LIFESTYLE FACTORS AND THE DEVELOPMENT OF BONE MASS AND BONE STRENGTH IN YOUNG WOMEN

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Objective To evaluate the contributions of adolescent calcium intake, oral contraceptive use, and exercise on bone mass and bone strength.

Study design Eighty white women participated in 10 years of the Penn State Young Women's Health Study, a longitudinal study of community participants. We measured bone mineral mass (g), density (BMD, g/cm^2), and body composition from dual energy x-ray absorptiometry and estimated proximal femur section modulus (bone bending strength). Calcium intake was determined from 45 days of prospective food records at regular intervals between the ages of 12 and 22 years. Exercise history and oral contraceptive use were assessed by questionnaire.

Results Daily calcium intakes between the ages of 12 and 22 years ranged from 500 to 1900 mg/d and were not significantly associated with bone gain or bone strength. Oral contraceptive use during adolescence was not correlated with bone or body composition measurements. Femoral neck BMD did not change from 17 to 22 years of age, but section modulus increased 3% ($P < .05$). Only exercise during adolescence was significantly associated with increased BMD and bone bending strength.

Conclusions Adolescent lifestyle patterns can influence young adult bone strength. Our data suggest that exercise is the predominant lifestyle determinant of bone strength for this cohort. *(J Pediatr 2004;144:776-82)*

It is currently believed that the bone strength changes that underlie osteoporotic fragility begin in the developing skeleton. This view is derived from observations that (1) fragile bones in the elderly have reduced skeletal mass, (2) the amount of mineral mass in the skeleton reaches a peak in early adulthood, and (3) most of the peak skeletal mass is accrued during childhood and adolescence. As much bone is laid down during the ages of 13 to 15 years in girls as is lost in the last 4 decades of their life.[1,2] Since the attainment of optimal young adult bone mass and bone strength during adolescence may well offer the best protection against osteoporosis when bone is lost in later life, understanding how modifiable lifestyle factors affect bone accrual and development of bone strength is of critical clinical importance.

The advent of dual energy x-ray absorptiometry (DEXA) in the late 1980s provided a technique to obtain quantitative measurements of bone mass and bone mineral density (BMD, g/cm^2). Precise knowledge of the relations between specific lifestyle factors and bone outcome measures can be made through the use of repeated measures and longitudinal study designs.[3-5]

Although BMD has been widely used as a surrogate for fracture risk, it is not a direct measurement of bone strength and is a 2-dimensional measurement (expressed as g/cm^2). Bone strength depends on both the material and structural properties of bone. New software has recently been developed to calculate specific measures of bone strength and geometric properties (ie, section modulus, cross-sectional area, subperiosteal width, and cortical thickness) from DEXA scan–derived bone measurements. Since hip fractures commonly occur as a result of bending and torsional loads, the distribution of the mass in the cross section is especially important to bone strength. Thus, measurement of section modulus (an engineering term that describes bending and torsional strength expressed in units of length to the third power) provides us with a clinically relevant measurement of bone strength.[6-8]

The objective of the current study was to use our longitudinal data set from healthy, white subjects over the ages of 12 to 22 years to obtain a comprehensive view of how

BMD	Bone mineral density	OCs	Oral contraceptives
DEXA	Dual energy x-ray absorptiometry		

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modifiable determinants of bone health, namely, calcium intake, oral contraceptive use, and exercise, are related to development of peak bone mass and to the development of young adult hip bone bending strength. We have previously reported interim data up to age 18 years. Data presented in this report use the final 4 years of measurement and add bone strength measurements.

METHODS

Subjects and Retention

The Penn State Young Women's Health Study is a prospective epidemiologic study, which was started in 1990 with the enrollment of 112 healthy, premenarchal girls, 11.9 ± 0.5 years of age. This population is representative of white adolescent girls attending public school in central Pennsylvania. Details of the recruitment, baseline measurements, and the effects of the calcium supplementation component on bone gain have been reported.[3,9-11] The study was approved by the Pennsylvania State University College of Medicine Institutional Review Board. Participants and their parents provided informed consent. During the first 4 years of the investigation, visits occurred every 6 months, then annually. All measurements in this report were from the 80 subjects who remained in the study 10 years later. Of the 1200 possible study subject visits ($15 \times 80 = 1200$), 1175 were completed, for an overall participation record of 98%. No differences in baseline age, height or weight, or bone measurements were present between subjects who dropped out and those who remained in the cohort.

Body Composition and Bone Measurements

The same Hologic QDR-2000W DEXA bone densitometer (Hologic, Waltham, Mass) was used throughout this study. The manufacturer's lumbar spine phantom was scanned daily for quality control and to correct for instrument drift. As has been reported by others, our observed coefficient of variation was <0.7% for the day-to-day quality control scans. Total body scans were made in the pencil beam mode in the presence of the manufacturer's 3-step acrylic and aluminum tissue phantom. Scans were analyzed for total body bone and body composition variables. Beginning at visit 10, when the cohort was on average 17 years of age, bilateral proximal femur scans were made in the array mode, with the use of an Osteodyne hip positioner (Osteodyne, Research Triangle Park, NC). The hip bone measurements reported are the average of those from the left and right hips.

Bone Geometry Analyses

Proximal femur scans were analyzed for bone structure by use of the Hip Structure Analysis program.[12] In brief, as shown in Figure 1, this program measures BMD and geometry of cross sections by using distributions of mineral mass traversing the bone, averaged along a length of approximately 5mm. Analysis regions were located across the femoral neck at its narrowest point and across the shaft 2 cm distal to the midpoint of the lesser trochanter. Because hip scans were bilateral, structural measurements were averaged over both hips. For the femoral neck and femoral shaft, conventional BMD (g/cm^2), bone cross-sectional area (cm^2), subperiosteal width (cm), and section modulus (cm^3) were measured. Cortical thickness was estimated by means of algorithms described previously.[12,13] We report BMD values for the total hip and section modulus values for the femoral neck and femoral shaft at age 22 years.

Calcium Intake Assessment

Prospective 3-day diet records were completed at baseline and every 6 months for the first 4 years (ages 12-16 years) and yearly thereafter. The records were analyzed with Nutritionist III, Version 7.0, and Nutritionist IV, Version 3.0, software (FirstDataBank, Inc, San Bruno, Calif). We calculated the time-averaged daily calcium intake for each participant by using her 15, 3-day diet records between the ages of 12 and 22 years and from her calcium supplementation data. This cohort also participated in a double-blinded, randomized, placebo-controlled calcium supplementation trial during ages 12 to 16 years.[9,10] Residual pill counts made every 6 months during the intervention periods allowed us to calculate calcium intake attributable to the supplementation program. The cumulative daily average calcium intake of each individual over ages 12 to 22 years is used in the analyses.

Oral Contraceptive Use

Oral contraceptive (OC) users (n = 33) were those individuals in the cohort who used OCs continuously for at least 6 months and were still using at age 22 years. Several low-dose preparations were used by the OC group. Nonusers (n = 17) had never used OCs. Individuals who had started and stopped using OCs or who had used OCs less than 6 months (n = 27) were excluded from these analyses. Three individuals who used depot medroxyprogesterone and the one individual with an incomplete OC use history were also excluded from analysis. OC use was by self-report. Because this cohort has performed well in the 4 years of calcium supplement pill counting and in the completion of 3-day prospective diet records every year, their OC use reports are believed to be accurate.

Physical Activity Assessment

Physical activity between ages 12 and 22 years was assessed with a sports exercise questionnaire that was based on existing instruments.[14,15] The questionnaire listed 28 activities, including (1) school-based activities, for example, soccer, cross-country, marching band; (2) outside-of-school organized activities, for example, swimming, dance, aerobic classes; and (3) individual activities, for example, walking, running, tennis.[16] The cumulative sports exercise score was the arithmetic sum, in arbitrary units, for the 10 years covered by the questionnaires.

Statistical Analyses

Statistical analyses were accomplished by using a range of procedures in SAS (SAS Institute, Cary, NC). Descriptive

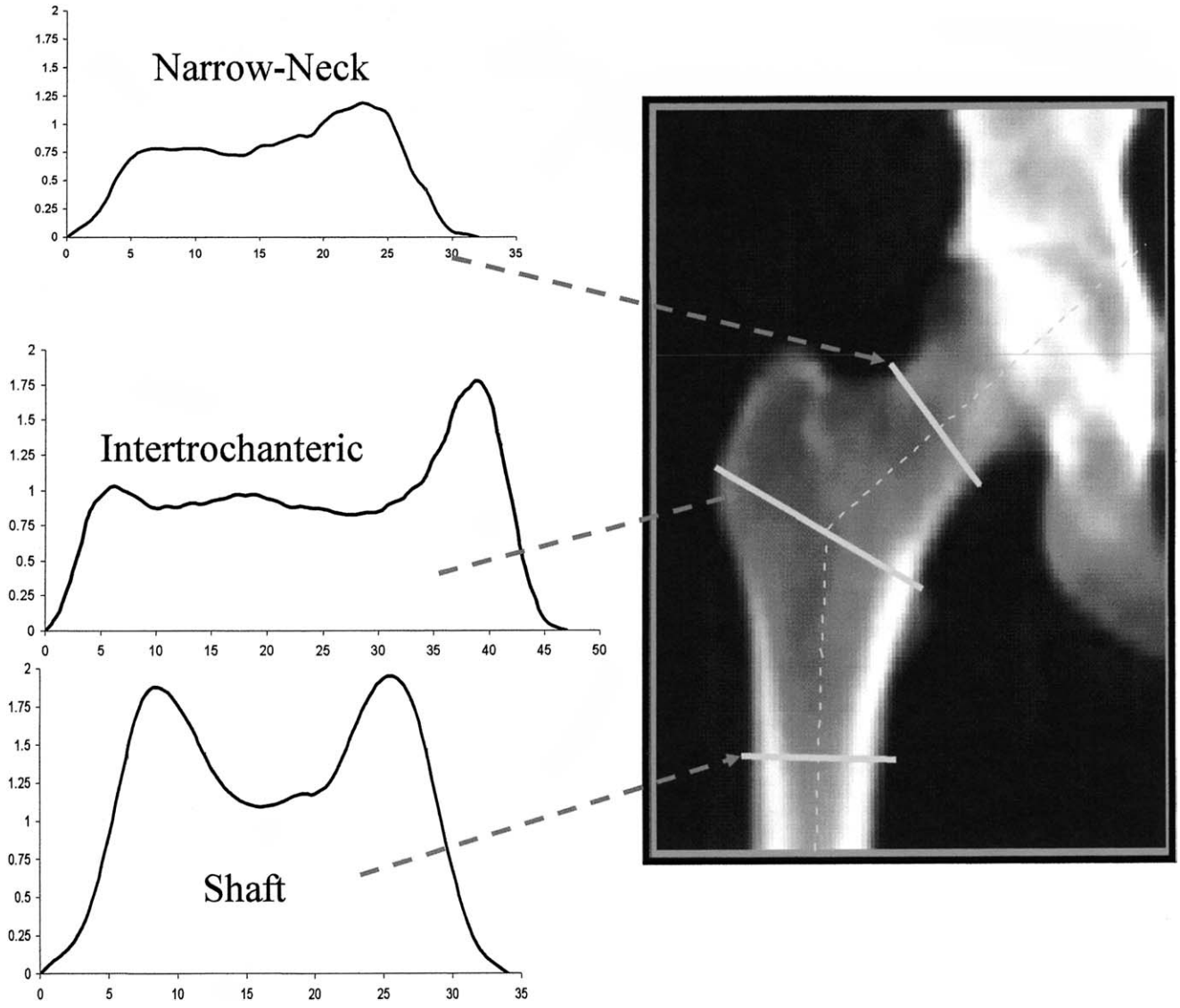

Fig 1. Hip structure analysis profile.

statistics (percentages, means, and standard deviations) were used to characterize the sample. The random-effects growth models were used to compare the yearly trends. The random-effects growth model is appropriate for longitudinal data analyses because it assumes an underlying fixed effect for the overall trend for each group but that the deviations of individual slope and intercept from the overall trend are random. Group and slope interactions were included in the model to test whether the yearly trends are similar between each set of cases and control subjects.

RESULTS

Natural History of Bone Gain and Bone Strength Changes, Ages 12 to 22 Years

The natural history of the gain of total body bone mineral content (g) for this cohort during ages 12 to 22 years is presented in Figure 2. During the 4 years, ages 12 to 16 years, the mean gain was approximately 850 g of bone mineral, which represents approximately 37% of the adult female skeleton. The change in total hip BMD and femoral neck and femoral shaft section modulus values during ages 17 to 22 years is shown in Table I. There was no change in BMD at the femoral neck and an increase at the femoral shaft. In contrast, section modulus values increased significantly over the same period at both the neck and the shaft.

Bone Gain and Calcium Intake, Ages 12 to 22 Years

The results of linear regression analyses to examine relations between daily calcium intake (ages 12 to 22 years) and bone gain and absolute bone mass are shown in Table II. Results indicate that no significant relation exists between average daily calcium intake across the range of 500 to 1900 mg/d and total body bone gain over ages 12 to 22 years, young adult hip BMD, or young adult bone section modulus values.

Table I. Change in BMD and section modulus values at the femoral neck and femoral shaft between ages 17 and 22 years

	Age 17 y	Age 22 y	% Change	P Value
Femoral neck				
BMD* (g/cm^2)	0.97 ± 0.11	0.96 ± 0.11	−0.7%	>.05
Section modulus (cm^3)	1.15 ± 0.22	1.19 ± 0.24	3.5%	.003
Femoral shaft				
BMD* (g/cm^2)	1.35 ± 0.13	1.39 ± 0.14	1.8%	.04
Section modulus (cm^3)	1.60 ± 0.27	1.65 ± 0.25	3.6%	<.001

*BMD values are from the Hip Structure Analysis program and vary slightly from DXA values due to a smaller region of interest.

Table II. Linear regression models for average daily calcium intake during adolescence and bone gain and bone strength variables

Dependent variable	β (slope)	R^2	P value
Total body bone gain, g from 12 to 22y	0.00197	0.021	.27
Hip BMD, g/cm^2 at 22 y	0.00005	0.02	.28
Femoral neck section modulus (cm^3) at 22 y	−0.00001	0.0002	.91
Femoral shaft section modulus (cm^3) at 22 y	0.00012	0.0127	.41

Oral Contraceptive Use and Body Composition of Teen Women

The OC users (n = 33) and nonusers (n = 17) were indistinguishable at age 12.5 years, with respect to anthropometric, endocrine, and bone measurements.[17] The mean age of menarche was similar among users and nonusers (13.4 years for both). A comparison of the anthropometric and body composition variables of OC users and nonusers at age 22 years is shown in Table III. The OC users and nonusers were indistinguishable with respect to age, height, weight, body mass index percent body fat, percent lean mass, total body and hip BMD, and hip section modulus values.

Sports-Exercise History Between Ages 12 and 22 Years Were Associated with Increased Young Adult Hip Bone Measurements

The cumulative sports-exercise score, which is a quantitative and integrated measurement of voluntary sports participation, was significantly related to hip BMD ($r = 0.40$, $P = .002$) at age 22 years and to section modulus values of the femoral neck ($r = 0.47$, $P < .001$) and shaft ($r = 0.41$, $P = .002$). The R^2 values indicate that variation in sport-exercise activities in adolescence explains 16% to 22% of the variation in hip bone mineral density and bending strength of the femoral neck and shaft.

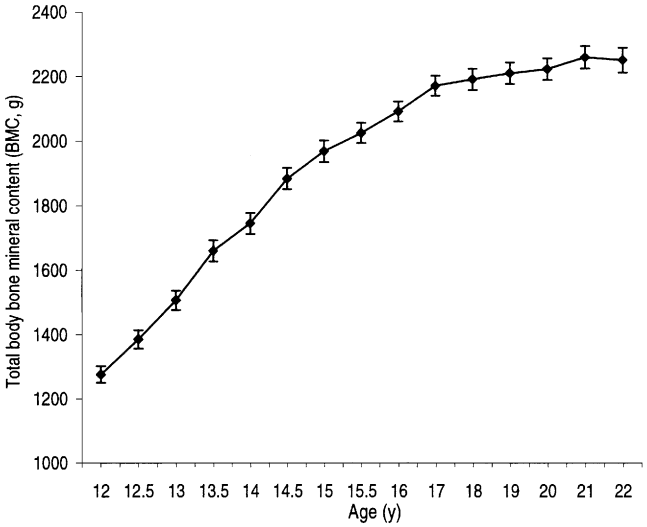

Fig 2. Total body bone mineral accretion from the Penn State Young Women's Health Study. Total body bone mineral content from ages 12 to 22 years is shown.

Table III. Bone and body composition variables of OC users and nonusers at age 22 y

	OC users (n = 33)	Nonusers (n = 17)
Age, y	21.7 ± 0.1	21.8 ± 0.1
Weight, kg	61.2 ± 1.3	64.4 ± 2.5
Body mass index, kg/m^2	22.0 ± 0.4	23.3 ± 0.75
Body fat %	29.1 ± 1.1	31.6 ± 1.6
Lean body mass, %	67.2 ± 1.1	64.7 ± 1.6
Total body BMC, g	2260 ± 55	2316 ± 66
Total body BMD, g/cm^2	1.14 ± 0.01	1.15 ± 0.02
Hip BMD, g/cm^2	1.0 ± 0.02	1.0 ± 0.02
Femoral neck section modulus (cm^3)	1.29 ± 0.05	1.32 ± 0.05
Femoral shaft section modulus (cm^3)	1.70 ± 0.06	1.74 ± 0.07

Values are mean ± SD.

DISCUSSION

The goal of this study was to make use of 15 regularly spaced measurements in a healthy cohort of young women as they aged from 12 to 22 years to evaluate overall contributions of 3 major modifiable lifestyle factors, namely, calcium intake, oral contraceptive use, and exercise, on the development of peak bone mass and young adult bone strength. We have shown that ages 12 to 16 years are important years for bone accretion and that adolescent physical activity is positively related to BMD and bone strength of the young adult hip. We also observed that neither variation in calcium intake >500 to 1900 mg/d during adolescence nor use of oral contraceptives during adolescence were associated with early adult bone

measurements. These findings confirm our previous reports[3,10,16-18] and show that (1) results persist into young adulthood, (2) femoral neck bone strength continues to increase from ages 17 to 22 years, whereas BMD does not, and (3) benefits of adolescent exercise are apparent in young adult bone strength values.

Most bone accrual occurs during ages 12 to 16. Peak hip BMD in female subjects is achieved in late adolescence (approximately age 16 years), and peak lumbar spine and total body BMD occur near age 20 years.[19,20] Peak BMD at all skeletal sites is approximately 1.0 g/cm^2, and peak total body bone mass is on average approximately 2300 g in women and 3000 g in men. We have documented the total body bone mineral accretion from repeated measurements of the 80 healthy women who completed 10 years of the Penn State Young Women's Health Study. Bone accretion proceeds in a nearly linear fashion between the ages of 12 and 16 years, and bone accretion is nearly complete by age 18 years, with only 2% to 3% additional gain between the ages of 18 and 23 years. Thus, between ages 12 and 16 years, young women gain approximately 850 g of bone mineral or approximately 40% of their adult skeleton. During these 4 critical years, yearly gain of approximately 212 g of bone mineral depends on the daily addition of 650 mg bone mineral to the skeleton per day. Since calcium constitutes 40% of bone mineral, approximately 250 mg of calcium is added to the skeleton each day during ages 12 to 16 years.

In contrast to the relatively early age at which peak bone mass is reached, femoral neck and shaft section modulus values continued to increase (3% to 5%) in this cohort in late adolescence (17-22 years). This suggests that bone bending strength is increasing during this period of life and suggests that the concept of "peak bone mass" may not correspond to maximal bone strength.

Habitual calcium intake between 500 and 1900 mg/d was not related to adolescent bone gain.

To rigorously determine whether long-term dietary differences in calcium intake affect bone gain and peak bone measures requires detailed long-term nutrient intake measurements. As an adolescent's nutritional intake varies greatly from day to day, the number of days of food intake data required to accurately estimate mean calcium intake is not widely appreciated. In two comprehensive studies, it was found that the number of days of food records needed to estimate mean daily calcium intakes for groups or individuals ranged from 7 to 88 days.[21,22] Thus, results of previous studies on calcium intake and bone gain that used one or two assessments may be misleading. The Penn State Young Women's Health Study collected nutrient intake measurements every 6 months for the first 4 years and yearly thereafter, which allowed for the calculation of the cumulative daily average intake of each individual as the cohort aged from 12 to 22 years. The range of spontaneous intake was 480 to 1958 mg/d, and total average calcium intake, which includes supplemental calcium, was 1058 ± 440 mg/d.

There was a small positive relation between calcium intake and bone variables, yet none reached significance ($P \leq .05$). If the relations had been significant, the variance (R^2) in calcium intake could only explain 2% to 4% of the difference in the bone measurements. Data indicate that daily calcium intake >500 mg/d during adolescence does not result in clinically appreciable increased body bone accrual or increased adult bone mass.

Bone density and body composition measurements were not related to OC use during adolescence. To date, most studies assessing effects of OCs on BMD have been cross-sectional or retrospective studies of adult women, with inconsistent results.[23-25] The longitudinal nature of this study allowed us to determine if OC use during adolescence might affect early adult peak bone strength and body composition. The results of our study indicate that OC use during adolescence does not affect body composition or young adult bone measures.[17] These results are strengthened by the homogeneity in age and ethnicity of the study subjects and by the repeated measurements that would more likely detect differences in body composition and peak bone measures caused by OC use. In contrast to our data, one longitudinal study in young women[26] and one in a primate model[27] showed a negative influence of oral contraceptive use on adolescent bone gain. A longitudinal and intervention study suggests that the combination of exercise and OCs can suppress bone gain in young women 18 years of age and older.[28,29] Other studies support our findings of no effect.[23-25] The effect of contraceptive use during adolescence on bone accrual has not been tested in a randomized, controlled trial.

Sports-exercise history is associated with young adult hip bone mass and bending strength. We showed a significant association between sports-exercise score and young adult bone mass and strength. These results support other convincing evidence that load-bearing activities during adolescence have significant osteogenic effects on the skeleton and that the effects are site-specific.[30-36] Furthermore, although load-bearing activities are believed to be the most osteogenic, we have little information on the osteogenic effects of low "load" (from ground reaction forces) activities that induce a high load from muscle activity such as swimming and cycling. There is even less information on the amount of daily activity needed to achieve optimal bone strength. Whether these gains in bone mineral and bone strength resulting from exercise in childhood reduce fracture risk in later life is a controversial issue.[37,38] This is due in part to the fact that only a few randomized, controlled trials have been performed, only short-term (7-10 months) interventions[33,39-42] have been done in children, and convincing multiyear follow-up studies have not yet been reported.

A second approach has been to examine the relations between quantifiable daily physical activities and adolescent bone gains. These studies are costly and difficult to perform and thus are rare. Data from one other longitudinal study of bone accrual supports our findings[36] by showing that girls and boys who were most active during adolescence gained more bone and had significantly higher bone mass values at age 16 years compared with their less active counterparts.[36] Our results extend these findings by showing that gains are

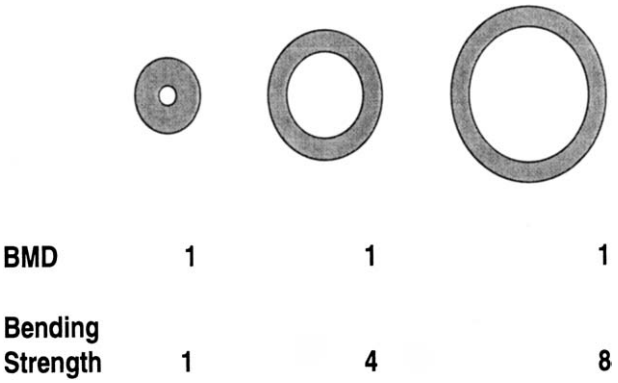

Fig 3. Three model bones with identical total cortical bone mass and cortical density may have an 8-fold difference in resistance to bending (section modulus), although their BMD, measured by DEXA, is not significantly different.

Table IV. Comparison of femoral neck bone mass and strength of two healthy young women

	Subject 1	Subject 2
Age	20	20
Height (cm)	170	170
Weight (kg)	53	51
Hip BMC (g)	28.6	36.4
Hip bone area (cm^2)	32.9	34.8
Hip BMD (g/cm^2)	0.87	1.05
Z-score (% peck)	−0.90	+0.42
Neck section modulus (cm^3)	1.26	1.23

maintained to age 21 years and are apparent in bone-bending strength measurements.

Assessment of Bone Strength

The use of BMD (g/cm^2) assumes that bone is an amorphous solid, for which size, shape, and the distribution of bone material within are irrelevant. Before and after puberty in both sexes, as long bones increase in length, the periosteal envelope widens, resulting in a thicker cortex that is displaced further and further from the neutral axis of the bone. To understand how this process contributes to increased bone strength requires the application of engineering principles and techniques. Section modulus, which describes bone-bending and torsional strength, offers a better representation of bone strength than BMD. For example, three model bones with different cross-sectional size but with identical total cortical bone mass and cortical density can have an 8-fold difference in resistance to bending,[43] although their BMD, measured by DEXA, would not be significantly different (Fig 3).

Section modulus takes into account the subperiosteal diameter as well as the amount and distribution of material in the subperiosteal envelope. Subtle changes in cross-sectional geometry can markedly affect structural properties.[7,8,44,45] Increases in subperiosteal diameter translate into considerable increases in section modulus values. For example, a 1-mm increase in cortical thickness will increase a child's bone bending strength 5 times.[46] A 15-year follow-up of Swedish women showed that despite increased bone loss after the menopause, the constantly increasing periosteal apposition could preserve bone strength.[47]

Case Study of Two Participants

To illustrate and compare the use of BMD and section modulus values, we present in Table IV the hip bone measurements of two healthy young women who are participants in our study and are of similar age, height, and weight. Subject 1 has substantially higher BMD (+17%) and a normal *z* score, compared with the low *z* score (−0.90) of subject 2. In contrast, the section modulus values are nearly identical between the two women. In this case, the use of BMD as a surrogate for bone strength would suggest that subject 1 had substantially better bone strength and that subject 2 was modestly osteopenic. However, BMD values do not take the bone size and structure into account. In contrast, the section modulus values are nearly identical for the two young women, indicating that the actual bone bending strength of their hips is the same. Section modulus has been applied to other populations, showing that it predicts stress fractures in military recruits[6]; explains sex and ethnic differences in fracture rates; and explains bone adaptation to weight change, estrogen use, and exercise intervention.

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