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Peak bone mass and patterns of change in total bone mineral density and bone mineral contents from childhood into young adulthood

Juan Lu, MD, M.P.H., Ph.D.¹, Yongyun Shin, Ph.D.², Miao-Shan Yen, MS², and Shumei S. Sun, Ph.D.²

¹Department of Family Medicine and Population Health, Division of Epidemiology, School of Medicine, Virginia Commonwealth University, Richmond, VA 23298-0032

²Department of Biostatistics, School of Medicine, Virginia Commonwealth University, Richmond, VA 23298-0032

Abstract

The literature has not reached a consensus on the age when peak bone mass is achieved. This study examines growth patterns of TBMC and TBMD, peak bone mass, effect of concurrent anthropometry measures and physical activity on growth patterns in a sample of 312 white males and 343 females aged eight to 30 years. We analyzed data from participants enrolled in Fels Longitudinal Study. Descriptive analysis was used to ascertain characteristics of participants and growth patterns of TBMC and TBMD. Mixed effects models were applied to predict ages at attainment of peak TBMC and TBMD and assess effects of height, weight, BMI and habitual physical activity on the attainment. Significant differences between sexes were observed for measures of TBMC and TBMD, and differences varied with age. For females, predicted median ages at peak TBMC and TBMD attainments are 21.96 (IQR: 21.81–22.21) and 22.31 (IQR: 21.95–22.59) years, respectively. For males, predicted median ages are 23.34 (IQR: 24.34–26.19) and 26.86 (IQR: 25.14–27.98) respectively. For females, height, weight and BMI, but not physical activity, had significant influences on attainment of TBMC and TBMD ($P < 0.01$). For males, weight and BMI, but not height and physical activity, exerted significant influence on attainment of TBMC and TBMD ($P < 0.01$), and also modified correlations between age and peak TBMC and TBMD. Our results suggest that (1) for both sexes, trajectories of TBMC and TBMD follow a curvilinear pattern between ages eight and 30 years; (2) predicted ages at peak TBMC and TBMD are from early to late 20s for both white males and females, with females reaching their peaks significantly earlier than males; and (3) concurrent height, weight and BMI, but not habitual physical activity, exert significant effects on trajectories of TBMC and TBMD.

Correspondence author: Shumei S. Sun, Ph.D., Professor and Chair, Department of Biostatistics, Professor of Epidemiology and Community Health, School of Medicine, Virginia Commonwealth University, 830 East Main Street, P.O. Box 980032, Richmond, VA 23298-0032, Tel: 804-827-2042, Fax: 804-827-2552, ssun@vcu.edu, <http://www.biostatistics.vcu.edu/>.

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Key words

body bone mineral content; body bone mineral density; Dual X-ray absorptiometry

Introduction

Osteoporosis is a major problem of public health and the leading cause of bone fractures. In the United States, about 10 million individuals are estimated to have osteoporosis; 18 million more are at risk of developing the disease; and another 34 million are at risk of having low bone mass, which is conducive to fractures. One in two women and one in four men in their sixth-decade will have an osteoporosis-related fracture some time during their remaining lifetime (1). The direct medical cost of osteoporosis reached \$17 billion in 2005 (2). As the age of the US population increases, the prevalence of osteoporosis and its associated costs will rise significantly.

Osteoporosis is a disease characterized by low bone mass and structural deterioration of bone tissue, leading to bone fragility and an increased risk of fractures (3). Bone mass is commonly measured by bone mineral content (BMC) and areal or volumetric bone mineral density (BMD) using dual X-ray absorptiometry (DXA) (4). Operationally, osteoporosis has been defined as having bone mineral density equal to or below 2.5 standard deviations of the average value for a young healthy woman (5). Bone mass of an individual in later life depends on the peak attained during growth and subsequent rate of bone loss (6). Previous studies suggest that peak adult bone density makes a greater contribution to bone density than subsequent rates of bone loss until at least 15 years post-menopause (7). A 10% increase in peak bone mass would reduce osteoporotic fracture risk in older adults by 50% (8). Hence, attaining a high peak bone mass in the first three decades of life would contribute significantly to prevention of osteoporosis (9, 10).

Bone mineral accumulation from infancy to post-puberty is a complex process. In general, peak bone mass is greater in men than women and in African Americans than in non-Hispanic whites (10, 11). Several interconnected factors influence bone mass accumulation. Quantitatively, non-modifiable genetic and family factors account for significant variation (12–14). Modifiable factors, including nutrition, physical activity, hormonal milieu, and smoking status, may account for 20–50% of the variation (14, 15).

The literature does not offer a consensus on the age when peak bone mass is achieved. Earlier studies using DXA have suggested that bone mass peaks long after sexual and skeletal maturity, potentially into an individual's third decade or beyond (16, 17). Other studies indicate that bone mass peaks earlier than is currently believed (18, 19). This lack of consensus arises from the paucity of long-term serial data, the use of cross-sectional data, and inconsistencies in accounting for potential risk factors. Therefore, the objective of this study is to use longitudinal data from Fels Longitudinal Study (FLS) to (1) examine the patterns of change in total body BMC (TBMC) and BMD (TBMD) in males and females ages eight-to-30 years; (2) predict the ages at which peak TBMC and TBMD are attained; and (3) determine the effects of concurrent height, weight, BMI and habitual physical activity (HPA) on the TBMC and TBMD trajectories.

Materials and Methods

Study sample

We analyzed data from 312 males and 343 females enrolled in FLS. Details of FLS participants and data collection process have been reported previously (16, 20). All FLS participants have been monitored since birth and have had serial measures of stature and weight taken at one, three, six, nine and 12 months, then semi-annually to 18 years, and biennially thereafter. Additional measurements, including BMC and BMD measures from DXA and self-reported physical activities were included when participants reached eight years of age. These variables were measured at annual intervals from ages eight to 18 years and biennially thereafter. Only 8% of FLS participants have been lost to follow-up, but data on all parameters measured at their last visit did not differ from those of the 92% who remain in the study. All procedures were approved by the institutional review board of Virginia Commonwealth University, and all study participants provided written consent to join FLS.

Measurements

Study Outcomes—The outcome of interest is the pattern of change in attainment of peak bone mass in males and females from ages eight-to-30 years. We selected TBMC (kg) and TBMD (kg/cm²) among other measures, as our initial step to study the trajectories of bone mass over time. In FLS, DXA measurements of body composition were made on all participants aged eight years and older at their regularly scheduled visits beginning 1989. DXA was measured through Hologic™ QDR 4500 Elite densitometer (Hologic, Waltham, MA) and a Lunar LPX machine. The calibration of the measurement and conversion between the Hologic and Lunar DXA machines were described in detail formerly (20). The number of DXA measurements and ages at which repeated DXA measurements were made vary and depend on the age of a participant when DXA measurements were introduced into FLS; age when the minimum weight was required for measurement of DXA; and whether annually scheduled examinations were missed. To be included in this analysis, a FLS subject must have had at least 3 out of 15 possible TBMC and TBMD measurements that were made a year apart. Approximately 56% of the subjects had six or more measurements.

Anthropometry—Age and annual measurements of height, weight and BMI were considered as time-varying covariates in analysis of the TBMC and TBMD trajectories. Measurements of weight and height in FLS subjects are taken recommendations in the Anthropometric Standardization Reference Manual (21). Height is measured to 0.1 cm on a Holtain stadiometer (Seritex, Carlstadt, NJ), and weight is measured to 0.1 kg on a beam balance scale. All measurements are made twice, and a third measurement is made if the difference between the first two exceeds established tolerance (0.3 kg for weight and 0.5 cm for height). BMI is expressed as kg/m². Sex-specific height-for-age, weight-for-age, and BMI-for-age Z-scores were calculated according to the Centers for Disease Control and Prevention (CDC) growth charts 2000 (22). These z-scores are used as time-varying covariates in the mixed effects models to extrapolate the impact of height, weight, and BMI on TBMC and TBMD trajectories. The age-specific z-values are based on rounded ages, for example, 9-year-olds comprise all children who are 8.5–9.4 years of age.

HPA—Mean levels of HPA were used as a covariant for deriving the patterns of attainment of peak bone mass. HPAs was determined by self-reported physical activity at work, sports and other physical activities during leisure time, as determined by the Baedeker Questionnaire of HPA (BQHPA) (23). For each individual, total physical activity was calculated based on three dimensions. The BQHPA is a validated 16-item instrument that has been shown to have high reproducibility (24).

Statistical analysis

Descriptive analysis was applied to study the characteristics of the study cohort and patterns of TBMC and TBMD across age. Mixed effects models were used to (1) determine the TBMC and TBMD trajectories and to predict the ages at which peak TBMC and TBMD were attained; and (2) determine the effects of concurrent height, weight, BMI and average HPA on attainment of peak TBMC and TBMD, controlling for the effects of age. The model allowed us to investigate the variations of mean TBMC and TBMD measurements within and between subjects simultaneously. Since the plots of mean TBMC and TBMD across age appear to be curvilinear, a quadratic random coefficient model was applied. All analyses were performed separately for males and females due to significant differences in the TBMC and TBMD between males and females.

The mixed effects model can be expressed as

$$y_{it} = \alpha_i + \beta_1 \lambda_t + \beta_2 \lambda_t^2 + \beta_3 x_{it} + \beta_4 x_{it} + \varepsilon_{it},$$

where y_{it} represents the values of repeated measurements, e.g., serial TBMC or TBMD measurements for individual i at time t , e.g., age in years; β_2 is a quadratic parameter, e.g., age in quadratic terms describing the deceleration or acceleration of change over time for individual i ; x_{it} represents covariates, e.g., weight; and ε_{it} is an error term. SAS software (SAS Institute Inc. Cary, NC, version 9.3) was used for all analyses.

Results

Baseline characteristics

Table 1 illustrates sex specific anthropometry measures at ages 8, 12 and 16 years from 312 men and 343 women in the study. Compared to the CDC growth chart 2000 (22), the FLS sample has similar average birth-weight for both sexes. However, the age-specific weight, height and BMI measures appear to be higher than shown in the CDC growth charts, particularly for male subjects and those at the 90th percentile.

Mean HPAs of the study cohort are shown in Table 2. These data were available from 132 men and 168 women. Compared to men, women self-reported having more leisure physical activity and fewer sports and work-related activities. The mean and SD of BQHPA leisure, sport and work indexes for women were 2.61 (± 0.47), 2.40 (± 0.67) and 2.68 (± 0.52); whereas the corresponding mean indexes for men were 2.50 (± 0.53), 2.69 (± 0.66) and 2.88

(± 0.60). Consequently, the mean and SD of BQHPA indexes of total physical activity were also higher for men (8.06 ± 1.09) than for women (7.68 ± 1.11).

Growth patterns of TBMC/TBMD

The growth pattern of TBMC in study participants is shown in Figure 1. From eight-to-30 years, the mean TBMC increased steadily until early or middle of the third decade for males and late teens to early 20s for females, then remained unchanged. Between eight and 10 years old, the mean accrual of TBMC was about the same for both sexes. However, (1) the mean accrual became different as males and females entered biological maturity at different chronological ages and (2) the variability (i.e., wide ranges of standard deviations) in the accrual among individuals became much larger, particularly among males. Between the ages of 11–14 years old, the average TBMC levels were slightly higher for females than for males; after 14 years old, the average levels of TBMC became noticeably higher for males than for females. Moreover, males attained significantly higher levels of TBMC and reached the maximum accumulation several years later than females. A similar growth pattern for TBMD by sex is shown in Figure 2.

Ages at peak bone mass attainment

The predicted median age [interquartile range (IQR)] at attainment of peak TBMC and TBMD are shown in Table 4. For males, the mixed effects models indicate that the predicted median ages at peak TBMC attainment were 23.34 (IQR: 24.34–26.19); and at peak TBMD are 26.86 (IQR: 25.14–27.98) years, respectively. For females, the predicted median ages at attainment of peak TBMC were 21.96 (IQR: 21.81–22.21); and at peak attainment of TBMD were 22.31 (IQR: 21.95–22.59) years, respectively. Overall, (1) the predicted ages at peak TBMC and TBMD attainment were later for males than for females, and (2) the ages at peak TBMC attainment were slightly earlier for both males and females than the ages at attainment of TBMD.

The effects of age, height, weight, BMI and HPA on attainment of peak TBMC and TBMD

The effects of chronological age and concurrent weight, height, BMI and average HPAs on attainment of TBMC are presented in Table 5. As expected, the result of the mixed effects model shows that chronological age is the most significant factor ($P < 0.0001$) affecting attainment of TBMC during the growth period for both sexes. For males, the concurrent anthropometry measures had a stronger impact on attainment of TBMC, as reflected by the significant influence on (1) the series of TBMC measures during the growth period (weight: $P < 0.0001$; BMI: $P = 0.0041$) with the exception of concurrent height ($p = 0.0590$); and (2) the modification of the relation between chronological age and attainment of TBMC. For example, in the null model, without the adjustment for weight, height or BMI, age exerts a significant effect on mean TBMC attainment ($P < 0.0001$); however, after the adjustment of weight, height or BMI, the effect of age on TBMC became less salient. The corresponding p-values were 0.4539, 0.5176 and 0.9095 respectively. For females, although the model shows that concurrent weight, height and BMI exerted significant influences on TBMC attainment (weight or height: $P < 0.0001$, BMI: $p = 0.0033$), the influence did not modify the significant association between chronological age and attainment of TBMC.

Furthermore, the results show that none of the averages HPAs, i.e., self-reported leisure, sports, work, or the summary of the three physical activities, exerted a significant influence on TBMC attainment, nor did such activities modify the association between chronological age and TBMC attainment for males and females.

Associations between chronological age and attainment of TBMD are given in Table 6. Again, for females, the association between chronological age and attainment of TBMD was not modified by concurrent anthropometry measures or by HPA; but for males, the association between chronological age and attainment of TBMD was modified by concurrent anthropometry measures, but not by HPA.

Discussion

Peak bone density acquired during the growth period is an important determinant of the risk for osteoporosis later in life. The objective of this study was to use longitudinal data from FLS to study the patterns of change in TBMC and TBMD in males and females across the age range of eight-to-30 years, and to assess the effect of concurrent anthropometry measures and self-reported HPA on patterns of change. The findings of this study focused on the trajectories of TBMC and TBMD from pre-puberty to early adulthood in healthy Caucasian males and females. This study is able to provide predicted age ranges at the peak attainment of TBMC and TBMD for the first time using longitudinal data gathered over the past 25 years. Currently, increasing numbers of children are being referred for DXA total body measurements in order to evaluate global and regional bone mineral content and body composition (25). Therefore, the knowledge gained from this study should help evaluate a variety of abnormalities in bone growth in childhood and early adulthood and to inform effective prevention and intervention programs for osteoporosis.

Comparison of our results with the literature

The results found in this study are in general agreement with the findings in the literature (Table 7), albeit to a different degree, owing to cohorts of different age, length of follow-up, approaches and designs applied, and potential risk factors adjusted for (16, 17, 19, 26–30). Our study exploits the unique opportunity to explore the trajectories of BMC and BMD generated by a large set of serial data collected in same individuals over a period of more than 25 years.

The application of the mixed effects model to these data allowed us to examine the linkage between levels of BMC and BMD collected at regular intervals in children to the risk of osteopenia and osteoporosis in same individuals as adults. Such linkages reveal how levels of BMC and BMD during childhood may lead to healthy or unhealthy BMC and BMD status in adulthood. The questions posed are of clinical and public health importance. Understanding how the timing of the attainment of peak bone mass may delay or accelerate the appearance of osteopenia and osteoporosis is desirable. Elucidating adverse relationships through such linkages can lead to early identification of children at increased risk for bone disease later in life.

Correlation between a high peak bone mass in early life and the acquisition of adult bone mass

Earlier studies have shown a high degree of tracking in bone mineral density from childhood to adolescence (31) and into early adulthood (32). Children with low bone mineral density will likely continue to have low BMD unless effective interventions are instituted (30). Studies (19, 33, 34) also show that late-maturing females (indexed by peak height velocity) had compromised BMC accrual compared with their early- and average-maturing peers. Results from these studies indicate that attaining a high peak bone mass in early life predicts a higher bone mass and reduced risk of osteopenia or osteoporosis later in life (10). Yet, thus far there is no clear evidence showing that the bone mass attained in early life is directly associated with bone mass attained in adults (35), nor the potential risk of osteoporosis in later life. Our analysis discloses a significant positive correlation ($p < 0.0001$) between peak BMD and BMC and adult bone BMD and BMC in both males and females. As shown in Table 8, the mean TBMC and TBMD measured between 30 and 50 years old are slightly below the means measured at peak attainment.

Study limitations

All of FLS participants are non-Hispanic Caucasians from southwestern Ohio who have been involved with FLS since birth. This may limit the ability to generalize the findings to other populations. However, analysis of this longitudinal data set that links childhood variables to the risk of osteoporosis or osteopenia in adulthood should be helpful to elucidate the biologic relationships that may apply to all races and ethnicities. Also, although DXA is the most widely used technique for measuring bone mass and density in children, there are technical limitations. DXA is a two-dimensional imaging technique in which BMD (g/cm^2) is derived by dividing the BMC (g) by the projected area of bone (cm^2). Thus, this BMD is not a measure of true volumetric density (g/cm^3) because no information about bone depth is included in the calculations. As such, DXA BMD results could potentially be confounded by skeletal size. Moreover, self-reported HPA and insensitivity of the two-dimensional DXA technique in BMD measurements may have hindered our ability to extrapolate the effect of physical activity on the TBMD attainments.

Conclusions

Based upon the findings of this study, we conclude that (1) for both sexes, trajectories of TBMC and TBMD follow a curvilinear pattern between ages eight and 30 years; (2) predicted ages at peak TBMC and TBMD are from early to late 20s for both white males and females, with females reaching their peaks significantly earlier than males; and (3) concurrent height, weight and BMI, but not HPA, exert significant effects on trajectories of TBMC and TBMD, controlling for the effects of age and quadratic age.

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Figure 1. Growth Pattern of Total Body BMC in Subjects 8 to 30 Years Old

Figure 1 shows the growth pattern of TBMC in study participants. Significant difference in measures of TBMC was observed between sexes and difference varied with age. Between eight and 10 years old, the mean TBMC accrual was about the same for both sexes. However, the mean accrual became different as males and females entered biological maturity at different chronological ages. Between ages 11–14 years old, the average TBMC levels were slightly higher for females than for males; after 14 years old, the average TBMC levels became noticeably higher for males than for females. Overall, males attained significantly higher levels of TBMC and reached the maximum accumulation several years later than females.

Figure 2. Growth Pattern of Total Body BMD in Subjects 8 to 30 Years Old

Figure 2 shows the growth pattern of TBMD in study participants. A similar curve linear growth pattern was observed as the growth pattern shown in Figure 1. In parallel, significant difference in measures of TBMD remained between sexes between ages eight and 30 years old.

Table 1

Characteristics of Anthropometry Measurements in Study Cohort

	Mean (SD)	Percentile				
		10 th	25 th	50 th	75 th	90 th
Birth weight (kg)						
Boys						
CDC growth chart, 2000 <i>l</i>	3.41 (0.55)	2.72	3.08	3.43	3.77	4.08
FLS ² participants	3.47 (0.54)	2.81	3.17	3.47	3.78	4.08
Girls						
CDC growth chart, 2000	3.29 (0.52)	2.64	2.98	3.29	3.63	3.92
FLS participants	3.26 (0.54)	2.61	2.95	3.26	3.60	3.88
Weight (Kg)						
Boys						
8-y-old CDC growth chart, 2000	26.01 (4.23)	21.61	23.25	25.46	28.01	31.13
8-y-old Fels study participants	26.87 (5.09)	23.80	23.70	25.50	28.20	31.60
12-y-old CDC growth chart, 2000	41.23 (9.82)	31.41	34.93	38.90	45.76	54.27
12-y-old FLS participants	42.57 (10.35)	32.35	35.10	39.30	50.00	59.10
16-y-old CDC growth chart, 2000	63.64 (11.76)	51.71	55.97	62.03	68.55	77.11
16-y-old FLS participants	66.00 (14.04)	53.00	56.20	62.69	71.90	93.60
Girls						
8-y-old CDC growth chart, 2000	25.84 (4.68)	20.75	22.51	25.06	28.24	31.87
8-y-old FLS participants	26.38 (2.22)	21.80	23.50	25.80	29.20	34.80
12-y-old CDC growth chart, 2000	43.63 (10.27)	31.98	36.52	41.73	48.76	57.38
12-y-old Fels study participants	43.75 (9.91)	34.30	37.77	43.70	50.90	61.90
16-y-old CDC growth chart, 2000	57.16 (10.76)	46.04	49.84	55.57	61.69	69.57
16-y-old Fels study participants	57.02 (9.17)	48.30	51.80	57.25	63.20	69.30
Height (cm)						
Boys						
8-y-old CDC growth chart, 2000	127.62 (5.83)	121.00	124.05	127.75	131.40	134.80

J CDC (Centers for Disease Control and Prevention) growth chart, 2000: http://www.cdc.gov/nchs/data/series/sr_11/sr11_246.pdf

	Mean (SD)	Percentile				
		10 th	25 th	50 th	75 th	90 th
8-y-old FLS participants	128.85 (5.21)	122.85	125.10	128.54	132.00	135.60
12-y-old CDC growth chart, 2000	149.67 (7.68)	140.45	145.05	149.05	154.55	160.15
12-y-old FLS participants	151.37 (6.82)	143.25	146.65	150.93	155.30	161.40
16-y-old CDC growth chart, 2000	172.85 (7.13)	163.45	168.40	173.20	177.60	181.65
16-y-old FLS participants	175.47 (6.61)	167.10	171.31	175.35	179.98	183.80
Girls						
8-y-old CDC growth chart, 2000	126.78 (6.10)	119.25	122.75	126.95	130.70	134.35
8-y-old FLS participants	127.91 (5.45)	120.60	124.07	127.87	131.45	135.00
12-y-old CDC growth chart, 2000	152.00 (7.69)	142.25	146.15	151.16	156.8	161.35
12-y-old Fels study participants	152.37 (7.03)	142.93	146.65	150.93	155.30	161.40
16-y-old CDC growth chart, 2000	163.17 (6.24)	155.30	158.85	163.40	167.10	171.20
16-y-old Fels study participants	164.23 (6.01)	156.67	159.82	164.15	167.99	183.80
BMI (kg/m²)						
Boys						
8-y-old CDC growth chart, 2000	16.03 (2.07)	14.19	14.89	15.64	16.71	18.16
8-y-old FLS participants	16.10 (2.22)	14.21	14.67	15.40	16.65	18.39
12-y-old CDC growth chart, 2000	18.44 (3.36)	15.37	16.32	17.50	19.71	22.98
12-y-old FLS participants	18.41 (3.39)	14.95	15.96	17.49	20.03	24.85
16-y-old CDC growth chart, 2000	21.25 (3.25)	18.05	19.30	20.65	22.37	25.37
16-y-old FLS participants	21.38 (4.10)	17.57	18.63	20.37	22.80	29.62
Girls						
8-y-old CDC growth chart, 2000	16.04 (2.07)	13.95	14.69	15.55	17.02	18.71
8-y-old FLS participants	16.02 (2.05)	14.09	14.88	15.72	17.42	19.52
12-y-old CDC growth chart, 2000	18.90 (3.44)	15.40	16.42	18.39	20.55	22.91
12-y-old FLS participants	18.69 (3.22)	15.70	16.77	18.75	21.26	24.18
16-y-old CDC growth chart, 2000	21.43 (3.71)	17.91	19.08	20.53	22.65	25.74
16-y-old FLS participants	21.13 (3.11)	18.27	19.31	21.27	23.44	26.94

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Table 2

Characteristics of Self-Reported Habitual Physical Activities

Characteristics	Male		Female	
	N	Mean (SD)	N	Mean (SD)
Leisure activity index	131	2.50 (0.53)	127	2.61 (0.47)
Sport activity index	132	2.69 (0.66)	127	2.40 (0.67)
Work activity index	132	2.88 (0.60)	127	2.68 (0.52)
Total activity index	131	8.06 (1.09)	127	7.68 (1.11)

Table 3

Predicted Ages at the Peak Total Body BMC or BMD Attainment

Peak Bone Mass	Age			
	Male		Female	
	N	Median (IQR)	N	Median (IQR)
Unadjusted				
TBMC ¹	312	24.34 (24.34–26.19)	343	21.96 (21.81–22.21)
TBMD ²	312	26.86 (25.14–27.98)	343	22.31 (21.95–22.59)

¹Total body bone mineral content;²Total body bone mineral density

Table 4

The Fixed Effect of Chronological Age and Concurrent Height, Weight, Body Mass Index or Mean Habitual Physical Activities on Peak Total Body BMC Attainment

Parameter	Male			Female		
	Estimate	SE	P	Estimate	SE	P
Age and quadratic age						
a	-2.3346	0.1290	<0.0001	-1.5104	0.00869	<0.0001
b	0.4425	0.0164	<0.0001	0.3569	0.0107	<0.0001
c	-0.0090	0.0005	<0.0001	-0.0813	0.0003	<0.0001
d	-	-	-	-	-	-
e	-	-	-	-	-	-
f	-	-	-	-	-	-
Weight (kg)						
a	-0.7131	0.1712	<0.0001	-1.9338	0.1180	<0.0001
b	0.1802	0.02624	<0.0001	0.4139	0.0184	<0.0001
c	0.0007	0.0009	0.4539	-0.0103	0.0006	<0.0001
d	-0.7408	0.1358	<0.0001	-0.4722	0.0998	<0.0001
e	0.1278	0.0207	<0.0001	0.1050	0.0153	<0.0001
f	0.0040	0.0008	<0.0001	-0.0038	0.0006	<0.0001
Height (m)						
a	-0.9877	0.1806	<0.0001	-2.2859	0.1455	<0.0001
b	0.2191	0.0771	<0.0001	0.4635	0.0215	<0.0001
c	-0.0007	0.0010	0.5176	-0.0119	0.0007	<0.0001
d	-0.3191	0.1687	0.0590	-0.6987	0.1326	<0.0001
e	0.0583	0.0259	0.0246	0.1221	0.0878	<0.0001
f	-0.0012	0.0010	0.2129	-0.0040	0.0006	<0.0001
BMI (kg/m²)						
a	-0.9022	0.1904	<0.0001	-2.1505	0.1325	<0.0001
b	0.2072	0.0294	<0.0001	0.4471	0.0206	<0.0001
c	0.0001	0.0010	0.9095	-0.0113	0.0007	<0.0001

Parameter	Male			Female		
	Estimate	SE	P	Estimate	SE	P
d	-0.4190	0.1421	0.0041	-0.3289	0.1114	0.0033
e	0.0704	0.02158	0.0011	0.0781	0.0167	<0.0001
f	-0.0021	0.0008	0.0064	-0.0029	0.0006	<0.0001
Habitual physical activity						
<i>Leisure activity index</i>						
a	-3.2218	0.6133	<0.0001	-2.0008	0.5431	0.0003
b	0.5625	0.0806	<0.0001	0.4210	0.0658	<0.0001
c	-0.0122	0.0023	<0.0001	-0.0104	0.0019	<0.0001
d	0.2681	0.2415	0.2686	0.2333	0.2092	0.2664
e	-0.0356	0.0316	0.2601	-0.0285	0.0252	0.2595
f	0.0009	0.0009	0.3065	0.0010	0.0007	0.1777
<i>Sport activity index</i>						
a	-1.7245	0.5196	0.0011	-0.8739	0.3565	0.0153
b	0.3740	0.0697	<0.0001	0.2970	0.0436	<0.0001
c	-0.0084	0.0020	<0.0001	-0.0073	0.0012	<0.0001
d	-0.3017	0.1862	0.1071	-0.2148	0.1417	0.1314
e	0.03590	0.0250	0.1512	0.0202	0.0174	0.2453
f	-0.0005	0.0007	0.4621	-0.0003	0.0005	0.6201
<i>Work activity index</i>						
a	-3.0421	0.6300	<0.0001	-1.6649	0.5184	0.0016
b	0.5161	0.0832	<0.0001	0.3627	0.0619	<0.0001
c	-0.0107	0.0023	<0.0001	-0.0079	0.0017	<0.0001
d	0.1772	0.2207	0.4234	0.0972	0.1889	0.6077
e	-0.0156	0.0292	0.5939	-0.0057	0.0226	0.8007
f	0.0003	0.0008	0.7095	-0.0000	0.0006	0.9707
<i>Total activity index</i>						
a	-2.4884	0.9411	0.0093	-1.0150	0.7221	0.1618
b	0.4636	0.1249	0.0002	0.3091	0.0085	0.0003

Parameter	Male			Female		
	Estimate	SE	P	Estimate	SE	P
c	−0.0107	0.0036	0.0027	−0.0077	0.0024	0.0012
d	−0.0098	0.1167	0.9334	−0.0497	0.0935	0.5960
e	0.0013	0.0155	0.9330	0.0050	0.0110	0.6507
f	0.0001	0.0004	0.8192	−0.0000	0.0003	0.9129

The model equations were as follows: Values of repeated measurements of total body bone mineral content (T BMC) = a (intercept) + b (parameter of age at the time of TBMC) + c (quadratic parameter of age) + d (parameter of covariable, e.g., concurrent BMI) + e (parameter of the age and a covariable) + e (parameter of the quadratic age and a covariable).

Table 5

The Fixed Effect of Chronological Age and Concurrent Height, Weight, Body Mass Index or Mean Habitual Physical Activities on Peak Total Body BMD Attainment

Parameter	Male			Female		
	Estimate	SE	P	Estimate	SE	P
Age and quadratic age						
a	0.2778	0.0275	<0.0001	0.3015	0.0220	<0.0001
b	0.0741	0.0036	<0.0001	0.0766	0.0028	<0.0001
c	-0.0014	0.0001	<0.0001	-0.0017	0.0001	<0.0001
d	-	-	-	-	-	-
e	-	-	-	-	-	-
f	-	-	-	-	-	-
Weight (kg)						
a	0.7310	0.0417	<0.0001	0.2741	0.0408	<0.0001
b	0.0047	0.0064	0.4636	0.0788	0.0063	<0.0001
c	0.0011	0.0002	<0.0001	-0.0018	0.0002	<0.0001
d	-0.1379	0.0347	<0.0001	-0.1227	0.0036	0.0007
e	0.0208	0.0052	<0.0001	0.0242	0.0054	<0.0001
f	-0.0006	0.0002	0.0014	-0.0009	0.0002	<0.0001
Height (m)						
a	0.6827	0.0405	<0.0001	0.2155	0.0450	<0.0001
b	0.0128	0.0063	0.0427	0.0871	0.0068	<0.0001
c	0.0008	0.0002	0.0006	-0.0021	0.0002	<0.0001
d	-0.0425	0.0404	0.2928	-0.1974	0.0410	<0.0001
e	0.0037	0.0061	0.5427	0.0308	0.0059	<0.0001
f	0.0001	0.0002	0.5852	-0.0010	0.0002	<0.0001
BMI (kg/m²)						
a	0.6941	0.0430	<0.0001	0.2311	0.0407	<0.0001
b	0.0096	0.0659	0.4636	0.0852	0.0063	<0.0001
c	0.0010	0.0002	<0.0001	-0.0020	0.0002	<0.0001

Parameter	Male			Female		
	Estimate	SE	P	Estimate	SE	P
d	-0.1370	0.0332	<0.0001	-0.0697	0.0353	0.0007
e	0.0137	0.0050	<0.0001	0.0157	0.0053	<0.0001
f	-0.0004	0.0002	0.0014	-0.0006	0.0002	<0.0001
Habitual physical activity						
<i>Leisure activity index</i>						
a	0.1265	0.1448	0.3837	0.1264	0.1256	0.3155
b	0.0977	0.0182	<0.0001	0.1989	0.0162	<0.0001
c	-0.0020	0.0005	<0.0001	-0.0025	0.0005	<0.0001
d	0.0371	0.0571	0.5162	0.0730	0.0482	0.1322
e	-0.0062	0.0072	0.3882	-0.0089	0.0062	0.1525
f	0.0002	0.0002	0.4158	0.0003	0.0002	0.1147
<i>Sport activity index</i>						
a	0.3917	0.1217	0.0016	0.4236	0.0826	<0.0001
b	0.0751	0.0155	<0.0001	0.0678	0.0109	<0.0001
c	-0.0014	0.0004	0.0008	-0.0017	0.0003	<0.0001
d	0.0624	0.0436	0.1540	-0.0436	0.0327	0.1848
e	0.0062	0.056	0.2662	0.0031	0.0043	0.4882
f	-0.0000	0.0002	0.6805	0.0000	0.0001	0.9705
<i>Work activity index</i>						
a	0.1861	0.1503	0.2175	Did not converge		
b	0.0848	0.0189	<0.0001			
c	-0.0017	0.0005	0.0011			
d	0.0134	0.0527	0.7999			
e	-0.0011	0.0066	0.8728			
f	0.0000	0.0002	0.8942			
<i>Total activity index</i>						
a	0.2730	0.2193	0.2151	0.3679	0.1684	0.0304
b	0.0818	0.0278	0.0033	0.0706	0.0211	0.0008

Parameter	Male			Female		
	Estimate	SE	P	Estimate	SE	P
c	−0.0019	0.0008	0.0119	−0.0018	0.0006	0.0036
d	−0.0068	0.0272	0.8043	−0.0069	0.0218	0.7511
e	0.0006	0.0035	0.9854	0.0007	0.0027	0.7962
f	0.0000	0.0001	0.6899	0.0000	0.0000	0.9052

The model equations were as follows: Values of repeated measurements of total body bone mineral density (TBMD) = a (intercept) + b (parameter of age at the time of TBMD) + c (quadratic parameter of age) + d (parameter of covariable, e.g., concurrent BMI) + e (parameter of the age and a covariable) + e (parameter of the quadratic age and a covariable).

Table 6
Predicted or Estimated Ages at the Peak of Total Body BMC/BMD Attainment in Literature

Reference	Designs	Samples Growth Periods	Methods of Analysis	Co-variables examined	Predicted (or Estimated) Ages at Peak Total Body BMC ¹ or BMD ²
Recker et al. 1992	Longitudinal, 3 yrs follow up	156 females Age 19.5–29.1 yrs	Bivariate and multiple regressions	Calcium intake, protein intake, physical activities	BMD Females: 30.26 yrs old
Slosman et al. 1994	Longitudinal,	60 white males/females Age 20 – 35	Descriptive, two-way ANOVA and linear regression	Sex, weight, height and BMI	BMC/BMD No substantial gain between ages 20 and 35 yrs for males and females
Faulker et al. 1996	Cross sectional	977 males and females Age 8 – 17 yrs	Descriptive and two-way ANOVA	Sex	BMC/BMD No significant difference between ages 17 and 21 yrs for males and females
Bachrach et al. 1999	Longitudinal Up to 4 yrs follow up	423 males and females Age 9–25	Mixed effects model and other model techniques	Sex, race/ethnicity,	BMD Females: reached plateau at 16.4 yrs Males: reached plateau at 17.6 yrs
Drake et al. 2000	Longitudinal, 3.6 yrs follow up	164 white females Age 18 – 22 yrs	Descriptive and ANOVA	Percentage change in body mass	BMC Females: Actual beyond 22 yrs
Nguyen et al. 2001	Longitudinal	186 white males and females Age 6 – 36 years	Descriptive, multiple linear model and mixed model for repeated measures	Sex	BMC³ Females: 20.8 yrs Males: 25.2 yrs
Kalkwarf et al. 2007	Longitudinal	1554 males and females Age 7 – 17 yrs	LMS ⁴ methods and centile curves, mixed and general linear models	Sex, race	BMC/BMD Values and variations increased with age; the plateau was not evident by age 16 (females) or age 17 (males); BMC/BMD were higher for Blacks at all skeletal sites
Baxter-Jones, et al. 2011	Multiple longitudinal, where repeated measurements were taken on more than one birth cohort	375 white males/females Age 8 – 30 yrs	Descriptive - the percentages of BMC actual were scaled at the biological age by the highest adult bone area or BMC value	Sex	BMC⁵ Depending on sites, the peak bone mass occurs by the end of second decade or very early in the third decade
Lu. et al.	Longitudinal	655 white males/females Age 8 – 30 yrs	Random coefficient model, male or female subjects were modeled separately	Concurrent weight, height, BMI, or fixed effect of self- reported habitual physical activities	BMC⁶ Median (IQR) Females: 21.96 (21.81–22.21) Males: 24.34 (24.34–26.19) Mean (95% CI) Females: 22.13 (21.99–22.27) Males: 26.72 (25.62–27.82) BMD⁶ Median (IQR) Females: 22.31 (21.95–22.59) Males: 26.86 (25.14–27.98) Mean (95% CI) Females: 22.84 (22.53–23.15)

Reference	Designs	Samples Growth Periods	Methods of Analysis	Co-variables examined	Predicted (or Estimated) Ages at Peak Total Body BMC ¹ or BMD ²
					Males: 19.89 (8.96–30.83)

¹Total body bone mineral content;
²Total body bone mineral density;
³Mixed model for repeated measures;
⁴LMS statistical methods which estimates the parameter of median, standard deviation and power on the Box-Cox transformation;
⁵Estimated from biological ages;
⁶Gender specific random coefficient model.

Table 7
Correlations between Peak Total Body BMC/BMD and Adult Total Body BMC/BMD

Sex	TBMC ¹				TBMD ²			
	N	Mean (SD)	Correlation	P-value	N	Mean (SD)	Correlation	P-value
Boys								
Peak	15	3.30 (0.35)	0.94	<0.0001	13	1.31 (0.09)	0.86	<0.0001
Adult ³	15	2.92 (0.36)			13	1.25 (0.09)		
Girls								
Peak	17	2.44 (0.55)	0.91	<0.0001	16	1.17 (0.08)	0.96	<0.0001
Adult	17	2.21 (0.36)			16	1.13 (0.09)		

¹Total body bone mineral content;

²Total body bone mineral density;

³Median BMC/BMD values derived between ages 30 and 50 years old