



## Original Full Length Article

## Socioeconomic status over the life-course and adult bone mineral density: The Midlife in the U.S. Study

Carolyn J. Crandall<sup>a,\*</sup>, Sharon Stein Merkin<sup>b</sup>, Teresa E. Seeman<sup>b</sup>, Gail A. Greendale<sup>b</sup>, Neil Binkley<sup>c</sup>, Arun S. Karlamangla<sup>b</sup><sup>a</sup> Division of General Internal Medicine, David Geffen School of Medicine at University of California, Los Angeles, USA<sup>b</sup> Division of Geriatrics, David Geffen School of Medicine at University of California, Los Angeles, USA<sup>c</sup> University of Wisconsin-Madison Osteoporosis Clinical Center and Research Program, Madison, WI, USA

## ARTICLE INFO

## Article history:

Received 16 December 2011

Revised 6 March 2012

Accepted 16 April 2012

Available online 21 April 2012

Edited by: Felicia Cosman

## Keywords:

Bone mineral density

Socioeconomic status

Poverty

Education

Income

## ABSTRACT

**Purpose:** Adult bone mass depends on acquisition in childhood and decline in adulthood, and may be influenced by socioeconomic conditions over the entire life course.

**Methods:** We examined associations of bone mineral density (BMD) in adulthood with life course socioeconomic status in 729 participants in the Midlife in the United States Biomarker Project, adjusting for age, menopausal transition stage, race, gender, body weight, smoking, physical activity in several life stages, and research site. Primary predictors were a) childhood socioeconomic advantage score (including parental education, self-rated financial status relative to others, not being on welfare), b) adult education level (no college vs. some college vs. college graduate), and c) adult current financial advantage score (including family-adjusted poverty to income ratio, self-assessed current financial situation, having enough money to meet needs, ease in paying bills).

**Results:** Mean age was 56.9 (range 34–85) years. After adjustment for covariates, childhood socioeconomic advantage and adult education level were positively associated with lumbar spine BMD: 0.27 standard deviations (SD) higher at 90th compared to 10th percentile of childhood advantage score ( $P = 0.009$ ), and 0.24 SD higher in college graduates compared to participants without college education ( $P = 0.01$ ). Adult current financial advantage was not associated with lumbar spine BMD. None of the three socioeconomic indicators was significantly associated with femoral neck BMD.

**Conclusions:** Childhood socioeconomic advantage and adult education level were associated with higher adult lumbar spine BMD. Current financial advantage was not associated with BMD. Childhood socioeconomic factors may influence acquisition of lumbar BMD.

© 2012 Elsevier Inc. All rights reserved.

## Introduction

Low socioeconomic status (SES) is associated with poor health and with multiple markers of sub-clinical disease. A large body of evidence documents SES gradients in biomarkers from nearly every major physiological system [1]. Many of the systems linked to SES, including the hypothalamic–pituitary–adrenal (HPA) axis, sympathetic nervous system, glucose metabolism, and inflammation [1], influence bone mineral density (BMD) [2–5]. Additionally, SES is linked to health behaviors which are known to influence bone mass, such as

smoking, physical activity, and excessive alcohol intake [6–9]. It has therefore been postulated that socioeconomic advantage positively influences bone mass.

A few U.S. studies have indeed found that higher adult SES is associated with higher total hip and femoral neck BMD [10,11]. However, because adult bone mass is a function of both acquisition in childhood and decline in adulthood, we hypothesized that both childhood and adult socioeconomic advantage positively influence adult BMD. Studies outside the U.S. support this hypothesis [12–14], but it has not been examined in the U.S.

Previous studies of SES and bone mass have focused exclusively on objective measures of SES, such as income and education, which do not completely capture the socioeconomic environment in which people live their daily lives. For example, subjective self-reports of SES (e.g., ranking oneself on a ladder, rating one's financial position relative to others) are independently associated with a variety of health outcomes, independent of education and income [15,16]. We therefore examined the associations of socioeconomic advantage

\* Corresponding author at: David Geffen School of Medicine, University of California at Los Angeles, UCLA Medicine/GIM, 911 Broxton Ave., 1st floor, Los Angeles, CA 90024. Fax: +1 310 794 0732.

E-mail addresses: [cgrundall@mednet.ucla.edu](mailto:cgrundall@mednet.ucla.edu) (C.J. Crandall), [smarkin@mednet.ucla.edu](mailto:smarkin@mednet.ucla.edu) (S.S. Merkin), [tseeman@mednet.ucla.edu](mailto:tseeman@mednet.ucla.edu) (T.E. Seeman), [GGreenda@mednet.ucla.edu](mailto:GGreenda@mednet.ucla.edu) (G.A. Greendale), [nbinkley@wisc.edu](mailto:nbinkley@wisc.edu) (N. Binkley), [akarlamangla@mednet.ucla.edu](mailto:akarlamangla@mednet.ucla.edu) (A.S. Karlamangla).

over the life course, assessed comprehensively using both objective and subjective SES measures, with lumbar spine and femoral neck BMD as measured by dual energy X-ray absorptiometry (DXA) in adulthood using data from the Midlife in the United States Study (MIDUS) Biomarker Project [17–19].

## Methods

### *The Midlife in the U.S. (MIDUS) recruitment and data collection methods*

The MIDUS National Study of Health and Well-Being [17–19] recruited a national sample of adults between 25 and 75 years of age residing in the coterminous United States in 1995–1996, and re-interviewed them 9–10 years later (MIDUS II); details of the study design, recruitment, and retention are available at <http://www.icpsr.umich.edu/icpsrweb/NACDA/>. Of the 3191 MIDUS II participants deemed medically able to travel, 1255 agreed to participate in the MIDUS II biomarker project, which required a 2-day commitment, including travel to one of the three clinical research centers University of California at Los Angeles, Georgetown University, and University of Wisconsin. Reasons given for nonparticipation were travel, family obligations, and being too busy. Participants provided medical history information and underwent anthropometric and BMD measurements according to standardized protocols. Data collection occurred between July 2004 and May 2009. Informed consent was provided by each participant. Each MIDUS center obtained institutional review board approval [17].

The characteristics of the MIDUS II participants were similar to those of the MIDUS I participants [19] and the characteristics of the MIDUS biomarker project participants (e.g. subjective health status, chronic health conditions, exercise, alcohol use) were similar to those of the MIDUS II participants as a whole [17].

Of the 1255 participants in the MIDUS II Biomarker Project, we excluded data from 126 participants who reported the use of medications known to influence bone density (oral corticosteroids, alendronate, anastrozole, calcitonin, ibandronate, leuprolide, letrozole, raloxifene, risedronate, tamoxifen, zoledronic acid, testosterone, finasteride, dutasteride), 137 female participants whose menopause transition stage classification could not be completed, 8 participants for whom we lacked complete SES information, and 255 without BMD measurement (which was added to the Biomarker Project part-way into data collection). Thus, the analytic sample for this study was composed of 729 participants (353 men, 376 women).

### *Childhood and adult socioeconomic advantage assessment*

Primary predictors in this analysis were 1) childhood socioeconomic advantage, 2) participant education, and 3) adult financial advantage. We separated participant education from adult financial advantage because educational attainment is relatively constant over adult life while financial status can vary over adult life, and at any point reflects current SES. Also, previous studies of SES relationships with BMD have found associations of BMD with participant education but not with income [10,20].

Participants were asked to recall three aspects of their socioeconomic environment during childhood. First, they were asked to rate the highest educational level attained by their father (or other male head of household) and mother (or other female head of household). Second, to assess welfare status in childhood, we asked participants whether they had ever been on welfare as a child (response choices: yes or no). Finally, we asked participants for a subjective self-assessment of childhood financial status relative to others (response choices: worse off, same as, or better than others.) We calculated a childhood socioeconomic advantage score (possible range 0–6) for each participant by summing three components: being on welfare during childhood (0: yes, 2: no), childhood financial level

relative to others (0: worse off, 1: same, 2: better), and highest parental education (0: <high school, 1: high school/general educational development [GED] certificate, 2: some college or more). Scores were calculated only for participants who supplied data regarding at least 2 of the 3 components; the missing component was imputed as the rounded mean of the other two components for 49 participants. Among MIDUS twin and siblings participants, the intra-class correlation coefficient for childhood advantage score was 0.84, indicating a high degree of reliability. We have previously shown associations between this childhood advantage score and a beneficial adult physiological profile [21].

The participants' educational level was also ascertained and collapsed to a 3-category variable: 1) no college vs. 2) some college or Associate's degree vs. 3) Bachelor's degree or more.

Data were available regarding 3 aspects of current adult financial advantage: the family-adjusted poverty-to-income ratio, a subjective rating of current financial situation, and a rating of the degree of difficulty paying bills. We describe each of these 3 measures of current adult financial advantage here. We calculated current family-adjusted poverty-to-income ratio (FPIR) for each participant as the ratio of the participant's total household income (sum of self-reported earnings, pension, social security, and government assistance for all household members) to the U.S. Census Bureau poverty threshold specific to the participant's age, presence of a spouse or partner in the household, the number of children under age 18 living in the household, and year of data collection. For example, an FPIR of 3 corresponds to a total household income 3 times the census bureau-defined poverty level for his/her family. Participants were also asked to rate their current financial situation (response choices of worst, average, or best) and to report whether they had enough money to meet their needs (response choices of not enough, just enough, or more than enough) and difficulty in paying bills (response choices of very, not very, or not at all).

We calculated an adult current financial advantage score (possible range 0–8) by summing 4 components: FPIR (0 for FPIR < 3, 1 for FPIR ≥ 3 but < 6, 2 for FPIR ≥ 6, reflecting approximate tertiles of its distribution), self-rated current financial situation (0: worst, 1: average, 2: best), money to meet needs (0: not enough, 1: just enough, 2: more than enough), and degree of difficulty paying bills (0: very, 1: not very, 2: not at all). Scores were calculated only for participants who supplied data regarding at least 3 of the 4 components; the missing component was imputed as the rounded mean of the other three components for 20 participants.

### *Bone mineral density measurement*

At the MIDUS II visit (2004–2009), BMD was measured in the lumbar spine (L<sub>1</sub>–L<sub>4</sub>) and left hip using dual-energy X-ray absorptiometry (DXA). DXA scans were performed using GE Healthcare Lunar Prodigy (Madison site) or Hologic 4500 (UCLA and Georgetown) technology by technologists certified by the International Society for Clinical Densitometry. Funding for DXA scanning at the UCLA and Georgetown sites was obtained after the Biomarker Project had commenced; thus, BMD data were not available for every participant at these sites. Adjudication of all DXA scans occurred centrally by physicians at the University of Wisconsin DXA center. Three times per week, and on all days on which scans were obtained, instruments were calibrated and phantom scan data were acquired. No densitometer shift or drift occurred during the course of this study. For BMD cross-calibration across the three clinical sites, a “bone-fide” phantom was scanned 10 times on the densitometers at each of the three study sites. The linear regression equation developed from these calibration scans were used to correct BMD values from two of the three sites to make the data comparable across study sites. The re-calibrated BMD values at the lumbar spine and left hip were reported in units of grams/cm-squared.

### Age and menopausal transition stage classification

From self-reported menstrual patterns and use (in the last year) of sex steroid hormones (from self report and examination of medication bottles brought to the clinical research center), we classified each female participant's menopausal stage as one of the following: premenopausal (no change in regularity of menses), early perimenopausal (had menses in last 3 months with change in regularity of menses), late perimenopausal (last menses 3–12 months previously with change in regularity of menses), postmenopausal (no menses in prior 12 months) not taking menopausal hormone therapy, and postmenopausal taking menopausal hormone therapy.

We classified each participant into one of seven age-gender-menopausal stage categories: male younger than 50 years, 50–59 year-old men, men 60 years or older, premenopausal women, early perimenopausal women, late peri-/post-menopausal women not taking menopausal hormone therapy, and postmenopausal taking menopausal hormone therapy. The choice of age categories in men was guided by previous observations that age-related bone loss in men does not start until age 50 years [22], and to age-match the oldest group to the post-menopausal women, because only 0.3% of occurrences of spontaneous menopause take place at or after 59 years of age [23].

### Assessment of race

Race/ethnicity was self-identified as white, black/African American, other, or multiracial. For this analyses, we classified race as black vs. not black; the latter group was mostly white, but included a small number ( $n = 32$ , 4.5%) that were neither white nor black/African American.

### Health behavior assessment

At the time of BMD measurement, questionnaires assessed total pack years of cigarette smoking (years smoked regularly multiplied by number of cigarettes per day divided by 20), alcohol consumption level, and levels of physical activity in different stages of life. Participants were asked to quantify their alcohol consumption at two time points: 1) during the past month, and 2) during the period in which they felt they consumed the most alcohol of their lives. We defined "heavy" alcohol consumption as regular consumption of >7 drinks per week or >3 drinks per day for female participants, and >14 drinks per week or >4 drinks per day for male participants [24].

Participants were asked to quantify levels of (recalled) physical activity during 3 stages of their lives: high school, young adulthood, and current (at the time of BMD measurement.) For the high school stage, participants reported the number of years of participation in competitive sports and in recreational sports (separately) between ages 14 and 18. For the young adult stage, participants reported the number of years of exercise performed between ages 20–35 years for each of 3 self-categorized intensity levels (light, moderate, and vigorous). For current physical activity, participants rated the average number of minutes per week currently spent doing light, moderate, and vigorous exercise. For each participants' young adulthood and current levels of physical activity, we created summary scores by adding the reported times for light (weight of 1), moderate (weight of 2), and vigorous (weight of 3) activity. Prior studies have validated the use of similar (recalled) self-reports of physical activity [25,26].

### Statistical analysis

Lumbar spine BMD and femoral neck BMD were the dependent variables in separate linear regressions that examined their associations with childhood socioeconomic advantage, adult education, and adult current financial advantage, both with and without controls for each other. Both advantage scores (childhood socioeconomic and

adult financial) had near-normal distributions and were treated as continuous predictors, but education was modeled as a 3-level, categorical predictor (1: no college, 2: some college or Associate's degree, 3: Bachelor's degree or more), because education effects on health are thought to operate through social advantages conferred by credentialing rather than directly by additional years of education ([27–29]), and because at least one previous study has suggested a threshold effect of education on BMD [10]. We controlled for age, gender, and menopausal status using a single categorical variable with the following seven categories: male <50 years-old, male 50–59 years-old, male  $\geq 60$  years-old, premenopausal female, early perimenopausal female, late peri-/post-menopausal female not taking menopausal hormone therapy, and postmenopausal female taking menopausal hormone therapy, and two continuous variables: one that tracked age in men 60 years and older, and one that tracked age in women who were late peri- or post-menopausal and not taking menopausal hormone therapy. We additionally controlled for race (black vs. non-black), study site, body weight (kg), smoking (pack-years), heavy alcohol consumption (yes/no), physical activity in high school (number of years in competitive sports and number of years in recreational sports), young adulthood physical activity score, and current physical activity score. We used linear mixed effects models with a random intercept at the family level to account for clustering between siblings and twins.

We tested for potential interactions of race (black vs. non-black), sex, and race-sex groups (black men, non-black men, black women, non-black women) with the 3 socioeconomic indicators.

All statistical tests were 2-sided. P values  $\leq 0.05$  were considered statistically significant. Statistical analyses were performed using SAS version 9.2 (SAS Institute Inc., Cary, North Carolina, U.S.A.).

### Results

Most demographic characteristics and health assessments of the MIDUS II biomarker study participants were comparable to those of the overall MIDUS II recruitment pool [17]. Compared to the entire MIDUS II biomarker study, a higher proportion of participants included in the current study were black (23.6% vs. 17.7%) and a slightly higher proportion were men (48.4% vs. 43.2%) (Table 1).

On average, participants of the current study were aged 56.9 years and 23.6% were black (Table 1). The proportion of men within each of the three age groups was similar. One-third of the women were late peri-/post-menopausal women who were not taking hormone therapy. Only a small minority of participants (16.5%) were current smokers. Average (both mean and median) childhood advantage score was 4.0 (standard deviation [SD] 1.5, inter-quartile range 3–5, 10th percentile 2, 90th percentile 6), and average adult financial advantage score was 3.9 (SD 2.5, median 4.0, inter-quartile range 2–6, 10th percentile 0, 90th percentile 7). Forty-one percent of the sample were college graduates or better educated, and an additional twenty-nine percent had some college level education. Adult education level (treated as a 3-level ordinal variable) was weakly correlated with childhood socioeconomic advantage (Spearman  $r = 0.35$ ) and adult current financial advantage (Spearman  $r = 0.36$ ), and correlations between childhood and current adult advantage scores were especially weak (Spearman  $r = 0.19$ ) (data not shown).

Childhood financial advantage scores were statistically significantly higher among non-black participants than among black participants (4.18 vs. 3.54), as were adult financial advantage score (4.48 vs. 2.17) and the proportion of participants with a college degree (47.5% vs. 19.8%) (each P value < 0.001), data not shown).

We first examined childhood advantage score, adult education level, and adult financial advantage score as predictors of BMD in separate multivariable regressions. After adjustment for race, study site, body weight, menopause transition stage (in women), and age, childhood advantage score and adult education level were positively

**Table 1**  
Descriptive statistics: n (%) or mean (SD).

	Analytic sample (n = 729)	MIDUS II biomarker sample (n = 1255)
Age (years)	56.9 (11.4)	57.3 (11.5)
Black race <sup>a</sup> *	172 (23.6%)	222 (17.7%)
Weight (kg) <sup>a</sup> *	86.7 (20.6)	84.7 (20.3)
Height (cm) <sup>a</sup> *	169.7 (9.5)	168.6 (9.4)
Body mass index (kg/m <sup>2</sup> )	30.1 (6.7)	29.8 (6.6)
Men <sup>a</sup> *	353 (48.4%)	542 (43.2%)
Age groups in men <sup>a</sup> *		
Ages <50 years	115 (32.6%)	156 (28.8%)
Ages 50–59 years	103 (29.2%)	153 (28.2%)
Ages ≥60 years	135 (38.2%)	233 (43.0%)
Menopause transition stage in women <sup>a</sup> *		
Premenopausal	62 (16.5%)	72 (12.7%)
Early perimenopausal	53 (14.1%)	56 (9.9%)
Late peri-/post-menopausal women (not taking hormone therapy)	224 (59.6%)	374 (65.9%)
Postmenopausal women taking hormone therapy	37 (5.1%)	66 (6.0%)
Current smoking	120 (16.5%)	187 (14.9%)
Smoking (pack-years)	9.1 (17.3)	8.8 (16.9)
Physical activity		
Recreational sports ages 14–18 years	1.7 (1.9)	1.6 (1.8)
Competitive sports ages 14–18 years <sup>a</sup> *	1.7 (1.8)	1.6 (1.8)
Summary score ages 20–35 years <sup>b</sup> *	34.5 (25.8)	33.3 (26.0)
Summary score current physical activity <sup>c</sup> *	692.1 (1214.9)	638.2 (1089.6)
Education		
No college	216 (30.0%)	344 (27.7%)
Some college or Associate's degree	210 (29.1%)	371 (29.9%)
College degree or more	295 (40.9%)	527 (42.4%)
Childhood socioeconomic advantage score	4.0 (1.5)	4.0 (1.5)
Adult financial advantage score	3.9 (2.5)	4.0 (2.5)
BMD femoral neck g/cm <sup>2</sup> <sup>a</sup> *	0.84 (0.14)	–
BMD lumbar spine g/cm <sup>2</sup> <sup>a</sup> *	1.06 (0.18)	–

<sup>a</sup>Represents statistically significant ( $P < 0.05$ ) difference ( $t$ -test for continuous variables and chi-squared test for categorical variables) between the analytic sample and those in the MIDUS II Biomarker Sample who were excluded from the analytic sample. Major reason for exclusion was unavailability of BMD measurement.

<sup>b</sup>Summary score of physical activity between ages 14 and 18 years = (number of years of light exercise \* 1) + (number of years of moderate exercise \* 2) + (number of years of vigorous exercise \* 3).

<sup>c</sup>Summary score current physical activity = (average number of minutes doing light exercise \* 1) + (average number of minutes doing moderate exercise \* 2) + (average number of minutes doing vigorous exercise \* 3).

associated with lumbar spine BMD. For every point increment of childhood advantage score, lumbar spine BMD was 0.011 g/cm<sup>2</sup> higher ( $P = 0.009$ ) and participants with a Bachelor's degree or more education had 0.047 g/cm<sup>2</sup> higher lumbar spine BMD ( $P = 0.002$ ) compared to participants with no college education (Table 2). Neither childhood advantage score nor adult education level was statistically significantly associated with femoral neck BMD (Table 3). Adult current financial advantage score was not statistically significantly associated with either lumbar spine or femoral neck BMD (Tables 2 and 3).

The positive associations of childhood socioeconomic advantage and adult education level with lumbar spine BMD persisted after adjustment for health behaviors, i.e. lifetime exposure to smoking, alcohol consumption, and physical activity at different life stages (high school years, young adulthood, and current); the adjusted effect size was 0.012 g/cm<sup>2</sup> per one-point increment in the childhood advantage score ( $P = 0.009$ ) and 0.044 g/cm<sup>2</sup> for college graduates compared to those without any college-level education ( $P = 0.01$ ) (Table 2). This translates to 0.27 SD higher lumbar spine BMD (95% confidence

interval 0.07 SD, 0.42 SD) at the 90th compared to the 10th percentile of childhood advantage score, and 0.24 SD higher lumbar spine BMD (95% confidence interval 0.06 SD, 0.41SD) in college graduates compared to those without any college-level education. When childhood advantage score and adult financial advantage score were included in the same model, the magnitude of the association between childhood advantage score and lumbar spine BMD remained unchanged (0.012 g/cm<sup>2</sup> higher lumbar spine BMD per one-point increment in the childhood advantage score,  $P = 0.009$ ). When all three socioeconomic advantage indicators were included together in one model, the associations of adult education and childhood advantage score with lumbar BMD became marginally significant (Table 2).

None of the interactions of race (black vs. non-black), sex, or race-sex groups (black men, non-black men, black women, non-black women) with the three socioeconomic indicators was statistically significant at the  $P < 0.05$  level (data not shown).

## Discussion

Adult bone mass is a function of bone acquisition in childhood and decline in adulthood. This study of 729 midlife adults in the U.S. was designed to determine whether socioeconomic advantage over different stages in the life course is associated with adult BMD. We found that greater childhood socioeconomic advantage and higher adult education level, but not adult current financial advantage, were associated with higher adult lumbar spine BMD. The associations of childhood socioeconomic advantage and adult education with lumbar spine BMD persisted after accounting for current financial advantage, and did not vary by race or sex. Femoral neck BMD was not significantly associated with any socioeconomic indicator. Because of differences in SES distributions between race groups in the U.S. and race differences in BMD [30], race is an important potential confounder of SES associations with BMD. Indeed, scores for each of the 3 indicators of socioeconomic advantage (childhood socioeconomic advantage, adult education, adult financial advantage) were more favorable among non-black than among black participants. The associations of childhood socioeconomic advantage and adult education with lumbar spine BMD in this study were independent of race. In addition, the associations between the three socioeconomic indicators and BMD did not vary significantly by race (black vs. non-black).

Our findings are consistent with findings from the Newcastle Thousand Families Cohort Study that prospectively examined the effects of an aggregate measure of fetal, infant, and childhood socioeconomic and health factors, which included occupational social class of the father at birth and of the main household wage earner at age 5 years, and found associations with lumbar spine BMD at ages 49–51 years [31]. However, the study did not separately report associations of childhood SES with BMD.

No previous U.S. study has examined associations of childhood SES with adult BMD. One prior U.S. study examined adult education in relation to femoral neck BMD. In the Third National Health and Nutrition Examination Survey, education was positively associated with femoral neck BMD in white women, but not in black women or white or black men [10]. However, the education effect was concentrated at the lowest end of the education distribution (in white women with less than 8 years of formal schooling), and was not adjusted for menopausal transition stage. In our study, which did not include many participants with less than 8 years of education and was adjusted for menopausal transition stage, we did not detect an association between educational level and femoral neck BMD. A second study using the NHANES III data examined total hip BMD in post-menopausal women and found a positive association with education, but the association did not persist after adjustment for health behaviors [11].

On the other hand, positive associations of adult education with lumbar spine BMD have been more consistently demonstrated; they

**Table 2**Adjusted associations of lumbar spine BMD (g/cm<sup>2</sup>) with socioeconomic indicators alone and together<sup>a</sup>.

		Model 1: childhood advantage alone	Model 2: adult education alone	Model 3: adult financial advantage alone	Model 4: childhood advantage and adult financial advantage	Model 5: All three SES indicators together
Without control for health behaviors						
Childhood advantage score (per unit; range 0–6)		0.011 (0.004)**	–	–	0.011 (0.004)**	0.007 (0.004)
Education	Some college or Associate's degree vs. no college	–	0.011 (0.016)	–	–	0.007 (0.016)
	College degree or more vs. no college	–	0.047 (0.015)**	–	–	0.042 (0.016)*
Adult financial advantage score (per unit; range 0–8)		–	–	0.001 (0.003)	0.00002 (0.003)	–0.001 (0.003)
With control for health behaviors <sup>b</sup>						
Childhood advantage score (per unit; range 0–6)		0.012 (0.004)**	–	–	0.012 (0.004)**	0.009 (0.005) <sup>~</sup>
Education	Some college or Associate's degree vs. no college	–	0.009 (0.017)	–	–	0.005 (0.018)
	College degree or more vs. no college	–	0.044 (0.016)*	–	–	0.035 (0.018) <sup>~</sup>
Adult financial advantage (per unit; range 0–8)		–	–	0.002 (0.003)	0.0005 (0.003)	–0.0002 (0.003)

<sup>a</sup> Cell entries are beta-coefficients from regression models examining adjusted associations of BMD with the SES indicators. Standard errors are presented within parentheses. All associations are adjusted for gender, menopause transition stage (in women), age (see text for specification), race, clinical research site, and body weight.

<sup>b</sup> Additional controls for smoking status, alcohol consumption, and physical activity level in childhood, in young adulthood, and currently.

\* P-value 0.05–0.01.

\*\* P-value 0.01–0.001.

<sup>~</sup> P-value 0.05–0.0.

were seen in our study as well as in an earlier study of postmenopausal women [20]. In both studies, the education associations persisted after adjustment for health behaviors. One potential reason for the stronger, more consistent with BMD at the lumbar spine than at the femoral neck may be the differing composition of bone at the two anatomical sites. The lumbar spine is composed predominantly of trabecular bone, whereas the femoral neck has a much

higher proportion of cortical bone than does the lumbar spine [32]. Some studies have suggested that weight-bearing and physical activity in the growing years are important determinants of cortical bone density, whereas cancellous vertebral bone density is more strongly affected by hormonal and/or metabolic factors which are sensitive to stressors during adolescence [33–35]. Changes in the hormonal milieu as a result of perceived stresses are the likely pathway from

**Table 3**Adjusted associations of femoral neck BMD (g/cm<sup>2</sup>) with socioeconomic indicators alone and together<sup>a</sup>.

		Model 1: childhood advantage alone	Model 2: adult education alone	Model 3: adult financial advantage alone	Model 4: childhood advantage and adult financial advantage	Model 5: all three SES indicators together
Without control for health behaviors						
Childhood advantage score (per unit; range 0–6)		0.005 (0.003)	–	–	0.005 (0.003)	0.005 (0.003)
Education	Some college or Associate's degree (vs. no college)	–	–0.015 (0.011)	–	–	–0.018 (0.011)
	College degree or more (vs. no college)	–	0.001 (0.011)	–	–	–0.007 (0.012)
Adult financial advantage score (per unit; range 0–8)		–	–	0.002 (0.002)	0.002 (0.002)	0.002 (0.002)
With control for health behaviors <sup>b</sup>						
Childhood advantage score (per unit; range 0–6)		0.005 (0.003)	–	–	0.005 (0.003)	0.006 (0.003) <sup>~</sup>
Education	Some college or Associate's degree (vs. no college)	–	–0.015 (0.012)	–	–	–0.019 (0.013)
	College degree or more (vs. no college)	–	–0.006 (0.012)	–	–	–0.015 (0.013)
Adult financial advantage score (per unit; range 0–8)		–	–	0.002 (0.002)	0.002 (0.002)	0.002 (0.002)

<sup>a</sup> Cell entries are beta-coefficients from regression models examining adjusted associations of BMD with the SES indicators. Standard errors are presented within parentheses. All associations are adjusted for gender, menopause transition stage (in women), age (see text for specification), race, clinical research site, and body weight.

<sup>b</sup> Additional controls for smoking status, alcohol consumption, and physical activity level in childhood, in young adulthood, and currently.

<sup>~</sup> P-value 0.05–0.0.

childhood and young adulthood social circumstances to adult bone health; thus, lumbar bone mass may be more susceptible to less favorable social circumstances in the growing years.

Associations with adult finances have also been seen only for lumbar spine BMD, and not femoral neck BMD. The previously-mentioned NHANES III study reported that family poverty-to-income ratio was not associated with femoral neck BMD [10]. However, a Spanish study of postmenopausal women found higher lumbar spine BMD in women with income above the Spanish Institute of Statistics poverty threshold compared to those living below the poverty threshold (after adjustment for smoking), but found no income association with femoral neck BMD [36]. Our study found no association of adult current financial advantage with either lumbar spine or femoral neck BMD.

In our study, childhood socioeconomic advantage and adult education were positively associated with lumbar spine BMD even when adjusted for current financial advantage. This is not surprising, given that education and current finances reflect different aspects of socioeconomic status, and are not strongly correlated [37,38]. Because adult education is affected by social conditions during childhood and young adulthood, and impacts adult socioeconomic status after attainment of the terminal credentials, our findings suggest that socioeconomic conditions over the life course are more relevant to adult bone mass than are current financial circumstances, and that socioeconomic advantage in childhood, during bone mass acquisition, may be especially relevant to adult bone mass.

It must be noted that the associations of childhood socioeconomic advantage and adult education with lumbar spine BMD in this study were not explained by differences in lifetime personal smoking behavior, excessive alcohol consumption, and levels of physical activity in high school and adulthood, suggesting that other factors may be responsible. One explanation that we could not explore in this study were SES differences in parental lifestyle choices (such as maternal smoking during pregnancy), which are known to influence children's bone mass [39]. Another potential mechanism by which childhood socioeconomic circumstances could affect bone mass is the effect of childhood stresses on physiological systems, such as the HPA axis, sympathetic nervous system, inflammation, and glucose regulation, all of which have been related to osteoporosis. SES differences in brain development and function begin at the earliest stages of life [1] and SES differences in cardiovascular and neuroendocrine profiles are seen in young children and adolescents [40–42] with persistent dysregulation seen in adults with low childhood SES [43]. In turn, dysregulation of these systems have been related to low BMD [1,44–48], and might represent the biological pathway from childhood socioeconomic disadvantage to osteoporosis.

Our study has some limitations. The cross-sectional observational design does not allow inference of causality. Moreover, childhood socioeconomic advantage was ascertained from recalled self-report and is therefore susceptible to bias. However, among twins and siblings, there is excellent agreement regarding recall of childhood social class and parental education [49,50]. Among MIDUS twin and sibling participants, the intra-class correlation coefficient for childhood advantage score was 0.84, indicating a high degree of reliability. The intra-class correlation coefficient was unchanged when we dropped non-twin siblings from the sample and when we examined parental education separately. In addition, we do not have direct measures of childhood nutrition which might have helped to explain BMD associations with childhood socioeconomic advantage. Poverty affects food choices and has profound impact on nutritional status [51]. Finally, information regarding physical activity in high school and young adult years was ascertained by recalled self-report and may be biased. Strengths of our study include the comprehensive assessment of socioeconomic advantage using both objective and subjective self-reports, the ability to separate current financial status from earlier socioeconomic advantage, measurement and rigorous classification

of menopausal transition stage based on strict criteria, the broad age range in the sample, the ability to exclude data from current users of medications that influence bone, and the inclusion of information regarding physical activity in different life stages.

In conclusion, socioeconomic advantage in childhood and adult education level were associated with higher adult lumbar spine, but not femoral neck, BMD, and current financial advantage was not associated with either lumbar spine or femoral neck BMD. This suggests that life-course, and especially childhood socioeconomic factors, may influence the acquisition of bone mass, especially trabecular bone mass, during the growing years.

## Acknowledgments

This research was supported by National Institutes of Health grant numbers 1R01AG033067, R01-AG-032271, and P01-AG-020166. The UCLA GCRC helped support this study (UCLA GCRC Grant # M01-RR000865).

Study design: CC and AK.

Study data analysis: SS-M.

Data interpretation: all authors.

Drafting manuscript: CC and AK.

Revising manuscript content and approving final version of manuscript: all authors.

SS-M takes responsibility for the integrity of the data analysis.

## References

- Seeman T, Epel E, Gruenewald T, Karlamangla A, McEwen BS. Socio-economic differentials in peripheral biology: cumulative allostatic load. *Ann N Y Acad Sci* 2010;1186:223–39.
- Eleftheriou F. Regulation of bone remodeling by the central and peripheral nervous system. *Arch Biochem Biophys* 2008;473:231–6.
- Isidro ML, Ruano B. Bone disease in diabetes. *Curr Diabetes Rev* 2010;6:144–55.
- McLean RR. Proinflammatory cytokines and osteoporosis. *Curr Osteoporos Rep* 2009;7:134–9.
- Merlotti D, Gennari L, Dotta F, Lauro D, Nuti R. Mechanisms of impaired bone strength in type 1 and 2 diabetes. *Nutr Metab Cardiovasc Dis* 2010;20:683–90.
- Iribarren C, Luepker RV, McGovern PG, Arnett DK, Blackburn H. Twelve-year trends in cardiovascular disease risk factors in the Minnesota Heart Survey. Are socioeconomic differences widening? *Arch Intern Med* 1997;157:873–81.
- Pierce JP, Fiore MC, Novotny TE, Hatziandreu EJ, Davis RM. Trends in cigarette smoking in the United States. Educational differences are increasing. *JAMA* 1989;261:56–60.
- Cummings SR, Melton LJ. Epidemiology and outcomes of osteoporotic fractures. *Lancet* 2002;359:1761–7.
- Karlamangla A, Zhou K, Reuben D, Greendale G, Moore A. Longitudinal trajectories of heavy drinking in adults in the United States of America. *Addiction* 2006;101:91–9.
- Lauderdale DS, Rathouz PJ. Does bone mineralization reflect economic conditions? An examination using a national US sample. *Econ Hum Biol* 2003;1:91–104.
- Wang MC, Dixon LB. Socioeconomic influences on bone health in postmenopausal women: findings from NHANES III, 1988–1994. *Osteoporos Int* 2006;17:91–8.
- Arabi A, Nabulsi M, Maalouf J, Choucair M, Khalife H, Vieth R, et al. Bone mineral density by age, gender, pubertal stages, and socioeconomic status in healthy Lebanese children and adolescents. *Bone* 2004;35:1169–79.
- Marwaha RK, Tandon N, Reddy DH, Mani K, Puri S, Aggarwal N, et al. Peripheral bone mineral density and its predictors in healthy school girls from two different socioeconomic groups in Delhi. *Osteoporos Int* 2007;18:375–83.
- del Rio Barquero L, Romera Baures M, Pavia Segura J, Setoain Quinquer J, Serra Majem L, Garces Ruiz P, et al. Bone mineral density in two different socioeconomic population groups. *Bone Miner* 1992;18:159–68.
- Demakakos P, Nazroo J, Breeze E, Marmot M. Socioeconomic status and health: the role of subjective social status. *Soc Sci Med* 2008;67:330–40.
- Adler NE, Epel ES, Castellazzo G, Ickovics JR. Relationship of subjective and objective social status with psychological and physiological functioning: preliminary data in healthy white women. *Health Psychol* 2000;19:586–92.
- Dienberg Love G, Seeman TE, Weinstein M, Ryff CD. Bioindicators in the MIDUS National Study: protocol, measures, sample, and comparative context. *J Aging Health* 2010;22:1059–80.
- Brim OG, Ryff CD, Kessler RC. How healthy are we? : a national study of well-being at midlife. Chicago: University of Chicago Press; 2004.
- Radler BT, Ryff CD. Who participates? Accounting for Longitudinal Retention in the MIDUS National Study of Health and Well-Being. *J Aging Health* 2010;22:307–31.
- Varena M, Binelli L, Zucchi F, Ghiringhelli D, Gallazzi M, Sinigaglia L. Prevalence of osteoporosis by educational level in a cohort of postmenopausal women. *Osteoporos Int* 1999;9:236–41.

- [21] Gruenewald TL, Karlamangla AS, Hu P, Stein-Merkin S, Crandall C, Koretz B, et al. History of socioeconomic disadvantage and allostatic load in later life. *Soc Sci Med* 2012;74(1):75–83 [Electronic publication ahead of print 2011 Nov 10. PubMed PMID: 22115943; PubMed Central PMCID: PMC3264490].
- [22] Riggs BL, Wahner HW, Dunn WL, Mazess RB, Offord KP, Melton III LJ. Differential changes in bone mineral density of the appendicular and axial skeleton with aging: relationship to spinal osteoporosis. *J Clin Invest* 1981;67:328–35.
- [23] Treloar AE. Menstrual cyclicity and the pre-menopause. *Maturitas* 1981;3:249–64.
- [24] National Institute on Alcohol Abuse and Alcoholism. Helping patient who drink too much: a clinician's guide updated 2005 edition. U.S. Department of Health and Human Services, National Institutes of Health, National Institute on Alcohol Abuse and Alcoholism; 2005.
- [25] Bernstein L, Patel AV, Ursin G, Sullivan-Halley J, Press MF, Deapen D, et al. Lifetime recreational exercise activity and breast cancer risk among black women and white women. *J Natl Cancer Inst* 2005;97:1671–9.
- [26] Friedenreich CM, Courneya KS, Bryant HE. The lifetime total physical activity questionnaire: development and reliability. *Med Sci Sports Exerc* 1998;30:266–74.
- [27] Grubb WN. The varied economic returns to postsecondary education — new evidence from the Class-of-1972 — Response. *J Hum Resour* 1995;30:222–8.
- [28] Muntaner C, Borrell C, Benach J, Pasarín MI, Fernandez E. The associations of social class and social stratification with patterns of general and mental health in a Spanish population. *Int J Epidemiol* 2003;32:950–8.
- [29] Backlund E, Sorlie PD, Johnson NJ. A comparison of the relationships of education and income with mortality: the national longitudinal mortality study. *Soc Sci Med* 1999;49:1373–84.
- [30] National Osteoporosis Foundation. Clinician's Guide to Prevention and Treatment of Osteoporosis. Washington, DC: National Osteoporosis Foundation; 2010. In.
- [31] Pearce MS, Birrell FN, Francis RM, Rawlings DJ, Tuck SP, Parker L. Lifecourse study of bone health at age 49–51 years: the Newcastle thousand families cohort study. *J Epidemiol Community Health* 2005;59:475–80.
- [32] Adams JS, Bishop N. DXA in adults and children. In: Rosen CJ, Compston JE, Lian JB, editors. *Primer on the metabolic bone diseases and disorders of mineral metabolism*. Seventh edition. Washington DC: American Society for Bone and Mineral Research; 2008.
- [33] Ott SM. Bone density in adolescents. *N Engl J Med* 1991;325:1646–7.
- [34] Mora S, Goodman WG, Loro ML, Roe TF, Sayre J, Gilsanz V. Age-related changes in cortical and cancellous vertebral bone density in girls: assessment with quantitative CT. *AJR Am J Roentgenol* 1994;162:405–9.
- [35] Nilsson M, Ohlsson C, Mellstrom D, Lorentzon M. Previous sport activity during childhood and adolescence is associated with increased cortical bone size in young adult men. *J Bone Miner Res* 2009;24:125–33.
- [36] Navarro MC, Sosa M, Saavedra P, Lainez P, Marrero M, Torres M, et al. Poverty is a risk factor for osteoporotic fractures. *Osteoporos Int* 2009;20:393–8.
- [37] Braveman PA, Cubbin C, Egerter S, Chideya S, Marchi KS, Metzler M, et al. Socioeconomic status in health research — one size does not fit all. *JAMA* 2005;294:2879–88.
- [38] Geyer S, Hemstrom O, Peter R, Vagero D. Education, income, and occupational class cannot be used interchangeably in social epidemiology. Empirical evidence against a common practice. *J Epidemiol Community Health* 2006;60:804–10.
- [39] Godfrey K, Walker-Bone K, Robinson S, Taylor P, Shore S, Wheeler T, et al. Neonatal bone mass: influence of parental birthweight, maternal smoking, body composition, and activity during pregnancy. *J Bone Miner Res* 2001;16:1694–703.
- [40] Evans GW. A multimethodological analysis of cumulative risk and allostatic load among rural children. *Dev Psychol* 2003;39:924–33.
- [41] Goodman E, McEwen BS, Huang B, Dolan LM, Adler NE. Social inequalities in biomarkers of cardiovascular risk in adolescence. *Psychosom Med* 2005;67:9–15.
- [42] Murali R, Chen E. Exposure to violence and cardiovascular and neuroendocrine measures in adolescents. *Ann Behav Med* 2005;30:155–63.
- [43] Miller GE, Chen E, Fok AK, Walker H, Lim A, Nicholls EF, et al. Low early-life social class leaves a biological residue manifested by decreased glucocorticoid and increased proinflammatory signaling. *Proc Natl Acad Sci U S A* 2009;106:14716–21.
- [44] Dennison E, Hindmarsh P, Fall C, Kellingray S, Barker D, Phillips D, et al. Profiles of endogenous circulating cortisol and bone mineral density in healthy elderly men. *J Clin Endocrinol Metab* 1999;84:3058–63.
- [45] Kann P, Laudes M, Piepkorn B, Heintz A, Beyer J. Suppressed levels of serum cortisol following high-dose oral dexamethasone administration differ between healthy postmenopausal females and patients with established primary vertebral osteoporosis. *Clin Rheumatol* 2001;20:25–9.
- [46] Reynolds RM, Dennison EM, Walker BR, Syddall HE, Wood PJ, Andrew R, et al. Cortisol secretion and rate of bone loss in a population-based cohort of elderly men and women. *Calcif Tissue Int* 2005;77:134–8.
- [47] Papanicolaou DA, Wilder RL, Manolagas SC, Chrousos GP. The pathophysiological roles of interleukin-6 in human disease. *Ann Intern Med* 1998;128:127–37.
- [48] Ganesan K, Teklehaimanot S, Tran TH, Asuncion M, Norris K. Relationship of C-reactive protein and bone mineral density in community-dwelling elderly females. *J Natl Med Assoc* 2005;97:329–33.
- [49] Krieger N, Okamoto A, Selby JV. Adult female twins' recall of childhood social class and father's education: a validation study for public health research. *Am J Epidemiol* 1998;147:704–8.
- [50] Robins LN, Schoenberg SP, Holmes SJ, Ratcliff KS, Benham A, Works J. Early home environment and retrospective recall: a test for concordance between siblings with and without psychiatric disorders. *Am J Orthopsychiatry* 1985;55:27–41.
- [51] Karp RJ, Shlomovich M, Bruno L. Diet and social disadvantage: the 'Medical Home' improves nutrition in childhood and diminishes likelihood of disease in adult life. *Maturitas* 2011;70:146–50.