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# Associations between apolipoprotein B and bone mineral density: a population-based study

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## Abstract

**Background** Lipids are critical in bone metabolism, and several studies have highlighted their importance. This study aimed to investigate the relationship between apolipoprotein B (apo B) and bone mineral density (BMD) at different skeletal sites (lumbar spine, femoral neck, and total femur) and to compare the influence of apo B with other traditional lipid markers.

**Methods** The study included participants from the National Health and Nutrition Examination Survey (NHANES) between 2011 and 2016 who had complete data for apo B and BMD at the three skeletal sites. We used weighted multivariate regression analysis, subgroup analysis, and interaction tests to examine associations. Restricted cubic spline (RCS) was used to examine the non-linear relationship.

**Results** A total of 4,258 adults were included in the study. Multivariate linear regression analysis showed that the relationship between apo B and BMD varied by skeletal site: a negative association was found with lumbar spine BMD [ $\beta = -0.054$ , 95%CI: (-0.073, -0.035)]. In contrast, a positive association was found with femoral neck BMD [ $\beta = 0.031$ , 95%CI: (0.011, 0.051)] and no significant association between apo B and total femur BMD.

**Conclusions** Our findings suggest that apo B is associated with BMD in a site-specific manner.

**Keywords** Apolipoprotein B, Bone mineral density, NHANES, Osteoporosis, Cross-sectional study

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## Background

Osteoporosis, a chronic disease that results in a decrease in bone mass and bone mineral density (BMD), poses a major health concern globally. Characterized by fragile bones and an increased susceptibility to bone disorders, it is estimated that approximately 200 million individuals are afflicted with osteoporosis or osteopenia [1, 2]. While aging is a significant risk factor, lifestyle and nutritional influences also contribute to the development and progression of the disease [3, 4].

Lipids play a vital role in various physiological processes, including bone metabolism. Several studies have underscored the influence of lipids on bone health [5], indicating a potential association between specific lipid



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components, such as apolipoprotein B (apo B), and BMD [6]. Apo B, a primary component of atherogenic lipoproteins with two major isoforms: apo B48 and apo B100 [7], is implicated in numerous metabolic processes besides cholesterol transport. Notably, apo B is involved in several inflammatory pathways such as the nuclear factor kappa-light-chain-enhancer of activated B cells (NF- $\kappa$ B) pathway and the mitogen-activated protein kinases (MAPK) pathway [8, 9]. Its direct involvement in bone metabolism, however, remains largely unexplored, which our study aims to address.

Given apo B's role as a marker for cardiovascular risk [10] and its potential impact on bone health, it is vital to examine the relationship between apo B levels and BMD. While it has been suggested that lipids, including apo B, may play a role in bone health [11], to the best of our knowledge, no research has directly investigated this relationship. This leaves a knowledge gap in understanding the factors influencing bone health. To contribute to fill this gap, our study seeks to investigate the association between apo B levels and lumbar BMD within the framework of the National Health and Nutrition Examination Survey (NHANES).

## Methods

### Study population

The NHANES is a comprehensive survey that provides valuable information on the health and nutritional status of the US population. It uses a complex, multistage, and probabilistic sampling process to ensure that the sample is representative of the overall population [12]. For this study, we used data from the 2011–2016 continuous cycle of the NHANES dataset. To ensure the quality of the data, we excluded participants with missing lumbar BMD data ( $n=15,042$ ), missing apo B data ( $n=9,339$ ), those younger than 20 years old ( $n=1,123$ ), and those with cancer, malignancy, or female hormone use ( $n=140$ ) from the initial sample of 29,902 eligible individuals. The final sample included 4,258 participants. The flow chart of the sample selection process is presented in Fig. 1. All human subjects involved in this study were treated in accordance with the ethical principles outlined in the Declaration of Helsinki, and the study was approved by the Research Ethics Review Board of the National Center for Health Statistics (NCHS).

### Study variables

In this study, we investigated the relationship between apo B and lumbar BMD, which was the dependent variable of interest. A light scattering immunochemical method was used to measure the concentration of apo B in human serum samples. In this assay, apo B in the sample forms immune complexes with specific antibodies.

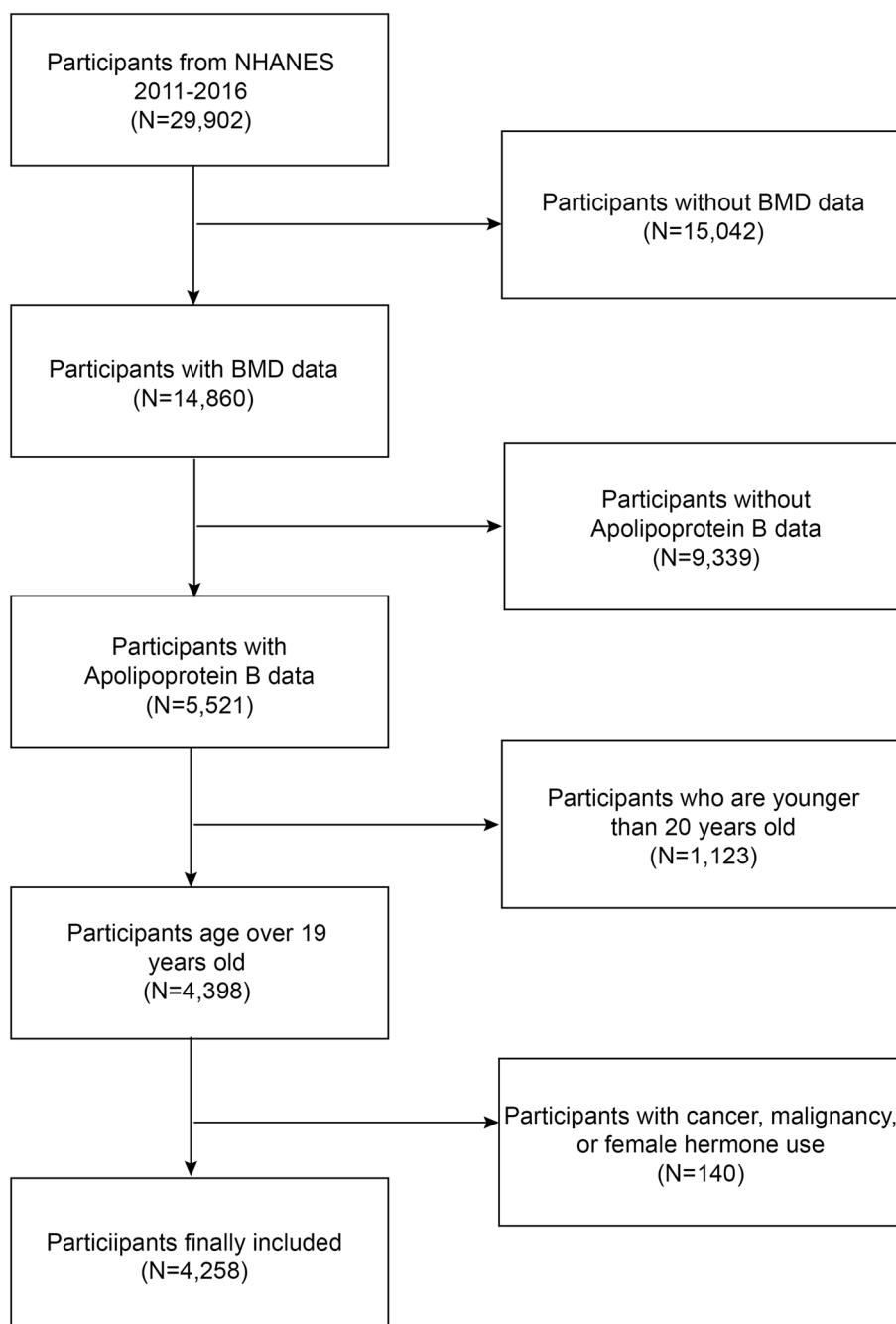
The formation of these complexes scatters a beam of light passed through the sample. The intensity of the scattered light is directly related to the concentration of apo B present. This method is a well-accepted and reliable technique for apo B measurement. Apo B, as the primary protein constituent of LDL and accounting for approximately 95% of LDL's total protein content, is integral to cholesterol transportation from the liver to vessel cells. Hence, elevated levels of Apo B, which can be accurately measured through the described method, often indicate atherosclerotic vascular changes, thereby serving as a risk factor for atherosclerosis. The quantification of apo B in this study is evaluated by comparison with a standard of known concentration.

Dual-energy X-ray absorptiometry (DXA) was used to quantify BMD in the lumbar, whole femur, and femoral neck. Total femur and lumbar spine BMD measurements were taken using the Hologic QDR-4500A fan-beam densitometer in 2017–2018, and with the Hologic Discovery A densitometers (Hologic, Inc., Bedford, MA) in 2013–2014. Only lumbar BMD measurements were taken with a Hologic Discovery A densitometer (Hologic, Inc., Bedford, MA) in 2011–2012 and 2015–2016. The APEX was used to assess femur and lumbar images from 2011 to 2014 and 2015 to 2018. As previously verified, there were no significant differences in mean BMD values when analyzed using Hologic Discovery and APEX [13]. A rigorous quality control program was implemented for DXA measurements throughout the study, ensuring that the coefficient of variation for DXA measurements was less than 1%.

The covariates in our study were selected based on previous literature, which includes gender, age, race, education level, and family income-to-poverty ratio have been shown to be associated with BMD in various studies [14, 15]. Similarly, body mass index is well-known factors related to bone health and lipid metabolism [16, 17]. The laboratory variables we included, such as alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase, total calcium, serum phosphorus, and globulin, are standard tests for assessing general health status and have been linked to BMD and/or lipid levels in previous research [18]. Finally, the questionnaire variables, including smoking status, alcohol drinking status, moderate physical activities status, prescription for cholesterol, diabetes status, and arthritis status, are lifestyle and health factors that are often considered in epidemiological studies of BMD and lipid metabolism [19, 20].

### Statistical analysis

We used R version 4.1.3 and Python version 3.10.4 to conduct the statistical analysis in this study. Multiple imputation was used to handle missing BMD and



**Fig. 1** Flow chart of participants selection. NHANES, National Health and Nutrition Examination Survey; BMD, bone mineral density

covariate data. Descriptive statistics for the baseline characteristics of the study population were presented using apo B subgroups for categorical variables and mean values with standard deviations for continuous variables. Weighted linear regression models were used to account for the complex survey design. We used multivariate linear regression analysis to estimate the beta values and 95% confidence intervals for the association between apo

B and lumbar BMD. Three models were created: Model 1 included no covariates, Model 2 adjusted for gender, age, and BMI, and Model 3 adjusted for all covariates. Stratified analyses were conducted for gender, age, race, education level, BMI, smoking status, drinking status, diabetes status, exercise status, and arthritis status. Interaction tests were used to investigate differences in associations across populations, the *P*-values for interaction were

examined by likelihood ratio tests. Restricted cubic spline (RCS) was applied to visualize the association between apo B and BMD. Correlation matrix heatmap was created to visually represent the relationships between Apo B, other traditional lipid markers, and BMD at different skeletal sites. Statistical significance was set at  $P < 0.05$ .

## Results

### Baseline characteristics

Table 1 displays the clinical features of the study sample, categorized by apo B quartiles. The study encompassed 4,258 participants who fulfilled the inclusion and exclusion criteria, with an average age of  $37.56 \pm 12.31$  years. Among these participants, 52.02% were male, 47.98% were female, and 23.27% of the females were menopausal. The racial/ethnic composition included 35.04% non-Hispanic white, 21.54% non-Hispanic black, 15.10% Mexican American, and 28.32% from other racial/ethnic backgrounds (Table 1).

Participants in the highest apo B quartile demonstrated a higher likelihood of being male, older, non-Hispanic white, or Mexican American. Additionally, they exhibited increased prevalence of arthritis, elevated rates of smoking, alcohol consumption, use of cholesterol prescription and higher levels of BMI, family income-to-poverty ratio, alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase, total calcium, globulin, and total femur BMD. However, they presented lower levels of prevalence of diabetes, educational attainment, serum phosphorus, and lumbar BMD ( $P < 0.05$ ).

In addition to the primary analyses, a correlation matrix heatmap was generated to visually represent the relationships between lipid biomarkers and BMD at different skeletal sites. Figure 2 shows the correlation coefficient between apo B, other lipid indicators, and BMD. There is significant collinearity between apo B, TC, and LDL-C.

### Association between apo B and BMD

Table 2 presents the associations between Apo B and BMD at three sites: lumbar, femoral neck, and total femur. In the unadjusted and minimally adjusted models, Apo B was negatively correlated with BMD at all three sites. For lumbar BMD, the fully adjusted model, after accounting for various covariates, revealed a negative correlation, with each unit increase in apo B associated with a decrease of  $0.054 \text{ g/cm}^2$  in lumbar BMD [ $\beta = -0.054$ , 95%CI: (-0.073, -0.035)]. Upon stratifying apo B into quartiles, participants in the highest quartile had a  $0.037 \text{ g/cm}^2$  lower lumbar BMD compared to those in the lowest quartile [ $\beta = -0.037$ , 95%CI: (-0.051, -0.023)]. Participants in the middle two quartiles also experienced a greater loss of lumbar BMD relative to those in the

lowest quartile. For femoral neck BMD, the fully adjusted model revealed a positive correlation, contrary to the unadjusted and minimally adjusted models. With each unit increase in apo B, femoral neck BMD increased by  $0.031 \text{ g/cm}^2$  [ $\beta = 0.031$ , 95%CI: (0.011, 0.051)]. When apo B was divided into quartiles, participants in the highest quartile demonstrated a  $0.023 \text{ g/cm}^2$  higher femoral neck BMD compared to those in the lowest quartile [ $\beta = 0.023$ , 95%CI: (0.011, 0.037)]. For total femur BMD, the association with apo B did not show statistical significance in all models. Additional file 1: Table S1 describes the results of the same analysis performed on the data set before imputation to avoid bias, and there was no significant difference in trend compared with the results after imputation. Figure 3 depicts the nonlinear association between apo B and BMD at different sites.

### Subgroup analysis

Subgroup analyses were performed to investigate the relationship between apo B and BMD across various subgroups at three sites: lumbar, femoral neck, and total femur (Table 3). For lumbar BMD, a negative association between apo B and lumbar BMD was observed in most of the subgroups stratified by sex, race/ethnicity, body mass index, and age. For femoral neck BMD, a negative association between apo B and femoral neck BMD was observed only in the body mass index  $\geq 30 \text{ kg/m}^2$  group, whereas no significant association was observed in the other groups. For total femoral BMD, the association was not significant in any of the subgroups. Interaction tests showed no significant differences between these strata in the association of Apo B with BMD at the three sites ( $P$  for interaction tests were  $> 0.05$ ).

## Discussion

Our study, analyzing a nationally representative sample of US adults, demonstrated complex associations between apo B levels and BMD at three sites: lumbar, femoral neck, and total femur. While a negative correlation was identified between apo B and lumbar BMD, a positive correlation was observed for femoral neck BMD. This indicates that the influence of apo B may vary across different skeletal sites. Subgroup analyses further revealed that these associations could potentially be influenced by factors such as sex, race, age, BMI, and diabetes status.

To the best of our knowledge, this is the first study to investigate the association between apo B and BMD. Apo B is a lipoprotein involved in lipid transportation and serves as a precursor to atherosclerosis. It is commonly utilized as a predictor of cardiovascular risk [9]. For instance, a recent case-control study proposed that apo B may function as a potential biomarker for atrial fibrillation, potentially playing a role in the initiation and

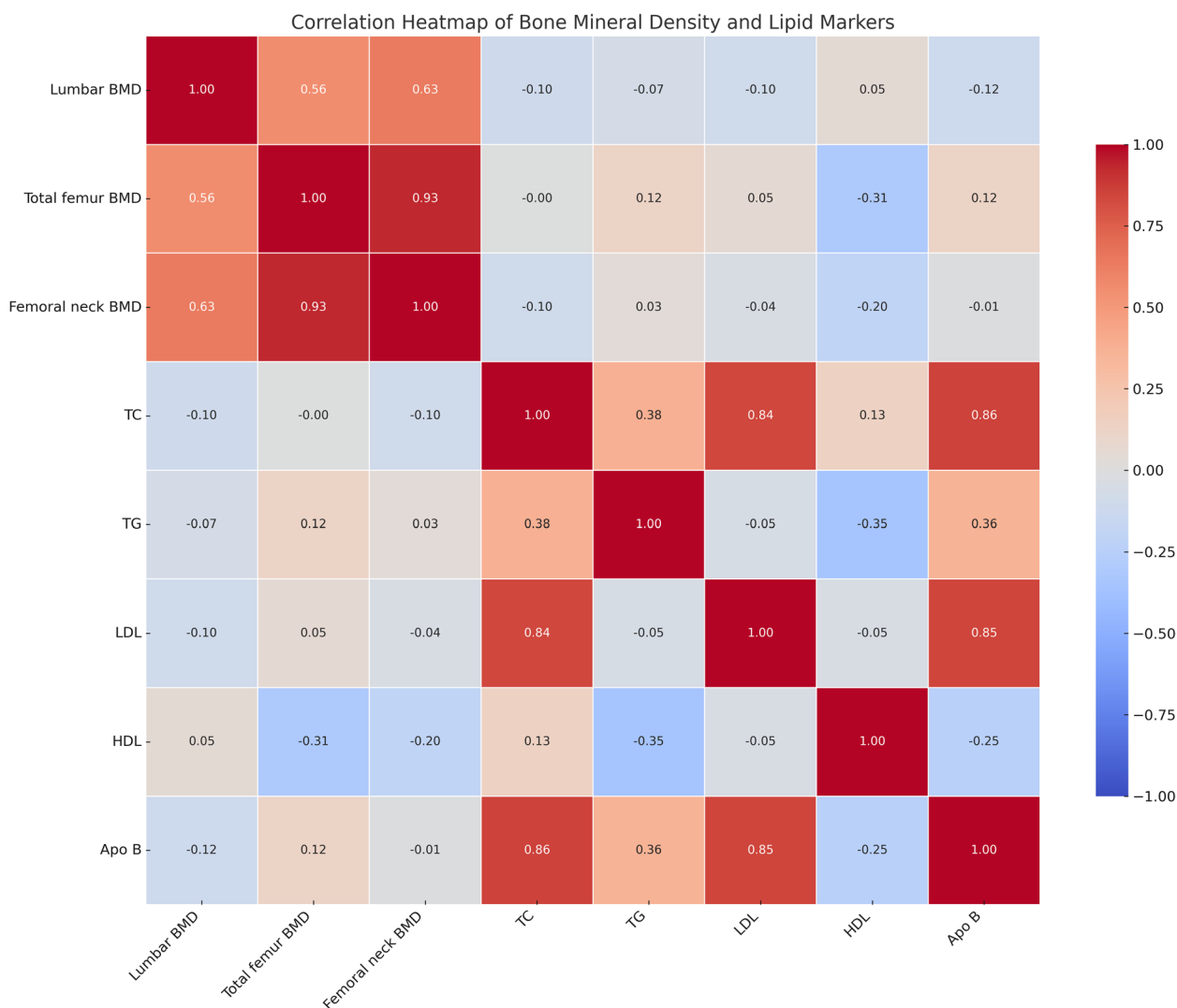
**Table 1** Weighted characteristics of the study population based on apolipoprotein B quartiles

| Apolipoprotein B (g/L)                          | Total<br>N = 4,258 | Q1 (≤0.70)<br>N = 1014 | Q2 (0.71–0.87)<br>N = 1100 | Q3 (0.88–1.04)<br>N = 1038 | Q4 (≥ 1.05)<br>N = 1106 | P-value |
|---|--------------------|------------------------|----------------------------|----------------------------|-------------------------|---------|
| Age (years)                                     | 37.555 ± 12.312    | 32.878 ± 12.063        | 36.894 ± 12.192            | 40.022 ± 11.795            | 43.481 ± 10.158         | < 0.001 |
| Sex, (%)  |                    |                        |                            |                            |                         | < 0.001 |
| Male  | 52.020             | 47.561                 | 49.789                     | 51.799                     | 61.100                  |         |
| Female  | 47.980             | 52.439                 | 50.211                     | 48.201                     | 38.900                  |         |
| Postmenopausal female                           | 11.165             | 8.542                  | 10.419                     | 12.498                     | 11.716                  |         |
| Premenopausal female                            | 36.815             | 43.897                 | 39.792                     | 35.703                     | 27.184                  |         |
| Race/Ethnicity (%)                              |                    |                        |                            |                            |                         | 0.037   |
| Non-Hispanic White                              | 35.040             | 60.395                 | 61.974                     | 61.937                     | 63.407                  |         |
| Non-Hispanic Black                              | 21.536             | 14.152                 | 11.881                     | 9.941                      | 9.652                   |         |
| Mexican American                                | 15.101             | 8.944                  | 10.126                     | 11.198                     | 11.692                  |         |
| Other race/ethnicity                            | 28.323             | 16.509                 | 16.020                     | 16.925                     | 15.249                  |         |
| Education level (%)                             |                    |                        |                            |                            |                         | < 0.001 |
| Less than high school                           | 15.176             | 12.818                 | 14.757                     | 14.933                     | 18.195                  |         |
| High school                                     | 20.229             | 19.163                 | 18.237                     | 19.882                     | 23.635                  |         |
| More than high school                           | 64.595             | 68.019                 | 67.006                     | 65.185                     | 58.170                  |         |
| Moderate activities (%)                         |                    |                        |                            |                            |                         | 0.048   |
| Yes   | 43.776             | 49.854                 | 47.320                     | 45.134                     | 44.159                  |         |
| No  | 56.224             | 50.146                 | 52.680                     | 54.866                     | 55.841                  |         |
| Smoked at least 100 cigarettes in life, n (%)   |                    |                        |                            |                            |                         | < 0.001 |
| Yes   | 39.027             | 33.536                 | 41.124                     | 40.876                     | 46.996                  |         |
| No  | 60.973             | 66.464                 | 58.876                     | 59.124                     | 53.004                  |         |
| Had at least 12 alcohol drinks in 1 year, n (%) |                    |                        |                            |                            |                         | 0.010   |
| Yes   | 73.258             | 76.667                 | 79.409                     | 78.790                     | 81.705                  |         |
| No  | 16.742             | 23.333                 | 20.591                     | 21.210                     | 18.295                  |         |
| Diabetes, n (%)                                 |                    |                        |                            |                            |                         | 0.008   |
| Yes   | 6.881              | 8.531                  | 5.194                      | 5.670                      | 7.776                   |         |
| No  | 93.119             | 91.469                 | 93.010                     | 92.708                     | 89.805                  |         |
| Take prescription for cholesterol, (%)          |                    |                        |                            |                            |                         | 0.019   |
| Yes   | 8.196              | 6.410                  | 7.818                      | 8.285                      | 10.127                  |         |
| No  | 91.804             | 93.590                 | 92.182                     | 91.715                     | 89.873                  |         |
| Arthritis, n (%)                                |                    |                        |                            |                            |                         | < 0.001 |
| Yes   | 13.434             | 9.758                  | 13.920                     | 15.647                     | 18.281                  |         |
| No  | 86.564             | 90.242                 | 86.080                     | 84.353                     | 81.719                  |         |
| Body mass index (kg/m <sup>2</sup> )            | 28.761 ± 7.102     | 26.508 ± 6.762         | 28.541 ± 6.989             | 29.683 ± 6.805             | 30.695 ± 6.670          | < 0.001 |
| Income to poverty ratio                         | 2.409 ± 1.662      | 2.6766 ± 1.6927        | 2.8033 ± 1.6928            | 2.9478 ± 1.6961            | 3.1525 ± 1.7327         | < 0.001 |
| ALT (U/L)                                       | 26.133 ± 19.656    | 21.376 ± 14.146        | 25.851 ± 21.278            | 27.169 ± 18.666            | 30.586 ± 18.620         | < 0.001 |
| AST (U/L)                                       | 25.700 ± 24.285    | 24.043 ± 24.677        | 25.962 ± 25.753            | 25.357 ± 14.509            | 27.010 ± 14.964         | 0.010   |
| ALP (U/L)                                       | 66.030 ± 22.041    | 61.745 ± 21.678        | 63.438 ± 20.193            | 65.566 ± 19.744            | 69.127 ± 27.203         | < 0.001 |
| Total calcium (mg/dL)                           | 9.353 ± 0.329      | 9.325 ± 0.312          | 9.338 ± 0.326              | 9.341 ± 0.336              | 9.390 ± 0.332           | < 0.001 |
| Serum phosphorus (mg/dL)                        | 3.729 ± 0.558      | 3.767 ± 0.561          | 3.722 ± 0.563              | 3.683 ± 0.539              | 3.638 ± 0.519           | < 0.001 |
| Globulin (g/dL)                                 | 2.868 ± 0.432      | 2.717 ± 0.410          | 2.785 ± 0.423              | 2.792 ± 0.404              | 2.831 ± 0.409           | < 0.001 |
| Lumbar BMD (g/cm <sup>2</sup> )                 | 1.031 ± 0.150      | 1.057 ± 0.151          | 1.038 ± 0.152              | 1.021 ± 0.147              | 1.252 ± 0.160           | < 0.001 |
| Total femur BMD (g/cm <sup>2</sup> )            | 0.977 ± 0.141      | 0.981 ± 0.153          | 0.981 ± 0.153              | 0.962 ± 0.143              | 0.994 ± 0.124           | 0.027   |
| Femoral neck BMD (g/cm <sup>2</sup> )           | 0.814 ± 0.138      | 0.813 ± 0.152          | 0.825 ± 0.152              | 0.804 ± 0.139              | 0.816 ± 0.120           | 0.502   |

Mean ± SD for continuous variables: the P value was calculated by the weighted linear regression model

(%) for categorical variables: the P value was calculated by the weighted chi-square test

Abbreviation: BMD bone mineral density, ALT alanine aminotransferase, AST aspartate aminotransferase, ALP alkaline phosphatase, HDL-C high density lipoprotein cholesterol, LDL-C low-density lipoprotein cholesterol



**Fig. 2** Correlation heatmap of bone mineral density and lipid markers. This heatmap illustrates the pairwise correlation coefficients between various bone mineral density measurements and lipid markers. The color intensity and the numeric values within each cell represent the strength and direction of the correlation. Darker shades of blue indicate a positive correlation, while darker shades of red indicate a negative correlation. The closer the value is to 1 or -1, the stronger the positive or negative correlation, respectively

maintenance of the condition in conjunction with several metabolic factors [21]. In addition, Marston et al. reported that the amount of apo B lipoprotein, compared to other lipid indicators, was the best predictor of myocardial infarction risk [10].

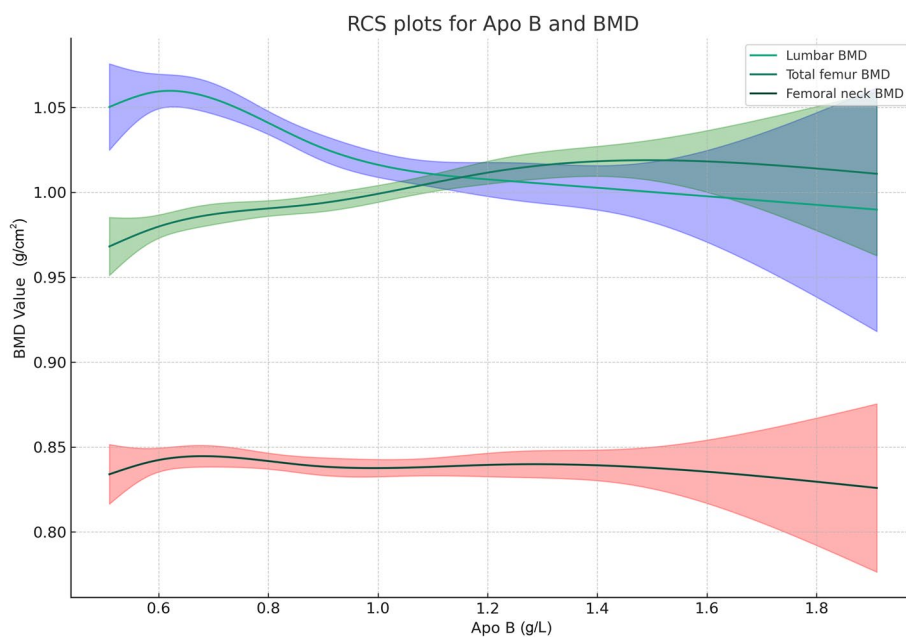
Currently, numerous epidemiological studies have demonstrated the correlation between lipid biomarkers and BMD [5, 22]. A multicenter cross-sectional study conducted in China revealed that high LDL-C levels are an independent risk factor for bone loss in both men and women. Moreover, increasing age and menopause exacerbate the negative effects on bone mass in women [23]. Yang et al. utilized Mendelian randomization analysis

to demonstrate a potential causal relationship between BMD and lipid profiles, including LDL-C, total cholesterol, triglycerides, and HDL-C [24]. Furthermore, LDL-C, a lipid biomarker significantly associated with apo B, has been shown to have a significant association with BMD in several studies [25, 26]. While past studies have concluded a negative association between LDL-C and BMD, some researchers have suggested a positive association or an invalid connection between LDL-C and BMD [27, 28]. A recent meta-analysis of ten studies found that individuals with osteoporosis had higher LDL-C levels than healthy controls [29]. This association may help elucidate the link between coronary vascular disease

**Table 2** The association between apolipoprotein B and bone mineral density

| Exposure                      | Model 1 [ $\beta$ (95% CI)] | Model 2 [ $\beta$ (95% CI)] | Model 3 [ $\beta$ (95% CI)] |
|-------------------------------|-----------------------------|-----------------------------|-----------------------------|
| Lumbar BMD (continuous)       | -0.067 (-0.085, -0.050)     | -0.039 (-0.058, -0.021)     | -0.054 (-0.072, -0.036)     |
| Lumbar BMD (quartile)         |                             |                             |                             |
| Quartile 1                    | Reference                   | Reference                   | Reference                   |
| Quartile 2                    | -0.019 (-0.032, -0.006)     | -0.018 (-0.031, -0.001)     | -0.013 (-0.026, -0.000)     |
| Quartile 3                    | -0.036 (-0.049, -0.023)     | -0.018 (-0.030, -0.002)     | -0.026 (-0.039, -0.012)     |
| Quartile 4                    | -0.049 (-0.062, -0.036)     | -0.033 (-0.044, -0.018)     | -0.037 (-0.050, -0.024)     |
| P for trend                   | < 0.001                     | < 0.001                     | < 0.001                     |
| Femoral neck BMD (continuous) | -0.010 (-0.050, 0.031)      | -0.083 (-0.161, -0.016)     | 0.031 (0.011, 0.051)        |
| Femoral neck BMD (quartile)   |                             |                             |                             |
| Quartile 1                    | Reference                   | Reference                   | Reference                   |
| Quartile 2                    | 0.011 (-0.022, 0.045)       | -0.040 (-0.075, -0.023)     | 0.016 (0.006, 0.031)        |
| Quartile 3                    | -0.009 (-0.042, 0.024)      | -0.045 (-0.080, -0.014)     | 0.021 (0.007, 0.035)        |
| Quartile 4                    | 0.034 (0.002, 0.067)        | -0.095 (-0.167, -0.011)     | 0.023 (0.011, 0.037)        |
| P for trend                   | < 0.001                     | < 0.001                     | 0.003                       |
| Total femur BMD (continuous)  | 0.036 (-0.005, 0.078)       | -0.001 (-0.038, 0.038)      | -0.025 (-0.063, 0.013)      |
| Total femur BMD (quartile)    |                             |                             |                             |
| Quartile 1                    | Reference                   | Reference                   | Reference                   |
| Quartile 2                    | 0.022 (-0.013, 0.056)       | 0.032 (0.000, 0.064)        | 0.015 (-0.014, 0.044)       |
| Quartile 3                    | 0.003 (-0.031, 0.036)       | 0.019 (-0.013, 0.050)       | 0.000 (-0.028, 0.028)       |
| Quartile 4                    | 0.034 (0.002, 0.067)        | 0.039 (0.008, 0.069)        | 0.016 (-0.012, 0.043)       |
| P for trend                   | 0.055                       | 0.044                       | 0.415                       |

Model 1: no covariates were adjusted. Model 2: age, gender, and BMI were adjusted. Model 3: age, gender, race, educational level, BMI, family income-to-poverty ratio, moderate activities, smoking status, alcohol use status, take prescription for cholesterol, prevalence of diabetes, prevalence of arthritis, ALT, AST, ALP, total calcium, globulin, female postmenopausal status, and serum phosphorus were adjusted



**Fig. 3** The nonlinear associations between apo B and bone mineral density. The solid line represents the smooth curve fit between variables. Translucent bands represent the 95% of confidence interval from the fit

**Table 3** Subgroup analysis of the association between apolipoprotein B and bone mineral density

| Subgroup               | Lumbar BMD [β (95%CI)]  | P for interaction | Total femur BMD [β (95%CI)] | P for interaction | Femoral neck BMD [β (95%CI)] | P for interaction |
|------------------------|-------------------------|-------------------|-----------------------------|-------------------|------------------------------|-------------------|
| Sex                    |                         | 0.245             |                             | 0.268             |                              | 0.266             |
| Male                   | -0.063 (-0.088, -0.037) |                   | -0.008 (-0.056, 0.039)      |                   | -0.039 (-0.087, 0.010)       |                   |
| Female                 | -0.040 (-0.068, -0.012) |                   | 0.030 (-0.020, 0.081)       |                   | 0.001 (-0.050, 0.052)        |                   |
| Race/ethnicity         |                         | 0.475             |                             | 0.441             |                              | 0.565             |
| Non-Hispanic White     | -0.039 (-0.070, -0.008) |                   | -0.019 (-0.073, 0.036)      |                   | -0.043 (-0.098, 0.012)       |                   |
| Non-Hispanic Black     | -0.081 (-0.120, -0.042) |                   | -0.020 (-0.097, 0.057)      |                   | -0.034 (-0.113, 0.045)       |                   |
| Mexican American       | -0.060 (-0.112, -0.008) |                   | 0.040 (-0.052, 0.132)       |                   | -0.007 (-0.100, 0.086)       |                   |
| Other race             | -0.028 (-0.090, 0.035)  |                   | 0.039 (-0.031, 0.110)       |                   | 0.019 (-0.053, 0.090)        |                   |
| BMI, kg/m <sup>2</sup> |                         | 0.335             |                             | 0.056             |                              | 0.100             |
| < 25                   | -0.035 (-0.071, 0.002)  |                   | 0.082 (-0.000, 0.164)       |                   | 0.043 (-0.040, 0.127)        |                   |
| 25–29.9                | -0.069 (-0.102, -0.036) |                   | -0.035 (-0.089, 0.019)      |                   | -0.046 (-0.101, 0.009)       |                   |
| ≥ 30                   | -0.042 (-0.072, -0.011) |                   | -0.038 (-0.098, 0.022)      |                   | -0.068 (-0.129, -0.007)      |                   |
| Age, years             |                         | 0.159             |                             | 0.290             |                              | 0.221             |
| < 50                   | -0.060 (-0.081, -0.039) |                   | 0.024 (-0.023, 0.070)       |                   | -0.004 (-0.051, 0.043)       |                   |
| ≥ 50                   | -0.030 (-0.067, 0.006)  |                   | -0.014 (-0.066, 0.039)      |                   | -0.048 (-0.101, 0.006)       |                   |
| Diabetes               |                         | 0.128             |                             | 0.610             |                              | 0.476             |
| Yes                    | 0.006 (-0.058, 0.070)   |                   | -0.010 (-0.097, 0.076)      |                   | -0.050 (-0.138, 0.038)       |                   |
| No                     | -0.056 (-0.077, -0.036) |                   | -0.010 (-0.097, 0.076)      |                   | -0.015 (-0.054, 0.023)       |                   |

Age, gender, race, educational level, BMI, family income-to-poverty ratio, moderate activities, smoking status, alcohol use status, take prescription for cholesterol, prevalence of diabetes, prevalence of arthritis, ALT, AST, ALP, total calcium, globulin and serum phosphorus were adjusted

and osteoporosis, where high LDL-C levels are a critical risk factor [30]. Our findings indicate that the inverse relationship between apo B and BMD is consistent with evidence from numerous epidemiological studies on the association between LDL-C and BMD, as well as the relationship between coronary vascular disease and osteoporosis [31–33].

The underlying mechanism explaining the inverse association between apo B and BMD remains unclear. Several hypotheses have been proposed to explain this phenomenon. One potential explanation is that oxidized lipids, including oxidized apolipoproteins, may exert direct harmful effects on bone cells. These effects could lead to the inhibition of osteoblast differentiation and bone formation, the promotion of adipogenesis in mesenchymal stem cells at the expense of their osteogenic differentiation, and the induction of osteoclast differentiation and bone resorption [34, 35]. Another possibility is that high apo B levels may trigger an inflammatory response, and emerging evidence suggests that inflammation can negatively impact bone mass by altering osteoclast activation or function [36, 37]. However, direct evidence to support these hypotheses is lacking, and further research is needed to confirm these mechanisms.

While our study provides important insights, it also has several limitations that should be acknowledged. First, because this is a cross-sectional study, causality cannot be established. Additionally, despite adjusting for

several relevant confounders, the possibility of residual confounding cannot be completely ruled out. Another important limitation is potential selection bias due to the exclusion of a substantial number of participants. This could have affected our results, and therefore, our findings should be interpreted with caution. Future research with more comprehensive inclusion criteria or strategies to minimize selection bias would be beneficial to verify and extend our findings. Despite these limitations, our study has several strengths. One key strength is the use of a nationally representative sample of US adults, making our findings generalizable to a diverse population. Additionally, the large sample size allowed for subgroup analyses, adding to the robustness of our results.

### Conclusion

Our study revealed a complex relationship between apo B levels and BMD at various sites. These findings highlight the unique role of apo B in bone metabolism and call for further investigations.

### Abbreviations

|        |  |
|--------|--|
| apo B  | Apolipoprotein B                                 |
| BMD    | Bone mineral density                             |
| NHANES | National Health and Nutrition Examination Survey |
| RCS    | Restricted cubic spline                          |
| ALT    | Alanine aminotransferase                         |
| AST    | Aspartate aminotransferase                       |
| ALP    | Alkaline phosphatase                             |



|       |  |
|-------|--|
| HDL-C | High-density lipoprotein cholesterol                           |
| LDL-C | Low-density lipoprotein cholesterol                            |
| NF-κB | Nuclear factor kappa-light-chain-enhancer of activated B cells |
| MAPK  | Mitogen-activated protein kinases                              |

## Supplementary Information

The online version contains supplementary material available at <https://doi.org/10.1186/s12891-023-06990-x>.

**Additional file 1: Table S1.** The association between apolipoprotein B and bone mineral density before imputation.

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### Authors' contributions

XZ, NT, HJ, MX and YZ designed the research. XZ, NT, ZN, ML, LL and YZ collected, analyzed the data, and drafted the manuscript. XZ, NT, and HJ revised the manuscript. All authors contributed to the article and approved the submitted version.

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### Availability of data and materials

The datasets generated and analysed during the current study are available in the NHANES repository, [[www.cdc.gov/nchs/nhanes/](http://www.cdc.gov/nchs/nhanes/)].

### Declarations

#### Ethics approval and consent to participate

All human subjects involved in this study were treated in accordance with the ethical principles outlined in the Declaration of Helsinki, and the study was approved by the Research Ethics Review Board of the National Center for Health Statistics (NCHS). The patients/participants provided their written informed consent to participate in this study.

#### Consent for publication

Not applicable.

#### Competing interests

The authors declare that they have no competing interests.

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