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Objectively measured physical activity trajectories predict adolescent bone strength: Iowa Bone Development Study

Kathleen F Janz[1,2], **Elena M Letuchy**[2], **Trudy L Burns**[2,3], **Julie M Eichenberger Gilmore**[4], **James C Torner**[2], and **Steven M Levy**[2,5]

[1]Department of Health and Human Physiology, The University of Iowa, Iowa City, Iowa, USA

[2]Department of Epidemiology, The University of Iowa, Iowa City, Iowa, USA

[3]Department of Pediatrics, The University of Iowa, Iowa City, Iowa, USA

[4]Department of Clinical and Translational Science, The University of Iowa, Iowa City, Iowa, USA

[5]Department of Preventive and Community Dentistry, The University of Iowa, Iowa City, Iowa, USA

Abstract

Background—Physical activity improves bone strength and reduces the risk for osteoporotic fractures. However, there are substantial gaps in our knowledge as to when, how and how much activity is optimal for bone health.

Purpose—In this cohort study, we examined developmental trajectories of objectively measured physical activity from childhood to adolescence to discern if moderate-and-vigorous intensity physical activity (MVPA) predicts bone strength.

Methods—Starting at age 5 and continuing at 8, 11, 13, 15 and 17 years, Iowa Bone Development Study participants (n=530) wore an accelerometer for 3–5 days. At age 17, we assessed dual X-ray energy absorptiometry outcomes of mass and estimated geometry (femoral neck cross-sectional area and section modulus). We also assessed geometric properties (bone stress index and polar moment of inertia) of the tibia using peripheral computer quantitative tomography. Latent class modelling was used to construct developmental trajectories of MVPA from childhood to late adolescence. General linear models were used to examine the trajectory groups as predictors of age 17 bone outcomes.

Correspondence to: Dr Kathleen F Janz, Department of Health and Human Physiology, E130 FH, University of Iowa, Iowa City, IA 52242, USA; kathleen-janz@uiowa.edu.

Contributors All authors conceptualised the research, collected data and wrote and edited the manuscript. KFJ is the guarantor of this work and, as such, takes full responsibility for the completed manuscript.

Competing interests None.

Patient consent Obtained.

Ethics approval University of Iowa Intuitional Review Board.

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Data sharing statement The Iowa Bone Development Study shares unpublished data including accelerometry and pQCT imaging data.

Results—Girls and boys who accumulated the most MVPA had greater bone mass and better geometry at 17 years when compared to less active peers. The proportion of participants achieving high levels of MVPA throughout childhood was very low (<6% in girls) and by late adolescence almost all girls were inactive.

Conclusions—Bone health benefits of physical activity are not being realised due to low levels of activity for most youth, especially in girls.

BACKGROUND

Osteoblasts initiate bone formation when stimulated mechanically by muscle and weight bearing forces associated with physical activity. Bone surfaces are covered with a greater proportion of active osteoblasts during childhood and adolescence as compared to adulthood, which suggests that regular physical activity during childhood and adolescence is crucial for favourable bone development and subsequent adult bone health.[1] Importantly, physical activity influences the amount of bone mineral mass and where the bone mineral mass is distributed, that is, whole bone geometry.[2,3] The latter is critical to bone health since the skeleton must be strong for load bearing and also light for mobility. Physical activity is particularly important for favourable geometric changes during prepuberty and early-puberty when periosteal apposition is the predominant bone response to increased mechanical loading, that is, mass primarily increases on the outside surface of the bone in children and adolescents. Theoretically, this phenomenon creates stronger bones whose shape remains advantageously altered even during times of decreased physical activity.[3]

Gunter *et al*[1] concluded that physical activity during childhood and adolescence improves bone mass and geometry and some of the benefits may be sustained later in life. However, they noted that a majority of the research has focused on changes in bone mineral mass rather than geometry, due to the predominant use of dual energy X-ray absorptiometry (DXA) technology in paediatric bone research. This is understandable since DXA is readily available, provides a low radiation dose (<1.0 mrem per scan) and can be used to scan clinically relevant sites such as the hip. Recently, investigators with the Saskatchewan Pediatric Bone Mineral Accrual Study (PBMAS)[4] reported geometric benefits to young adult bone associated with adolescent physical activity. Their findings suggest that habitual physical activity can have long-term, sustained benefits for a bone by changing the shape of the bone. Although PBMAS used a valid questionnaire to measure physical activity, the questionnaire's units were arbitrary and specific dimensions of physical activity (intensity, frequency, duration) could not be discerned. This limitation reduces the understanding of the dose–response effects of early and accumulated physical activity on bone strength and makes it difficult to compare findings with other studies.

In this paper, we conceptualised physical activity as a behavioural process that evolves over time and examined its longitudinal effect on late adolescent bone strength including bone mineral mass and geometry. Our strategy for measuring and analysing physical activity included an objective measure of physical activity (ActiGraph) and group-based physical activity trajectory models. These models identify clusters of individuals who followed a similar progression of physical activity behaviour over time and as such provided developmental trajectories for the behaviour.[5] The analytical strategy provided advantages

over other approaches for summarising longitudinal physical activity data since it considers the timing, tempo, pattern and cumulative effect of the behaviour. The physical activity variable of moderate-and-vigorous intensity physical activity (MVPA) was modelled since it is commonly tracked in national surveillance systems and used to assess adherence to federal physical activity guidelines.[6-8] Quantifying the timing, magnitude, pattern and cumulative effect of MVPA on bone strength can guide public health policymakers, paediatric healthcare providers and health promotion specialists in structuring guidelines and delivering programmes to maximise bone health throughout the life course.[9]

METHODS

The Iowa Bone Development Study (IBDS) is an ongoing longitudinal study of bone health during childhood, adolescence and young adulthood. Participants are a subset of the Iowa Fluoride Study birth cohort; 1882 families from eight Iowa hospital postpartum wards who were recruited between 1993 and 1997.[10] Initial recruitment and examination of the IBDS cohort was conducted between 1998 and 2002 when participants were approximately 5 years of (child) age. The IBDS uses rolling admission to allow Fluoride Study members to participate in any follow-up examinations. Approximately 95% of the IBDS participants are white and two-thirds of parents have college degrees. Further information about the study design and demographic characteristics of participants is available in previous publications.[1112] The current analysis focused on data collected from 1998 to 2013. The study was approved by the University of Iowa Institutional Review Board (Human Subjects).

Sample design and data collection

At approximately ages 5, 8, 11, 13, 15 and 17 years, accelerometer measures of physical activity were obtained and a clinical examination that included anthropometry and DXA was conducted. At ages 11, 13, 15 and 17 years, peripheral quantitative CT (pQCT) measures were added to the clinical examination. Each measurement wave was conducted over a 3-year period and the age SD for each wave was ~0.4 years resulting in 4 and 6-year-olds within the 5-year-old wave, 7 and 9-year-olds within the 8-year-old wave, etc.

Measures

Accelerometry—At each clinical examination, participants and their parents were given instructions on accelerometer wear. ActiGraph accelerometers (Pensacola, Florida, USA) were mailed to participants during the autumn season (September–November). Owing to availability, model 7164 was used for ages 5, 8, 11 and 13 years, GT1M for age 15 and GT3X for age 17. The detailed procedure for accelerometer data collection is described in previous publications.[1112] Briefly, at ages 5 and 8, participants were asked to wear the monitor during all waking hours for four consecutive days, including one weekend day. At the other examination ages, they were asked to wear for five consecutive days, including both weekend days. Accelerometry movement counts were collected in a 1 min epoch at ages 5, 8, 11 and 13 years. Accelerometry data at age 15 were collected in a 5 s epoch and raw acceleration data were collected at age 17. Age 15 and 17 accelerometry data were re-integrated to 1 min epochs.

Accelerometers were considered as having not been worn if a period of 60 consecutive minutes of zero accelerometry counts (with allowance for two non-zero interruptions) was encountered in the accelerometry data array. Accelerometry data were only used from participants who wore an accelerometer for a minimum of 10 h/day and 3 days at each examination. MVPA was defined as 2296 or greater accelerometry counts per minute.[13,14]

Dual energy X-ray absorptiometry—At age 17, DXA measures were conducted using the Hologic QDR 4500A DXA (Delphi upgrade) with software V.12.3 in the fan-beam mode. Previous research suggests that skull size confounds whole body bone data in the youth[15]; therefore, whole body bone mineral content (BMC, g) results exclude the skull. Software-specific Global Regions of Interest (ROI) were used to designate the general boundaries of the hip images. A review of the bone within the ROI box was confirmed by the operator and edited to ensure appropriate bone-edge detection. DXA measures of mass used in this study included whole body BMC, hip BMC and hip areal bone mineral density (aBMD, g/cm^2). Structural geometry was estimated from hip DXA images using the Hip Structure Analysis program (Hologic Apex 3.0 software). The program, part of the Hologic software, is based on the principle first described by Martin and Burr,[16] that the mass in a pixel value calibrated in g/cm^2 of hydroxyapatite can be converted to linear thickness in cm by dividing it by the effective mineral density of a fully mineralised bone. A line of pixels traversing the bone axis is thus a projection of the surface area of a bone in cross-section and can yield some of its geometry.[17] The Hologic software program locates cross-sections traversing the femoral neck at its narrowest point. Bone cross-sectional area (CSA in cm^2) at the femoral neck and cross-sectional moment of inertia (in cm^4) for bending in the image plane at the femoral neck were calculated. Section modulus (Z in cm^3) was derived from these variables. CSA is a surrogate measure of compressive strength and Z of bending or torsional strength. Both represent geometric constructs of a bone.

Peripheral quantitative CT—At age 17, tibial measures were acquired using pQCT (XCT 2000, Stratec, Inc; Pforzheim, Germany). The left leg was scanned, unless there had been a history of fracture (<1% of children). Measurements were obtained from the cortical bone of the diaphyseal (mid-shaft) to manufacturer's standard protocol, using software V. 6.0. The tibial length was measured from the centre of the medial malleolus to the proximal tibia plateau, with the participants resting the lateral side of one foot on the contralateral knee. The region of interest was identified automatically from a set distance proximal from a reference line of 4%, 38% and 66% of the tibia and a tomographic slice of 2.2 mm trans-sectional thickness was measured at a voxel size of 0.4 mm^2 at each site. Specific pQCT measures at the tibia sites included bone stress index (tibia 4% site, mg^2/mm^4) and polar moment of inertia (tibia 38% and 66% site, mm^4). Bone stress index is a measure of compressive strength and polar moment of inertia measures bending strength. DXA and pQCT scans were acquired by one of the three International Society of Clinical Densitometry (ISCD)-certified technicians. The manufacturers' hydroxyapatite phantoms for DXA and pQCT were scanned daily.

Other measures

At each clinical examination, research nurses trained in anthropometry measured the participant's height (cm) and weight (kg). Sitting height was measured for each participant at ages ≥11 to calculate the year from peak height velocity using predictive equations established by Mirwald *et al*.[18] Based on estimated age at peak height velocity, physical maturity status was quantified as years from pre-peak height velocity or years at/post-peak height velocity.

Data analysis

Gender-specific means and SDs were calculated to describe the distributional properties of the measures. Each participant's MVPA (approximate ages 5, 8, 11, 13, 15 and 17 years) was grouped within a pattern of conditional probabilities based on structural equation modelling theory that assumes individuals differ qualitatively as members of homogeneous (latent) subgroups.[5] Individual-specific probabilities of belonging to each subgroup allowed assignment to a subgroup based on the highest probability. The relationship between MVPA and age was fitted up to a third-degree polynomial model that included the latent subgroup variable. Under the assumption that data were missing at random, individuals with incomplete data were included; however, at least two time points with a least one of the time points at age 13, 15 or 17 years were required. The best fitting polynomial model was determined by comparing the Bayesian Information Criterion for models with different numbers of subgroups. After identifying latent MVPA subgroups that followed similar profiles, the time-dependent physical attribute of maturity associated with subgroup membership was examined. The subgroups were then used to predict bone outcomes at age 17 by fitting a general linear model (GLM) with adjustment for age 17, height and weight and estimating subgroup-specific least squares means. Outcomes from DXA included whole body BMC, hip BMC, hip aBMD, femoral neck CSA, femoral neck Z. Outcomes from pQCT of the tibia included bone stress index, polar moment of inertia 38% and polar moment of inertia 66%. Procedures from the Statistical Analysis System (SAS), V.9.2 including SAS procedure TRAJ, were used for the statistical analyses. A p Value of 0.05 was specified as statistical significance.

RESULTS

Accelerometry data from ages 5 to 17 years were available for 530 participants and provided 2661 data points for modelling the MVPA trajectories. Three hundred and sixty-four participants had age 17 DXA and pQCT data. Table 1 presents a description of the participants by age and table 2 describes the age 17 maturity status and bone outcomes. For girls and boys, the most parsimonious modelling solution and the solution with the best goodness-of-fit consisted of three (sub)groups. These trajectories are presented in figure 1 (girls) and figure 2 (boys). The three distinct groups for girls are characterised by (1) persistently inactive with decreasing MVPA levels, (2) moderately active with decreasing MVPA levels and (3) active with severely decreasing MVPA levels. The proportion of individuals in each group was 49.5%, 44.6% and 5.9%, respectively. On average, group 1 girls participated in approximately 40 min/day of MVPA at age 5 which steadily declined to 20 min by age 17 (50% reduction). Group 2 girls participated in 55 min/day of MVPA at

ages 5 and 8 which declined to 28 min/day by age 17 (50% reduction). When compared to peers, group 3 girls were much more active during childhood (on average 85 min/day at age 5); this group experienced the steepest decline in MVPA and members were only slightly more active (30 min/day MVPA) than peers at age 17; a reduction of 65%. Importantly by age 17, the 95% CIs for all three groups overlapped. For boys, the three distinct groups were characterised by (1) persistently inactive with decreasing MVPA levels, (2) moderately active with increasing MVPA levels during middle childhood followed by decreasing levels and (3) active with increasing MVPA levels during middle childhood followed by decreasing levels. The proportion of individuals in each group was 39.5%, 37.4%, and 23%, respectively. On average, group 1 boys participated in approximately 46 min/day of MVPA at age 5, which declined steadily to 34 min/day by age 17 (26% reduction). Group 2 boys participated in 64 min/day of MVPA at age 5 and increased at age 8 before steadily declining to 30 min/day by age 17 (54% reduction from ages 5 to 17). Finally, group 3 boys participated in 76 min/day of MVPA at age 5 and increased at age 8 before declining to 50 min/day by age 17 (34% reduction from ages 5 to 17). Similar to girls, by age 17, 95% CIs for all three groups overlapped.

Height-adjusted and weight-adjusted age 17 bone outcomes for groups 1, 2 and 3 were compared by constructing a contrast between the relevant least squares means (table 3). There were also no significant differences in the predicted age of peak height velocity among these groups for girls or boys. Group 3 (most active) girls had significantly greater whole body BMC, hip BMC, femoral neck Z and polar moment of inertia (38% site) than group 1 or 2 girls. Additionally, group 3 girls had significantly greater hip aBMD, femoral neck CSA, bone stress index and polar moment of inertia (66% site) than group 1 girls. Group 2 girls had significantly greater hip aBMD, femoral neck CSA, femoral neck Z, bone stress index and polar moment of inertia (38% site) than group 1 girls. Group 3 (most active) boys had significantly greater whole body BMC, hip BMC, hip aBMD, femoral neck CSA, femoral neck Z, bone stress index and polar moment of inertia (38% site) than group 1 boys. Group 2 boys had significantly greater polar moment of inertia (38% site) than group 1 boys. While group 3 boys trended towards greater mean values when compared to group 2 boys, there were no significant differences between the groups.

DISCUSSION

Using an objective measure of physical activity and a 12-year follow-up, this study predicted future group membership for physical activity using known probabilities and subsequently tested distinct trajectories of physical activity for their effect on bone strength. Results indicated that a persistently high level of physical activity during childhood was associated with greater bone strength in girls and boys including measures of geometry at the hip, distal tibia and proximal tibia. The physical activity and bone strength relationship was significant despite markedly decreased physical activity during adolescence. These results are in agreement with PBMAS findings, which found physical activity to be associated with greater bone strength in young adulthood.[4]

We also report that very few girls (<6%) were highly active during childhood and by age 15, the mean for the highly active group fell below the recommended level of 60 min/day of

activity. By age 17 this group of once highly active girls had similar (low) levels of activity as inactive peers. These results suggest that by late adolescence nearly all girls are at risk for the hypokinetic conditions associated with inactivity. Collectively, they are not optimising the known benefits of physical activity to bone health during a time when peak bone mass is rapidly accruing and the bone is most sensitive to the effects of mechanical loading. Therefore, targeted interventions for 'high-risk' girls during late adolescence are inappropriate and physical inactivity in adolescent girls should be viewed as endemic.

The use of waist-worn accelerometers strengthens the internal validity of this study. When an accelerometer is placed on the waist above the hip, it measures the weight bearing characteristic of physical activity that influences adaptive bone modelling such as skipping, running and jumping.[1] Although our cut point for MVPA (2296 counts/min) was based on the relationship of movement counts to energy expenditure[13] and selected due to its widespread use in the literature, we previously showed a positive relationship for ambulatory movement counts and ground reaction forces using a similar movement cut point (2113 counts/min as predictive of ground reaction forces of 1.2 times body weight).[19] Given the required magnitude of mechanical loading decreases as the frequency of loading increases, minutes of MVPA provide a defensible measure of bone-loading physical activity in population-based studies and results that can be compared across studies.[1]

Limitations of our study include the age 17 cross-sectional nature of the DXA and pQCT measures, it is possible that participants in group 3 (most active) had greater bone strength due to genetics or other factors that were not measured. Also study participants were drawn from a regional sample of babies born in Iowa. Thus, generalisation of study results to other geographic areas, particularly with more ethnic and racial variability, should be performed with caution.

This study is novel in combining the conceptualisation of physical activity as a behavioural process with an objective measure of physical activity. In addition, our bone imaging strategies provided a comprehensive look at several essential characteristics of a bone that contribute to strength. The ROI examined are important since fracture of the femur is the most serious osteoporotic fracture incurred in older adults. The femur and tibia are sites that are influenced by mechanical loading throughout the life course suggesting that physical activity behaviour can be modified to reduce fracture risk.[20] Whole body BMC (adjusted for height) provided an additional important bone outcome since it is a marker of overall bone growth and development.[21] While opportunities for the prevention of osteoporotic fractures start at birth and continue throughout the life cycle, ~40% of bone accrual occurs during the adolescent growth period that is associated with the pubertal growth spurt.[921] This suggests that the age 17 bone outcomes used in this study are predictive of adult values.

CONCLUSIONS

In conclusion, this study indicates that in girls and boys, high levels of childhood physical activity are positively associated with bone strength in late adolescence even after drastic reductions in physical activity levels during puberty. The results suggest the possibility of

sustained effects of early physical activity to bone health as well as the importance of physical activity throughout childhood and adolescence.

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What are the new findings?

- Early levels and accumulative levels of physical activity predict bone strength.
- Objective measures of physical activity show distinct trajectories of activity from childhood (age 5 years) to middle adolescence (17 years).
- By middle adolescence almost all girls in a midwestern cohort were inactive.

How might it impact on clinical practice in the near future?

- Physicians should be aware that bone mass is not a complete measure of bone strength.
- Physicians should increase their efforts to screen for and promote bone-strengthening physical activity.
- Adolescent girls should be seen as a population-at-risk with respect to health-enhancing physical activity.

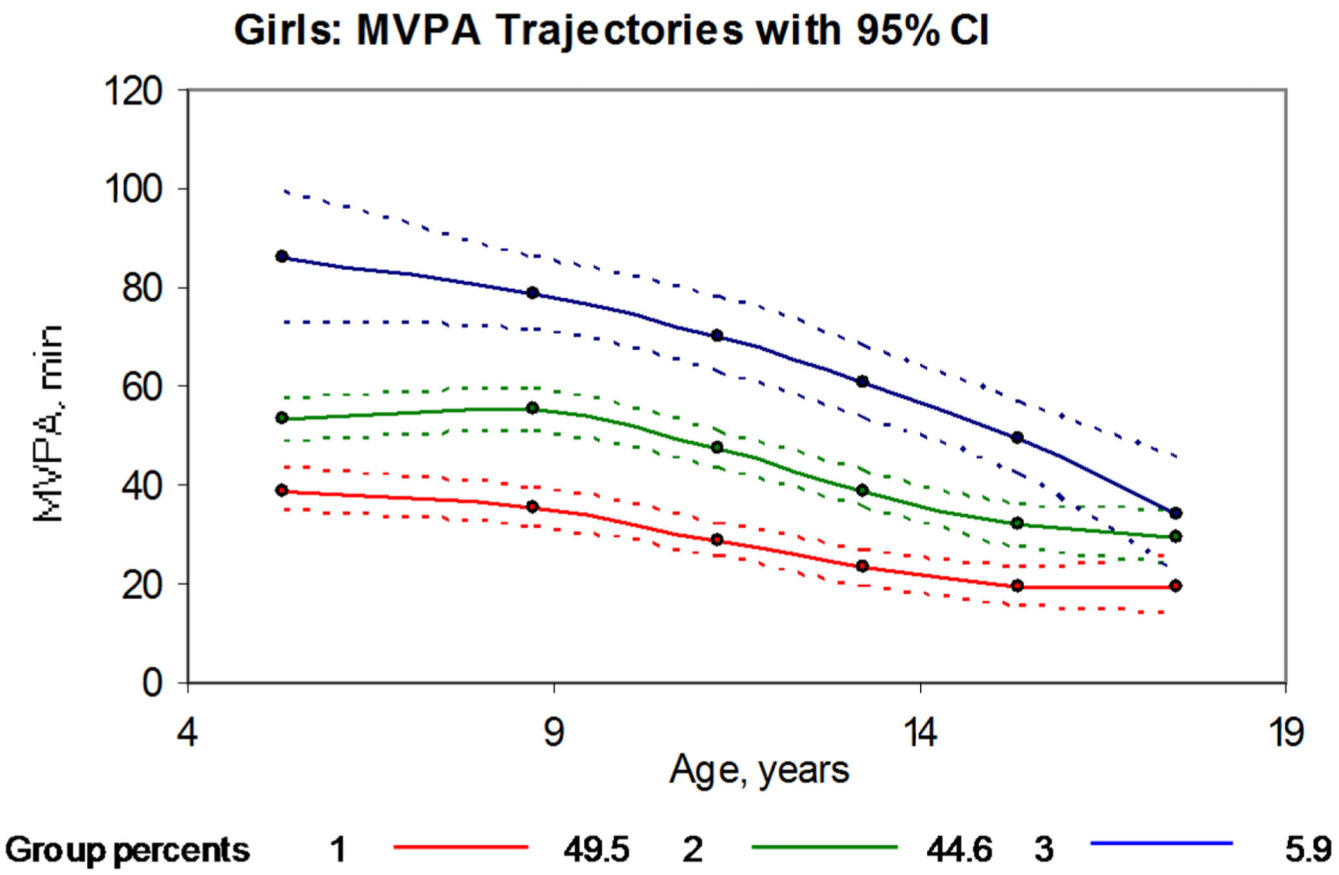

Figure 1.

Trajectories of moderate-and-vigorous intensity physical activity (minutes/day) across childhood and adolescence (girls) based on latent group membership. Each line represents a percentage of the Iowa Bone Development Cohort which clustered within a discrete physical activity pattern.

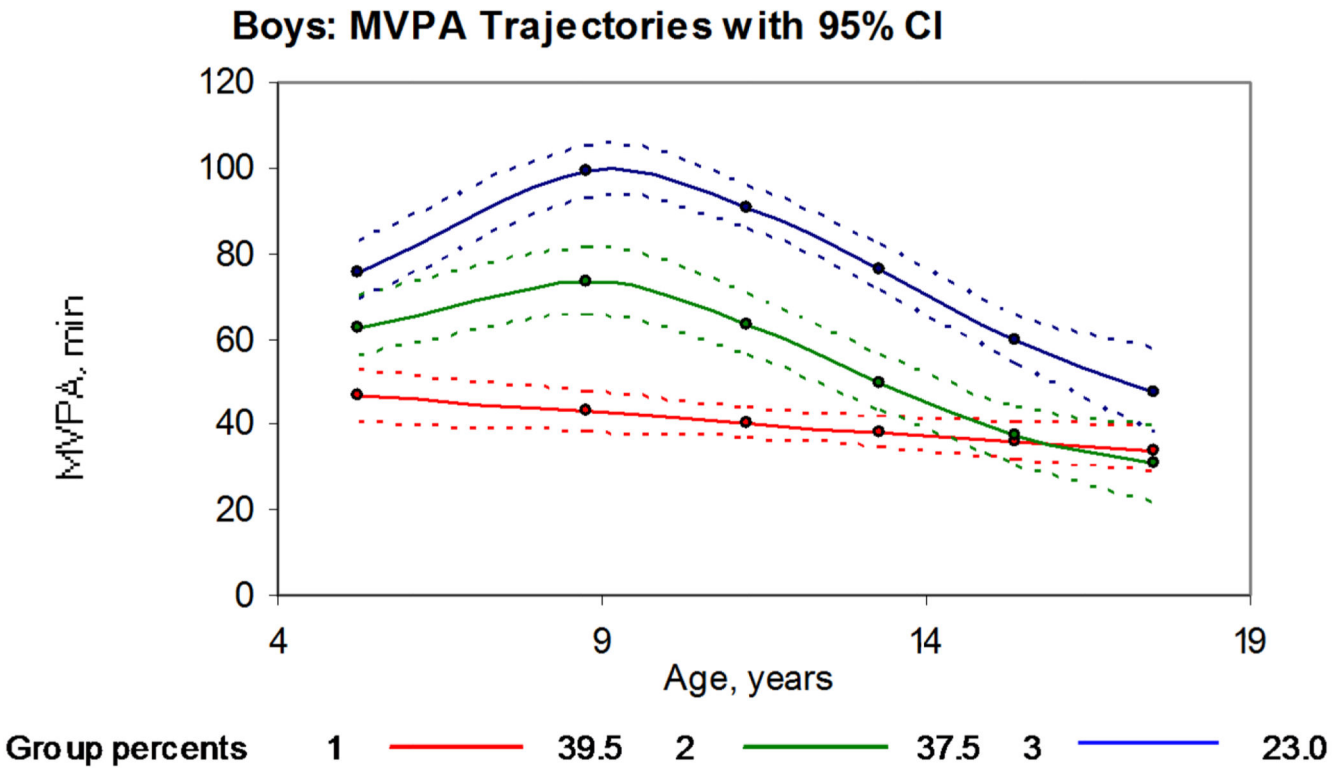

Figure 2.

Trajectories of moderate-and-vigorous intensity physical activity (minutes/day) across childhood and adolescence (boys) based on latent group membership. Each line represents a percentage of the Iowa Bone Development Cohort which clustered within a discrete physical activity pattern.

Table 1

Description of Iowa Bone Development Study participants by wave and gender

		Age, years	Height, cm	Weight, kg	MVPA, min/day
Wave	**N***	**Mean**	**Mean**	**Mean**	**Mean**
Girls (n=263)					
1	203	5.3±0.4	111.0±5.4	20.0±4.0	47.7±19.8
2	248	8.7±0.6	132.9±6.9	32.0±8.7	46.3±20.3
3	247	11.2±0.3	149.1±7.5	44.5±12.4	39.7±19.2
4	238	13.3±0.4	160.7±6.6	56.3±14.6	32.9±19.3
5	204	15.3±0.3	164.5±6.5	62.1±14.7	25.7±16.7
6	195	17.5±0.4	165.6±6.7	66.8±16.8	23.7±15.5
Boys (n=267))					
1	184	5.2±0.4	112.2±5.7	20.6±3.6	59.5±23.7
2	245	8.8±0.7	135.0±7.3	33.8±9.6	65.4±28.7
3	250	11.2±0.3	149.1±7.5	45.4±13.0	64.1±28.6
4	243	13.3±0.4	163.1±9.3	58.5±15.9	52.1±25.3
5	212	15.4±0.3	175.3±7.8	70.8±16.1	38.0±20.3
6	192	17.5±0.4	178.7±7.5	78.7±17.2	35.8±21.4

Age at PHV: mean=11.8±0.6, range=10.2–14.5.

Age at PHV: mean=13.6±0.8, range=10.5–16.1.

MVPA, moderate-and-vigorous intensity physical activity; PHV, peak height velocity.

* Number of observations per wave for MVPA, a few participants did not have scanning visits (body size measurements) for corresponding waves.

Table 2

Description of maturity, body size and bone outcomes in Iowa Bone Development Study participants at age 17

	Girls (n=186)		Boys (n=160)	
	Mean	**SD**	**Mean**	**SD**
Age at PHV, years	11.8	0.6	13.7	0.7
Height, cm	165.6	6.7	178.7	7.5
Weight, kg	66.8	16.8	78.7	17.2
Whole body BMC, g	1794.0	325.8	2376.4	446.6
Hip BMC, g	32.98	6.27	47.09	9.85
Hip BMD, g/cm^2	1.018	0.139	1.133	0.159
Femoral Neck CSA, cm^2	3.23	0.60	4.16	0.81
Femoral Neck Section Modulus, cm^3	1.48	0.37	2.17	0.51
Bone Stress Index (tibia 4% site), mg^2/mm^4	98.4	23.7	133.5	31.6
Polar moment of inertia (tibia 38% site), mm^4	1496.4	338.9	2028.3	437.1
Polar moment of inertia (tibia 66% site), mm^4	2217.4	506.3	3029.1	673.1

BMC, bone mineral content; BMD, bone mineral density; CSA, cross-sectional area; PHV, peak height velocity.

Table 3

Least squares means for peak height velocity and age 17 bone outcomes (adjusted for height and weight) by MVPA trajectory group membership*

	Girls (N=189)			Pairwise comparisons (p Values)		
	Group 1 N=92	**Group 2 N=86**	**Group 3 N=11**	**Group 1 v 2**	**Group 1 v 3**	**Group 2 v 3**
Age at PHV, years	11.8	11.8	12.0			
DXA and hip structural analysis						
Whole body BMC, g	1756.8	1812.4	1956.9	0.0402	0.0004	0.0111
Hip BMC, g	32.07	33.44	37.03	0.0347	0.0003	0.0084
Hip BMD, g/cm^2	0.994	1.036	1.082	0.0146	0.0156	0.2133
Femoral Neck CSA, cm^2	3.13	3.29	3.50	0.0117	0.0041	0.0962
Femoral Neck Section Modulus, cm^3	1.40	1.52	1.70	0.0009	<0.0001	0.0159
Bone strength (pQCT)						
Bone Stress Index (tibia 4% site), mg^2/mm^4	93.84	101.30	112.08	0.0110	0.0029	0.0782
Polar moment of inertia (tibia 38% site), mm^4	1445.8	1521.5	1714.9	0.0089	<.0001	0.0015
Polar moment of inertia (tibia 66% site), mm^4	2158.9	2251.0	2431.3	0.0260	0.0016	0.0364

	Boys (N=160)			Pairwise comparisons (p Values)		
	Group 1 N=68	**Group 2 N=60**	**Group 3 N=32**	**Group 1 v 2**	**Group 1 v 3**	**Group 2 v 3**
Age at PHV, years	13.6	13.5	13.8			
DXA and hip structural analysis						
Whole Body BMC, g	2310.1	2393.3	2485.5	0.1018	0.0048	0.1352
Hip BMC, g	45.67	47.02	50.26	0.3063	0.0046	0.0448
Hip BMD, g/cm^2	1.105	1.130	1.198	0.3112	0.0015	0.0185
Femoral Neck CSA, cm^2	4.05	4.15	4.43	0.3588	0.0057	0.0433
Femoral Neck Section Modulus, cm^3	2.12	2.14	2.32	0.7451	0.0159	0.0319
Bone strength (pQCT)						
Bone Stress Index (tibia 4% site), mg^2/mm^4	126.44	136.31	142.58	0.0415	0.0061	0.2798
Polar moment of inertia (tibia 38% site), mm^4	1940.4	2088.1	2102.9	0.0046	0.0099	0.8132
Polar moment of inertia (tibia 66% site), mm^4	2940.9	3102.2	3078.7	0.0483	0.1601	0.8104

SAS GLM procedure was used for comparison: group 3—most active over time, group—consistently low activity.

p Values from pairwise comparisons not adjusted for multiple comparisons (p Value<=0.05/3 corresponds to Bonferroni adjustment for multiple comparisons).

BMC, bone mineral content; BMD, bone mineral density; CSA, cross-sectional area; MVPA, moderate-and-vigorous intensity physical activity; PHV, peak height velocity; pQCT, peripheral quantitative CT.