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# Association between serum uric acid levels and bone mineral density in Chinese and American: a cross-sectional study

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**Despite extensive studies conducted on the relationship between serum uric acid (UA) and bone mineral density (BMD), their association remains controversial. In this study, we investigated whether UA levels are independently associated with BMD in Chinese and American populations to elucidate their association. Herein, the data of 12,344 individuals (age > 20 years) from the National Health and Nutrition Examination Survey (2005–2018) and those of 768 individuals from the inpatient medical records and physical examination center systems of the Tertiary Class A Hospital (2021–2023) from China were included. The association between UA and BMD was analyzed by employing multivariate regression models with covariate adjustments. In addition, population description, stratified analysis, single-factor analysis, smooth-curve fitting, and threshold and saturation effect analyses were performed. After covariate adjustments, UA exhibited an association with BMD of the femur (β = 0.008, 95% confidence interval [CI] 0.001–0.015, *P* = 0.02), femoral neck (β = 0.011, 95% CI 0.004–0.018, *P* = 0.002), and lumbar spine (β = 0.014, 95% CI 0.06–0.022, *P* < 0.001) in American subjects. Similarly, UA exhibited association with BMD of the femur (β = 0.079, 95% CI 0.042–0.117, *P* < 0.001), femoral neck (β = 0.171, 95% CI 0.121–0.22, *P* < 0.001), and lumbar spine (β = 0.052, 95% CI 0.007–0.097, *P* = 0.024) in Chinese subjects. Notably, the relationship between UA levels and BMD was nonlinear. The saturated utility values for determining the UA level with BMD of the femur and femoral neck using a two-stage linear regression model were 429.9 and 468 µmol/L, respectively, in the Chinese population. In the American population, the saturated utility values of UA level with BMD of the femur, femoral neck, and lumbar spine were 410.4, 410.4, and 452 µmol/L, respectively. Altogether, the present findings suggested a positive association between the UA levels and overall BMD in adults, implying that maintaining saturated UA levels can facilitate osteoporosis prevention.**

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**Keywords** Uric acid, Bone mineral density, Threshold effect

Osteoporosis (OP) is a metabolic bone disease characterized by decreased bone mineral density (BMD) and bone mass, along with damage to the bone microstructures, which further increases bone fragility and fracture risk[1]. OP pathogenesis has been associated with various factors, including hormonal changes, calcium and vitamin D deficiencies, oxidative stress, and enhanced osteoclast bone resorption-mediated bone loss[2–4]. Reportedly, increasing low BMD-associated disability and mortality rates in both developed and developing countries[5] and increasing OP incidences considerably raise the social and economic burden on the affected population[6]. Hence, identifying the therapeutic factors that can reduce OP risk and improve overall bone health is critical for global public health.

Uric acid (UA) is the final product of purine catabolism in organisms[7], and its high levels can increase the risk of various adverse outcomes, including diabetes mellitus (DM), metabolic syndrome, chronic kidney disease (CKD), and cardiovascular diseases[8–10]. Reportedly, some observational studies suggest that UA may be beneficial

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to BMD[11–13], as owing to its free-radical-scavenging activity, extracellular UA acts as an antioxidant and may exert a protective effect on bone metabolism based on its physiological state[14]. However, the antioxidant effects of UA in vivo and its protective effects on bone metabolism and BMD are not well established, making the present findings controversial[15]. UA has been positively associated with BMD mainly in the Asian populations[16–19], but not in the American population[20,21]. Furthermore, Li[21] highlighted that several important factors affecting bone metabolism, including serum alkaline phosphatase (ALP), serum calcium, serum phosphorus, and vitamin D, have not been fully adjusted for confounders[12,16,18,19] warranting further investigations.

Altogether, studies on the relationship between UA and BMD are limited, which underscores the importance of exploring their relationship across different ethnic groups in clinical settings for the development of OP prevention and treatment strategies. Therefore, this cross-sectional study explored the UA–BMD relationship in two different populations, namely Chinese and American. The representative certified sample of the American population was derived from the National Health and Nutrition Examination Survey (NHANES) and that of the Chinese population was from a Tertiary Class A hospital in China.

## Materials and methods

### Study design and population

The data analyzed in this study were sourced from the National Health and Nutrition Examination Survey (NHANES) (2005–2018), a complex, stratified, multistage, uninstitutionalized sample of the US population probability. These cross-sectional surveys were conducted by the National Center for Health Statistics (NCHS). For methodological details on NHANES, visit www.cdc.gov/nchs/NHANES/. The study population was limited to those aged > 20 years with complete BMD data available. After excluding subjects who did not meet the inclusion criteria (Figure S1), a total of 12,344 subjects aged > 20 years were included in the final analysis.

The data of the 768 Chinese participant subjects in the study were collected between January 2021 and December 2023 from the inpatient medical record and physical examination center systems, respectively, of the Tertiary Class A Hospital (Figure S3). All research activities were performed in accordance with the relevant guidelines/regulations. Research involving human research participants was performed in accordance with the Declaration of Helsinki. The need for informed consent was waived off by the ethics committee considering the retrospective nature of the study.

### Statement of ethics

The study was approved by the ethics review board of the National Center for Health Statistics, and written consent was obtained from each participant[22]. Clinical Ethics Committee of People's Hospital of Leshan ((LYLL [2023] KY 052)).

### Variables

In American participant, the exposure variable was serum UA. As a part of the routine serum biochemical analysis, serum UA was determined by using the timing end-point method using Beckerman and Coulter Unicel DXC800 instrument. The outcome variables were lumbar BMD, femoral BMD, and femoral neck BMD measured by dual-energy X-ray absorptiometry (DXA). All scans were performed with the Hologic QDR 4500A sector beam density instrument (Hologic, Inc., Bedford, Mass.). All measured BMD values were collected and standardized by professionals. In addition, the study included the following covariates: age, sex, race, body mass index (BMI), income, education, blood urea nitrogen, creatinine, total cholesterol, triglyceride, low-density lipoprotein, high-density lipoprotein, serum phosphorus, serum calcium, vitamin D, gamma-glutamyltransferase, alkaline phosphatase, aspartate transaminase, alanine transaminase, drinking behavior, and smoking behavior. Detailed information on UA, lumbar BMD, femoral BMD, and femoral neck BMD are available on the NHANES website along with measurement procedures and other covariate acquisition procedures (Table S1).

In the Chinese participant, the exposure variable was serum UA. The outcome variables were lumbar BMD, femoral BMD, and femoral neck BMD measured by dual-energy X-ray absorptiometry (DXA). The instrument used to measure bone density is a DXA body scan (GE Lunar Prodigy Advance), which was operated by a professional technician. Actual data (both clinical and laboratory) collected from participants included the following: sex, age, BMI, T2DM or not, alanine aminotransferase, aspartic acid aminotransferase, ALP, gamma-glutamyl transferase, total bilirubin, high-density lipoprotein, low-density lipoprotein, total cholesterol, triglyceride, urea, and creatinine (Table S4).

### Statistical analysis

Data were expressed as the mean ± standard error (SE) for continuous variables and as a percentage of categorical variables. To compare between-group differences, weighted Chi-square tests and weighted linear regression models were employed for continuous variables and categories, respectively. The participants were characterized by quartiles of UA. The association among UA and lumbar BMD, femoral BMD, and femoral neck BMD was evaluated by using a weighted multivariate logistic regression model. Multiple regression analysis was stratified by type 2 diabetes, sex, and race. Then, the nonlinear relationship between UA and BMD was analyzed by using smooth curve fitting and a generalized additive model. Finally, the inflection points of the relationship between UA and lumbar BMD, femoral BMD, and femoral neck BMD were calculated based on the threshold effect and saturation effect analysis. R packages (http://www.R-project.org, The R Foundation) and EmpowerStats (http://www.empowerstats.com, X&Y Solutions, Inc., MA, USA) were used for all analyses, with a two-sided $P < 0.05$ serving as a significance threshold.

## Results

In total, 12,344 American participants (age ≥ 20 years) were included in this study and classified as per the quartile of UA (Category 1: ≤ 261.7 μmol/L; Category 2: 261.7–315.2 μmol/L; Category 3: 315.2–368.8 μmol/L; Category 4: > 368.8 μmol/L). In addition to the income, significant differences were noted in the baseline characteristics among the UA quartiles (Table 1). When compared with other subgroups, the participants in the highest quartile of UA were more likely to be male, non-Hispanic white, and non-Hispanic black. The prevalence of age, BMI, serum calcium, blood urea nitrogen, creatinine, ALP, gamma-glutamyl transferase, TC, TG, LDL, ALT, AST, bilirubin, T2DM, and BMD of the lumbar spine, femur, and femoral neck were all higher, whereas that of vitamin D and blood phosphorus was lower. Additionally, individuals in the top quartile of the UA may be more educated and more likely to drink and smoke. Multiple regression analysis of the association between UA and BMD in American subjects (Table 2) revealed that in unadjusted models, UA was associated with BMD of the femur (β = 0.099, 95% confidence interval [CI] 0.092–0.107, $P < 0.001$), femoral neck (β = 0.063, 95% CI 0.055–0.07, $P < 0.001$), and lumbar spine (β = 0.071, 95% CI 0.064–0.079, $P < 0.001$). After adjusting for covariates (covariates requiring correction were selected based on the results of the univariate analysis with $P < 0.001$; Table S2), the following results were obtained: Model 1 (β = 0.01, 95% CI 0.003–0.017, $P = 0.004$; β = 0.011, 95% CI 0.004–0.018, $P = 0.001$; and β = 0.019, 95% CI 0.011–0.028, $P < 0.001$; respectively) and Model 2 (β = 0.008, 95% CI 0.001–0.015, $P = 0.02$; β = 0.011, 95% CI 0.004–0.018, $P = 0.002$; and β = 0.014, 95% CI 0.06–0.022, $P < 0.001$; respectively). Notably, UA and BMD exhibited a significant positive correlation. The smooth-curve fitting and generalized additive model indicated that the relationship of UA with BMD of the femur, femoral neck, and lumbar spine was nonlinear. The saturated utility values of UA with BMD of the femur, femoral neck, and lumbar spine were 410.4, 410.4, and 452 μmol/L, respectively (Table S3).

Subgroup analyses were performed by their stratifying the individuals by gender, race, age, and presence or absence of T2DM (Table 3). Notably, UA was positively correlated with BMD of the femoral neck and lumbar spine in both males (β = 0.012, 95% CI 0.00–0.024, $P = 0.044$ and β = 0.029, 95% CI 0.015–0.042, $P < 0.001$, respectively) and females (β = 0.013, 95% CI 0.003–0.023, $P = 0.0087$ and β = 0.016, 95% CI 0.004–0.028, $P = 0.009$, respectively); there was no significant correlation between UA and total femur BMD in both the genders. The positive association between UA and BMD of femur (β = 0.028, 95% CI 0.011–0.045, $P = 0.001$) and femoral neck (β = 0.025, 95% CI 0.008–0.042, $P = 0.003$) was more pronounced in non-Hispanic black, while that between UA and femoral neck was more pronounced in non-Hispanic white (β = 0.015, 95% CI 0.005–0.026, $P = 0.004$). In contrast, UA did not show any association with the lumbar spine BMD in all racial subgroups. In the age group of > 60 years, UA exhibited a significant positive correlation with BMD of the femur (β = 0.036, 95% CI 0.014–0.057, $P < 0.001$), femoral neck (β = 0.028, 95% CI 0.009–0.047, $P = 0.004$), and lumbar spine (β = 0.038, 95% CI 0.013–0.063, $P = 0.002$). In contrast, although UA positively correlated with femoral BMD (β = 0.02, 95% CI 0.007–0.033, $P = 0.002$) in the age group of ≤ 60 years, it displayed no association with BMD of the femoral neck and lumbar spine. Interestingly, the positive association of UA with BMD of the femur (β = 0.009, 95% CI 0.001–0.017, $P = 0.002$), femoral neck (β = 0.011, 95% CI 0.004–0.019, $P = 0.0029$), and lumbar spine (β = 0.015, 95% CI 0.006–0.024, $P = 0.001$) was significant in the population without T2DM. In contrast, there was no significant correlation between UA and BMD of the femur, femoral neck, and lumbar spine in populations with T2DM and prediabetes.

Moreover, the included 768 Chinese participants (age ≥ 20 years) were classified according to the quartile of UA (Category 1: ≤ 257.3 μmol/L; Category 2: 257.3–311 μmol/L; Category 3: 311–384 μmol/L; Category 4: > 384 μmol/L). Except for age, ALT, AST, TC, and ALP, significant differences were observed in the baseline characteristics among the UA quartiles (Table 4). When compared with other subgroups, participants in the top quartile of UA were more likely to be male, and their BMI, gamma-glutamyl transferase, TG, urea, creatinine, bilirubin, and BMD of the lumbar spine, femur, and femoral neck were all higher, whereas the HDL and T2DM were values lower.

Multiple regression analysis was performed to assess the UA–BMD association in the Chinese subjects (Table 5). In the unadjusted model, UA was positively correlated with BMD of the femur (β = 0.089, 95% CI 0.058–0.119, $P < 0.001$), femoral neck (β = 0.161, 95% CI 0.122–0.199, $P < 0.001$), and lumbar spine (β = 0.066, 95% CI 0.03–0.102, $P < 0.001$) in Chinese subjects. After adjustments for covariates (covariates requiring correction were selected based on the results of the univariate analysis at $P < 0.001$; Table S5), the following results were obtained: UA exhibited association with BMD in both Model 1 (β = 0.074, 95% CI 0.038–0.111, $P < 0.001$; β = 0.167, 95% CI 0.119–0.216, $P < 0.001$; and β = 0.043, 95% CI − 0.001–0.086, $P = 0.057$; respectively) and Model 2 (β = 0.079, 95% CI 0.042–0.117, $P < 0.001$; β = 0.171, 95% CI 0.121–0.22, $P < 0.001$; β = 0.052, 95% CI 0.007–0.097, $P = 0.024$; respectively). Smooth-curve fitting and generalized additive model revealed the nonlinear relationship between UA and BMD of the femur, femoral neck, and lumbar spine (Figure S4). The data analyses revealed that the saturated utility values for determining UA with femoral and femoral neck BMDs using a two-stage linear regression model were 429.9 and 468 μmol/L, respectively (Table S6). However, because the log-likelihood ratio test results in the two-stage linear regression model analysis between UA and lumbar spine BMD were not significant ($P > 0.05$), the general linear correlation analysis was performed between UA and lumbar spine BMD, which indicated a significant positive correlation (correlation coefficient = 0.1325, $P < 0.001$) (Table S7).

Subgroup analyses stratified by gender, age, and T2DM revealed a significantly positive association between UA and femur BMD in the female population (β = 0.089, 95% CI 0.047–0.131, $P < 0.001$) (Table 6). Furthermore, BMDs of the femoral neck in males (β = 0.018, 95% CI 0.028–0.208, $P = 0.001$) and females (β = 0.216, 95% CI 0.15–0.282, $P < 0.001$) exhibited a significant positive correlation, albeit no significant correlation was detected between UA and BMD of the lumbar spine in male and female. UA exhibited a significant positive association with BMD of the femur and femoral neck in the age groups of > 60 years (β = 0.052, 95% CI 0.012–0.092, $P = 0.01$ and β = 0.156, 95% CI 0.095–0.217, $P < 0.001$; respectively) and ≤ 60 years (β = 0.196, 95% CI 0.096–0.29, $P < 0.001$ and β = 0.208, 95% CI 0.12–0.297, $P < 0.001$; respectively); the correlation between UA and BMD of the lumbar

| UA (umol/L) | Q1 (≤261.7 umol/L) | Q2 (261.7–315.2 umol/L) | Q3 (315.2–368.8 umol/L) | Q4 (>368.8 umol/L) | P-value |
|---|---|---|---|---|---|
| Patients, n | 3368 | 3154 | 2812 | 3010 | |
| Age (years) | 49.549 ± 14.868 | 51.062 ± 15.447 | 52.100 ± 15.749 | 53.413 ± 15.753 | < 0.001 |
| Gender | | | | | < 0.001 |
| Male | 584 (17.340%) | 1222 (38.744%) | 1700 (60.455%) | 2207 (73.322%) | |
| Female | 2784 (82.660%) | 1932 (61.256%) | 1112 (39.545%) | 803 (26.678%) | |
| BMI (kg/m$^2$) | 26.250 ± 5.625 | 27.826 ± 5.613 | 28.667 ± 5.556 | 29.873 ± 5.636 | < 0.001 |
| ALT (U/L) | 21.084 ± 12.897 | 24.178 ± 22.870 | 25.958 ± 15.592 | 29.203 ± 19.596 | < 0.001 |
| AST (U/L) | 23.052 ± 9.090 | 24.472 ± 14.201 | 25.359 ± 10.689 | 27.815 ± 19.538 | < 0.001 |
| Alkaline phosphotase (U/L) | 68.080 ± 25.134 | 71.222 ± 26.634 | 71.230 ± 23.249 | 71.722 ± 22.400 | < 0.001 |
| Gamma glutamyl transferase (U/L) | 22.737 ± 28.217 | 27.024 ± 48.891 | 30.422 ± 32.218 | 39.194 ± 58.959 | < 0.001 |
| Bilirubin, total (umol/L) | 10.522 ± 6.598 | 11.280 ± 5.068 | 11.917 ± 5.675 | 12.417 ± 5.243 | < 0.001 |
| Ca(mmol/L) | 2.350 ± 0.090 | 2.360 ± 0.088 | 2.363 ± 0.088 | 2.375 ± 0.094 | < 0.001 |
| Phosphorus (mmol/L) | 1.224 ± 0.176 | 1.212 ± 0.176 | 1.202 ± 0.176 | 1.191 ± 0.189 | < 0.001 |
| Vitamin D (nmol/L) | 67.034 ± 28.801 | 65.720 ± 27.087 | 64.119 ± 25.813 | 63.906 ± 27.114 | < 0.001 |
| TC (mmol/L) | 5.038 ± 1.028 | 5.158 ± 1.081 | 5.133 ± 1.063 | 5.189 ± 1.146 | < 0.001 |
| TG (mmol/L) | 1.443 ± 2.036 | 1.653 ± 1.240 | 1.768 ± 1.273 | 2.118 ± 1.720 | < 0.001 |
| LDH (mmol/L) | 130.238 ± 29.856 | 134.366 ± 46.344 | 134.567 ± 29.381 | 137.778 ± 43.331 | < 0.001 |
| HDL (mmol/L) | 1.550 ± 0.438 | 1.424 ± 0.409 | 1.344 ± 0.395 | 1.256 ± 0.380 | < 0.001 |
| Creatinine (umol/L) | 68.098 ± 29.627 | 75.369 ± 34.264 | 82.676 ± 34.662 | 93.138 ± 43.864 | < 0.001 |
| BU (mmol/L) | 4.300 ± 1.545 | 4.573 ± 1.522 | 4.862 ± 1.828 | 5.419 ± 2.301 | < 0.001 |
| Smoking status | | | | | < 0.001 |
| Some days | 108 (8.554%) | 120 (8.811%) | 101 (7.787%) | 108 (7.458%) | |
| Every day | 551 (43.730%) | 550 (40.382%) | 501 (38.628%) | 437 (30.180%) | |
| Never | 601 (47.698%) | 692 (50.808%) | 695 (53.585%) | 903 (62.362%) | |
| Education, n (%) | | | | | 0.023 |
| Less than 9th grade | 362 (10.748%) | 368 (11.668%) | 295 (10.491%) | 288 (9.568%) | |
| 9–11th grade | 445 (13.213%) | 433 (13.729%) | 390 (13.869%) | 392 (13.023%) | |
| High School Grad/GED or Equivalent | 703 (20.873%) | 703 (22.289%) | 680 (24.182%) | 705 (23.422%) | |
| Some College or AA degree | 989 (29.365%) | 863 (27.362%) | 813 (28.912%) | 893 (29.668%) | |
| College Graduate or above | 865 (25.683%) | 784 (24.857%) | 633 (22.511%) | 730 (24.252%) | |
| Income (%) | | | | | 0.715 |
| Less than $25,000 | 228 (29.008%) | 216 (30.725%) | 197 (30.076%) | 196 (28.283%) | |
| $25,000–74,999 | 349 (44.402%) | 311 (44.239%) | 302 (46.107%) | 295 (42.569%) | |
| More than$75,000 | 198 (25.191%) | 165 (23.471%) | 146 (22.290%) | 191 (27.561%) | |
| Race/ethnicity (%) | | | | | < 0.001 |
| Non-Hispanic Black | 595 (17.666%) | 540 (17.121%) | 536 (19.061%) | 698 (23.189%) | |
| Non-Hispanic White | 1386 (41.152%) | 1357 (43.025%) | 1235 (43.919%) | 1325 (44.020%) | |
| Mexican American | 663 (19.685%) | 617 (19.562%) | 525 (18.670%) | 406 (13.488%) | |
| Other Race—Including Multi-Racial | 353 (10.481%) | 336 (10.653%) | 306 (10.882%) | 352 (11.694%) | |
| Other Hispanic | 371 (11.015%) | 304 (9.639%) | 210 (7.468%) | 229 (7.608%) | |
| Alcohol Intake | | | | | < 0.001 |
| Non-drinker | 903 (26.811%) | 751 (23.811%) | 526 (18.706%) | 542 (18.007%) | |
| 1 to < 5 drinks/month | 1994 (59.204%) | 1869 (59.258%) | 1704 (60.597%) | 1640 (54.485%) | |
| 5 to < 10 drinks/month | 179 (5.315%) | 201 (6.373%) | 187 (6.650%) | 273 (9.070%) | |
| 10+ drinks/month | 292 (8.670%) | 333 (10.558%) | 395 (14.047%) | 555 (18.439%) | |
| T2DM (%) | | | | | < 0.001 |
| Non-T2DM | 2887 (85.719%) | 2617 (82.974%) | 2347 (83.464%) | 2426 (80.598%) | |
| Prediabetes | 184 (5.463%) | 210 (6.658%) | 190 (6.757%) | 229 (7.608%) | |
| T2DM | 297 (8.818%) | 327 (10.368%) | 275 (9.780%) | 355 (11.794%) | |
| Total femur BMD (g/cm$^2$) | 0.907 ± 0.149 | 0.945 ± 0.157 | 0.978 ± 0.156 | 1.006 ± 0.158 | < 0.001 |
| Femoral neck BMD (g/cm$^2$) | 0.780 ± 0.143 | 0.803 ± 0.155 | 0.825 ± 0.154 | 0.842 ± 0.153 | < 0.001 |
| Lumbar spine BMD (g/cm$^2$) | 0.987 ± 0.155 | 1.004 ± 0.157 | 1.028 ± 0.151 | 1.058 ± 0.158 | < 0.001 |

**Table 1**. Baseline characteristics of the study population based on UA quartiles among the American subjects. ALT: Alanine aminotransferase, AST: Aspartate aminotransferase, BU: Blood urea nitrogen, Ca: Total calcium, TC: Cholesterol, LDL: Lactate dehydrogenase, TG: Triglycerides, HbA1c: Glycohemoglobin, HDL: Direct HDL-Cholesterol, T2DM: Type 2 diabetes, UA: Uric acid, BMD: Bone mineral density; BMI: body mass index.

| Exposure | Non-adjusted | Adjust I | Adjust II |
|---|---|---|---|
| Total femur BMD (g/cm$^2$) | | | |
| UA (umol/L) | | | |
| Q1 (≤ 261.7 mmol/L) | Ref | Ref | Ref |
| Q2 (261.7–315.2 mmol/L) | 0.038 (0.030, 0.045) < 0.00001 | 0.001 (− 0.005, 0.007) 0.83105 | 0.003 (− 0.003, 0.009) 0.32804 |
| Q3 (315.2–368.8 mmol/L) | 0.071 (0.063, 0.078) < 0.00001 | 0.004 (− 0.003, 0.010) 0.28511 | 0.005 (− 0.001, 0.012) 0.12881 |
| Q4 (> 368.8 mmol/L) | 0.099 (0.092, 0.107) < 0.00001 | 0.010 (0.003, 0.017) 0.00453 | 0.008 (0.001, 0.015) 0.02913 |
| Femoral neck BMD (g/cm$^2$) | | | |
| UA (umol/L) | | | |
| Q1 (≤ 261.7 mmol/L) | Ref | Ref | Ref |
| Q2 (261.7–315.2 mmol/L) | 0.023 (0.016, 0.031) < 0.00001 | 0.001 (− 0.005, 0.007) 0.70351 | 0.005 (− 0.001, 0.010) 0.12372 |
| Q3 (315.2–368.8 mmol/L) | 0.046 (0.038, 0.053) < 0.00001 | 0.006 (− 0.001, 0.013) 0.07151 | 0.008 (0.002, 0.015) 0.01140 |
| Q4 (> 368.8 mmol/L) | 0.063 (0.055, 0.070) < 0.00001 | 0.011 (0.004, 0.018) 0.00123 | 0.011 (0.004, 0.018) 0.00220 |
| Lumbar spine BMD (g/cm$^2$) | | | |
| UA (umol/L) | | | |
| Q1 (≤ 261.7 mmol/L) | Ref | Ref | Ref |
| Q2 (261.7–315.2 mmol/L) | 0.017 (0.010, 0.025) < 0.00001 | − 0.004 (− 0.012, 0.003) 0.24641 | − 0.002 (− 0.009, 0.005) 0.65903 |
| Q3 (315.2–368.8 mmol/L) | 0.041 (0.034, 0.049) < 0.00001 | 0.004 (− 0.004, 0.011) 0.38190 | 0.004 (− 0.003, 0.012) 0.28539 |
| Q4 (> 368.8 mmol/L) | 0.071 (0.064, 0.079) < 0.00001 | 0.019 (0.011, 0.028) < 0.00001 | 0.014 (0.006, 0.022) 0.00085 |

**Table 2**. Multivariable adjusted associations among quartile of uric acid and bone mass density among the American subjects. Adjust I for: age, gender, body mass index; Adjust II for: age, gender, race, body mass index, diabetes, drinking behavior, smoking behavior, calcium, phosphorus, ALT, AST, alkaline phosphotase, gamma glutamyl transferase, bilirubin, Vitamin D, TC, TG, HDL, LDL, creatinine, blood urea nitrogen.

spine was significant in both the age groups. Interestingly, the positive association of UA with BMD of the femur (β = 0.13, 95% CI 0.08–0.018, $P < 0.001$), femoral neck (β = 0.27, 95% CI 0.2–0.34, $P < 0.001$), and lumbar spine (β = 0.08, 95% CI 0.017–0.142, $P = 0.012$) was significant in the population without T2DM, whereas no association was detected in patients with T2DM.

## Discussion

The present cross-sectional analyses assessed the association of UA and BMD of the lumbar spine, femur, and femoral neck using the representative data of the American population from the NHANES (12,344 individuals; age ≥ 20 years; 2005–2018) and the clinical data of the Chinese population from the Chinese Grade III, Class A hospital (768 subjects; 2021–2023). The results of the multiple regression analysis revealed that, after adjusting for age, gender, race, BMI, and other confounding factors, UA exhibited a notable positive correlation with BMD of the lumbar spine, femur, and femoral neck in both the American and Chinese populations, especially in patients without T2DM. Additionally, a nonlinear relationship between UA and BMD was observed at different sites, and a UA was detected inflection between BMD at different sites. Altogether, the results suggested that controlling SUA within a reasonable range may lead to a better BMD, thereby preventing OP and osteoporotic fractures.

OP is a systemic disease characterized by a decrease in bone mass and strength per unit volume, which leads to bone fractures, making it is a leading cause of morbidity and mortality in the elderly population across the world[23]. Rapid urbanization, lifestyle changes, and obesity have considerably increased the prevalence of hyperuricemia in the general population, with increasing incidences over the past few decades[24,25]. Recently, various epidemiological and laboratory studies have associated UA with multiple biological processes and diseases, including obesity, hypertension, and CKD[4,24,26].

Notably, clinical studies on the association between UA and BMD are limited and have controversial findings. Nevertheless, the findings of this study suggested that, in different ethnic groups, the UA levels within a certain range served as a protective factor for BMD.

Several cross-sectional studies have been reported in Asian populations. A cross-sectional study in the Korean population (2,991 men; age ≥ 50 years) reported a positive association of the serum UA levels with BMDs at three sites (namely L1–L4, femoral neck, and total femur)[27]. In a Chinese population of 631 adult male patients with T2DM (mean age = 57.3 years), increased UA levels prevented OP and bone loss[28]. In an elderly population (men aged ≥ 65 years), higher UA levels were associated with a higher BMD and a lower incidence of brittle fractures at skeletal sites[29]. Another cross-sectional study in the Chinese population (943 men and 4,256 postmenopausal women) reported that the UA levels in the Chinese postmenopausal women exerted a protective effect on bone metabolism[18]. These findings indicated that higher UA levels in different physiological states are positively associated with higher BMD, mainly in the Asian populations[21]. In the American population, a prospective cohort study of fracture cases (total of 1,680 men; 387 men with non-spinal fractures and 1,383 randomized samples) associated higher SUA levels with a lower risk of non-spinal fractures, suggesting the protective effects of UA on BMD[30]. In another study, the analysis of the data of 5,895 individuals (age ≥ 20 years; 3,061 men and 2,834 women) from the NHANES (2005–2008) revealed an inverse association between adult UA and total

| Exposure | Gender | | T2DM or not | | | Race | | | | | Age | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Male | Female | Non-T2DM | Prediabetes | T2DM | Non-Hispanic white | Non-Hispanic black | Mexican American | Other race/ ethnicity | Other Hispanic | >60 | ≤ 60 |
| Total femur BMD (g/cm$^2$) | | | | | | | | | | | | |
| Non-adjusted | | | | | | | | | | | | |
| UA (umol/L) | | | | | | | | | | | | |
| Q1 (≤ 261.7 mmol/L) | Ref | Ref | Ref | Ref | Ref | Ref | Ref | Ref | Ref | Ref | Ref | Ref |
| Q2 (261.7–315.2 mmol/L) | 0.018 (0.004, 0.032) 0.01326 | 0.017 (0.009, 0.026) 0.00009 | 0.039 (0.031, 0.047) < 0.00001 | 0.024 (− 0.005, 0.053) 0.10531 | 0.035 (0.009, 0.061) 0.00780 | 0.041 (0.030, 0.053) < 0.00001 | 0.050 (0.030, 0.069) < 0.00001 | 0.041 (0.025, 0.056) < 0.00001 | 0.021 (− 0.000, 0.043) 0.05523 | 0.021 (0.000, 0.043) 0.04691 | 0.042 (0.028, 0.057) < 0.00001 | 0.042 (0.033, 0.050) < 0.00001 |
| Q3 (315.2–368.8 mmol/L) | 0.034 (0.021, 0.048) < 0.00001 | 0.024 (0.014, 0.034) < 0.00001 | 0.074 (0.066, 0.083) < 0.00001 | 0.051 (0.021, 0.080) 0.00088 | 0.051 (0.024, 0.078) 0.00024 | 0.079 (0.067, 0.090) < 0.00001 | 0.074 (0.054, 0.093) < 0.00001 | 0.065 (0.048, 0.081) < 0.00001 | 0.067 (0.042, 0.091) < 0.00001 | 0.048 (0.027, 0.070) 0.00001 | 0.086 (0.072, 0.101) < 0.00001 | 0.077 (0.069, 0.086) < 0.00001 |
| Q4 (> 368.8 mmol/L) | 0.057 (0.044, 0.071) < 0.00001 | 0.018 (0.007, 0.030) 0.00221 | 0.107 (0.099, 0.115) < 0.00001 | 0.086 (0.057, 0.114) < 0.00001 | 0.052 (0.027, 0.078) 0.00006 | 0.109 (0.098, 0.120) < 0.00001 | 0.094 (0.075, 0.112) < 0.00001 | 0.078 (0.061, 0.096) < 0.00001 | 0.111 (0.088, 0.135) < 0.00001 | 0.090 (0.069, 0.111) < 0.00001 | 0.117 (0.103, 0.131) < 0.00001 | 0.108 (0.099, 0.116) < 0.00001 |
| Adjust I | | | | | | | | | | | | |
| UA (umol/L) | | | | | | | | | | | | |
| Q1 (≤ 261.7 mmol/L) | Ref | Ref | Ref | Ref | Ref | Ref | Ref | Ref | Ref | Ref | Ref | Ref |
| Q2 (261.7–315.2 mmol/L) | 0.002 (− 0.011, 0.015) 0.73865 | 0.004 (− 0.003, 0.011) 0.23896 | 0.029 (0.022, 0.036) < 0.00001 | 0.007 (− 0.019, 0.034) 0.59850 | 0.032 (0.008, 0.056) 0.00956 | 0.027 (0.018, 0.037) < 0.00001 | 0.047 (0.030, 0.064) < 0.00001 | 0.029 (0.015, 0.043) 0.00005 | 0.020 (0.001, 0.039) 0.03935 | 0.016 (− 0.003, 0.034) 0.09312 | 0.032 (0.019, 0.046) < 0.00001 | 0.029 (0.022, 0.036) < 0.00001 |
| Q3 (315.2–368.8 mmol/L) | 0.008 (− 0.004, 0.020) 0.20202 | 0.008 (− 0.001, 0.016) 0.07134 | 0.061 (0.053, 0.068) < 0.00001 | 0.032 (0.004, 0.059) 0.02651 | 0.047 (0.022, 0.072) 0.00027 | 0.057 (0.047, 0.067) < 0.00001 | 0.072 (0.055, 0.089) < 0.00001 | 0.055 (0.040, 0.069) < 0.00001 | 0.066 (0.044, 0.087) < 0.00001 | 0.044 (0.025, 0.062) < 0.00001 | 0.069 (0.055, 0.082) < 0.00001 | 0.056 (0.048, 0.063) < 0.00001 |
| Q4 (> 368.8 mmol/L) | 0.016 (0.004, 0.028) 0.01041 | 0.013 (0.004, 0.023) 0.00777 | 0.085 (0.078, 0.092) < 0.00001 | 0.073 (0.046, 0.099) < 0.00001 | 0.050 (0.026, 0.074) 0.00006 | 0.079 (0.069, 0.089) < 0.00001 | 0.103 (0.087, 0.119) < 0.00001 | 0.061 (0.045, 0.077) < 0.00001 | 0.084 (0.062, 0.105) < 0.00001 | 0.065 (0.047, 0.084) < 0.00001 | 0.089 (0.076, 0.103) < 0.00001 | 0.079 (0.071, 0.086) < 0.00001 |
| Adjust II | | | | | | | | | | | | |
| UA (umol/L) | | | | | | | | | | | | |
| Q1 (≤ 261.7 mmol/L) | Ref | Ref | Ref | Ref | Ref | Ref | Ref | Ref | Ref | Ref | Ref | Ref |
| Q2 (261.7–315.2 mmol/L) | 0.003 (− 0.009, 0.016) 0.58940 | 0.005 (− 0.001, 0.012) 0.11575 | 0.003 (− 0.003, 0.010) 0.35428 | − 0.006 (− 0.031, 0.018) 0.60503 | 0.015 (− 0.007, 0.037) 0.16999 | − 0.000 (− 0.009, 0.009) 0.96797 | 0.023 (0.007, 0.039) 0.00469 | − 0.002 (− 0.016, 0.011) 0.72060 | − 0.007 (− 0.026, 0.011) 0.42804 | − 0.004 (− 0.020, 0.013) 0.66955 | 0.005 (− 0.016, 0.026) 0.64908 | 0.009 (− 0.002, 0.020) 0.11024 |
| Q3 (315.2–368.8 mmol/L) | 0.008 (− 0.004, 0.020) 0.18647 | 0.007 (− 0.001, 0.016) 0.10091 | 0.005 (− 0.002, 0.012) 0.19969 | 0.016 (− 0.010, 0.042) 0.23022 | 0.013 (− 0.010, 0.036) 0.26356 | 0.003 (− 0.008, 0.013) 0.62305 | 0.019 (0.002, 0.035) 0.02506 | − 0.000 (− 0.015, 0.015) 0.96955 | 0.009 (− 0.013, 0.030) 0.43056 | − 0.006 (− 0.025, 0.012) 0.48691 | 0.032 (0.011, 0.052) 0.00271 | 0.019 (0.006, 0.031) 0.00276 |
| Q4 (> 368.8 mmol/L) | 0.011 (− 0.001, 0.023) 0.06227 | 0.009 (− 0.001, 0.020) 0.07670 | 0.009 (0.001, 0.017) 0.02092 | 0.018 (− 0.009, 0.046) 0.18396 | 0.006 (− 0.017, 0.030) 0.60706 | 0.007 (− 0.004, 0.018) 0.20260 | 0.028 (0.011, 0.045) 0.00127 | − 0.016 (− 0.034, 0.002) 0.08228 | 0.011 (− 0.012, 0.035) 0.34917 | − 0.002 (− 0.022, 0.017) 0.82322 | 0.036 (0.014, 0.057) 0.00113 | 0.020 (0.007, 0.033) 0.00272 |
| Femoral neck BMD (g/cm$^2$) | | | | | | | | | | | | |
| Non-adjusted | | | | | | | | | | | | |
| UA (umol/L) | | | | | | | | | | | | |
| Q1 (≤ 261.7 mmol/L) | Ref | Ref | Ref | Ref | Ref | Ref | Ref | Ref | Ref | Ref | Ref | Ref |
| Q2 (261.7–315.2 mmol/L) | 0.020 (0.005, 0.034) 0.00856 | 0.009 (0.000, 0.017) 0.04610 | 0.026 (0.018, 0.034) < 0.00001 | 0.006 (− 0.021, 0.033) 0.66884 | 0.015 (− 0.010, 0.039) 0.24041 | 0.023 (0.012, 0.034) 0.00003 | 0.041 (0.022, 0.061) 0.00002 | 0.026 (0.011, 0.041) 0.00075 | 0.010 (− 0.012, 0.031) 0.37457 | 0.012 (− 0.008, 0.032) 0.25411 | 0.027 (0.014, 0.040) 0.00004 | 0.028 (0.020, 0.036) < 0.00001 |
| Q3 (315.2–368.8 mmol/L) | 0.031 (0.017, 0.045) 0.00001 | 0.014 (0.004, 0.025) 0.00603 | 0.048 (0.039, 0.056) < 0.00001 | 0.027 (− 0.000, 0.055) 0.05211 | 0.041 (0.015, 0.066) 0.00185 | 0.047 (0.036, 0.058) < 0.00001 | 0.055 (0.036, 0.074) < 0.00001 | 0.043 (0.027, 0.059) < 0.00001 | 0.040 (0.016, 0.063) 0.00094 | 0.031 (0.010, 0.052) 0.00344 | 0.063 (0.050, 0.075) < 0.00001 | 0.053 (0.045, 0.062) < 0.00001 |
| Q4 (> 368.8 mmol/L) | 0.048 (0.035, 0.062) < 0.00001 | 0.001 (− 0.010, 0.013) 0.81946 | 0.069 (0.061, 0.077) < 0.00001 | 0.048 (0.021, 0.074) 0.00042 | 0.032 (0.008, 0.056) 0.00832 | 0.070 (0.059, 0.081) < 0.00001 | 0.054 (0.036, 0.072) < 0.00001 | 0.047 (0.030, 0.064) < 0.00001 | 0.071 (0.048, 0.093) < 0.00001 | 0.056 (0.035, 0.076) < 0.00001 | 0.085 (0.073, 0.098) < 0.00001 | 0.071 (0.063, 0.079) < 0.00001 |
| Adjust I | | | | | | | | | | | | |
| Continued | | | | | | | | | | | | |

| Exposure | Gender | | T2DM or not | | | Race | | | | | Age | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Male | Female | Non-T2DM | Prediabetes | T2DM | Non-Hispanic white | Non-Hispanic black | Mexican American | Other race/ ethnicity | Other Hispanic | >60 | ≤60 |
| UA (umol/L) | | | | | | | | | | | | |
| Q1 (≤261.7 mmol/L) | Ref | Ref | Ref | Ref | Ref | Ref | Ref | Ref | Ref | Ref | Ref | Ref |
| Q2 (261.7–315.2 mmol/L) | 0.003 (−0.010, 0.016) 0.62808 | 0.002 (−0.005, 0.008) 0.60882 | 0.020 (0.013, 0.026) < 0.00001 | −0.011 (−0.035, 0.013) 0.37528 | 0.011 (−0.012, 0.034) 0.34400 | 0.015 (0.006, 0.024) 0.00074 | 0.039 (0.023, 0.056) < 0.00001 | 0.018 (0.005, 0.030) 0.00661 | 0.013 (−0.004, 0.030) 0.13910 | 0.011 (−0.006, 0.028) 0.21580 | 0.019 (0.007, 0.031) 0.00202 | 0.019 (0.013, 0.026) < 0.00001 |
| Q3 (315.2–368.8 mmol/L) | 0.007 (−0.005, 0.019) 0.26152 | 0.009 (0.001, 0.018) 0.02713 | 0.040 (0.033, 0.046) < 0.00001 | 0.014 (−0.011, 0.039) 0.28279 | 0.039 (0.015, 0.062) 0.00152 | 0.035 (0.026, 0.044) < 0.00001 | 0.054 (0.037, 0.070) < 0.00001 | 0.039 (0.026, 0.053) < 0.00001 | 0.043 (0.024, 0.062) < 0.00001 | 0.032 (0.014, 0.049) 0.00038 | 0.047 (0.035, 0.059) < 0.00001 | 0.035 (0.028, 0.042) < 0.00001 |
| Q4 (>368.8 mmol/L) | 0.013 (0.001, 0.025) 0.02907 | 0.015 (0.006, 0.025) 0.00202 | 0.055 (0.048, 0.062) < 0.00001 | 0.047 (0.023, 0.072) 0.00016 | 0.037 (0.014, 0.060) 0.00143 | 0.054 (0.045, 0.063) < 0.00001 | 0.066 (0.050, 0.081) < 0.00001 | 0.041 (0.027, 0.056) < 0.00001 | 0.048 (0.029, 0.067) < 0.00001 | 0.041 (0.024, 0.059) < 0.00001 | 0.061 (0.049, 0.073) < 0.00001 | 0.048 (0.041, 0.055) < 0.00001 |
| Adjust II | | | | | | | | | | | | |
| UA (umol/L) | | | | | | | | | | | | |
| Q1 (≤261.7 mmol/L) | Ref | Ref | Ref | Ref | Ref | Ref | Ref | Ref | Ref | Ref | Ref | Ref |
| Q2 (261.7–315.2 mmol/L) | 0.007 (−0.006, 0.019) 0.28953 | 0.005 (−0.001, 0.012) 0.12831 | 0.007 (0.000, 0.013) 0.03876 | −0.017 (−0.041, 0.006) 0.15338 | 0.002 (−0.020, 0.024) 0.85870 | 0.001 (−0.008, 0.010) 0.86060 | 0.027 (0.011, 0.042) 0.00090 | −0.002 (−0.015, 0.010) 0.70390 | −0.001 (−0.018, 0.017) 0.92179 | −0.001 (−0.018, 0.015) 0.89115 | 0.000 (−0.018, 0.019) 0.98088 | 0.009 (−0.002, 0.019) 0.11289 |
| Q3 (315.2–368.8 mmol/L) | 0.009 (−0.002, 0.021) 0.12112 | 0.011 (0.003, 0.019) 0.00981 | 0.008 (0.001, 0.015) 0.02847 | 0.010 (−0.016, 0.035) 0.45995 | 0.017 (−0.006, 0.040) 0.15979 | 0.006 (−0.004, 0.015) 0.26322 | 0.023 (0.006, 0.039) 0.00653 | 0.004 (−0.010, 0.018) 0.56786 | 0.013 (−0.007, 0.034) 0.20544 | 0.000 (−0.018, 0.018) 0.96587 | 0.017 (−0.002, 0.035) 0.07851 | 0.013 (0.001, 0.024) 0.02751 |
| Q4 (>368.8 mmol/L) | 0.012 (0.000, 0.024) 0.04472 | 0.013 (0.003, 0.023) 0.00873 | 0.011 (0.004, 0.019) 0.00290 | 0.018 (−0.008, 0.044) 0.16686 | 0.009 (−0.014, 0.033) 0.43345 | 0.015 (0.005, 0.026) 0.00411 | 0.025 (0.008, 0.042) 0.00362 | −0.010 (−0.027, 0.007) 0.23917 | 0.009 (−0.013, 0.031) 0.42773 | 0.001 (−0.018, 0.020) 0.92420 | 0.028 (0.009, 0.047) 0.00410 | 0.011 (−0.001, 0.024) 0.07041 |
| Lumbar spine BMD ($g/cm^2$) | | | | | | | | | | | | |
| Non-adjusted | | | | | | | | | | | | |
| UA (umol/L) | | | | | | | | | | | | |
| Q1 (≤261.7 mmol/L) | Ref | Ref | Ref | Ref | Ref | Ref | Ref | Ref | Ref | Ref | Ref | Ref |
| Q2 (261.7–315.2 mmol/L) | 0.016 (0.001, 0.030) 0.03298 | 0.006 (−0.003, 0.016) 0.16673 | 0.016 (0.007, 0.024) 0.00018 | 0.015 (−0.015, 0.045) 0.32768 | 0.033 (0.007, 0.060) 0.01485 | 0.022 (0.011, 0.034) 0.00011 | 0.023 (0.004, 0.042) 0.01547 | 0.012 (−0.004, 0.027) 0.13149 | −0.009 (−0.031, 0.013) 0.43764 | 0.021 (−0.001, 0.044) 0.06584 | 0.052 (0.036, 0.068) < 0.00001 | 0.009 (0.001, 0.017) 0.03260 |
| Q3 (315.2–368.8 mmol/L) | 0.031 (0.017, 0.045) 0.00002 | 0.021 (0.010, 0.032) 0.00015 | 0.040 (0.031, 0.048) < 0.00001 | 0.049 (0.018, 0.081) 0.00186 | 0.052 (0.023, 0.080) 0.00034 | 0.045 (0.034, 0.057) < 0.00001 | 0.045 (0.026, 0.064) < 0.00001 | 0.028 (0.012, 0.044) 0.00057 | 0.025 (0.000, 0.049) 0.04935 | 0.038 (0.015, 0.061) 0.00141 | 0.097 (0.081, 0.113) < 0.00001 | 0.027 (0.019, 0.036) < 0.00001 |
| Q4 (>368.8 mmol/L) | 0.063 (0.049, 0.076) < 0.00001 | 0.024 (0.012, 0.037) 0.00013 | 0.070 (0.062, 0.078) < 0.00001 | 0.081 (0.052, 0.111) < 0.00001 | 0.075 (0.049, 0.102) < 0.00001 | 0.070 (0.058, 0.081) < 0.00001 | 0.062 (0.044, 0.080) < 0.00001 | 0.060 (0.043, 0.078) < 0.00001 | 0.076 (0.052, 0.099) < 0.00001 | 0.065 (0.043, 0.087) < 0.00001 | 0.132 (0.116, 0.147) < 0.00001 | 0.056 (0.047, 0.064) < 0.00001 |
| Adjust I | | | | | | | | | | | | |
| UA (umol/L) | | | | | | | | | | | | |
| Continued | | | | | | | | | | | | |

| Exposure | Gender | | T2DM or not | | | Race | | | | | Age | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Male | Female | Non-T2DM | Prediabetes | T2DM | Non-Hispanic white | Non-Hispanic black | Mexican American | Other race/ ethnicity | Other Hispanic | > 60 | ≤ 60 |
| Q1 (≤ 261.7 mmol/L) | Ref | Ref | Ref | Ref | Ref | Ref | Ref | Ref | Ref | Ref | Ref | Ref |
| Q2 (261.7–315.2 mmol/L) | 0.008 (− 0.006, 0.023) 0.26206 | − 0.001 (− 0.009, 0.007) 0.85992 | 0.007 (− 0.001, 0.015) 0.07215 | − 0.002 (− 0.032, 0.029) 0.91345 | 0.037 (0.010, 0.064) 0.00779 | 0.011 (− 0.000, 0.021) 0.05652 | 0.020 (0.001, 0.038) 0.03545 | 0.002 (− 0.013, 0.016) 0.81408 | − 0.010 (− 0.031, 0.011) 0.33732 | 0.016 (− 0.005, 0.037) 0.13131 | 0.039 (0.024, 0.055) < 0.00001 | − 0.001 (− 0.008, 0.007) 0.83861 |
| Q3 (315.2–368.8 mmol/L) | 0.016 (0.002, 0.029) 0.02495 | 0.014 (0.004, 0.025) 0.00522 | 0.028 (0.020, 0.036) < 0.00001 | 0.030 (− 0.001, 0.062) 0.05865 | 0.050 (0.021, 0.078) 0.00064 | 0.026 (0.015, 0.038) < 0.00001 | 0.042 (0.024, 0.060) < 0.00001 | 0.019 (0.004, 0.035) 0.01380 | 0.022 (− 0.001, 0.045) 0.06275 | 0.032 (0.011, 0.053) 0.00351 | 0.075 (0.060, 0.091) < 0.00001 | 0.010 (0.002, 0.018) 0.01478 |
| Q4 (> 368.8 mmol/L) | 0.036 (0.022, 0.049) < 0.00001 | 0.031 (0.019, 0.042) < 0.00001 | 0.051 (0.043, 0.059) < 0.00001 | 0.066 (0.036, 0.097) 0.00002 | 0.069 (0.041, 0.096) < 0.00001 | 0.043 (0.031, 0.054) < 0.00001 | 0.064 (0.046, 0.081) < 0.00001 | 0.043 (0.026, 0.060) < 0.00001 | 0.053 (0.030, 0.076) < 0.00001 | 0.043 (0.022, 0.064) 0.00008 | 0.094 (0.078, 0.109) < 0.00001 | 0.030 (0.022, 0.038) < 0.00001 |
| Adjust II | | | | | | | | | | | | |
| UA (umol/L) | | | | | | | | | | | | |
| Q1 (≤ 261.7 mmol/L) | Ref | Ref | Ref | Ref | Ref | Ref | Ref | Ref | Ref | Ref | Ref | Ref |
| Q2 (261.7–315.2 mmol/L) | 0.010 (− 0.004, 0.024) 0.14700 | − 0.001 (− 0.009, 0.007) 0.76226 | − 0.002 (− 0.009, 0.006) 0.68716 | − 0.020 (− 0.049, 0.009) 0.16920 | 0.015 (− 0.010, 0.041) 0.24350 | − 0.002 (− 0.013, 0.008) 0.65147 | 0.013 (− 0.006, 0.031) 0.17245 | − 0.014 (− 0.029, 0.001) 0.06439 | − 0.024 (− 0.045, − 0.003) 0.02559 | 0.003 (− 0.017, 0.023) 0.76220 | 0.019 (− 0.005, 0.044) 0.12214 | − 0.006 (− 0.018, 0.006) 0.32314 |
| Q3 (315.2–368.8 mmol/L) | 0.015 (0.002, 0.029) 0.02552 | 0.009 (− 0.000, 0.019) 0.06152 | 0.003 (− 0.005, 0.012) 0.45149 | 0.026 (− 0.005, 0.056) 0.10163 | 0.017 (− 0.010, 0.045) 0.20890 | 0.002 (− 0.010, 0.014) 0.77475 | 0.019 (− 0.000, 0.038) 0.05555 | − 0.010 (− 0.027, 0.006) 0.22717 | − 0.010 (− 0.035, 0.015) 0.44017 | − 0.000 (− 0.022, 0.022) 0.98406 | 0.042 (0.018, 0.066) 0.00061 | − 0.005 (− 0.018, 0.008) 0.43676 |
| Q4 (> 368.8 mmol/L) | 0.029 (0.015, 0.042) 0.00003 | 0.016 (0.004, 0.028) 0.00905 | 0.015 (0.006, 0.024) 0.00123 | 0.014 (− 0.018, 0.045) 0.40314 | 0.019 (− 0.008, 0.047) 0.17390 | 0.009 (− 0.004, 0.021) 0.18621 | 0.028 (0.008, 0.048) 0.00543 | − 0.003 (− 0.022, 0.017) 0.78069 | 0.011 (− 0.016, 0.038) 0.43499 | 0.003 (− 0.020, 0.027) 0.79302 | 0.038 (0.013, 0.063) 0.00260 | 0.003 (− 0.011, 0.017) 0.67141 |

**Table 3**. Multivariable adjusted stratified analysis associations among quartile of uric acid and bone mass density among the American subjects. Adjust I for: age, gender, body mass index; Adjust II for: age, gender, race, body mass index, diabetes, drinking behavior, smoking behavior, calcium, phosphorus, ALT, AST, alkaline phosphotase, gamma glutamyl transferase, bilirubin, Vitamin D, TC, TG, HDL, LDL, creatinine, blood urea nitrogen.

| UA (umol/L) | Q1 (≤ 257.3 umol/L) | Q2 (257.3–311 umol/L) | Q3 (311–384 umol/L) | Q4 (> 384 umol/L) | P-value |
|---|---|---|---|---|---|
| Patients, n | 192 | 193 | 193 | 190 | |
| Age (years) | 63.177 ± 12.084 | 63.409 ± 10.394 | 63.922 ± 10.865 | 62.663 ± 13.136 | 0.875 |
| Gender | | | | | < 0.001 |
| Male | 46 (23.958%) | 50 (25.907%) | 74 (38.342%) | 114 (60.000%) | |
| Female | 146 (76.042%) | 143 (74.093%) | 119 (61.658%) | 76 (40.000%) | |
| BMI (kg/m$^2$) | 22.492 ± 3.072 | 23.986 ± 3.666 | 24.741 ± 3.225 | 24.891 ± 3.025 | < 0.001 |
| ALT (U/L) | 22.398 ± 13.819 | 25.225 ± 37.262 | 25.314 ± 30.163 | 24.777 ± 15.701 | 0.265 |
| AST (U/L) | 23.655 ± 11.750 | 24.461 ± 27.519 | 24.659 ± 16.990 | 24.075 ± 10.043 | 0.187 |
| Alkaline phosphotase (U/L) | 90.271 ± 34.636 | 87.743 ± 30.406 | 86.256 ± 25.564 | 93.901 ± 30.469 | 0.241 |
| Gamma glutamyl transferase (U/L) | 30.971 ± 44.268 | 34.555 ± 49.047 | 34.103 ± 41.767 | 41.719 ± 41.717 | < 0.001 |
| Bilirubin, total (umol/L) | 10.607 ± 6.372 | 11.713 ± 5.089 | 11.586 ± 5.716 | 10.492 ± 5.480 | 0.004 |
| TC (mmol/L) | 4.969 ± 1.170 | 5.202 ± 1.116 | 5.082 ± 1.070 | 5.434 ± 5.548 | 0.119 |
| TG (mmol/L) | 1.545 ± 1.393 | 1.835 ± 1.810 | 1.711 ± 1.128 | 2.432 ± 2.518 | < 0.001 |
| HDL (mmol/L) | 1.436 ± 0.456 | 1.438 ± 0.497 | 1.369 ± 0.387 | 1.200 ± 0.352 | < 0.001 |
| LDL (mmol/L) | 2.807 ± 0.966 | 3.042 ± 0.902 | 3.080 ± 0.909 | 2.966 ± 0.976 | 0.009 |
| Creatinine (umol/L) | 56.873 ± 17.324 | 64.188 ± 48.026 | 71.078 ± 34.558 | 91.201 ± 61.975 | < 0.001 |
| BU (mmol/L) | 5.158 ± 1.576 | 5.586 ± 1.886 | 6.188 ± 2.229 | 7.643 ± 4.211 | < 0.001 |
| T2DM (%) | | | | | < 0.001 |
| Yes | 86 (44.792%) | 108 (55.959%) | 118 (61.140%) | 79 (41.579%) | |
| No | 106 (55.208%) | 85 (44.041%) | 75 (38.860%) | 111 (58.421%) | |
| Lumbar spine BMD (g/cm$^2$) | 0.931 ± 0.168 | 0.943 ± 0.156 | 0.967 ± 0.200 | 0.997 ± 0.192 | 0.008 |
| Femoral neck BMD (g/cm$^2$) | 0.772 ± 0.155 | 0.818 ± 0.177 | 0.823 ± 0.130 | 0.933 ± 0.239 | < 0.001 |
| Total femur BMD (g/cm$^2$) | 0.835 ± 0.149 | 0.851 ± 0.134 | 0.873 ± 0.116 | 0.923 ± 0.176 | < 0.001 |

**Table 4**. Baseline characteristics of the study population based on UA quartiles in the Chinese. ALT: Alanine aminotransferase, AST: Aspartate aminotransferase, BU: Blood urea nitrogen, TC: Cholesterol, LDL: Lactate dehydrogenase, TG: Triglycerides, HbA1c: Glycohemoglobin, HDL: Direct HDL-Cholesterol, T2DM: Type 2 diabetes, UA: Uric acid, BMD: bone mineral density; BMI: body mass index.

| Exposure | Non-adjusted | Adjust I | Adjust II |
|---|---|---|---|
| Total femur BMD (g/cm$^2$) | | | |
| UA (umol/L) | | | |
| Q1 (≤ 257.3 mmol/L) | Ref | Ref | Ref |
| Q2 (257.3–311 mmol/L) | 0.016 (− 0.014, 0.047) 0.29217 | 0.031 (− 0.003, 0.064) 0.07058 | 0.034 (0.001, 0.068) 0.04627 |
| Q3 (311–384 mmol/L) | 0.038 (0.008, 0.069) 0.01379 | 0.040 (0.006, 0.075) 0.02072 | 0.044 (0.009, 0.079) 0.01305 |
| Q4 (> 384 mmol/L) | 0.089 (0.058, 0.119) < 0.00001 | 0.074 (0.038, 0.111) 0.00008 | 0.079 (0.042, 0.117) 0.00004 |
| Femoral neck BMD(g/cm$^2$) | | | |
| UA (umol/L) | | | |
| Q1 (≤ 257.3 mmol/L) | Ref | Ref | Ref |
| Q2 (257.3–311 mmol/L) | 0.046 (0.008, 0.084) 0.01685 | 0.078 (0.034, 0.121) 0.00051 | 0.079 (0.035, 0.123) 0.00052 |
| Q3 (311–384 mmol/L) | 0.051 (0.013, 0.088) 0.00828 | 0.069 (0.025, 0.114) 0.00238 | 0.067 (0.022, 0.113) 0.00391 |
| Q4 (> 384 mmol/L) | 0.161 (0.122, 0.199) < 0.00001 | 0.167 (0.119, 0.216) < 0.00001 | 0.171 (0.121, 0.220) < 0.00001 |
| Lumbar spine BMD (g/cm$^2$) | | | |
| UA (umol/L) | | | |
| Q1 (≤ 257.3 mmol/L) | Ref | Ref | Ref |
| Q2 (257.3–311 mmol/L) | 0.012 (− 0.024, 0.049) 0.50498 | 0.013 (− 0.028, 0.053) 0.53243 | 0.017 (− 0.023, 0.058) 0.40581 |
| Q3 (311–384 mmol/L) | 0.036 (− 0.000, 0.072) 0.05272 | 0.019 (− 0.023, 0.060) 0.37593 | 0.027 (− 0.015, 0.069) 0.20438 |
| Q4 (> 384 mmol/L) | 0.066 (0.030, 0.102) 0.00039 | 0.043 (− 0.001, 0.086) 0.05744 | 0.052 (0.007, 0.097) 0.02459 |

**Table 5**. Multivariable adjusted stratified analysis associations among quartile of uric acid and bone mass density in the Chinese. Adjust I for: age, gender, body mass index; Adjust II for: age, gender, body mass index, diabetes, alkaline phosphotase, HDL.

| | T2DM or not | | Gender | | Age | |
|---|---|---|---|---|---|---|
| | Non-T2DM | T2DM | Male | Female | > 60 | ≤ 60 |
| Total femur BMD (g/cm$^2$) | | | | | | |
| Non-adjusted | | | | | | |
| UA (umol/L) | | | | | | |
| Q1 (≤ 257.3 mmol/L) | Ref | Ref | Ref | Ref | Ref | Ref |
| Q2 (257.3–311 mmol/L) | 0.043 (0.002, 0.085) 0.04146 | 0.014 (− 0.029, 0.058) 0.51336 | − 0.001 (− 0.068, 0.066) 0.97078 | 0.022 (− 0.009, 0.054) 0.16925 | 0.011 (− 0.023, 0.044) 0.52442 | 0.035 (− 0.038, 0.107) 0.34802 |
| Q3 (311–384 mmol/L) | 0.073 (0.032, 0.113) 0.00053 | 0.031 (− 0.013, 0.075) 0.16687 | − 0.014 (− 0.074, 0.047) 0.65852 | 0.048 (0.015, 0.081) 0.00451 | 0.039 (0.006, 0.072) 0.02012 | 0.037 (− 0.037, 0.111) 0.32637 |
| Q4 (> 384 mmol/L) | 0.136 (0.091, 0.181) < 0.00001 | 0.047 (0.007, 0.087) 0.02208 | 0.033 (− 0.023, 0.090) 0.24920 | 0.076 (0.038, 0.115) 0.00013 | 0.069 (0.036, 0.102) 0.00005 | 0.184 (0.104, 0.264) 0.00001 |
| Adjust I | | | | | | |
| UA (umol/L) | | | | | | |
| Q1 (≤ 257.3 mmol/L) | Ref | Ref | Ref | Ref | Ref | Ref |
| Q2 (257.3–311 mmol/L) | 0.045 (0.004, 0.086) 0.03138 | 0.016 (− 0.039, 0.072) 0.56615 | 0.026 (− 0.066, 0.118) 0.57800 | 0.034 (0.002, 0.066) 0.04044 | 0.030 (− 0.006, 0.066) 0.10664 | 0.033 (− 0.040, 0.106) 0.37773 |
| Q3 (311–384 mmol/L) | 0.061 (0.019, 0.102) 0.00442 | 0.025 (− 0.034, 0.083) 0.40763 | − 0.011 (− 0.095, 0.073) 0.78992 | 0.062 (0.027, 0.096) 0.00047 | 0.054 (0.017, 0.091) 0.00428 | 0.026 (− 0.051, 0.104) 0.51047 |
| Q4 (> 384 mmol/L) | 0.125 (0.076, 0.173) < 0.00001 | 0.021 (− 0.034, 0.075) 0.45685 | 0.032 (− 0.049, 0.112) 0.43953 | 0.096 (0.055, 0.137) < 0.00001 | 0.053 (0.015, 0.091) 0.00697 | 0.162 (0.068, 0.256) 0.00098 |
| Adjust II | | | | | | |
| UA(umol/L) | | | | | | |
| Q1 (≤ 257.3 mmol/L) | Ref | Ref | Ref | Ref | Ref | Ref |
| Q2 (257.3–311 mmol/L) | 0.044 (0.002, 0.086) 0.03980 | 0.015 (− 0.042, 0.071) 0.60855 | 0.046 (− 0.052, 0.143) 0.36015 | 0.035 (0.003, 0.067) 0.03360 | 0.031 (− 0.006, 0.068) 0.10483 | 0.053 (− 0.026, 0.132) 0.18941 |
| Q3 (311–384 mmol/L) | 0.060 (0.017, 0.102) 0.00594 | 0.025 (− 0.035, 0.085) 0.40919 | 0.010 (− 0.082, 0.101) 0.83326 | 0.060 (0.026, 0.095) 0.00073 | 0.052 (0.014, 0.089) 0.00779 | 0.036 (− 0.047, 0.118) 0.39953 |
| Q4 (> 384 mmol/L) | 0.130 (0.080, 0.180) < 0.00001 | 0.022 (− 0.035, 0.079) 0.44980 | 0.053 (− 0.034, 0.140) 0.23689 | 0.089 (0.047, 0.131) 0.00004 | 0.052 (0.012, 0.092) 0.01095 | 0.196 (0.096, 0.297) 0.00019 |
| Femoral neck BMD (g/cm$^2$) | | | | | | |
| Non-adjusted | | | | | | |
| UA (umol/L) | | | | | | |
| Q1 (≤ 257.3 mmol/L) | Ref | Ref | Ref | Ref | Ref | Ref |
| Q2 (257.3–311 mmol/L) | 0.130 (0.075, 0.186) < 0.00001 | − 0.043 (− 0.092, 0.006) 0.08728 | − 0.058 (− 0.131, 0.015) 0.12315 | 0.080 (0.037, 0.124) 0.00034 | 0.037 (− 0.007, 0.082) 0.10097 | 0.079 (0.013, 0.144) 0.01986 |
| Q3 (311–384 mmol/L) | 0.101 (0.047, 0.155) 0.00028 | 0.016 (− 0.035, 0.066) 0.54233 | 0.003 (− 0.064, 0.069) 0.93949 | 0.058 (0.012, 0.103) 0.01286 | 0.047 (0.003, 0.091) 0.03691 | 0.068 (0.002, 0.135) 0.04564 |
| Q4 (> 384 mmol/L) | 0.248 (0.188, 0.308) < 0.00001 | 0.086 (0.039, 0.132) 0.00033 | 0.083 (0.020, 0.145) 0.01014 | 0.185 (0.131, 0.239) < 0.00001 | 0.152 (0.107, 0.196) < 0.00001 | 0.204 (0.131, 0.276) < 0.00001 |
| Adjust I | | | | | | |
| UA (umol/L) | | | | | | |
| Q1 (≤ 257.3 mmol/L) | Ref | Ref | Ref | Ref | Ref | Ref |
| Q2 (257.3–311 mmol/L) | 0.139 (0.082, 0.197) < 0.00001 | − 0.044 (− 0.101, 0.013) 0.13218 | − 0.013 (− 0.108, 0.083) 0.79749 | 0.100 (0.051, 0.149) 0.00007 | 0.073 (0.018, 0.128) 0.00955 | 0.083 (0.016, 0.149) 0.01583 |
| Q3 (311–384 mmol/L) | 0.102 (0.044, 0.161) 0.00066 | 0.022 (− 0.039, 0.083) 0.48013 | 0.026 (− 0.062, 0.114) 0.56142 | 0.078 (0.025, 0.130) 0.00396 | 0.063 (0.007, 0.119) 0.02884 | 0.071 (0.001, 0.141) 0.04905 |
| Q4 (> 384 mmol/L) | 0.262 (0.194, 0.330) < 0.00001 | 0.035 (− 0.022, 0.092) 0.22735 | 0.093 (0.009, 0.177) 0.03160 | 0.208 (0.144, 0.271) < 0.00001 | 0.154 (0.095, 0.212) < 0.00001 | 0.206 (0.122, 0.291) < 0.00001 |
| Adjust II | | | | | | |
| UA (umol/L) | | | | | | |
| Q1 (≤ 257.3 mmol/L) | Ref | Ref | Ref | Ref | Ref | Ref |
| Q2 (257.3–311 mmol/L) | 0.142 (0.084, 0.201) < 0.00001 | − 0.045 (− 0.104, 0.014) 0.13648 | 0.019 (− 0.082, 0.120) 0.71184 | 0.094 (0.045, 0.144) 0.00023 | 0.077 (0.021, 0.132) 0.00731 | 0.082 (0.012, 0.151) 0.02269 |
| Q3 (311–384 mmol/L) | 0.106 (0.047, 0.165) 0.00050 | 0.020 (− 0.043, 0.083) 0.53836 | 0.051 (− 0.044, 0.146) 0.29241 | 0.067 (0.014, 0.121) 0.01457 | 0.064 (0.007, 0.121) 0.02949 | 0.062 (− 0.010, 0.135) 0.09553 |
| Q4 (> 384 mmol/L) | 0.270 (0.200, 0.340) < 0.00001 | 0.035 (− 0.025, 0.095) 0.25915 | 0.118 (0.028, 0.208) 0.01113 | 0.216 (0.150, 0.282) < 0.00001 | 0.156 (0.095, 0.217) < 0.00001 | 0.208 (0.120, 0.297) < 0.00001 |
| Lumbar spine BMD (g/cm$^2$) | | | | | | |
| Non-adjusted | | | | | | |
| Continued | | | | | | |

| | T2DM or not | | Gender | | Age | |
|---|---|---|---|---|---|---|
| | Non-T2DM | T2DM | Male | Female | > 60 | ≤ 60 |
| UA (umol/L) | | | | | | |
| Q1 (≤ 257.3 mmol/L) | Ref | Ref | Ref | Ref | Ref | Ref |
| Q2 (257.3–311 mmol/L) | 0.042 (− 0.008, 0.092) 0.09861 | − 0.002 (− 0.053, 0.049) 0.93441 | − 0.006 (− 0.079, 0.067) 0.86765 | 0.017 (− 0.023, 0.057) 0.40713 | 0.005 (− 0.037, 0.047) 0.80591 | 0.040 (− 0.030, 0.111) 0.26495 |
| Q3 (311–384 mmol/L) | 0.042 (− 0.007, 0.092) 0.09100 | 0.062 (0.009, 0.114) 0.02154 | 0.058 (− 0.009, 0.126) 0.09206 | 0.006 (− 0.036, 0.048) 0.76454 | 0.034 (− 0.008, 0.076) 0.10890 | 0.046 (− 0.026, 0.117) 0.21074 |
| Q4 (> 384 mmol/L) | 0.067 (0.013, 0.121) 0.01470 | 0.061 (0.013, 0.108) 0.01235 | 0.042 (− 0.020, 0.105) 0.18699 | 0.038 (− 0.010, 0.086) 0.11851 | 0.061 (0.020, 0.102) 0.00339 | 0.093 (0.014, 0.171) 0.02211 |
| Adjust I | | | | | | |
| UA (umol/L) | | | | | | |
| Q1 (≤ 257.3 mmol/L) | Ref | Ref | Ref | Ref | Ref | Ref |
| Q2 (257.3–311 mmol/L) | 0.040 (− 0.012, 0.092) 0.13374 | − 0.022 (− 0.086, 0.042) 0.50418 | 0.004 (− 0.089, 0.097) 0.93861 | 0.016 (− 0.029, 0.061) 0.48991 | 0.005 (− 0.044, 0.054) 0.83592 | 0.044 (− 0.027, 0.115) 0.22290 |
| Q3 (311–384 mmol/L) | 0.040 (− 0.012, 0.093) 0.13343 | 0.009 (− 0.058, 0.076) 0.79467 | 0.043 (− 0.042, 0.129) 0.32238 | 0.006 (− 0.042, 0.054) 0.80226 | 0.020 (− 0.029, 0.070) 0.42477 | 0.038 (− 0.036, 0.111) 0.31900 |
| Q4 (> 384 mmol/L) | 0.071 (0.010, 0.133) 0.02409 | 0.015 (− 0.047, 0.077) 0.62870 | 0.038 (− 0.043, 0.119) 0.35706 | 0.051 (− 0.005, 0.107) 0.07339 | 0.037 (− 0.014, 0.087) 0.15523 | 0.059 (− 0.031, 0.150) 0.19990 |
| Adjust II | | | | | | |
| UA (umol/L) | | | | | | |
| Q1 (≤ 257.3 mmol/L) | Ref | Ref | Ref | Ref | Ref | Ref |
| Q2 (257.3–311 mmol/L) | 0.041 (− 0.011, 0.093) 0.12055 | − 0.026 (− 0.091, 0.040) 0.44629 | − 0.015 (− 0.113, 0.082) 0.75977 | 0.027 (− 0.018, 0.072) 0.24746 | 0.004 (− 0.045, 0.054) 0.86405 | 0.037 (− 0.038, 0.113) 0.33565 |
| Q3 (311–384 mmol/L) | 0.044 (− 0.009, 0.096) 0.10462 | 0.006 (− 0.063, 0.075) 0.86589 | 0.039 (− 0.053, 0.131) 0.41054 | 0.018 (− 0.031, 0.066) 0.47177 | 0.020 (− 0.031, 0.070) 0.44938 | 0.033 (− 0.045, 0.111) 0.40755 |
| Q4 (> 384 mmol/L) | 0.080 (0.017, 0.142) 0.01264 | 0.018 (− 0.048, 0.083) 0.59788 | 0.042 (− 0.045, 0.129) 0.34138 | 0.056 (− 0.002, 0.113) 0.05720 | 0.044 (− 0.009, 0.097) 0.10295 | 0.050 (− 0.046, 0.146) 0.31068 |

**Table 6**. Multivariable adjusted stratified analysis associations among quartile of uric acid and bone mass density in the Chinese. Adjust I for: age, gender, body mass index; Adjust II for: age, gender, body mass index, diabetes, alkaline phosphotase, HDL.

TBS, suggesting that maintaining serum UA at the saturation levels facilitated OP and fracture prevention[31]. However, a study in the American population reported no association between UA and lumbar BMD after full adjustment for potential confounders[21]. Additionally, a Mendelian randomization analysis study including 28,141 participants of European descent and a Biobank (4,807 cases and 332,352 controls) of gout data sets from the United Kingdom, reported no causal relationship between UA and BMD[32]. Such controversial results of the UA–BMD relationship may be attributed to the heterogeneity between the corresponding studies, including different study designs, study samples, ethnic distribution, and controlled confounding variables[33]. Hence, the data of both American (NHANES) and Chinese subjects was included in this study, and adjustments were made for multiple confounders.

Oxidative stress has been reported to inhibit bone formation and promote bone resorption. Changes in the redox state are associated with bone remodeling processes that allow for sustained bone regeneration through the synergistic action of osteocytes (i.e., osteoclasts, osteoblasts, and osteocytes). Changes in the antioxidant system seem to be involved in the pathogenesis of bone loss. The antioxidant system induces apoptosis of osteoblasts and osteoblasts, which favors osteoclastogenesis and inhibits mineralization and osteogenesis. Excessive osteocyte apoptosis has been associated with oxidative stress, which causes an imbalance that favors osteoclastogenesis, leading to increased bone remodeling and bone loss. Antioxidants contribute to the activation of osteoblast differentiation, mineralization processes, and a decrease in osteoclast activity, either directly or by counteracting the effects of oxidants[34]. UA is an important antioxidant in living organisms and scavenges peroxidase, hydroxyl, and singlet oxygen free radicals[35–37]. Consequently, lower UA concentrations reduce resistance to oxidative stress, thereby promoting osteoclast differentiation and decreasing osteoblast activity, resulting in enhanced bone resorption and bone loss[34,38]. Reportedly, UA plays an important role in expanding bone marrow mesenchymal stem cells and promoting osteogenic differentiation in humans[34,38]. Nutritional supplementation is critical to preventing OP[35], indicating that individuals with high UA levels may have obtained more nutrients than those with low UA levels[4,13,39]. UA can serve as an indicator of the nutritional status of an individual. The main source of UA is purine-rich foods, which are also high in protein. People with better living conditions and better nutritional intake may present a higher BMD than those with low UA levels[24,39]. Herein, the results of multiple regression models revealed that the the positive association between UA and BMD was more significant in non-T2DM subjects in both the American and Chinese populations. Obesity is an independent risk factor for T2DM[40,41], and individuals with high UA levels exhibit more lean body mass and less fat mass, which has been positively correlated with BMD[42].

The results of smooth-curve fitting (Figures S2 and S4) and threshold effect analysis (Tables S3 and S6) indicated that, in the American population, the saturated utility values of UA with BMD of the femur, femoral neck, and lumbar spine were 410.4, 410.4, and 452 μmol/L, respectively (Table S3). In the Chinese population, the saturated utility values of UA with femoral BMD and femoral neck BMD were 429.9 and 468 μmol/L, respectively (Table S6).

The present study offers several advantages. First, as it is based on a large sample data from NHANES and real clinical data from the Chinese Grade III, Class A hospital, the sample included in this study is multi-layer random, making the data highly reliable and standardized. Second, subjects from two different demographics, namely Chinese and American subjects, were included, and racial subgroup analyses were performed on the American subjects to further elucidate the differences in the relationship between UA and BMD among different races. Third, this study excluded or controlled for many important confounding factors, including age, sex, race, BMI, T2DM, serum urea nitrogen, and creatinine. Fourth, the relationships between SUA and BMD of three different sites, namely the lumbar spine, femur, and femoral neck, were discussed. Finally, a two-stage linear regression model was employed to determine the saturation utility values between UA and BMD of different body parts.

This study has some limitations. First, despite the association between UA levels and BMD, no causal relationship could be established. Second, no other impact of medications (e.g., urate-lowering drugs, calcium supplements, osteoporosis treatment), and relevant biochemical markers were analyzed in this study, including bone metabolism markers such as parathyroid hormone and bone turnover markers such as type I procollagen N-terminal propeptide, osteocalcin, and type I collagen cross-linked c-terminal peptide. Third, owing to the retrospective nature of the study, the data on confounding factors such as alcohol consumption, smoking, and serum phosphorus in the Chinese population was lacking. Fourth, Chinese participants had spontaneous full medical examinations or hospitalizations, which may have induced bias, as the characteristics of the participants probably differed from those of the general population. Finally, no fracture history was examined. Hence, conducting large-scale, follow-up studies incorporating additional biochemical indicators and following a multicenter randomized design are essential to validate the reliability and reproducibility of the present results.

Nevertheless, the present study included Chinese and American subjects and is based on the results of multiple regression models suggesting the protective effects of SUA on BMD. The protective effect could be found even after adjusting for confounders such as age, BMI, race, and sex. The saturation effect value between the serum UA levels and BMD at different sites was determined by the threshold effect analysis. These findings highlight the importance of recognizing the dual role of UA in clinical practice. In medical activities, we should pay attention to the high-risk population for uric acid screening. In health education, emphasis on reasonable diet, appropriate exercise, to keep serum UA in a reasonable range is very important. Future studies should include longitudinal or interventional studies to examine the causal relationship between UA levels and BMD and explore the role of other potential biomarkers in bone health.

## Data availability

The datasets used and/or analysed during the current study available from the corresponding author on reasonable request.

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## Author contributions

WL and XL had full access to all of the data in the study and takes responsibility. for the integrity of the data and the accuracy of the data analysis. Study concept and design: WL, XL, YP, YZ and KC. Acquisition of data: WL and XL. Analysis and interpretation of data: WL and XL. Drafting of the manuscript: WL. Critical revision of the manuscript for important intellectual content: All authors. Statistical analysis: WL and XL. Study supervision: KC and YP.

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## Declarations

## Competing interests

The authors declare no competing interests.

## Additional information

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