	0.08	0.026	Wt (kg)	0.07	0.01	<.001
				Concurrent MVPA (10 min/d)	0.08	0.05	0.076
				Age 5 MVPA (10 min/d)	0.04	0.06	0.551
				Age 5 Hip BMC (g)	0.78	0.08	<.001

Note: β = regression parameter estimate, WB BMC = whole body, MVPA = moderate and vigorous physical activity in ten minutes intervals to avoid small coefficients. Unstructured within person error-covariance was used for repeated measures, variance-covariance values were highly significant ($p < 0.001$). Akaike's Information Criterion (AIC) values indicated that this strategy improved the model fit when compared to a compound symmetric structure.

Table 3

Mixed regression model analysis of BMC for boys ($n = 148$) at age 8 and age 11 as predicted by MVPA at age 5 years

Panel A without Age 5 BMC in the Model						Panel B with Age 5 BMC in the Model					
	Effect	β	SE	p-value	Effect		β	SE	p-value		
WB BMC	Intercept	-608.93	258.70	0.020	Intercept		-176.01	248.36	0.48		
	Age (yr)	-82.50	51.87	0.114	Age (yr)		-134.44	49.56	0.008		
	Age ² (yr ²)	5.69	2.64	0.033	Age ² (yr ²)		9.68	2.56	0.002		
	Ht (cm)	7.78	1.07	<.001	Ht (cm)		4.96	0.92	<.001		
	Wt (kg)	12.44	0.81	<.001	Wt (kg)		10.08	0.75	<.001		
	Concurrent MVPA (10 min/d)	0.57	2.07	0.784	Concurrent MVPA (10 min/d)		1.06	1.87	0.574		
	Age 5 MVPA (10 min/d)	8.95	3.40	0.009	Age 5 MVPA (10 min/d)		5.77	2.87	0.046		
Spine BMC	Intercept	-15.69	7.03	0.027	Intercept		0.72	0.08	<.001		
	Age (yr)	-2.87	1.38	0.04	Age (yr)		-8.03	7.21	0.267		
	Age ² (yr ²)	0.15	0.07	0.031	Age ² (yr ²)		-2.60	1.43	0.072		
	Ht (cm)	0.34	0.04	<.001	Ht (cm)		0.19	0.07	0.009		
	Wt (kg)	0.12	0.02	<.001	Wt (kg)		0.16	0.04	<.001		
	Concurrent MVPA (10 min/d)	0.02	0.06	0.779	Concurrent MVPA (10 min/d)		0.10	0.02	<.001		
	Age 5 MVPA (10 min/d)	0.75	0.14	<.001	Age 5 MVPA (min/d)		0.44	0.11	0.002		
Hip BMC	Intercept	-9.43	4.35	0.032	Intercept		0.8838	0.08	<.001		
	Age (yr)	-2.00	0.86	0.023	Age (yr)		-2.03	4.43	0.647		
	Age ² (yr ²)	0.14	0.04	0.003	Age ² (yr ²)		-2.58	0.88	0.004		
	Ht (cm)	0.18	0.02	<.001	Ht (cm)		0.19	0.04	<.001		
	Wt (kg)	0.13	0.02	<.001	Wt (kg)		0.09	0.02	<.001		
	Concurrent MVPA (10 min/d)	0.11	0.04	0.004	Concurrent MVPA (10 min/d)		0.12	0.03	0.005		
	Age 5 MVPA (10 min/d)	0.26	0.07	0.004	Age 5 MVPA (min/d)		0.13	0.06	0.039		
					Age 5 Hip BMC (g)		0.81	0.08	<.001		

Note: β = regression parameter estimate, WB BMC = whole body, MVPA = moderate and vigorous physical activity in ten minutes intervals to avoid small coefficients. The models for boys were not adjusted for maturity, because no boys were categorized as mature. Unstructured within person error-covariance was used for repeated measures, variance-covariance values were highly significant ($p < 0.001$). Akaike's Information Criterion (AIC) values indicated that this strategy improved the model fit when compared to a compound symmetric structure.

Table 4
Characteristics of children in the lowest (n=84) and highest quartiles (n=84) of age 5 MVPA

	Age 5		Age 8		Age 11	
	Lowest	Highest	Lowest	Highest	Lowest	Highest
	Mean $\pm$ SD	Mean $\pm$ SD	Mean $\pm$ SD	Mean $\pm$ SD	Mean $\pm$ SD	Mean $\pm$ SD
Girls						
Ht (cm)	111.4 $\pm$ 6.2	111.0 $\pm$ 5.0	133.2 $\pm$ 7.4	131.8 $\pm$ 6.0	149.2 $\pm$ 8.6	149.0 $\pm$ 6.4
Wt (kg)	20.9 [*] $\pm$ 5.1	19.7 $\pm$ 2.5	33.6 [*] $\pm$ 11.3	30.0 $\pm$ 6.2	45.8 $\pm$ 14.5	43.6 $\pm$ 9.6
Age at DXA (yr)	5.3 $\pm$ 0.5	5.3 $\pm$ 0.4	8.7 $\pm$ 0.6	8.6 $\pm$ 0.7	11.3 $\pm$ 0.3	11.2 $\pm$ 0.3
MVPA (min/d)	11.2 [*] $\pm$ 3.5	45.4 $\pm$ 10.0	19.4 [*] $\pm$ 10.7	34.1 $\pm$ 13.7	19.3 [*] $\pm$ 10.8	30.4 $\pm$ 17.7
Boys						
Ht (cm)	111.8 $\pm$ 7.3	112.6 $\pm$ 5.4	134.3 $\pm$ 9.2	134.8 $\pm$ 6.9	148.6 $\pm$ 9.3	149.8 $\pm$ 7.5
Wt (kg)	21.5 $\pm$ 5.4	20.1 $\pm$ 2.5	34.6 $\pm$ 12.1	31.8 $\pm$ 7.0	47.1 $\pm$ 16.4	43.8 $\pm$ 10.4
Age at DXA (yr)	5.2 $\pm$ 0.4	5.3 $\pm$ 0.4	8.6 $\pm$ 0.6	8.7 $\pm$ 0.6	11.1 [*] $\pm$ 0.3	11.3 $\pm$ 0.3
MVPA (min/d)	9.55 [*] $\pm$ 3.6	50.7 $\pm$ 11.0	20.4 [*] $\pm$ 14.4	50.5 $\pm$ 22.2	29.4 [*] $\pm$ 16.9	53.5 $\pm$ 26.0

Note: 59 girls and 25 boys in lowest age 5 MVPA quartile; 37 girls and 47 boys in highest age 5 MVPA quartile.

^{*} $p < 0.05$ for lowest vs. highest age 5 MVPA.

Table 5

Mixed-model least-squares means for BMC in children in the lowest and highest quartiles of MVPA at age 5 years

	Age 5		Age 8		Age 11	
	Age 5 Lowest LS Mean(SE)	Age 5 Highest LS Mean(SE)	Age 5 Lowest LS Mean(SE)	Age 5 Highest LS Mean(SE)	Age 5 Lowest LS Mean(SE)	Age 5 Highest LS Mean(SE)
Boys						
WB BMC	225.31 (7.29)	259.93 (5.30) ***	551.15 (13.56)	593.98 (9.16) *	894.6 (15.99)	937.43 (12.94) *
Spine BMC	13.62 (0.32)	15.49 (0.23) ***	21.41 (0.59)	24.37 (0.43) ***	29.21 (0.39)	31.15 (0.46) ***
Hip BMC	5.41 (0.18)	6.52 (0.13) ***	11.21 (0.30)	12.42 (0.21) **	17.29 (0.34)	18.50 (0.27) **
Girls						
WB BMC	236.11 (4.44)	259.05 (5.55) **	541.23 (7.85)	574.77 (10.06) *	930.78 (11.09)	964.33 (12.17) *
Spine BMC	13.64 (0.25)	14.48 (0.31) *	21.11 (0.38)	22.86 (0.49) **	31.15 (0.49)	32.90(0.58) **
Hip BMC	5.63 (0.11)	6.22 (0.13) ***	10.82 (0.18)	11.63 (0.23) **	17.39 (0.22)	18.20 (0.26) **

 $p < 0.001$,

**
 $p < 0.01$,

*
 $p < 0.05$

Note: WB BMC = whole body BMC. BMC at age 5 years was adjusted for concurrent (age 5 years) age, height, and weight. BMC at age 8 years and age 11 years was adjusted for concurrent age, height, weight, maturity, and MVPA (moderate and vigorous physical activity)

Mixed-model least-squares means for BMC in children in the lowest and highest quartiles of MVPA at age 5 years, with adjustment for age 5 BMC

Table 6

	Age 8			Age 11		
	Age 5 Lowest	Age 5 Highest	LS Mean(SE)	Age 5 Lowest	Age 5 Highest	LS Mean(SE)
	LS Mean(SE)	LS Mean(SE)		LS Mean(SE)	LS Mean(SE)	
Boys						
WB BMC	557.14 (11.05)	584.83 (7.97)		901.74 (11.16)	929.43 (11.33)	
Spine BMC	22.16 (0.45)	23.62 (0.32) *		28.95 (0.48)	30.41 (0.37) *	
Hip BMC	11.49 (0.24)	12.12 (0.17) *		17.57 (0.28)	18.20 (0.23) *	
Girls						
WB BMC	544.68 (6.17)	560.83 (8.01)		932.89 (10.1 9)	949.03 (11.43)	
Spine BMC	21.37 (0.24)	22.14 (0.32)		31.36 (0.40)	33.13 (0.44)	
Hip BMC	10.93 (0.14)	11.30 (0.18)		17.50 (0.19)	17.86 (0.22)	

* p-value<0.05

Note: WB BMC = whole body BMC. . . BMC at age 8 years and age 11 years was adjusted for concurrent age, height, weight, maturity, MVPA (moderate and vigorous physical activity), and age 5 BMC.