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# Associations between Body Composition and Bone Density and Structure in Men and Women across the Adult Age Spectrum

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## Abstract

**Background/Purpose—**The objective of this study was identify independent associations between body composition and bone outcomes, including cortical structure and cortical and trabecular volumetric bone mineral density (vBMD) across the adult age spectrum.

**Methods—**This cross-sectional study evaluated over 400 healthy adults (48% male, 44% black race), ages 21–78 years. Multivariable linear regression models evaluated associations between whole-body DXA measures of lean body mass index (LBMI) and fat mass index (FMI) and tibia peripheral quantitative CT (pQCT) measures of cortical section modulus, cortical and trabecular vBMD and muscle density (as a measure of intramuscular fat), adjusted for age, sex, and race. All associations reported below were statistically significant ($p < 0.05$).

**Results—**Older age and female sex were associated with lower LBMI and muscle strength. Black race was associated with greater LBMI but lower muscle density. Greater FMI was associated with lower muscle density. Cortical section modulus was positively associated with LBMI and muscle strength and negatively associated with FMI. Adjustment for body composition eliminated the greater section modulus observed in black participants and attenuated the lower section modulus in females. Greater LBMI was associated with lower cortical BMD and greater

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**Conflicts of Interest**
The authors have no potential conflicts of interest to disclose.

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trabecular BMD. FMI was not associated with either BMD outcome. Greater muscle density was associated with greater trabecular and cortical BMD. Associations between body composition and bone outcomes did not vary by sex (no significant tests for interaction).

**Conclusions—**These data highlight age, sex- and race-specific differences in body composition, muscle strength and muscle density, and demonstrate discrete associations with bone density and structure. These data also show that age, sex- and race- related patterns of bone density and strength are independent of differences in body composition. Longitudinal studies are needed to examine the temporal relations between changes in bone and body composition.

### Keywords

DXA; lean mass; pQCT; section modulus; bone mineral density; muscle density

## Introduction

Body composition varies according to age, sex, and racial background, and contributes to the normal variability in bone structure and bone mineral density (BMD) among adults. Aging is associated with loss of muscle mass and quality, and age-related muscle loss is accompanied by fat gain in older adults [1]. It is well established that low body mass index (BMI) is a risk factor for osteoporosis and fracture [2]; however, studies of the independent contributions of lean mass and fat mass to bone health have yielded conflicting results. For example, an early dual energy x-ray absorptiometry (DXA) report from the Health, Aging, and Body Composition Study (Health-ABC) of men and women, ages 70 to 79 years, concluded that lean mass and fat mass were both positively associated with BMD, however, the associations varied according to sex, measurement site, and the index used to adjust for bone size [3]. A subsequent Women's Health Initiative study reported that femur BMD and cross-sectional area (CSA) were greater in women with higher BMI and values scaled in proportion to lean mass but not fat or total body mass [4]. More recent studies suggested differential effects of subcutaneous versus visceral fat mass. The majority of studies employing computed tomography (CT) measures of fat distribution demonstrated that visceral adipose tissue was negatively associated with BMD and bone structure [5–8].

The "functional muscle-bone unit" approach posits that bone adapts to the mechanical forces to which it is subjected in order to keep the bone strength at a constant set point [9]. A recent peripheral quantitative computed tomography (pQCT) study in men ages > 65 years, enrolled in the Osteoporotic Fractures in Men Study (MrOS) demonstrated that leg power and physical activity were positively associated with bone size and estimates of bone compressive strength [10]. Muscle metabolism may also affect bone health; fatty infiltration of muscle was associated with a higher risk of fracture in Health-ABC participants, independent of BMD, muscle CSA, and muscle strength [11, 12]. These data support the concept that differences in lean mass and muscle quality between subjects of varying age, sex, race, and total fat mass play a critical role in determining epidemiologic associations between these variables and bone outcomes, including fractures.

Prior studies of the functional muscle-bone unit and the impact of adiposity on BMD and bone structure were largely limited to elderly or adolescent participants, were frequently restricted to males or females, and usually did not examine race differences. A recent study demonstrated positive associations between skeletal muscle mass and bone density and structure at multiple skeletal sites; however, the cohort was > 96% white, and the study did not include measures of adiposity [13]. To our knowledge, no prior studies examined measures of volumetric BMD, cortical structure, body composition, muscle strength, and muscle density across the age range from young adults to the elderly in a multiethnic sample.



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This cross-sectional study in 500 adults, ages 21 to 78 years included DXA measures of whole body and regional lean and fat mass, tibia pQCT measures of muscle area, muscle density, trabecular and cortical volumetric BMD and cortical structure, and dynamometric measures of isometric muscle strength. The objectives were to (1) determine the effects of age, sex, and race on lean body mass, muscle strength, and muscle density, and (2) determine the effects of age, sex and race on trabecular and cortical BMD, cortical section modulus (a summary measure of cortical dimensions), and examine associations between body composition and bone outcomes.

## Material and Methods

### Study Setting and Participants

Adults, ages 21 to 78 years, were enrolled as healthy reference participants for bone studies at the Children's Hospital of Philadelphia (CHOP) and University of Pennsylvania (UPENN) between March of 2004 and June of 2008. Participants were recruited from UPENN internal medicine clinics and the surrounding community using flyers and newspaper advertisements. Exclusion criteria included a history of chronic diseases or medications known to affect nutrition or bone health, such as a reported history of diabetes, malabsorption syndromes, chronic kidney disease, liver disease, thyroid disease or malignancy. The protocols were approved by the Institutional Review Boards at CHOP and UPENN. Informed consent was obtained from all participants. A total of 90 participants less than 35 years of age were included in a prior study of bone and body composition in children and young adults [14].

Of the 500 total subjects, data were missing for section modulus (15 subjects), cortical density (15 subjects), trabecular density (20 subjects), muscle density (36 subjects), muscle strength (11 subjects), and body composition (43 subjects).

### Assessment of Anthropometrics and Race

Weight and height were measured using a digital scale (Scaltronix, White Plains, NY) and stadiometer (Holtain Ltd., Crymych, UK), respectively. Participants self-identified race according to National Institute of Health categories. Among 500 participants, 255 and 221 self-identified as black or white, respectively. The remaining 25 included 20 Asians, one Native American, and three Native Hawaiian or other Pacific Islander.

### Peripheral Quantitative Computed Tomography (pQCT)

Bone, muscle and fat measures in the left tibia were obtained by pQCT (Stratec XCT2000 12-detector unit, Orthometrix, Inc.) with a voxel size of 0.4 mm, slice thickness of 2.3 mm, and scan speed of 25 mm/sec. All scans were analyzed with Stratec software version 6.00. A scout view was obtained to place the reference line at the proximal border of the distal endplate. The bone measurements were obtained at 3% and 38% of tibia length proximal to the reference line. At the 3% metaphyseal site, scans were analyzed for trabecular volumetric BMD ($mg/cm^3$) with contour mode 3 threshold 169 $mg/cm^3$, and peel mode 4 threshold 650 $mg/cm^3$ with an additional 10% concentric peel. At the 38% diaphyseal site, scans were analyzed for cortical volumetric BMD ($mg/cm^3$) using a threshold of 710 $mg/cm^3$ to separate bone from soft tissue. Polar section modulus ($mm^3$) was defined using a threshold of 480 $mg/cm^3$. Section modulus provides a composite measure of the effects of cortical periosteal and endosteal dimensions on fracture load [15]. Calf muscle and subcutaneous fat CSA ($mm^2$) were assessed 66% proximal to the distal physis using threshold 40 $mg/cm^3$ for fat/lean separation and 711 $mg/cm^3$ for lean/bone separation. Quality control was monitored daily using a phantom. The *in vivo* coefficient of variation (CV) ranged from 0.5–1.6% for pQCT outcomes.

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The pQCT measure of muscle density (mg/cm$^3$) was used as a composite index of intra and extra-myocellular fat content, as previously described [11, 16]. Prior studies have documented that skeletal muscle attenuation determined by CT was associated with skeletal muscle lipid content on tissue biopsy,[17] and pQCT studies of muscle density demonstrated significant associations with insulin resistance, independent of total body and subcutaneous fat[18]. Edge-detection and threshold techniques were used to separate tissues (fat, muscle, and bone) based on attenuation characteristics that are directly related to tissue composition and density [17, 19]. Images were filtered prior to being analyzed using contour mode 3 (−101 mg/cm$^3$) to find skin, and peel mode 2 (40 mg/cm$^3$) to separate adipose and muscle/bone, respectively. Images were filtered subsequently with a combination 3×3, and double 5×5 kernal image filter that clearly defined the edge of the muscle using contour mode 31 (40 mg/cm$^3$). All bone was identified using a threshold of 150 mg/cm$^3$ and mathematically removed to generate results for muscle density. The CV for muscle density using this method was 0.9% [16].

### Dynamometric Measurement of Muscle Strength

Muscle strength was assessed using Biodex Multi-Joint System 3 Pro Dynamometer (Biodex Medical Systems, Inc, Shirley, NY). High intra-rater (0.97 to 0.99) and inter-rater (0.93 to 0.96) intra-class correlation coefficients have been reported [20]. Peak isometric torque [Newton-meters (N-m)] was measured in triplicate at −10, 0, 10, and 20 degrees and the highest value recorded for both dorsiflexion and plantarflexion. We report strength as peak isometric torque (ft-lbs) in dorsiflexion (with the foot placed in 20 degrees of plantarflexion), since this measurement had the best reproducibility in our lab (coefficient of variation, 4.3%) and had the best fit ($R^2$) in prior regression models [21]. Further, the tibialis anterior attaches directly to the tibia (the bone of interest in this study) and causes dorsiflexion of the ankle.

### Whole-Body Dual Energy X-Ray Absorptiometry (DXA)

Whole-body fat mass and lean mass were assessed by DXA using a Hologic densitometer (Delphi Systems, Hologic, Inc., Bedford, MA). The measurements were performed in the array mode using standard positioning techniques. Quality control scans were performed daily using a simulated L1–4 lumbar spine made of hydroxyapatite encased in epoxy resin. In our institution, the in vitro coefficient of variation was less than 0.6% and the in vivo coefficient of variation in adults was less than 1% [22]. Fat mass and lean body mass were converted to fat mass index (FMI, kg/m$^2$) and lean body mass index (LBMI, kg/m$^2$) using height. The decision to use body composition indices was based on the observation women had greater tibia length relative to height (compared with men) and black participants had greater tibia length relative to height (compared with non-black participants). We concluded that adjusting for tibia length or height alone would not adequately characterize these effects, potentially resulting in residual confounding in bone models that included measures of body composition.

### Physical Activity Questionnaire

Physical activity was assessed using a detailed questionnaire developed for the Multi-Ethnic Study of Atherosclerosis (MESA) [23]. The MESA physical activity questionnaire uses 28 questions to assess physical activity during a typical week in the past month in a number of domains. Participants report the number of days per week and the number of hours and/or minutes per day the activity was performed. Each activity included in the questionnaire has an assigned metabolic equivalent level from the Compendium of Physical Activities. The intra-class correlations compare favorably with other accepted and commonly used physical activity surveys [24]. We used a definition of intentional exercise (the sum of walking for exercise, sports/dancing, and conditioning MET-hours/week) that has been previously

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defined [25]. The variable was highly skewed, therefore, results were considered in three categories: data were categorized as either no intentional exercise, or as above or below the median number of MET-hours/week among those reporting intentional exercise.

### Statistical Analysis

Statistical analysis was performed using Stata 11 software (*StataCorp, College Station, TX).* Differences in means were assessed using Student's *t* test or the Wilcoxon rank sum test as appropriate. Group differences in categorical variables were assessed using the $\chi^2$ test.

Natural log transformations resulted in linear relations between tibia length and cortical section modulus, muscle CSA, and muscle strength; therefore, these measures were log transformed in all analyses. The correlations (R) between log transformed tibia length and musculoskeletal outcomes were 0.67 for section modulus, 0.33 for muscle area, and 0.44 for muscle strength (all $p<0.001$); therefore, all multivariable models incorporating these outcomes were adjusted for tibia length.

Linear regression models of muscle outcomes (DXA LBMI, pQCT muscle density, and isometric muscle strength) evaluated the independent effects of age, sex, race, DXA FMI, and physical activity. Linear regression models of bone outcomes (cortical section modulus, cortical BMD and trabecular BMD) first examined associations with age, sex and race, and then subsequent models evaluated the independent associations with LBMI, FMI, muscle density, muscle strength, and physical activity. Beta coefficients were converted to standardized coefficients (difference in outcome per every 1 standard deviation difference in the independent variable). Scatter plots were created to illustrate observed associations between body composition and bone outcomes. Multiplicative interaction terms were used to assess interactions between age and sex, age and race, and sex and race for all muscle and bone outcomes. Multiplicative interaction terms were also used to determine if the muscle-bone relations varied according to age, sex and race. Repeated analyses stratified by gender confirmed the study findings.

Multiple comparisons were performed across numerous correlated bone and body composition outcomes. A Bonferroni correction is not appropriate since it assumes the outcomes are independent. Therefore, we interpreted isolated findings with caution and examined the consistency of the overall results.

## Results

### Subject Characteristics

The participant characteristics are summarized in Table 1 according to sex and race. Black women had significantly greater BMI and FMI, compared to all other groups. Within males and females, tibia length was significantly greater in blacks compared with non-blacks ($p<0.001$), relative to height.

### Muscle Outcomes

Table 2 summarizes the multivariable models for DXA whole body LBMI, pQCT muscle density, and muscle strength. LBMI was lower in older participants and women, greater in blacks, and positively associated with FMI (Table 2). The greater LBMI among black participants was significantly less pronounced among women (test for interaction, $p<0.05$), compared with men. Tests for age-by-sex and age-by-race interactions were not significant.

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Muscle density was significantly lower in older adults, women and blacks. However, in models adjusted for FMI (Table 2) muscle density did not differ according to sex. Greater FMI was significantly associated with lower muscle density.

Muscle strength was significantly lower in older participants and females in models adjusted for LBMI, but did not vary significantly according to race (Table 2). Greater LBMI was positively associated with muscle strength and greater FMI was negatively associated with muscle strength. When pQCT muscle CSA was substituted for DXA LBMI in the muscle strength models, similar results were observed.

Reported exercise was not associated with LBMI, muscle strength, or muscle density in any of the models described above.

## Cortical Section Modulus

Table 3 summarizes the model for cortical section modulus, adjusted for age, sex, race and tibia length (Model 1) with sequential adjustment for muscle and fat covariates (Models 2–4). In Model 1, female sex was associated with a lower section modulus with a significant interaction with age, indicating that the difference between men and women was more pronounced with greater age. The positive β-coefficient for age indicates that section modulus is greater in older males. Section modulus was significantly greater in black, compared with non-black participants. The adjustment for tibia length confirmed that the lower section modulus in females was independent of their significantly shorter tibia length, and the greater section modulus in black participants was independent of their greater tibia length. Figure 1 demonstrates the association between observed section modulus and age, according to sex and race.

Model 2 demonstrates that greater LBMI was strongly associated with greater section modulus, and adjustment for LBMI markedly attenuated the race differences observed in Model 1. In Model 3, LBMI and muscle strength, but not muscle density, were independently and positively associated with section modulus. Similar results were obtained when pQCT muscle CSA was substituted for DXA LBMI ($R^2 = 0.71$, model not shown). The association between DXA LBMI and section modulus was similar in men and women; however, the association was slightly attenuated among black participants [Interaction β: −0.038 (−0.068, −0.0090) p=0.01], compared with non-black participants.

Model 4 incorporated measures of fat mass, demonstrating that greater FMI was associated with significantly lower section modulus, while greater LBMI and muscle strength were independently associated with greater section modulus. Similar results were obtained when pQCT muscle and subcutaneous fat CSA, or BMI were substituted for DXA LBMI and FMI ($R^2 = 0.71$). Figure 2a illustrates the unadjusted opposing associations of fat mass and lean mass with cortical section modulus using DXA FMI and LBMI. Figure 2b illustrates unadjusted associations of pQCT muscle and subcutaneous fat CSA with section modulus.

## Cortical and Trabecular BMD

Table 4 summarizes the models for cortical and trabecular BMD, adjusted for age, sex, race, with subsequent adjustment for muscle and fat covariates. In the first model, cortical BMD was greater in females, and declined with age in females only (age-sex interaction p<0.001). This interaction demonstrated that post-menopausal females had lower cortical density than men. Within females, the inverse association of cortical BMD with age was greater among post-menopausal women compared with pre-menopausal women (interaction term p<0.01). Cortical BMD was greater in black men compared to non-black men, but this race effect was not present among females (interaction p < 0.001).

The second cortical BMD model examined associations with body composition. Greater LBMI was associated with significantly lower cortical BMD. Similar results were obtained when pQCT muscle CSA was substituted for DXA LBMI (model $R^2$=0.30). Muscle strength and physical activity were not associated with cortical BMD with or without adjustment for measures of muscle mass (DXA FMI or pQCT muscle CSA). Greater muscle density was associated with greater cortical BMD. LBMI did not modify the association of cortical BMD with sex or race.

Trabecular BMD was lower in older participants and was lower in females (Table 4). The impact of age did not vary according to sex. Black race was associated with lower trabecular BMD in men, but not women (interaction $p < 0.001$). The second trabecular BMD model examined the effect of body composition. Greater LBMI was significantly associated with greater trabecular BMD; however, FMI was not. Greater reported exercise and greater muscle density were also associated with greater trabecular BMD. In contrast, muscle strength was not associated with trabecular BMD, independent of age, sex, and race effects. LBMI did not modify the association of cortical BMD with sex or race.

## Discussion

These data demonstrated distinct associations between body composition and cortical dimensions, trabecular BMD and cortical BMD (summarized in Table 5). Greater LBMI and muscle strength were independently associated with greater section modulus, while greater FMI was associated with lower section modulus after adjustment for LBMI. Travison, et al reported a positive effect of LBMI and negative effect of FMI on DXA-based estimates of cortical structure in the proximal femur in men [26]. Similar to our results, the study demonstrated that adjustment for lean mass significantly attenuated the greater cortical dimensions observed in black participants. Our study extends these findings to women, and is strengthened by the use of three-dimensional QCT methods to measure cortical dimensions. Furthermore, our data demonstrated that age was inversely associated with section modulus in women only, and this sex effect was not explained by sex- or age- related differences in LBMI.

The mechanisms underlying the association between greater LBMI and superior cortical dimensions and trabecular BMD have not been established; potential mediators include mechanical and biologic signals [27–31]. Sex steroids (estrogen and testosterone) and other hormonal signaling pathways, including growth hormone and insulin-like growth factors, have been implicated [13, 32, 33]. Physical forces applied to bone may also regulate bone modeling through mechanical signals including mechanical receptors and hemichannels on osteocytes [34, 35]. Finally, other, more novel biologic mechanisms are being studied including sclerostin [36], myokines [29, 37], and muscle-derived progenitor cells [38].

The mechanism for the negative association between FMI and cortical dimensions is not known. Gilsanz, et al recently used QCT to measure cortical dimensions in the femur, and visceral and subcutaneous adipose tissue in the abdomen in young women, ages 15 to 25 years. In multivariate models, thigh muscle and abdominal subcutaneous fat CSA were positively associated with cortical dimensions while visceral fat CSA was negatively associated with cortical area. Visceral adiposity is associated with increased levels of inflammatory cytokines that may have adverse effects on bone metabolism [39]. A recent longitudinal study in elderly adults demonstrated that, although greater fat mass was associated with greater lean mass at baseline, greater fat mass was associated with greater declines in leg lean mass over an 8-year period [1]. Therefore, the negative effect of FMI on section modulus observed here may reflect declines in muscle mass. Longitudinal studies are



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needed to assess the independent effects of changes in lean mass, visceral fat, and subcutaneous fat on changes in cortical dimensions in adults.

Our study showed that cortical BMD was greater in females, compared with males, and declined with age to a greater extent in females. These data extend our observation that female sex was associated with greater cortical BMD in children, adolescents and young women (age < 30 years) [14]. This is also consistent with estrogen effects on bone turnover and cortical density. Greater LBMI was associated with lower cortical BMD. Since calcium apatite is primarily important in resisting compression, and the primary role of cortical bone is to resist torque, less mineralized cortical bone may not always represent an adverse outcome [40]. In individuals with greater LBMI, less dense cortical bone may be evidence of greater ductility which is compensated to absorb energy through greater compliance [41].

Trabecular BMD was lower in females than males and declined with age. After multivariable adjustment, trabecular BMD was positively associated with LBMI, but not FMI. These data confirm similar observations made recently by LeBrasseur et al. This group also utilized high-resolution techniques to show subjects with greater appendicular muscle mass index had greater trabecular number and thickness. PQCT measures of trabecular compartment BMD do not distinguish between trabecular bone volume fraction and material BMD. This may explain the opposing associations of LBMI with cortical (lower material density) and trabecular (lower material density but greater trabecular microarchitecture) BMD.

While our data do not support an additional independent association of total FMI with trabecular or cortical BMD, we found that muscle density (an inverse correlate of intramuscular fat) was independently associated with BMD. This supports previous data pointing to the importance of fat distribution. These findings are similar to results in a recent study of adolescent girls [16]. Previously reported associations between muscle density at the thigh and subsequent fracture risk [11] could thus be related to greater mineralization of bone in those with greater muscle density. Low muscle density may be associated with greater visceral fat and clinical comorbidities such as insulin resistance and the metabolic syndrome [18]. Fracture risk could be increased in these participants through associations with these comorbidities. Lang et al. noted that inclusion of clinical comorbidities attenuated the association between muscle density and fracture risk [11]. Further study is needed to further clarify the mechanism by which muscle density is associated with cortical and trabecular density and with fracture risk. In contrast to the study in young girls [16], we found that lower muscle density (greater intramuscular fat) was not associated with cortical dimensions (section modulus), adjusted for LBMI and muscle strength among adults.

Prior DXA based studies suggested that the relations between lean mass and bone outcomes (bone mineral content or areal BMD) differed according to sex [42, 43]. Ferretti, et al hypothesized that estrogen modified the mechanical set-point for bone remodeling in response to biomechanical loads [42]. LeBrasseur also found evidence of an interaction between sex and muscle on pQCT bone outcomes [13]. Our analyses did not provide evidence of a sex-muscle interaction in the models for cortical section modulus, cortical BMD or trabecular BMD. For example, the highly significant positive association between LBMI and section modulus did not differ significantly between males and females in the multivariate models adjusted for age, race, muscle strength, and tibia length. Possible explanations for our different results include different age of subjects and the use of different measurement sites and techniques. In addition, differences in the statistical methods may have contributed to the observed differences. The use of ratios to assess bone mineral content – lean mass relations does not incorporate adjustments for sex differences in tibia lengths, and potentially introduces statistical errors since muscle area and bone

measures do not scale isometrically [44]. In our dataset, no interaction was identified after adjusting for sex differences in tibia length. Our observations among adult participants across the age spectrum confirm our previous findings in children, adolescents and young adults [14].

The greatest limitation of this study is the cross-sectional design. Longitudinal studies are needed to establish the temporal relations between body composition and bone density and structure. The fracture implications of these findings are not known and measures in the tibia may not reflect bone strength at the hip or other sites. PQCT does not have sufficient resolution to assess trabecular microarchitecture or cortical porosity. Additional limitations include lack of dietary intake and measures of vitamin D, parathyroid hormone, sex hormones, and growth factors (such as IGFBP-2) [13] to potentially explain the age, sex and race differences in BMD and dimensions. Last, visceral fat may have distinct effects on bone and these data were not available. However, to our knowledge, this is the first study to examine relations of fat and lean mass with bone density and structure in a diverse sample of men and women from young adulthood through the elderly. These data highlight age, sex- and race-specific differences in body composition, muscle strength and muscle density, and demonstrated discrete associations with bone density and structure.

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## Abbreviations

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| **BMD** | bone mineral density |
| **BMI** | body mass index |
| **DXA** | dual energy x-ray absorptiometry |
| **CSA** | cross-sectional area |
| **CT** | computed tomography |
| **pQCT** | peripheral quantitative computed tomography |
| **MrOS** | Osteoporotic Fractures in Men Study |
| **CHOP** | Children’s Hospital of Pennsylvania |
| **UPENN** | University of Pennsylvania |
| **N-m** | Newton-meters |
| **CV** | coefficient of variation |
| **FMI** | fat mass index |
| **LBMI** | lean body mass index |
| **MESA** | Multi-ethnic Study of Atherosclerosis |

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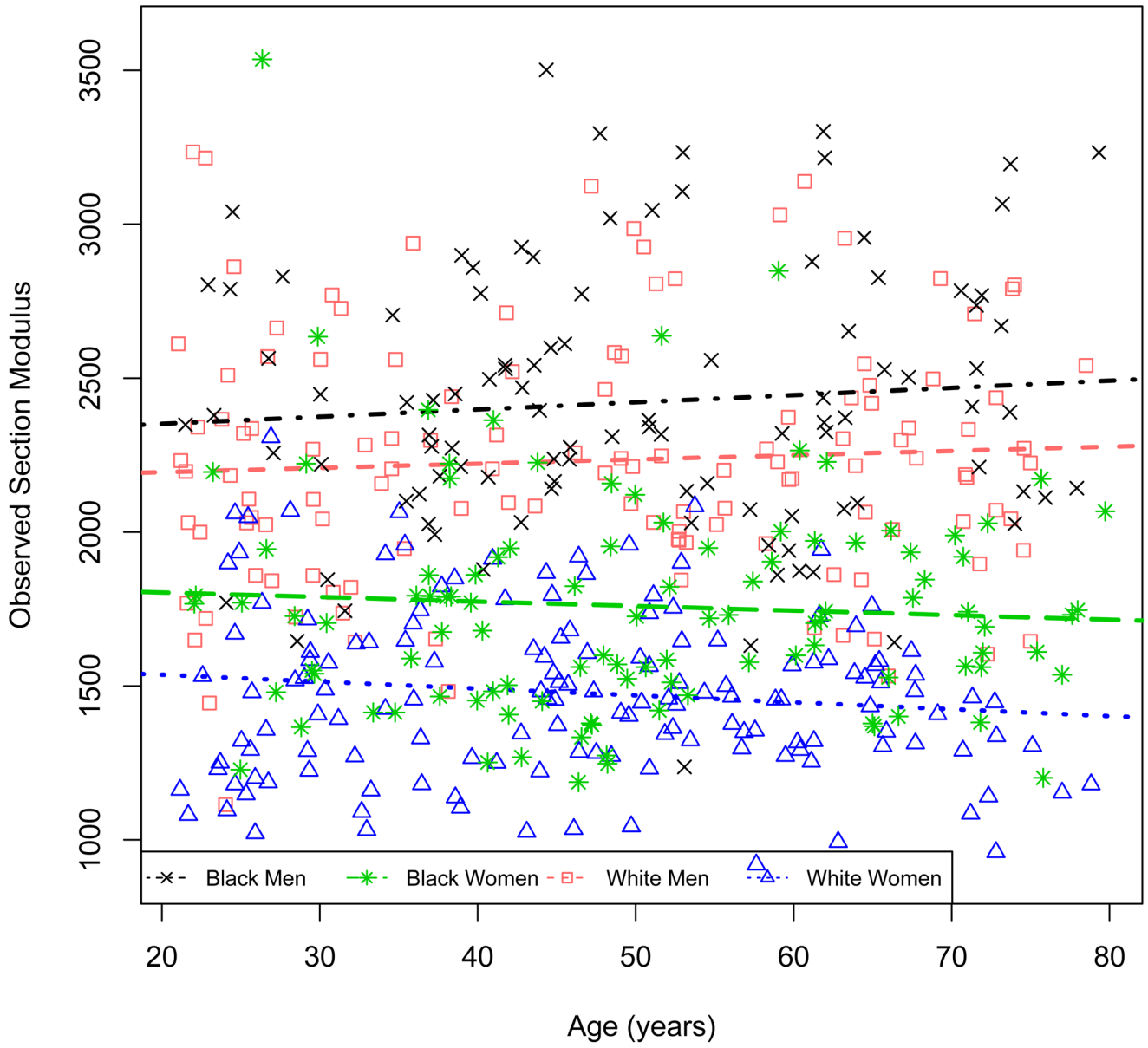
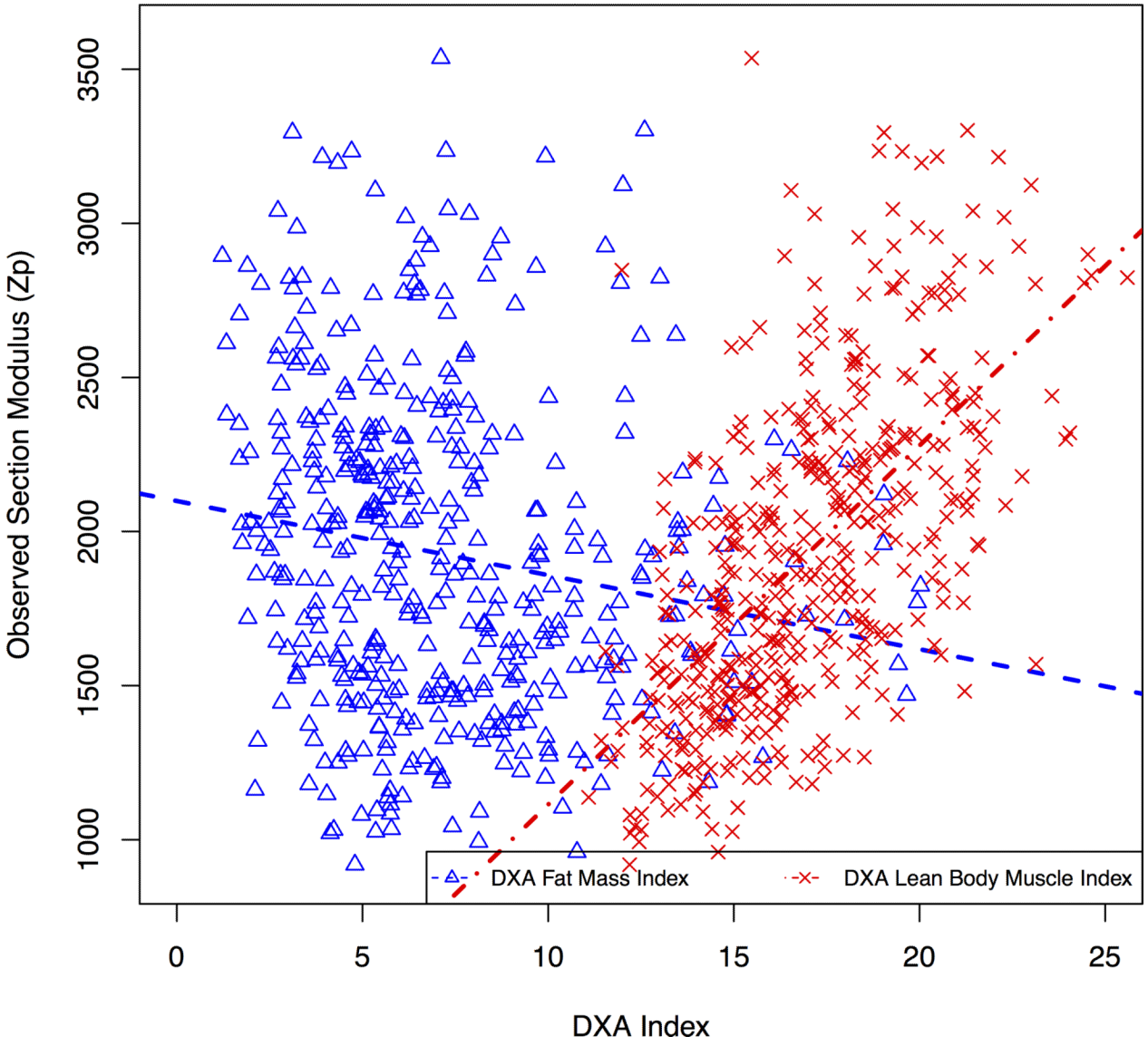



**Figure 1.**
Age-related differences in section modulus by sex and race group.

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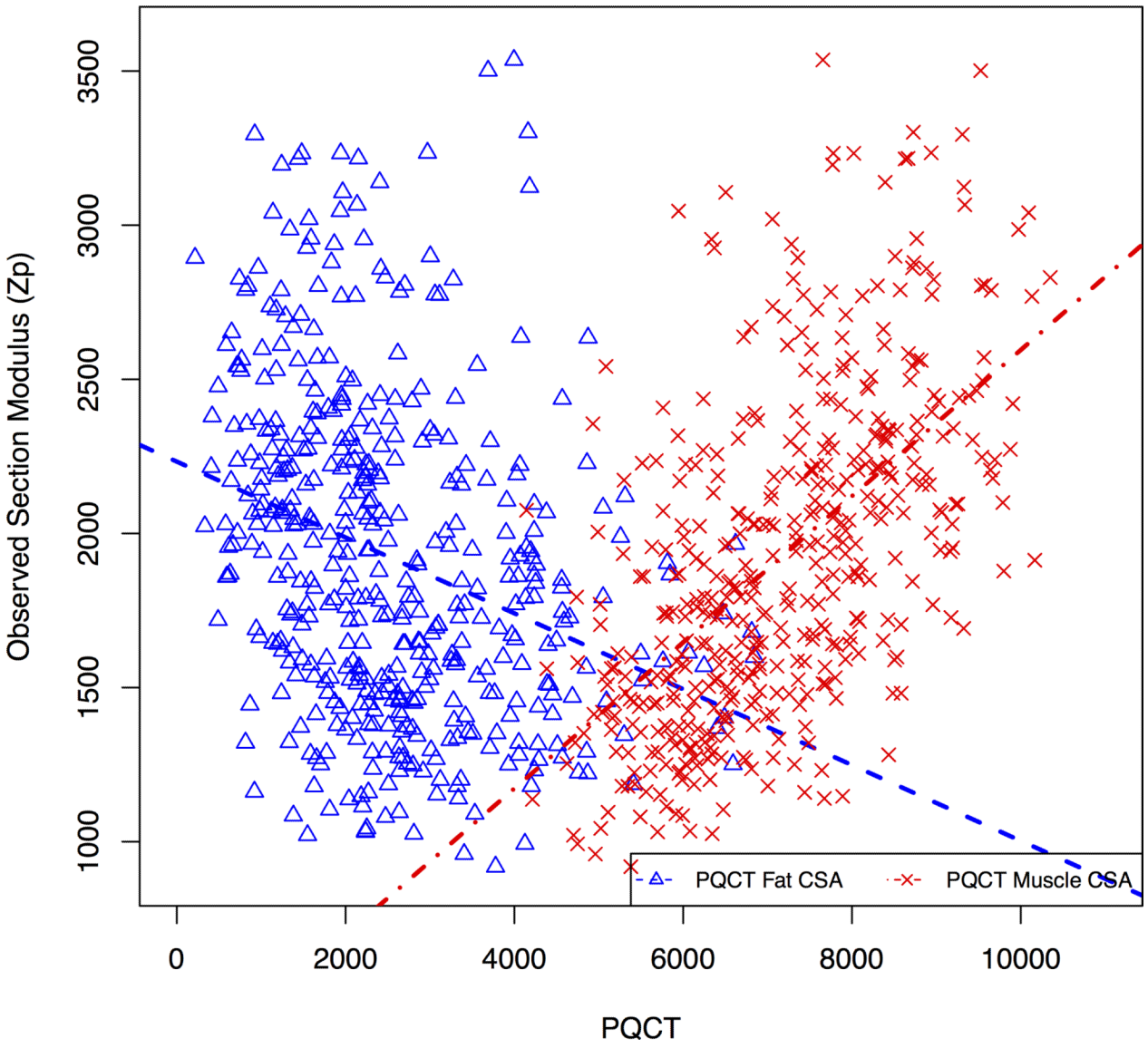


**Figure 2.**
Associations between predicted cortical section modulus and (a) DXA measures of LBMI and FMI, and (b) pQCT measures of muscle and subcutaneous fat CSA.

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## Table 1

Participant Characteristics According to Sex and Race

| | Males | | Females | |
|---|---|---|---|---|
| | **Non-Black** | **Black** | **Non-Black** | **Black** |
| **N** | 130 | 109 | 150 | 111 |
| **Age (yrs)** | 46.8 (17.8) | 49.7 (15.2) | 46.3 (15.1) | 50.0 (15.4) |
| **Post-menopausal** | N/A | N/A | 63 (42%) | 61 (55%) |
| **Height (m)** | 1.77 (0.07) | 1.75 (0.07) | 1.64 (0.07) | 1.64 (0.07) |
| **Weight (kg)** | 82.6 (14.5) | 82.6 (15.1) | 65.2 (13.8) | 80.5 (18.2) |
| **BMI ($kg/m^2$)** | 25.5 (23.0, 27.8) | 26.7 (23.4, 29.5) | 23.0 (20.4, 26.4) | 27.5 (24.7, 32.6) |
| **Tibia length (mm)** | 410 (394, 423) | 421 (401, 436) | 372 (356, 389) | 394 (376, 410) |
| **Calf muscle CSA ($mm^2$)** | 80.7 (74.0, 87.0) | 77.5 (68.6, 87.7) | 63.4 (57.2, 70.7) | 64.0 (58.1, 73.0) |
| **Muscle strength (N-m)** | 40.5 (33.9, 43.7) | 40.3 (33.5, 45.4) | 25.5 (20.7, 29.3) | 25.6 (22.1, 32.1) |
| **Calf muscle density ($mg/cm^3$)** | 75.5 (74.0, 76.4) | 75.3 (72.9, 76.5) | 75.2 (73.9, 76.4) | 73.7 (71.7, 75.0) |
| **Whole body LBMI ($kg/m^2$)** | 18.4 (2.3) | 18.9 (2.5) | 14.9 (2.0) | 16.4 (2.3) |
| **Whole body FMI ($kg/m^2$)** | 5.8 (2.9) | 5.4 (2.4) | 7.4 (3.2) | 10.6 (4.0) |
| **Trabecular BMD ($mg/cm^3$)** | 264 (236, 293) | 244 (215, 265) | 222 (203, 245) | 231 (209, 257) |
| **Cortical BMD ($mg/cm^3$)** | 1176 (1157, 1196) | 1200 (1182, 1211) | 1203 (1182, 1219) | 1201 (1172, 1220) |
| **Cortical section modulus ($mm^3$)** | 2230 (1110, 3230) | 2420 (1240, 3500) | 1480 (919, 2310) | 1760 (1190, 3540) |
| **Regular exercise (n, %)** | 113 (87%) | 87 (80%) | 135 (90%) | 90 (81%) |
| **Exercise (MET-hr/week)** | 31 (10.5, 72) | 32.7 (5.5, 99.8) | 24.5 (10.5, 52.8) | 24.5 (5.3, 65.5) |

Results are presented as mean (SD) for normally distributed data and median (inter-quartile range) for skewed data.

CSA: cross-sectional area

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## Table 2

Multivariable Linear Regression Models of Muscle Outcomes

| | DXA LBMI ($R^2$ = 0.63) N = 457 | pQCT Muscle Density ($R^2$ = 0.43) N = 417 | Muscle Strength ($R^2$ = 0.41) N = 417 |
|---|---|---|---|
| | β (95% CI) | β (95% CI) | β (95% CI) |
| **Age** | −0.51 (−0.68, −0.35) *c* | −0.014 (−0.017, −0.012) *c* | −0.069 (−0.10, −0.035) *c* |
| **Female sex** | −1.70 (−1.85, −1.55) *c* | −0.00079 (−0.0091, 0.0076) | −0.14 (−0.25, −0.035) *b* |
| **Black race** | 0.84 (0.38, 1.30) *c* | −0.0073 (−0.012, −0.0022) *b* | −0.030 (−0.094, 0.034) |
| **Black race * Female** | −0.67 (−1.33, −0.015) *a* | -- | -- |
| **FMI** | 1.80 (1.61, 1.99) *c* | −0.012 (−0.015, −0.0080) *c* | −0.072 (−0.12, −0.025) *b* |
| **LBMI** | -- | 0.00052 (−0.0034, 0.0044) | 0.12 (0.071, 0.17) *c* |
| **Muscle Density** | -- | -- | 0.65 (−0.50, 1.79) |
| **Tibia Length** | -- | -- | 0.080 (0.044, 0.12) *c* |

Results are presented as standardized beta-coefficients for continuous variables (effect per 1 SD). Tibia length, muscle strength, and muscle density were log-transformed in all models.

*a* p<0.05,

*b* p<0.01,

*c* p<0.001

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**Table 3**

Multivariable Models Assessing the Impact of Muscle and Fat Covariates on Natural Log-Transformed Cortical Section Modulus.

| | Section Modulus Model 1 $R^2$ = 0.64 N = 405 | Section Modulus Model 2 $R^2$ = 0.71 N = 405 | Section Modulus Model 3 $R^2$ = 0.72 N= 405 | Section Modulus Model 4 $R^2$ = 0.73 N = 405 |
|---|---|---|---|---|
| | **β (95% CI)** | **β (95% CI)** | **β (95% CI)** | **β (95% CI)** |
| **Age** | 0.020 (−0.0029, 0.042) | 0.030 (0.010, 0.051) [b] | 0.036 (0.013, 0.058) [b] | 0.040 (0.017, 0.062) [b] |
| **Female sex** | −0.16 (−0.27, −0.058) [b] | −0.018 (−0.11, 0.079) | 0.00062 (−0.098, 0.099) | 0.066 (−0.034, 0.17) |
| **Female * Age** | −0.038 (−0.070, −0.0048) [a] | −0.050 (−0.080, −0.021) [b] | −0.051 (−0.080, −0.023) [c] | −0.049 (−0.078, −0.021) [b] |
| **Black race** | 0.065 (0.030, 0.10) [c] | 0.022 (0.010, 0.054) [a] | 0.023 (−0.0089, 0.056) | 0.021 (−0.010, 0.053) |
| **Tibia length** | 0.10 (0.084, 0.12) [c] | 0.11 (0.088, 0.12) [c] | 0.10 (0.083, 0.12) [c] | 0.11 (0.088, 0.12) [c] |
| **LBMI** | -- | 0.095 (0.077, 0.11) [c] | 0.090 (0.071, 0.11) [c] | 0.12 (0.098, 0.14) [c] |
| **Muscle strength** | -- | -- | 0.026 (0.0074, 0.045) [b] | 0.021 (0.0022, 0.040) [a] |
| **Muscle density** | -- | -- | −0.0035 (−0.022, 0.015) | −0.015 (−0.034, 0.0040) |
| **FMI** | -- | -- | -- | −0.049 (−0.072, −0.026) [c] |

Results are presented as standardized beta-coefficients for continuous variables (effect per 1 SD). Tibia length, muscle strength, and muscle density, were log-transformed in all models.

[a] p <0.05,

[b] p<0.01,

[c] p<0.001

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**Table 4**

Multivariable Models of Log-Transformed Cortical and Trabecular BMD

| | Cortical BMD Model 1 $R^2$ = 0.23 N = 415 | Cortical BMD Model 2 $R^2$ = 0.27 N = 415 | Trabecular BMD Model 1 $R^2$ = 0.21 N = 411 | Trabecular BMD Model 2 $R^2$ = 0.27 N = 411 |
|---|---|---|---|---|
| | | β (95% CI) | | β (95% CI) |
| **Age** | −0.0036 (−0.0070, −0.00020) [a] | −0.0017 (−0.0054, 0.0021) | −0.044 (−0.059, −0.029) [c] | −0.028 (−0.045, −0.011) [c] |
| **Female sex** | 0.053 (0.038, 0.069) [c] | 0.048 (0.032, 0.065) [c] | −0.16 (−0.20, −0.12) [c] | −0.11 (−0.16, −0.056) [c] |
| **Female sex * Age** | −0.012 (−0.017, −0.0073) [c] | −0.012 (−0.017, −0.0072) [c] | -- | -- |
| **Black race** | 0.019 (0.012, 0.026) [c] | 0.014 (0.0089, 0.019) [c] | −0.088 (−0.13, −0.045) [c] | −0.088 (−0.13, −0.046) [c] |
| **Female sex * Black race** | −0.017 (−0.026, −0.0067) [c] | −0.013 (−0.023, −0.0026) [a] | 0.12 (0.060, 0.18) [c] | 0.10 (0.045, 0.16) [c] |
| **LBMI** | | −0.0044 (−0.0077, −0.00046) [a] | | 0.044 (0.021, 0.067) [c] |
| **Muscle strength** | | -- | | -- |
| **Muscle density** | | 0.0044 (0.0012, 0.0076) [b] | | 0.033 (0.014, 0.052) [c] |
| **FMI** | | −0.00047 (−0.0044, 0.0036) | | 0.015 (−0.0086, 0.039) |
| **Exercise (v. 0 MET-hr/wk)** | | | | |
| **<27 MET-hr/wk** | | 0.0018 (−0.0059, 0.0094) | | 0.048 (0.0036, 0.093) [a] |
| **≥27 MET-hr/wk** | | 0.0014 (−0.0060, 0.0088) | | 0.054 (0.011, 0.098) [a] |

Results are presented as standardized beta-coefficients for continuous variables (effect per 1 SD). Tibia length, muscle strength, and muscle density, were log-transformed in all models.

[a] p≤0.05,

[b] p<0.01,

[c] p<0.001

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## Table 5

Summary of Associations between Body Composition and Bone Outcomes

| | **Section Modulus Model 4 $R^2$ = 0.73 N = 405** | **Cortical BMD Model 2 $R^2$ = 0.27 N = 415** | **Trabecular BMD Model 2 $R^2$ = 0.27 N = 411** |
|---|---|---|---|
| | **β (95% CI)** | **β (95% CI)** | **β (95% CI)** |
| **Age** | Positive in men | Negative | Negative |
| **Female sex and age effects** | Lower in females and the sex differences are more pronounced with greater age | Greater in younger females but the decline with age is more pronounced in females. Lower in post-menopausal women compared with men | Lower in females |
| **Black race and sex effects** | Greater in blacks compared with non-blacks; however these differences are eliminated with adjustment for LBMI | Greater in black men compared with non-black men | Lower in black men |
| **Tibia Length** | Positive | NS | NS |
| **LBMI** | Positive | Negative | Positive |
| **Muscle Strength** | Positive | NS | NS |
| **Muscle Density** | NS | Positive | Positive |
| **FMI** | Negative | NS | NS |
| **Exercise (v. 0 MET-hr/wk)** | | | |
| **<27 MET-hr/wk** | NS | NS | Positive |
| **≥27 MET-hr/wk** | NS | NS | Positive |