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Sustained Effects of Physical Activity on Bone Health: Iowa Bone Development Study

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Abstract

Studies of youth athletics and interventions have shown some maintenance of bone mineral content (BMC; g) after cessation of training, but less is known about sustained effects of everyday physical activity (PA). Using a prospective cohort, this report examined potential effects of childhood PA on adolescent BMC. Participants ($N = 156$ boys, 170 girls) had exams at ages 5, 13, and 15. Body size and maturity were determined using anthropometry. Moderate-to-vigorousintensity PA (MVPA) and vigorous-intensity PA (vigorous PA) were measured using accelerometry. BMC of the spine and hip was measured using dual-energy x-ray absorptiometry. Mixed regression models tested whether PA at age 5 affected BMC at ages 13 and 15 after adjustment for age (yr), height (cm), weight (kg), maturity (pre-peak height velocity or post), and activity level (min•day⁻¹). Analysis was repeated to control for age 5 BMC. On average, boys participated in 59, 52, and 38 min of MVPA and 13, 17, and 11 min of Vigorous PA at ages 5, 13, and 15, respectively. MVPA ($\beta = 0.799$) and Vigorous PA ($\beta = 1.338$) at age 5 predicted later spine BMC (p<0.05). MVPA (β = 0.480) at age 5 predicted hip BMC. Girls participated in 47, 33, and 26 min of MVPA and 10, 9 and 7 min of Vigorous PA at ages 5, 13, and 15, respectively. Neither MVPA nor Vigorous PA predicted later spine BMC. MVPA (β = 0.302) at age 5 predicted hip BMC. After controlling for BMC at age 5 as well as the other covariates, the effect of MVPA (β = 0.695) and Vigorous PA (β = 1.079) at age 5 remained significant for boys at the spine. For girls, neither MVPA nor Vigorous PA at age 5 predicted spine or hip BMC. Children's early PA appears

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Authors' roles: SL and KJ participated in the study design, acquisition of the data, and revising the manuscript. EL conducted the data analysis and revised the manuscript. SF drafted the manuscript. All authors participated in data interpretation and approved the final version of the manuscript.

^{5.0} DISCLOSURES

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to have a modest effect on adolescent BMC at the critical regions of spine and hip; benefits may be greater for geometric changes, which future studies should include.

Keywords

DXA; longitudinal; bone mineral content; children; adolescence

1.0 INTRODUCTION

Mechanical loading via physical activity (PA) places strains on bone greater than those needed for steady state remodeling, leading to a response that increases bone mass and improves its overall strength via changes in geometry and micro-architecture (1–4). The potential of PA to increase bone mass depends on the magnitude of the load, the rate at which the load is applied, the duration of the loading bout, and the novelty of the load (5). Loads of greater force that are delivered quickly, such as jumping, appear to provide the greatest opportunity for bone mineralization, or bone mineral content (BMC) accrual (6).

Loads necessary for bone accrual have been found in activities ranging from competitive sport to exercise interventions to self-selected activity. Previous research on competitive sport found that 9- to 12-year-old female gymnasts had 15.5% higher bone mineral density (BMD) at the mid-radius, 33% at the distal radius, 11.0% at the L2 – L4 vertebrae, 15.0% at the femoral neck, and 15.0% at Ward's triangle than controls of the same age (7, 8). A study examining the playing versus non-playing arms of 16- to 50-year-old female tennis and squash athletes found that the athletes had greater between-arm BMC differences when compared to controls (15.5% at the proximal humerus, 16.2% at the humeral shaft, 8.5% at the radial shaft, and 12.5% at the distal radius) (9). Exercise interventions have also provided evidence of skeletal benefits from targeted impact activities. Gunter et al. (6) and Fuchs et al. (10) found BMC gains in prepubescent boys and girls of 3.5% – 8.0% at the hip and lumbar spine resulting from a targeted, high-impact jumping intervention. Higher levels of everyday PA, examined by a prospective observational study, showed that highly active 8- to 14-year-olds had 18.0% greater BMC at the lumbar spine in both boys and girls, 7.0% greater BMC at the femoral neck in boys, and 11.0% greater BMC at the femoral neck in girls compared to the least active group (11).

Cross-sectional, longitudinal, and randomized controlled trials demonstrate the benefits of PA on bone health in children (12–15). However, as children progress into and through adolescence, they tend to reduce their activity levels and it is less clear if the BMC benefits obtained from early PA can be sustained into adolescence despite this reduction in activity (16–18). A previous report from the Iowa Bone Development Study found that, even though PA levels decreased as children aged, those who were most active at age 5 had greater BMC at ages 8 and 11 than those were less active. After adjusting for concurrent age, height, weight, and MVPA, boys in the highest MVPA quartile at age 5 had 14.0% more BMC at the spine and 11.0% more BMC at the hip at age 8 than those in the lowest MVPA quartile. Girls in the highest MVPA quartile at age 5 had 8.0% more spine and hip BMC at age 8 than those in the lowest MVPA quartile. These values decreased to 7.0% for the spine and hip in boys at age 11. For girls, the values decreased to 6.0% for the spine and 5.0% for the hip at

age 11 (19). Baxter-Jones and colleagues (20) also examined the sustainability of BMC over time and reported that active adolescent males had 8.0% more hip BMC as adults than their inactive or moderately-active peers after adjustment for age, maturity age, height, weight, adult PA, calcium intake, and BMC one year after peak height velocity (PHV). These males also had 9.0% greater adjusted femoral neck BMC. The active adolescent females in the study had 9.0% and 10.0% greater BMC at the hip and femoral neck, respectively (20).

These studies provide some evidence that increased BMC associated with PA can be maintained into the future. Using objective PA monitors, dual-energy x-ray absorptiometry (DXA), and a ten-year, longitudinal design, this report extends the previous Iowa Bone Development Study results to examine whether childhood PA is associated with greater BMC during adolescence.

2.0 MATERIALS AND METHODS

2.1 Participants

Study participants were members of the Iowa Bone Development Study- a longitudinal study of bone health during childhood, adolescence, and young adulthood- recruited from 1998 to 2001 from a cohort of families participating in the Iowa Fluoride Study. Additional information about the study design and demographic characteristics of the participants has been described elsewhere (21–24). Baseline measures were assessed at age 5 ($N = 156$ boys, 170 girls) and follow-up measures were assessed at ages 13 ($N = 143$ boys, 160 girls) and 15 $(N = 114$ boys, 117 girls). For inclusion in these analyses, participants were required to have one measurement at either age 13 or 15; however, 56% of boys and 63% of girls had both. Approval for this study was obtained from the University of Iowa Institutional Review Board (Human Subjects). Parents provided written informed consent and children provided assent.

2.2 Physical activity

ActiGraph activity monitor model number 7164 was worn by participants at ages 5 and 13 yr. Due to the unavailability of this model at the 15 yr measurement, model GT1M was used. Previous research has shown a high correlation in movement counts between the two monitors $(r = 0.99)(25)$. Movement counts were collected in one-minute epochs for ages 5 and 13 and five-second epochs for age 15. The five-second epochs for age 15 were reintegrated to one-minute epochs to maintain consistency with the earlier measurements. Procedures for PA measurement using the ActiGraph and validation of these monitors have been described elsewhere (26–28). Children at age 5 were asked to wear the monitor all day during waking hours for four consecutive days, including one weekend day. The number of wear days for children at ages 13 and 15 was increased to five consecutive days, including both weekend days, to account for increased day-to-day variability in accelerometrymeasured PA in older children when compared to younger children (27). To be included in the analyses, participants were required to have three valid days of monitor wear for each measurement period. A day was considered valid if the monitor was worn for at least eight hours per day. Using the Spearman-Brown Prophecy formula, this corresponds to a 60%

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reliability coefficient (29). To reduce seasonal effects, PA was only monitored during the autumn months.

The PA variables of interest were time spent in moderate through vigorous-intensity physical activity (MVPA) (minutes) and time spent in vigorous-intensity PA (Vigorous PA) (minutes). Mean values were obtained from all minutes of all valid days of wear. As specified by Evenson and colleagues (in a sample of 5- to 8-year-olds) (30), cut-points were defined as < 100 counts per minute for sedentary, ≥ 2,296 counts per minute for MVPA, and ≥4,012 counts per minute for Vigorous PA. The moderate-intensity and vigorous-intensity PA cut-points have been evaluated using area-under-the-receiver operating characteristic curve (ROC-AUC) and have been shown to exhibit fair (ROC-AUC = 0.74) to good (ROC- $AUC = 0.84$) classification accuracy, respectively. When combined (MVPA), the cut-points exhibited excellent classification accuracy ($ROC-AUC = 0.90$). Based on a comparison of five independently developed sets of cut-points (in samples ranging from 5- to 18-yearolds), Trost and colleagues recommended that researchers use the Evenson cut-points (31).

2.3 Bone mineral content

At age 5, left hip scans were obtained using a Hologic QDR 2000 DXA (Hologic, Inc., Bedford, MA) with software version 7.20B, using the pencil-beam mode. At ages 13 and 15, the Hologic QDR 4500 DXA (Delphi upgrade) with software version 12.3 and the fan-beam mode were used. All scans were reanalyzed using Hologic software version 12.6, and BMC (g) was derived from these scanned images. Software-specific global regions of interest were used to designate the general boundaries of the images. A review of the bone within the region of interest 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. Translational equations for 4500 DXA measures to 2000 DXA measures were used to adjust for the differences between the two DXA machines. A separate study where 60 children (32 boys and 28 girls) aged 9.9 to 12.4 were scanned on each machine in random order during one clinic visit was conducted. The actual observations were closely aligned around the translational equation regression line, and the coefficient of determination (\mathbb{R}^2) for the 4500 DXA regressed on to the 2000 DXA data was 0.99 (unpublished observation).

2.4 Height, Weight, and Somatic Maturity

Research-trained nurses measured the participants' height (cm) using a Harpenden stadiometer (Holtain, Crymych, UK) and body mass (kg) using a Healthometer physician's scale (Continental, Bridgeview, IL) at each visit. At ages 13 and 15, sitting height was used to estimate maturity offset (year from PHV) using predictive equations established by Mirwald and colleagues (32). These equations include age, sex, weight, height, sitting height, and leg length as predictors of years from PHV, or somatic maturity. The method of Mirwald (32) has been validated in white Canadian children and adolescents ($\mathbb{R}^2 = 0.91$ – 0.92, SEE = $0.49 - 0.50$). The maturity offset variable was dichotomized as 0 (before PHV, or premature) or 1 (after PHV, or mature).

2.5 Statistical analysis

Descriptive statistics (means, standard deviations) were calculated for the anthropometric, BMC, and PA characteristics of the participants. Student's t-tests were used to examine sex differences. Longitudinal linear mixed regression models were used to determine whether age 5 PA could predict age 13 or 15 spine or hip BMC after adjusting for age (13/15 yr), height (cm), weight (kg), maturity ($0 = pre-PHV/1 = post$; boys, age 13 only), and concurrent (age 13/15) MVPA/Vigorous PA (as relevant) activity level (min/day). The residual observations within children were correlated through the within-person variancecovariance matrix. Matrix structure type was determined based on Akaike's Information Criterion (AIC) for goodness of fit. An unstructured variance-covariance matrix was chosen because it allowed for an assumption of higher variance for age 15 measures together with the within-person covariance. The longitudinal analyses were repeated to also control for BMC at age 5. All statistical analyses were conducted using SAS version 9.2 and were sexspecific. Results with $p < 0.05$ were considered statistically significant.

3.0 RESULTS

3.1 Participant characteristics

The distribution of the participants' characteristics at ages 5, 13, and 15 are shown in Table 1. The boys were significantly taller than the girls at all ages ($p < 0.05$). The boys were significantly heavier than the girls at age 15 ($p < 0.01$). The boys were more active than the girls at all ages, for both MVPA and Vigorous PA ($p < 0.01$). In addition, a higher percentage of the boys participated in 60 minutes or more of MVPA per day than the girls at every measurement age. For both boys and girls, the percentage of participants meeting the 60 minutes threshold was highest at age 5 (44% boys; 25% girls) and decreased thereafter. The boys had significantly greater spine BMC than the girls at age 5 ($p < 0.05$), but the girls had significantly greater spine BMC than the boys at age 13 ($p < 0.01$). The boys had significantly greater hip BMC than the girls at age 15 ($p < 0.01$). At age 13, 29% of boys and 99% of girls were classified as mature. At age 15, 97% of boys and 100% of girls were classified as mature.

Loss to follow-up did occur over the 10 years of data collection. Baseline comparisons for the participants who remained in the study until age 15 versus those who were lost to follow-up after age 13 are shown in Table 2. For boys, those who were lost after age 13 were slightly taller, heavier, had more BMC at both the spine and the hip, and participated in a few more minutes of MVPA at baseline than those who remained in the study until age 15, but none of these differences were statistically significant ($p > 0.05$). For girls, those who were lost after age 13 were slightly taller and heavier at baseline than those who participated until age 15, but again, these differences were not statistically significant ($p > 0.05$).

3.2 Effect of early PA on later BMC

Gender-specific regression models for spine BMC, without BMC at age 5 as a covariate, are presented in Panel A of Tables 3 and 4. For boys (Table 3), after adjustment for concurrent (age 13 and/or 15) age, height, weight, maturity, and PA, age 5 MVPA was a significant predictor of BMC at ages 13 and/or 15 at the spine and hip ($p < 0.05$). Age 5 Vigorous PA

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was a significant predictor of BMC at ages 13 and/or 15 in boys at the spine only ($p < 0.05$). Neither concurrent MVPA nor concurrent Vigorous PA was a significant predictor of age 13 and/or 15 BMC at the spine or hip in boys ($p > 0.05$). In girls (Table 4), age 5 MVPA was a significant predictor of BMC at ages 13 and/or 15 at the hip only ($p < 0.05$). The MVPA and Vigorous PA β coefficients (slopes) indicate that the contribution of age 5 PA to BMC at age 13 and/or 15 was greater in boys than in girls. Similar to the boys, neither concurrent MVPA nor concurrent Vigorous PA was a significant predictor of age 13 and/or 15 BMC at the spine or hip in girls ($p > 0.05$).

Models that include age 5 BMC measures as a covariate are presented in Panel B of Tables 3 and 4. For boys (Table 3), both age 5 MVPA and age 5 Vigorous PA remained significant predictors of BMC at ages 13 and/or 15 at the spine ($p < 0.05$), but were no longer significant at the hip ($p > 0.05$). However, age 5 MVPA approached significance ($p =$ 0.057), so it is possible that a larger sample size might have reached statistical significance. Again, neither concurrent MVPA nor concurrent Vigorous PA was a significant predictor of age 13 and/or 15 BMC at the spine or hip in boys ($p > 0.05$). In girls (Table 4), neither age 5 MVPA nor age 5 Vigorous PA was a significant predictor of spine or hip BMC at ages 13 and/or 15 ($p > 0.05$). Concurrent MVPA and concurrent Vigorous PA remained insignificant for prediction of age 13 and/or 15 BMC at the spine and hip in girls ($p > 0.05$). The MVPA and Vigorous PA β coefficients (slopes) indicate that the contribution of age 5 PA to BMC at age 13 and/or 15 was greater in boys than in girls, even when age 5 BMC values were included as a covariate.

4.0 DISCUSSION

This report provides limited evidence that everyday PA during early childhood is associated with BMC during adolescence. Our findings for boys suggest that early PA predicts later hip and spine BMC prior to adjusting for early BMC. However, when models were adjusted for early (age 5) BMC, the effect of early PA was seen only at the spine in boys. Adjustment for age 5 BMC is a conservative approach that tests the impact of PA beyond age 5 and would be expected to attenuate associations due to controlling for the immediate benefit of PA at age 5 on BMC at age 5. Using this conservative approach, we did not see sustained benefits of early PA on later BMC in girls. One possible explanation for this could relate to the fact that boys were more active than girls at every age in our sample. Perhaps girls are not reaching some critical (and unknown) threshold of PA in early life and are missing out on potential benefits as they grow and mature. Or, perhaps the types of activities favored by girls are not conducive to bone adaptation.

Applying our significant results for boys, the average change in BMC at age 15 was calculated based on a one standard deviation increase in MVPA at age 5, which corresponds to approximately 20 minutes per day for the boys in our sample. A one standard deviation (20 minutes) increase of MVPA at age 5 would result in ~80 minutes of MVPA. Assuming all other factors remained constant, this would result in an increase of 1.2 g of spine BMC at age 15 (a 2.0% change). This expected magnitude of increase is smaller than that seen in a previous randomized controlled trial that resulted in a 3.1% increase at the spine (10). However, this randomized controlled trial targeted bone –adaptation exercises, whereas we

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measured general physical activity, so a smaller effect is expected. The male-specific effect that we report suggests a need to maintain PA throughout childhood and adolescence and not rely on early PA as protective. Maintaining on-going high levels of PA will be challenging given the decrease in activity that occurs during adolescence and continues into adulthood (17–19). This might also be a possible explanation for why neither concurrent MVPA nor Vigorous PA were significant predictors of age 13 and/or 15 BMC at the spine or hip. It is possible that our participants were participating in an insufficient number of minutes of physical activity, or perhaps the types of activity they chose to engage in were not sufficient for bone building.

This report focused on the spine and hip BMC of children and adolescents with the ultimate goals of obtaining a better understanding of and suggesting possible ways to reduce incidence rates of osteoporosis in the future. Osteoporosis has been defined as "a skeletal disorder characterized by compromised bone strength leading to an increased risk of fracture" (33). We used BMC as a measure of bone mass and a surrogate of strength because DXA is considered a gold standard in evaluating bone health and risk for osteoporosis (33). Similarly, DXA allows scanning at clinically relevant sites for future fractures, such as the spine and hip, while requiring only a low dose of radiation exposure to the participants (less than 1.0 mrem). However, the ability of a bone to resist fracture is known to depend on more than BMC alone. The shape of the bone and the distribution of the mass throughout the bone (i.e., microarchitecture and geometry) also play a vital role in its fragility (34). Studies combining measures of bone geometry and mass will contribute to a better understanding of the bone benefits gained by participation in PA, as well as whether or not those benefits are sustained over time.

Limitations of this report include the use of a mostly white, low minority, convenience sample with relatively high socioeconomic status. In addition, it is possible that other factors, not controlled for, such as diet or genetic factors, could cause active participants to differ from those who are inactive. While accelerometry-based monitoring is the preferred, objective means of measuring PA, it does not provide any context, and activities that involve moderate-to-high intensity might not necessarily be associated with bone adaptation. Also, use of a 1-minute epoch for our data could have led to the misclassification of vigorousintensity activity as moderate-intensity. However, this objective monitoring is still preferred over self-reported PA and should be considered a strength of this report. Additional strengths include the use of a relatively large sample size and a longitudinal design that spanned 10 years.

4.1 Conclusions

In summary, this report provides limited evidence of sustained increases of BMC from childhood to adolescence, particularly in boys, and that those who are less active at an early age may miss the opportunity to obtain their optimal peak BMC later in life. An important implication of our work is that PA programming should begin early, be maintained over time, and include targeted activities for bone mineral accrual to optimize bone health throughout life.

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Highlights

- **•** We examine effect of childhood physical activity on adolescent bone mineral content
- **•** Children's physical activity has a modest effect on adolescent bone mineral content
- **•** Age 5 physical activity contributed to later bone mineral content more in boys than girls

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Characteristics of the participants. Characteristics of the participants.

Untransformed MVPA and Vigorous PA minutes reported here; Box-Cox transformed values used in all inferential analyses. Untransformed MVPA and Vigorous PA minutes reported here; Box-Cox transformed values used in all inferential analyses.

BMC, bone mineral content; MVPA, moderate and vigorous-intensity physical activity; PA, physical activity. BMC, bone mineral content; MVPA, moderate and vigorous-intensity physical activity; PA, physical activity.

*** $p < 0.05$,

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p < 0.01 Student's t-test of boys vs. girls. p < 0.01 Student's t-test of boys vs. girls.

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ß regression parameter estimate; BMC, bone mineral content; MVPA, moderate and vigorous-intensity physical activity; PA, physical activity β, regression parameter estimate; BMC, bone mineral content; MVPA, moderate and vigorous-intensity physical activity; PA, physical activity

Box-Cox transformed MVPA and Vigorous PA minutes used for inferential analyses. Box-Cox transformed MVPA and Vigorous PA minutes used for inferential analyses.

 d Concurrent = 13 and/or 15 yr for Panels (A) and (B) $a_{\text{Concurrent}} = 13$ and/or 15 yr for Panels (A) and (B)

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Table 4

Longitudinal mixed regression model analysis of BMC for girls ($n = 170$) at ages 13 and 15 as predicted by MVPA and Vigorous PA at age 5. Longitudinal mixed regression model analysis of BMC for girls (n = 170) at ages 13 and 15 as predicted by MVPA and Vigorous PA at age 5.

ß regression parameter estimate; BMC, bone mineral content; MVPA, moderate and vigorous-intensity physical activity; PA, physical activity β, regression parameter estimate; BMC, bone mineral content; MVPA, moderate and vigorous-intensity physical activity; PA, physical activity

Box-Cox transformed MVPA and Vigorous PA minutes used for inferential analyses. Box-Cox transformed MVPA and Vigorous PA minutes used for inferential analyses.

 $\alpha_{\rm Concurrent}$ = 13 and/or 15 yr for Panels (A) and (B) $a_{\text{Concurrent}} = 13$ and/or 15 yr for Panels (A) and (B)

Note: maturity offset not included since 98.8% were mature at age 13 and 100% were mature at age 15 Note: maturity offset not included since 98.8% were mature at age 13 and 100% were mature at age 15