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Optimal Serum Cholesterol Concentrations are Associated with Accelerated Bone Loss in African Ancestry Men

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Abstract

Purpose—Studies of lipid and lipoprotein cholesterol associations with bone mineral density (BMD) and bone loss have been inconclusive, and longitudinal data are sparse. Therefore, the aim of this study was to test if fasting serum lipid and lipoprotein cholesterol levels are associated with areal and volumetric BMD and BMD change,

Methods—We determined the association of serum triglycerides, high-density lipoprotein (HDL) and low-density lipoprotein (LDL) cholesterol concentrations with cross-sectional and longitudinal (mean follow-up: 6.1 years) measures of BMD in a cohort of 1289 in African ancestry men (mean age: 56.4 years). Fasting serum triglycerides, HDL and LDL were measured at baseline concurrent with BMD assessments. Dual-energy X-ray absorptiometry was used to quantify integral hip BMD and peripheral quantitative computed tomography at the radius and tibia was used to quantify volumetric BMD. Men were categorized as optimal, borderline or high-risk for triglyceride, HDL and LDL concentrations based on adult treatment panel III guidelines.

Results—Lower serum triglyceride or LDL and higher HDL concentrations were associated with lower trabecular BMD at baseline (all $p < 0.05$). Similarly, men classified as having optimal levels of LDL, HDL or triglycerides at baseline experienced the greatest integral BMD loss at the hip and trabecular BMD loss at the tibia (all $p < 0.05$), independent of potential confounding factors.

Conclusions—We found that clinically optimal serum lipid and lipoprotein cholesterol concentrations were associated with accelerated bone loss among Afro-Caribbean men. Further studies are needed to better understand the mechanisms involved and potential clinical significance of these findings.

Keywords

lipids; lipoproteins; cholesterol; triglycerides; bone mineral density; African ancestry

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INTRODUCTION

Serum lipid and lipoprotein cholesterol levels are well-established risk factors for cardiovascular diseases[1]. A high serum level of low-density lipoprotein cholesterol (LDL-c) and triglycerides or low high-density lipoprotein cholesterol (HDL-c) beyond the recommended clinical guidelines confers an increased risk of coronary heart disease[2]. Therefore, clinical guidelines recommend monitoring serum lipoprotein cholesterol levels in all adults at least every 5 years[3] because as adults age their lipid and lipoprotein profiles tend to worsen[4]. Aging is also associated with bone loss, which can lead to osteoporosis and its associated fractures. Studies examining the relationship between serum lipid and lipoprotein cholesterol concentrations and bone mineral density (BMD) in adults have yielded inconsistent results[5–23]. However, longitudinal studies of this relationship and studies among African ancestry men are sparse. Therefore, we tested if fasting serum lipid and lipoprotein cholesterol concentrations are associated with cross-sectional and longitudinal measures of BMD in a well-characterized cohort of middle-aged and elderly African ancestry men. We hypothesized that optimal concentrations of serum lipid and lipoprotein cholesterol would be associated with greater cross-sectional BMD and with less BMD-loss across the follow-up time.

MATERIALS AND METHODS

Study Population

The population-based Tobago Health Study began in 2000 on the Caribbean island of Tobago[24]. Tobago residents are predominantly descendants of West African slaves that settled on the island between 1765 and 1808[25]. There has been remarkably little immigration since that time. The country is an independent democracy with English as the official language. We previously estimated that non-African ancestry genetic admixture is <6% in this population[26]. Men were recruited from the general population by word of mouth, hospital flyers, and radio broadcasting to the general population of Tobago. To be eligible, men had to be 40 years and older, ambulatory and not terminally ill. Between 2004 and 2007, men were invited to complete both DXA and quantitative computed tomography (QCT) assessment of BMD. Questionnaires were administered to obtain information on demographic characteristics, medical history, and lifestyle related factors. A total of 2,206 men had complete clinical assessment including BMD scans at this visit, which represents the baseline for the current analysis. Between 2010 and 2013, these men were invited to have repeat DXA and QCT scans and clinical examinations. A total of 1,605 men (80% of survivors) returned for the follow-up exam including BMD assessment. Serum lipid and lipoprotein variables were available in 1385 of the men with complete follow-up data. In addition, we excluded any man on lipid-lowering medication (N=52; 4%), androgen deprivation therapy (N=41; 3%), or both therapies (N=3) leaving 1289 men for the current analysis. Studies of the correlates of bone[24, 27] and cardiovascular health[28] in Tobago have been published previously. The Institutional Review Boards of the University of Pittsburgh and the Tobago Division of Health and Social Services approved this study. All participants provided written informed consent before data collection.

Densitometry

Areal BMD was measured at the whole body and total hip at both the baseline and follow-up visits using a single Hologic QDR 4500W densitometer (Hologic, Inc., Bedford, MA). The left hip was scanned unless the participant had a fracture or a total hip replacement. Trained and certified technicians performed the DXA scans and followed a strict protocol for both visits. Longitudinal machine stability was assessed from plots of daily spine phantom scans, and reviewed monthly. A weekly print out of QC plots was generated to detect short-term inconsistencies and long-term drift. The scanner was stable throughout the course of the study. The long-term coefficient of variation for BMD was 0.499%.

Volumetric BMD at the non-dominant forearm (radius) and left tibia was measured by peripheral QCT at both the baseline and follow-up visits using an XCT-2000 scanner (Stratec Medizintechnik, Pforzheim, Germany). Technicians followed stringent protocols for patient positioning and scanning. A scout view was obtained prior to the QCT scan to define an anatomic reference line for the relative location of the subsequent scans (4% and 33% of the total length) at the radius and tibia. Tibia length was measured from the medial malleolus to the medial condyle of the tibia, and radius length was measured from the olecranon to the ulna styloid process. A single axial slice of 2.5 mm thickness with a voxel size of 0.5 mm and a speed of 20 mm/s was taken at all locations. Image processing was performed using the Stratec software package (Version 5.5E). To determine the cortical volumetric BMD (mg/cm^3) at the 33% site of the radius and tibia, identical parameters were: mode 2, Threshold=169 mg/cm^3 ; cortmode 1, Threshold=710 mg/cm^3 . To determine the trabecular volumetric BMD (mg/cm^3) at the 4% site of the radius and tibia, identical parameters for contour finding and separation of trabecular and cortical bone were: contour mode 2, Threshold=169 mg/cm^3 ; peel mode 1, area=45%. The short-term *in vivo* precision of the pQCT measurements for 15 subjects ranged from 0.65% (for cortical density at the tibia) to 2.1% (for trabecular density at the tibia).

Serum Lipid and Lipoprotein Cholesterol Concentrations

All assays were performed in the Heinz Nutrition Laboratory at the University of Pittsburgh's Graduate School of Public Health, which has met the accuracy and precision standards of the Centers for Disease Control and Prevention and is Clinical Laboratory Improvement Amendment accredited. Blood was drawn in Tobago in the morning after an overnight fast. Serum was separated from the rest of the blood sample by centrifugation in the Tobago clinic. Samples were then aliquotted into 1mL vials and stored at -80°C until overnight shipment on dry ice to the laboratory at the University of Pittsburgh. High-density lipoprotein cholesterol was determined using the selective heparin/manganese chloride precipitation method and had an inter-assay coefficient of variation (CV) of 2.1%. LDL-c was calculated by means of the Friedewald equation. Triglycerides were determined enzymatically using the procedure of Bucolo and David[29] and had an interassay CV of 1.7%.

Clinical Assessment and Health History

Body weight was measured in kilograms with participants wearing light clothing and without shoes, using a calibrated balance beam scale. Height was measured in centimeters

without shoes, using a wall-mounted height board. BMI was measured as weight divided by height in m². Hypertension was measured by taking three blood pressure measurements after five minutes of seated rest using an automated blood pressure machine (Omron model HEM-705CP, Illinois). The average of the second and third measurements was used to calculate systolic and diastolic pressures. Hypertension was defined as systolic pressure equal or greater than 140mmHg or diastolic pressure equal or greater than 90mmHg or anti-hypertension medication use. Diabetes was defined as fasting serum glucose ≥126mg/dl or anti-diabetic medication use. Estimated glomerular filtration rate (eGFR), a marker of kidney function, was calculated from serum creatinine measures using the MDRD equation[30]. Height, weight and BMI were also assessed at follow-up and absolute change measures were calculated.

Trained interviewers and nurses administered questionnaires to obtain information on demographic characteristics, lifestyle factors and medical history. In the current analysis, we used information from the baseline exam to assess potential covariates, including current cigarette smoking, alcohol consumption, time spent watching television, and medical history including history of cardiovascular disease or cancer, a self-perceived rating of their overall health compared to others of their age. Genetic admixture was determined using principal component analysis of genotypes from 119 ancestry informative markers[31].

Statistical Analysis

We tested the association of baseline serum lipid and lipoprotein concentrations with potential covariates, baseline BMD or change in BMD (%) using chi-square, ANOVA or multivariable linear regression, as appropriate. For analyses of baseline BMD, our model included adjustment for potential confounding factors including height, weight, smoking, alcohol intake, watching TV, overall health perception, diabetes, hypertension, cardiovascular disease (CVD), cancer, having ≥3 co-morbid diseases, eGFR and genetic admixture. For longitudinal analyses of BMD, we also adjusted for follow-up time, weight change and the corresponding baseline BMD measure. Lastly, we grouped men into categories of lipid and lipoprotein concentrations as optimal, borderline, or high risk (LDL-c: <100, 100–<160, ≥160; HDL-c: ≥60, 40–<60, <40; triglycerides: <150, 150–<200, ≥200, respectively) based on adult treatment panel III (ATPIII) recommendations[32]. We then tested for a linear trend association between category of serum lipid and lipoproteins (from optimal to high risk) and change in BMD using multivariable linear regression adjusting for all potential confounders. Statistical significance was based on an α of 0.05 for all analyses and analyses were performed using SAS (Version 9.3, SAS Institute, Cary, NC).

RESULTS

Baseline Characteristics

Men were aged 56.4±9 years (range: 41 – 88 years) at study entry and followed for a mean of 6.1 years (Table 1). Only 11% of men reported that they currently smoked, 37% reported watching ≥14 hours of TV a week and 94% rated their health status as good or excellent at baseline. Intake of alcohol was low with only 10% of men drinking 4 or more alcoholic beverages per week and only 3% drinking 1 or more alcoholic drinks per day. At baseline,

17% of men were diabetic, 46% were hypertensive, 4% had a history of cardiovascular disease and 4% had a history of cancer.

Distribution of Serum Lipid and Lipoprotein Concentrations

Twenty percent of men had optimal versus 22% with high-risk LDL-c concentrations based on the Adult Treatment Panel III guidelines (Table 2). Similarly, 22% had optimal versus 19% with high-risk HDL-c concentrations. However, men in our cohort on average had optimal concentrations of triglycerides (mean $\pm$ SD: 111 $\pm$ 59 mg/dL) with only 6% having levels that were considered high-risk.

Association of Serum Lipids and Lipoprotein Cholesterol with Baseline Bone Mineral Density

At baseline, serum lipid and lipoprotein cholesterol concentrations were associated with trabecular volumetric BMD after adjustment for all potential confounding factors including age, height, body weight, smoking, alcohol, TV watching, diabetes, hypertension, CVD, cancer, having ≥ 3 co-morbid diseases, self-reported health status, eGFR and genetic admixture (Table 3). For example, each 1 SD greater LDL-c or triglyceride level was associated with a 4–5 mg/cm³ greater trabecular volumetric BMD at the radius and tibia ($p < 0.01$ for all). A 1 SD greater HDL-cholesterol was associated with a 3 mg/cm³ lower trabecular volumetric BMD at the tibia ($p = 0.012$). There were no significant associations between lipid or lipoprotein cholesterol concentrations with whole body or total hip areal BMD or with cortical BMD.

Association of Baseline Serum Lipids and Lipoprotein Cholesterol with Change in Bone Mineral Density

A greater level of serum triglycerides at baseline was associated with less bone loss at all skeletal sites ($p < 0.05$ for all) except volumetric BMD at the radius after adjustment for follow-up time, change in body weight and the following baseline covariates: baseline bone measure, age, height, body weight, smoking, alcohol intake, TV watching, diabetes, hypertension, CVD, cancer, having ≥ 3 co-morbid diseases, self-reported health status, eGFR and genetic admixture (Table 4). For example, compared to a man with mean triglyceride concentration (111 mg/dL) who lost 0.86% total hip BMD over the follow-up period, a man with 1 SD (59 mg/dL) greater baseline triglycerides lost only 0.48% total hip BMD ($p < 0.0001$). A similar direction of effect was seen for LDL-c, but only changes in total hip areal BMD and trabecular volumetric BMD at the tibia were statistically significant ($p < 0.05$ for both). A greater serum level of HDL-c at baseline was associated with a greater loss of total hip and whole body BMD, and trabecular and cortical volumetric BMD at the tibia ($p < 0.01$ for all). Baseline serum HDL-c was not statistically significantly associated with BMD loss at the radius.

Depictions of the association of ATPIII optimal lipid and lipoprotein concentration categories with bone loss are displayed in Figure 1. Men with the highest risk LDL-c, HDL-c or triglyceride category experienced the least BMD loss, while men with optimal categorization had the greatest BMD loss at the total hip or tibial trabecular compartment independent of potential confounding factors ($p < 0.05$ for both LDL-c; $p < 0.01$ for both

HDL-c; $p < 0.0001$ for both triglycerides). Patterns of results for ATPIII category and BMD loss were similar for whole body BMD and tibia cortical volumetric BMD for HDL-c and triglycerides (all $p < 0.05$) but were not statistically significant for LDL-c (data not shown).

DISCUSSION

In the current study, we found that African ancestry men with more favorable fasting serum lipid and lipoprotein profiles had lower BMD at baseline and experienced more rapid bone loss during 6 years of follow-up. Specifically, men with optimal LDL-c or triglyceride concentrations had significantly lower trabecular BMD at baseline than other men even after adjusting for a number of potential confounders, including body weight. Moreover, men with optimal serum HDL-c or triglyceride levels experienced the most bone loss during follow-up compared to men with borderline or high-risk levels. Bone loss trends were similar, although not always significant, for serum LDL-c concentrations. While the overall magnitude of effect was small for each association (1SD of cholesterol was associated with 0.1–0.5% difference in BMD measure), they are equivalent to the magnitude of effect of 10 years of increased age or a 1 SD greater body weight in the same population[27]. Therefore, we conclude that, in this population, serum lipid and lipoprotein cholesterol may have a potentially important association with BMD change.

Studies examining the relationship between lipid or lipoprotein cholesterol concentrations and bone have yielded conflicting results[5–23]. However, our findings of an inverse association between HDL-c and BMD are consistent with several reports[6–12]. Variability in study designs may explain at least some of the inconsistency in findings between reports. For example, most studies were cross-sectional and also relied on DXA measures of integral BMD, which is a composite measure of cortical and trabecular BMD. Indeed, in our study we found a cross-sectional association with trabecular BMD only and not with either cortical or DXA measures of integral BMD at the hip or whole body. Interestingly, the Longitudinal Study of Aging in Amsterdam found an inverse correlation between HDL-c and ultrasound measures at the calcaneus, a predominantly trabecular skeletal site, among 1255 older men and women[12], in line with our results. Our findings raise the possibility of a skeletal compartment specific association with lipid and lipoprotein cholesterol. The mechanisms underlying such associations are unclear and will require further investigation.

We did not find a consistent significant association between LDL-c concentrations with BMD loss, although trends were similar to results for triglycerides. The inflammatory response elicited by oxidized LDL (oxLDL) contributes to atherosclerotic lesions[33] and has a hypothesized role in lipid-induced bone loss[34]. Studies have shown that osteoblasts treated with high concentrations of oxLDL have decreased mineralization and undergo cell death[35, 36]. However, studies also show that at low concentrations, oxLDL has the opposite effect and may promote osteoblast proliferation[37]. These contradictory, concentration-dependent actions of oxLDL may explain some inconsistent results of studies examining the association of LDL-c and BMD[7, 13–23]. Further studies of oxLDL, LDL-related apolipoproteins and bone metabolism in humans are needed.

There is a growing appreciation in recent years that circulating lipids and lipoproteins may directly impact bone metabolism. At least part of the energy demands of the skeleton are met by fatty acid oxidation[38] and postprandial lipoproteins are a major delivery system of this fuel source to bone cells[39]. Along with energy metabolism, there is also evidence that lipoproteins may regulate stem cell differentiation into mature bone cells[40, 41]. In line with these observations, it would stand to reason that having more lipid and lipoproteins available in the circulation could potentially lead to more favorable bone mass and explain the direction of effect seen in the current study. Despite the growing recognition of a potential functional link between lipoprotein and bone metabolism, including pleiotropic effects by their genes[5], little remains known about the physiology of lipoprotein and bone cell interactions. Our findings in a large, well-characterized human population sample suggest a need to further explore these relationships and to better define the underlying mechanisms involved.

One potential limitation of the current study is that our analyses relied on a single fasting measure of serum lipids and lipoprotein cholesterol at the baseline exam as comparable measures were not available at the follow-up visit. It is possible that single measures may not accurately reflect the lifetime exposure to and impact of serum lipids and lipoprotein cholesterol concentrations on bone. Our study also did not include measures of apolipoproteins, lipoprotein subfractions or bioactive lipids such as oxLDL or phospholipids, which may have provided mechanistic insight on the observed associations. Future studies of BMD loss in this population will focus on both longitudinal measures of serum lipid and lipoprotein cholesterol, as well as, other subclasses and types of lipids and lipoproteins.

Our study focused on African ancestry men, whereas previous studies largely included Caucasian or Asian subjects and focused mainly on postmenopausal women. While this is the first study in African ancestry individuals and, thus, may not be directly comparable to a previous study, our serum LDL and HDL cholesterol levels are generally similar to those reported in other adult African American men in studies across the US[42, 43], as well as, in African men in Nigeria[44]. However, triglyceride levels and the proportion of men with high-risk triglyceride levels in our study appear to be lower (on average ~10mg/dL and 10%, respectively) compared to other studies of African ancestry men[42–44]. Compared to African American cohorts, our sample of Tobago men also has a greater prevalence of diabetes and prostate cancer, but lower prevalence of smoking, alcohol intake, and coronary artery atherosclerosis. While we did not have detailed information on nutrition or physical activity, it is likely that these exposures are somewhat different than those of African American men as well. Thus, it is possible that serum lipid and lipoprotein cholesterol associations with BMD and bone loss are context specific and modified by race and/or gender. Finally, while we were able to adjust for many potential confounding factors such as age, body size, co-morbid conditions, lifestyle factors and genetic admixture, we also cannot exclude the possibility of residual confounding by unmeasured variables. Nonetheless, the current study has several notable strengths including its large community-dwelling sample size, cross-sectional and longitudinal design, rich database of potential confounding factors, and detailed measures of the skeletal phenotype including DXA and QCT measures of integral, cortical and trabecular bone.

In conclusion, we found that clinically optimal serum triglyceride and HDL-c concentrations were associated with lower BMD and accelerated bone loss over time in a large cohort of middle-aged and elderly African ancestry men. These findings were independent of age, lifestyle factors, body composition, medication use and co-morbid medical conditions. This association is potentially very important given the widespread usage and strong treatment effects of current lipid-lowering therapies[45]. Future studies are needed to determine if this association exists in other longitudinal cohorts of men and women and to examine potential mechanisms underlying these findings.

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Figure 1. Multivariable Adjusted Percent Change in Bone Mineral Density by Baseline ATPIII Category of Serum Lipid and Lipoprotein Cholesterol Concentration in African Ancestry Men Percent change in total hip BMD (a) and trabecular BMD at the tibia (b) according to optimal serum lipid and lipoprotein cholesterol categories defined by the adult treatment panel III (ATPIII). Black bars are optimal category; dark grey are borderline category; and light grey are high-risk categories. All results are presented as means with standard error bars and are adjusted for follow-up time, change in body weight and the following at baseline: corresponding bone measure, age, height, body weight, smoking, alcohol intake, TV watching, diabetes, hypertension, CVD, cancer, having 3+ co-morbid diseases, health status, eGFR and genetic admixture. BMD change is significantly different by ATPIII category for all serum lipid and lipoprotein cholesterol concentrations ($p < 0.05$ for both LDL-c; $p < 0.01$ for both HDL-c; $p < 0.0001$ for both triglycerides).

Table 1

Baseline Characteristics of the 1289 African Ancestry Men

Trait	Mean (SD) or %
Age (years)	56.4 (9.0)
Standing Height (cm)	175.5 (6.7)
Body Weight (kg)	84.5 (15.2)
Absolute Weight Change (kg)	0.1 (5.9)
BMI (kg/m ²)	27.4 (4.6)
Absolute BMI Change (kg/m ²)	−0.1 (2.3)
Current Smoker (%)	10.9
Alcohol (< 4 drinks/week, %)	10.3
Watch television (< 14 hours/week, %)	37.3
Health Status, Good/Excellent (%)	94.2
Diabetes (%)	16.6
Hypertension (%)	45.9
Cardiovascular Disease (%)	3.8
Cancer (%)	3.8
eGFR (ml/min/1.73m ²)	81.0 (17.1)
3 Comorbid Chronic Diseases (%)	3.7
Any Non-African Genetic Admixture (%)	2.4

eGFR: estimated glomerular filtration rate

Table 2

Unadjusted Distribution of Baseline Serum Lipid and Lipoprotein Cholesterol Concentrations in African Ancestry Men

	Mean $\pm$ SD (mg/dl)	Number (%) of Men in ATPIII* Categories		
		<i>Optimal</i>	<i>Borderline</i>	<i>High Risk</i>
LDL-c [#]	133 $\pm$ 40	258 (20.1)	747 (58.0)	282 (21.9)
HDL-c	50 $\pm$ 13	288 (22.3)	761 (59.0)	240 (18.6)
Triglycerides	111 $\pm$ 59	1064 (82.5)	147 (11.4)	78 (6.1)

* Adult Treatment Panel III guidelines as follows: LDL-c optimal: <100, borderline: 100–<160, high risk: $\geq$ 160; HDL-c optimal: $\geq$ 60, borderline: 40–<60, high risk: <40; triglycerides optimal: <150, borderline 150–<200, high risk: $\geq$ 200.

[#] LDL-c was not able to be measured in 2 men at baseline (N=1287, all other N=1289).

Table 3

Multivariable Adjusted* Association of Serum Lipid or Lipoprotein Cholesterol Concentrations with BMD at Baseline

Skeletal Site	Unadjusted Mean (SD)	LDL-c (SD=40)	HDL-c (SD=13)	Triglycerides (SD=59)
<i>Areal BMD (g/cm²)</i>				
Whole Body	1.27 (0.11)	0.003 (0.003)	0.003 (0.003)	−0.004 (0.003)
Total Hip	1.16 (0.15)	0.004 (0.004)	−0.002 (0.004)	0.001 (0.004)
<i>Volumetric BMD (mg/cm³)</i>				
Cortical, Radius	1214 (24)	−1.01 (0.67)	0.55 (0.70)	−0.14 (0.68)
Cortical, Tibia	1178 (25)	−1.11 (0.72)	0.00 (0.75)	−0.29 (0.73)
Trabecular, Radius	208 (50)	4.79 (1.41)	−2.69 (1.49)	3.82 (1.44)
Trabecular, Tibia	227 (41)	4.45 (1.16)	−3.04 (1.22)	4.10 (1.17)

BOLD signifies statistically significant (p<0.05).

Values for multivariable models are presented as β (SE) difference in baseline BMD per 1 standard deviation (SD) higher baseline lipid or lipoprotein cholesterol concentration.

* All models are adjusted for baseline age, height, body weight, smoking, alcohol intake, TV watching, diabetes, hypertension, CVD, cancer, having 3+ co-morbid diseases, health status, eGFR and genetic admixture

Table 4

Multivariable Adjusted* Association of Serum Lipid or Lipoprotein Cholesterol Concentration with Percent Change in Bone Mineral Density

Skeletal Site	Unadjusted Mean (SD)	LDL-c (SD=40)	HDL-c (SD=13)	Triglycerides (SD=59)
<i>Areal BMD</i>				
Whole Body	0.49 (2.36)	0.11 (0.07)	-0.23 (0.07)	0.17 (0.07)
Total Hip	-0.86 (3.36)	0.19 (0.09)	-0.25 (0.10)	0.38 (0.09)
<i>Volumetric BMD</i>				
Cortical, Radius	-1.54 (1.35)	-0.02 (0.04)	-0.03 (0.04)	-0.03 (0.04)
Cortical, Tibia	-1.62 (1.19)	-0.02 (0.04)	-0.11 (0.04)	0.08 (0.04)
Trabecular, Radius	-0.22 (4.49)	0.08 (0.14)	-0.25 (0.14)	0.34 (0.14)
Trabecular, Tibia	0.12 (3.60)	0.24 (0.11)	-0.34 (0.11)	0.47 (0.11)

BOLD signifies statistically significant (p<0.05).

Values are displayed as percent change (standard error) in BMD per 1 SD higher baseline serum lipid or lipoprotein cholesterol concentration.

* All models are adjusted for follow-up time, change in body weight and the following at baseline: corresponding baseline bone measure, age, height, body weight, smoking, alcohol intake, TV watching, diabetes, hypertension, CVD, cancer, having 3+ co-morbid diseases, health status, eGFR and genetic admixture