



# OPEN Association between serum vitamin A and bone mineral density in adolescents

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Vitamin A is essential for growth and development, immune function, vision, and gene expression. The association between adult bone mineral density (BMD) and vitamin A has been extensively studied, the findings are heterogeneous. Studies investigating the direct correlation between vitamin A and BMD in children are, nonetheless, few. The purpose of this study is to investigate the link between vitamin A and BMD in American teenagers. In this cross-sectional investigation, 6,002 adolescents between the ages of 12 and 19 participated in the National Health and Nutrition Examination Survey (NHANES), which was performed between 2001 and 2006. The relationship between serum Vitamin A and BMD was assessed using a weighted multivariate linear regression model and smooth-fitting curves. Increased serum Vitamin A is substantially positively linked with BMD of the thoracic spine, lumbar spine, pelvis, trunk bone, and total BMD after controlling for pertinent factors. According to the threshold effect curve, the impact of Vitamin A is significant ( $P < 0.05$ ) when it is below the saturation threshold. Males exhibit a stronger positive association, according to subgroup analysis. According to our research, there is a strong positive connection and saturation effect between serum Vitamin A and BMD in American adolescents.

**Keywords** Serum vitamin A, Bone mineral density, Adolescents, NHANES

As an essential component of the human body, bones serve a wide range of functions such as hematopoiesis, storage, mobility, support, and protection<sup>1</sup>. Bone development consists of both straight growth and bone mass buildup<sup>2</sup>. During adolescence, bone mass can reach 40–60% of adult bone mass, and by the age of 18, up to 90% of peak bone mass can be accumulated, which is critical for building a strong skeletal system<sup>3,4</sup>. Adolescence is a vital phase for fast bone growth and development. Establishing appropriate nutritional status during this time is essential for obtaining peak bone mass<sup>5,6</sup>.

Vitamin A, known chemically as retinol when found in the plasma, is a fat-soluble nutrient that our bodies cannot produce on their own. It must be obtained through diet, predominantly from retinyl esters present in animal-derived foods and from beta-carotene, which is abundant in a variety of vegetables and fruits<sup>7</sup>. Vitamin A is essential for human health since it affects not only eyesight but also immunological response, cell division, and organ development<sup>7–10</sup>. According to recent research, the relationship between vitamin A and bone mineral density (BMD) varies. A study has indicated that there is a positive correlation between serum vitamin A and BMD among Chinese adults aged 40–75, including 2,101 females and 10,53 males<sup>11</sup>. A study conducted in 2021 pointed out that among non-Hispanic participants (aged  $\geq 18$  years), there is a positive correlation between vitamin A and BMD at the femoral neck and total hip joints<sup>12</sup>. On the other hand, a longitudinal study of 2,322 males (aged 49 to 51) found that men with retinol levels ( $> 103.12$  micrograms per deciliter [3.60 micromoles per liter]) had a 7-fold increased overall risk of fracture compared to men with lower levels ( $P < 0.001$ )<sup>13</sup>. However, in a Norwegian study of 21,774 individuals aged 65 to 79, serum vitamin A and hip fractures in both men and women has no significant correlation<sup>14</sup>. This study was conducted in adolescents, and currently, there is still a scarcity of research in adolescent and pediatric populations.

The research aims to investigate the correlation between serum vitamin A and BMD among adolescents between the ages of 12 and 19, utilizing data obtained from the National Health and Nutrition Examination Survey (NHANES).

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## Procedures and materials

### Research population and data sources

The Centers for Disease Control and Prevention (CDC) in the NHANES, a cross-sectional population study intended to evaluate the health and nutritional status of adults and children (<https://www.cdc.gov/nchs/nhanes/index.htm>). The NHANES has been conducted every two years since 1999, using a nationally representative sample. Numerous types of data are included in NHANES, such as questionnaires, laboratory, examination, nutritional, and demographic data. This study gathered data from the NHANES database for teenagers aged 12 to 19 between 2001 and 2006, resulting in 31,509 individuals. We excluded participants who were not aged 12–19 ( $n=24,431$ ), did not have BMD information ( $n=430$ ), or serum vitamin A information ( $n=646$ ). In the end, 6,002 people took part in the research. (Fig. 1).

### Serum vitamin A measurement

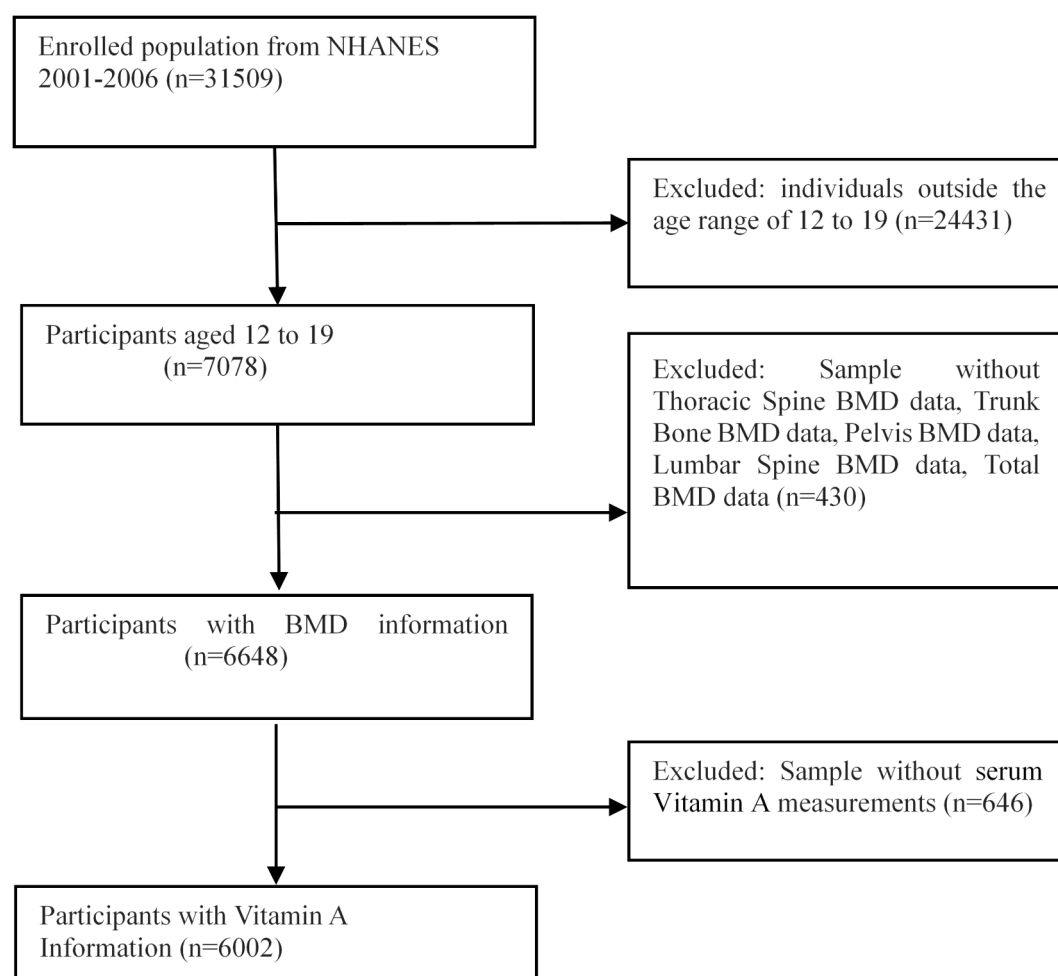
Photodiode array detection and high-performance liquid chromatography (HPLC) were used to assess the amounts of serum vitamin A (retinol).

### BMD examination

In the NHANES mobile examination centers, dual-energy X-ray absorptiometry (DXA), performed by certified and trained radiology technologists, is used to determine BMD, expressed in ( $\text{g}/\text{cm}^2$ ). DXA scans are capable of measuring the soft tissue and bone in every part of the body, including the head, arms, legs, and trunk. Furthermore, measures of particular regional skeletal structures, including the lumbar spine, thoracic spine, pelvis, and ribs, can be acquired. A Hologic QDR-4500 A fan-beam densitometer (Hologic, Inc., Bedford, Massachusetts) was used to obtain the whole-body DXA scans.

### Covariate

In the study, the following covariates were assessed: age (years), gender (male/female), height (cm), race (Mexican American, Other Hispanic, White Non-Hispanic, Black Non-Hispanic, Other Race), poverty income



**Fig. 1.** A flow chart showing the participants in NHANES between 2001 and 2006. *NHANES* National Health and Nutrition Examination Survey, *BMD* bone mineral density.

ratio (PIR), phosphorus levels (mg/dL), vitamin D levels (nmol/L), total calcium (mg/dL), carbohydrate intake (gm), protein intake (gm), and Vitamin A Retinol Activity Equivalents (RAE) (mcg). To learn more about the measurement techniques and data collecting for serum Vitamin A, BMD, and other variables, check out the NHANES website at (<http://www.cdc.gov/nchs/nhanes/index.htm>).

### Analysis using statistics

Using a significance level of  $p < 0.05$ , all analyses in this study were carried out using R (<http://www.r-project.org>) and EmpowerStats (<http://www.empowerstats.com>). Serum Vitamin A concentrations (ug/dL) were sorted from lowest to highest and grouped into the following four quartiles (Q1: 11.50–38.15; Q2: 38.16–44.79; Q3: 44.80–52.22; Q4: 52.30–149.00) for analysis, following the NHANES analytical criteria. Weighted NHANES samples were utilized. Three models were created in order to investigate the relationship between serum Vitamin A levels and BMD: Model 1 without covariate correction. Model 2 with age, gender, and race adjustments. Model 3 evaluated the relationship between serum Vitamin A and BMD by using a weighted multivariate linear regression model and smooth fitting curves after controlling for age, gender, race, poverty income ratio, standing height, protein, carbohydrates, Vitamin A RAE, total calcium, phosphorus, and Vitamin D. The relationship between Vitamin A and BMD was assessed using the threshold effect, and subgroup analyses were carried out as well.

### Ethics permission and participation consent

The National Center for Health Statistics Ethics Review Board approved the acquisition of the publicly accessible NHANES data, which were used for this study's analysis (<https://www.cdc.gov/nchs/nhanes/index.htm>). Written informed consent was obtained from all participants or their parents or guardians for individuals under 18 years of age prior to participation in the study. The research methods were conducted in strict accordance with established standards and legal constraints.

## Result

### Participant characteristics

The study included 6,002 individuals, with a mean age of  $15.46 \pm 2.28$  and 51.62% being male. Serum Vitamin A levels differed significantly by age, gender, race, poverty income ratio, standing height, protein, carbohydrate, Vitamin A RAE, total calcium, phosphorus, vitamin D, thoracic spine BMD, lumbar spine BMD, pelvis BMD, trunk bone BMD, and total BMD ( $p < 0.05$ ). In contrast to the first quartile (Q1) group, the fourth quartile (Q4) group has a higher percentage of males and non-Hispanic whites, as well as higher family income and higher levels of carbohydrate and protein content, Vitamin D levels, thoracic Spine BMD, lumbar Spine BMD, Pelvis BMD, trunk BMD, and total BMD. In contrast to the Q1 group, the Q4 group exhibited decreased serum phosphorus ( $p < 0.05$ ) (Table 1).

### Relationships between BMD of various bony sites and serum vitamin A

The study illustrates the association between serum vitamin A and BMD. In Model 2, it was discovered that a 10-unit rise in serum Vitamin A was significantly associated with enhanced BMD levels at all five locations, in spite of age, gender, and race controls. In Model 3, after controlling for additional factors such as age, gender, race, poverty income ratio, standing height (cm), protein (gm), carbohydrate (gm), Vitamin A RAE (mcg), total calcium (mg/dL), phosphorus (mg/dL), and Vitamin D (nmol/L), there was a significant correlation found between each 10-unit increase in serum Vitamin A and the following BMD measurements: thoracic spine ( $\beta = 0.0064$ , 95% CI: 0.0042 to 0.0086), lumbar spine ( $\beta = 0.0081$ , 95% CI: 0.0049 to 0.0113), pelvis ( $\beta = 0.0251$ , 95% CI: 0.0208 to 0.0294), trunk bone ( $\beta = 0.0100$ , 95% CI: 0.0074 to 0.0125), and total BMD ( $\beta = 0.0098$ , 95% CI: 0.0075 to 0.0121) (Table 2).

### Analysis of threshold effects and smoothed curve fitting

A nonlinear positive connection between serum Vitamin A and BMD for the thoracic spine, lumbar spine, pelvis, trunk bones, and whole body was confirmed by smooth curve fitting (Fig. 2). The association between Vitamin A and thoracic spine BMD, lumbar spine BMD, pelvis BMD, trunk Bone, and total BMD are 52.7ug/dL, 53.62ug/dL, 53.4ug/dL, 53.4 ug/dL, and 66 ug/dL, respectively. When Vitamin A is below the saturation threshold values, the effects are significant. ( $P < 0.05$ ) (Table 3).

### Subgroup analysis

We also performed a gender-based subgroup analysis. Serum Vitamin A strongly positively linked with the BMDs of the thoracic spine, lumbar spine, pelvis, trunk bone, and total body in male adolescents ( $P < 0.05$ ). Serum Vitamin A, however, only had a significant positive correlation with pelvic BMD, Trunk Bone BMD, and Total BMD in teenage females ( $P < 0.05$ ) (Table 4).

## Discussion

We used NHANES data from 2001 to 2006 to investigate the association between serum vitamin A and BMD in adolescents aged 12 to 19. After accounting for relevant variables, we discovered that elevated serum vitamin A was substantially and positively linked with BMD of the thoracic spine, lumbar spine, pelvic, and trunk bones. The threshold effect curve shows that vitamin A has a substantial influence when below the saturation threshold ( $P < 0.05$ ). A subgroup analysis found a robust positive correlation between serum Vitamin A and BMD of the thoracic spine, lumbar spine, pelvis, trunk bone, and whole body in male adolescents ( $P < 0.05$ ). However, serum

Characteristic	Serum vitamin A quartiles (ug/dL)				P-value
	Q1 (11.50–38.15)	Q2 (38.16–44.79)	Q3 (44.80–52.22)	Q4 (52.30–149.00)	
Number	1501	1496	1500	1505	
Age (years, mean $\pm$ SD)	14.835 $\pm$ 2.272	15.235 $\pm$ 2.269	15.426 $\pm$ 2.226	16.321 $\pm$ 2.084	< 0.001
Gender, n (%)					< 0.001
Male	568 (37.841%)	684 (45.722%)	839 (55.933%)	1007 (66.910%)	
Female	933 (62.159%)	812 (54.278%)	661 (44.067%)	498 (33.090%)	
Race, n (%)					< 0.001
Mexican American	464 (30.913%)	493 (32.955%)	468 (31.200%)	478 (31.761%)	
Other Hispanic	39 (2.598%)	59 (3.944%)	60 (4.000%)	55 (3.654%)	
Non-Hispanic White	219 (14.590%)	367 (24.532%)	446 (29.733%)	613 (40.731%)	
Non-Hispanic Black	733 (48.834%)	524 (35.027%)	444 (29.600%)	303 (20.133%)	
Other Race	46 (3.065%)	53 (3.543%)	82 (5.467%)	56 (3.721%)	
PIR (mean $\pm$ SD)	1.889 $\pm$ 1.462	2.051 $\pm$ 1.544	2.170 $\pm$ 1.558	2.307 $\pm$ 1.566	< 0.001
Standing height (cm, mean $\pm$ SD)	162.105 $\pm$ 9.550	164.309 $\pm$ 10.091	166.432 $\pm$ 10.135	169.429 $\pm$ 10.077	< 0.001
Protein (gm, Median, Q1–Q3)	63.105 (45.185–88.535)	69.830 (48.040–96.750)	74.015 (49.680–100.270)	79.220 (56.310–111.540)	< 0.001
Carbohydrate (gm, Median, Q1–Q3)	256.650 (191.220–346.832)	281.450 (206.260–376.515)	286.475 (208.995–378.752)	305.050 (220.080–423.900)	< 0.001
Vitamin A, RAE (mcg, Median, Q1–Q3)	342.500 (164.000–573.250)	391.000 (198.000–673.000)	396.000 (212.250–694.750)	480.000 (261.000–819.000)	< 0.001
Total calcium (mg/dL, mean $\pm$ SD)	9.600 $\pm$ 0.315	9.685 $\pm$ 0.298	9.736 $\pm$ 0.309	9.794 $\pm$ 0.339	< 0.001
Phosphorus (mg/dL, mean $\pm$ SD)	4.487 $\pm$ 0.678	4.428 $\pm$ 0.646	4.421 $\pm$ 0.675	4.307 $\pm$ 0.643	< 0.001
Vitamin D (nmol/L, mean $\pm$ SD)	46.507 $\pm$ 18.699	52.544 $\pm$ 19.525	55.234 $\pm$ 19.041	62.720 $\pm$ 22.967	< 0.001
Thoracic Spine BMD (g/cm <sup>2</sup> , mean $\pm$ SD)	0.771 $\pm$ 0.113	0.789 $\pm$ 0.109	0.799 $\pm$ 0.110	0.822 $\pm$ 0.106	< 0.001
Lumbar Spine BMD (g/cm <sup>2</sup> , mean $\pm$ SD)	0.960 $\pm$ 0.169	0.979 $\pm$ 0.161	0.987 $\pm$ 0.163	1.011 $\pm$ 0.153	< 0.001
Pelvis BMD (g/cm <sup>2</sup> , mean $\pm$ SD)	1.206 $\pm$ 0.204	1.238 $\pm$ 0.199	1.267 $\pm$ 0.206	1.309 $\pm$ 0.206	< 0.001
Trunk Bone BMD (g/cm <sup>2</sup> , mean $\pm$ SD)	0.882 $\pm$ 0.131	0.906 $\pm$ 0.134	0.924 $\pm$ 0.136	0.957 $\pm$ 0.135	< 0.001
Total BMD (g/cm <sup>2</sup> , mean $\pm$ SD)	1.057 $\pm$ 0.123	1.081 $\pm$ 0.126	1.095 $\pm$ 0.127	1.129 $\pm$ 0.126	< 0.001

**Table 1.** Baseline characteristics of participants ( $N = 6,002$ ). *BMD* bone mineral density, *RAE* retinol activity equivalents, *PIR* poverty income ratio.

Vitamin A was only substantially favorably associated to pelvic BMD, trunk bone BMD, and total BMD in female adolescents ( $P < 0.05$ ).

In our study, serum vitamin A exhibits a nonlinear association with BMD, with saturation effect values for skeletal health being Thoracic Spine BMD: 52.7  $\mu\text{g/dL}$  (1.84  $\mu\text{mol/L}$ ), Lumbar Spine BMD: 53.62  $\mu\text{g/dL}$  (1.87  $\mu\text{mol/L}$ ), Pelvis BMD: 53.4  $\mu\text{g/dL}$  (1.86  $\mu\text{mol/L}$ ), Trunk Bone BMD: 53.4  $\mu\text{g/dL}$  (1.86  $\mu\text{mol/L}$ ), and Total BMD: 66  $\mu\text{g/dL}$  (2.31  $\mu\text{mol/L}$ ). Within this range, increased levels of vitamin A contribute to enhancing BMD; however, once this threshold is exceeded, further increases in vitamin A may not confer additional benefits. To date, studies on the relationship between serum vitamin A and BMD have primarily focused on adult populations, with very limited epidemiological research based on individuals under 20 years of age. For instance, a recent study indicated a positive correlation between BMD at the hip and femoral neck joints and vitamin A levels in a population of adults excluding Hispanics<sup>12</sup>. In mouse experiments, long-term intake of clinically relevant doses of vitamin A has a negative impact on cortical bone BMD<sup>15</sup>. However, in another study of Norwegian adolescents aged 15–19, Teigmo et al. found no independent association between vitamin A levels and BMD<sup>16</sup>. Zhang et al. (2021) found that in children aged 6 to 9, there is an inverted U-shaped association between serum retinol levels and BMD, with the inflection point for plasma retinol concentration and skeletal health being approximately 1.2  $\mu\text{mol/L}$ , lower than the results of our study<sup>17</sup>. The results of existing studies are heterogeneous, which may be related to the age of the population, study design, genetics, and so on. More prospective studies are needed in the future to further verify these findings.

During adolescence, individuals experience a spike in the growth of their skeletal structure, with a considerable deposit of bone minerals; this time is crucial for creating the basis of optimal bone mass<sup>18</sup>. Some related studies have shown a positive correlation between vitamin A and BMD, which is consistent with our research. This may be due to the following mechanisms: First, Within the body, retinol-binding protein (RBP) can carry serum retinol to target tissues in the plasma, where it is transformed into all-trans retinoic acid (ATRA). By binding to retinoic acid receptors (RARs), ATRA can suppress nuclear factor kappa B (NF- $\kappa\text{B}$ ) activity, boosting bone growth and blocking osteoclast development and maturation<sup>7</sup>. Second, during adolescence, a period of vigorous growth, vitamin A can influence the production of growth hormone and insulin-like growth factor 1 (IGF1), therefore promoting skeletal growth<sup>19,20</sup>. Third, vitamin A may reduce the excessive release of parathyroid hormone, which, at high levels, can damage bone health<sup>21</sup>. Additionally, our study indicates that once the levels of vitamin A exceed the saturation threshold, there is no association between the two. This could be related to the excessive vitamin A affecting osteoblasts and bone-related peptides through RAR signaling, impacting osteocytic function and the ossification process, thereby inhibiting the formation of healthy bone density<sup>10</sup>. Therefore, it is crucial to ensure that adolescents receive an adequate, not excessive, amount of vitamin A.

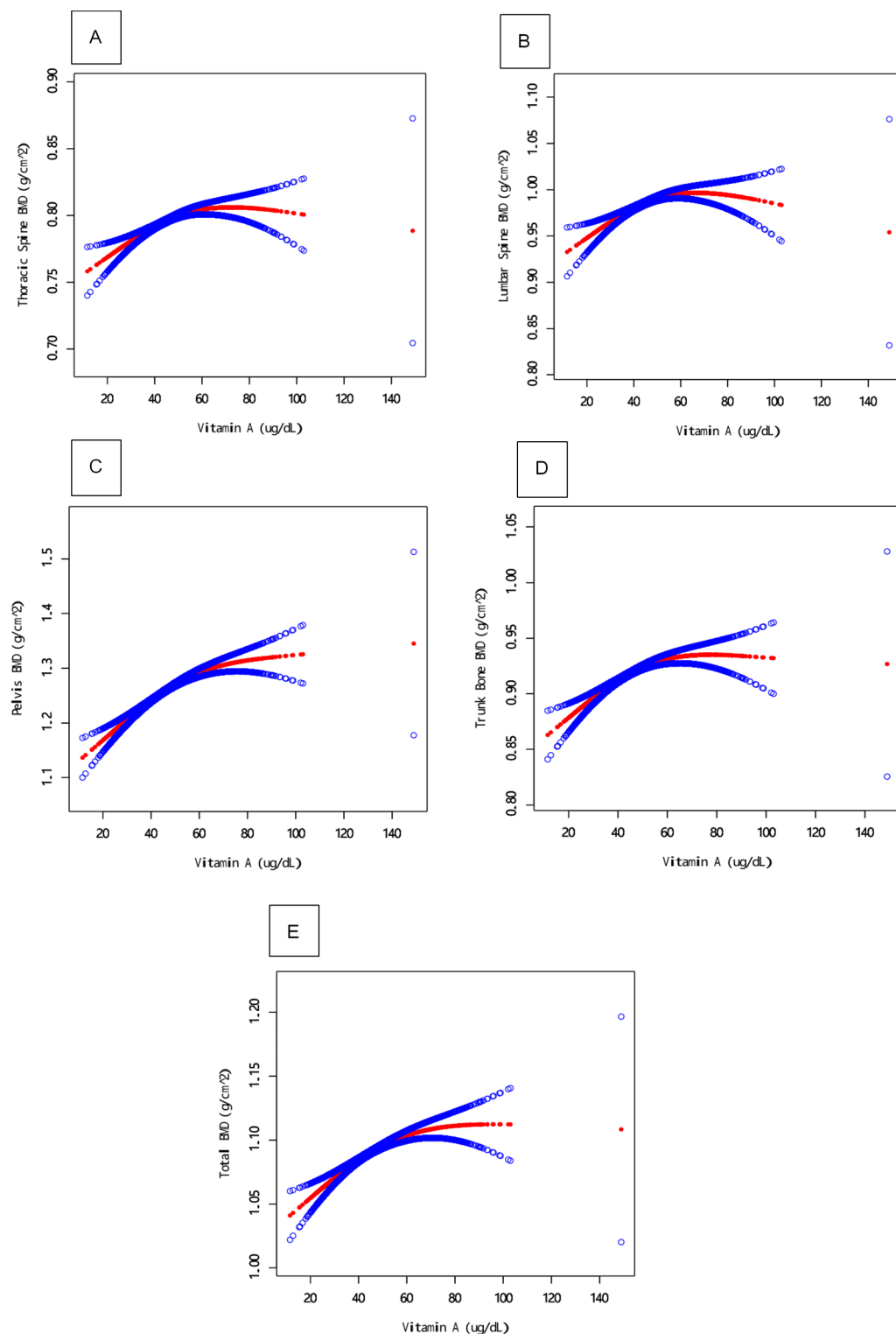
Exposure	Model 1	Model 2	Model 3
	[ $\beta$ (95% CI)] <i>P</i> -value	[ $\beta$ (95% CI)] <i>P</i> -value	[ $\beta$ (95% CI)] <i>P</i> -value
Thoracic spine BMD (g/cm <sup>2</sup> )			
Continuous vitamin A per 10-unit (ug/dL)	0.0166 (0.0141, 0.0190) < 0.0001	0.0062 (0.0040, 0.0084) < 0.0001	0.0064 (0.0042, 0.0086) < 0.0001
Vitamin A quartile			
Q1	Reference	Reference	Reference
Q2	0.018 (0.010, 0.026) < 0.0001	0.013 (0.006, 0.019) 0.0001	0.010 (0.004, 0.016) 0.0014
Q3	0.027 (0.019, 0.035) < 0.0001	0.020 (0.013, 0.027) < 0.0001	0.015 (0.008, 0.021) < 0.0001
Q4	0.051 (0.043, 0.059) < 0.0001	0.027 (0.020, 0.035) < 0.0001	0.020 (0.013, 0.027) < 0.0001
Lumbar spine BMD (g/cm <sup>2</sup> )			
Continuous Vitamin A per 10-unit (ug/dL)	0.0166 (0.0130, 0.0201) < 0.0001	0.0077 (0.0045, 0.0109) < 0.0001	0.0081 (0.0049, 0.0113) < 0.0001
Vitamin A quartile			
Q1	Reference	Reference	Reference
Q2	0.018 (0.007, 0.030) 0.0020	0.019 (0.010, 0.029) < 0.0001	0.013 (0.004, 0.022) 0.0037
Q3	0.026 (0.015, 0.038) < 0.0001	0.031 (0.021, 0.040) < 0.0001	0.021 (0.012, 0.030) < 0.0001
Q4	0.050 (0.039, 0.062) < 0.0001	0.040 (0.030, 0.051) < 0.0001	0.026 (0.016, 0.036) < 0.0001
Pelvis BMD (g/cm <sup>2</sup> )			
Continuous vitamin A per 10-unit (ug/dL)	0.0335 (0.0290, 0.0380) < 0.0001	0.0246 (0.0203, 0.0289) < 0.0001	0.0251 (0.0208, 0.0294) < 0.0001
Vitamin A quartile			
Q1	Reference	Reference	Reference
Q2	0.032 (0.018, 0.047) < 0.0001	0.031 (0.019, 0.044) < 0.0001	0.027 (0.015, 0.039) < 0.0001
Q3	0.061 (0.046, 0.075) < 0.0001	0.058 (0.045, 0.071) < 0.0001	0.049 (0.037, 0.062) < 0.0001
Q4	0.103 (0.088, 0.117) < 0.0001	0.081 (0.067, 0.095) < 0.0001	0.073 (0.059, 0.086) < 0.0001
Trunk bone BMD (g/cm <sup>2</sup> )			
Continuous vitamin A per 10-unit (ug/dL)	0.0240 (0.0210, 0.0270) < 0.0001	0.0094 (0.0068, 0.0120) < 0.0001	0.0100 (0.0074, 0.0125) < 0.0001
Vitamin A quartile			
Q1	Reference	Reference	Reference
Q2	0.024 (0.015, 0.034) < 0.0001	0.018 (0.010, 0.026) < 0.0001	0.013 (0.006, 0.020) 0.0004
Q3	0.041 (0.032, 0.051) < 0.0001	0.030 (0.022, 0.038) < 0.0001	0.021 (0.013, 0.028) < 0.0001
Q4	0.075 (0.065, 0.084) < 0.0001	0.042 (0.034, 0.051) < 0.0001	0.029 (0.021, 0.038) < 0.0001
Total BMD (g/cm <sup>2</sup> )			
Continuous vitamin A per 10-unit (ug/dL)	0.0233 (0.0205, 0.0261) < 0.0001	0.0093 (0.0069, 0.0116) < 0.0001	0.0098 (0.0075, 0.0121) < 0.0001
Vitamin A quartile			
Q1	Reference	Reference	Reference
Q2	0.023 (0.014, 0.032) < 0.0001	0.018 (0.011, 0.025) < 0.0001	0.014 (0.007, 0.020) < 0.0001
Q3	0.037 (0.028, 0.046) < 0.0001	0.026 (0.019, 0.034) < 0.0001	0.019 (0.013, 0.026) < 0.0001
Q4	0.071 (0.062, 0.080) < 0.0001	0.039 (0.031, 0.046) < 0.0001	0.028 (0.020, 0.035) < 0.0001

**Table 2.** Relationship between serum vitamin A and bone mineral density. *BMD* bone mineral density, *RAE* retinol activity equivalents, *PIR* poverty income ratio. Model 1: no covariates were adjusted. Model 2: adjusts for Age; Gender; Race. Model 3: adjusts for Age; Gender; Race; Poverty Income Ratio; Standing Height (cm); Protein (gm); Carbohydrate (gm); Vitamin A, RAE (mcg); Total calcium (mg/dL); Phosphorus (mg/dL); Vitamin D (nmol/L).

## Limitation and strengths

This research offers some benefits. First off, In this study, serum Vitamin A levels and BMD in teenagers aged 12 to 19 are evaluated for the first time, and it confirmed the nonlinear correlation between the two by analyzing bone mineral density at several sites, including the thoracic spine, lumbar spine, pelvis, trunk bone, and total bone; Second, the study examined the saturation effect values for the link between serum Vitamin A and BMD in the thoracic spine, lumbar spine, pelvis, trunk, and total bone. Finally, to acquire more reliable results, the study conducted a gender-specific subgroup analysis among teenagers.

This study is not without limits, though. First off, because the study's foundation is the NHANES database from the United States, its findings could not apply to other populations because of possible ethnic, genetic, and environmental variations. Secondly, because this study was cross-sectional, it is impossible to determine a causal link between serum Vitamin A levels and bone mineral density; additional cohort studies are needed to validate the findings of this study. Third, even with a large number of variables incorporated into our analytic models, it is not possible to entirely rule out the residual confounding effects resulting from incompletely or not at all assessed factors.



**Fig. 2.** The relationship between serum Vitamin A and Thoracic Spine BMD (A), Lumbar Spine BMD (B), Pelvis BMD (C), Trunk Bone BMD (D), and Total BMD (E). The red line represents the smooth curve fit between variables. The blue line represents the 95% confidence interval of the fit. adjusts for: Age; Gender; Race; poverty Income Ratio; Standing Height (cm); Protein (gm); Carbohydrate (gm); Vitamin A, RAE (mcg); Total calcium (mg/dL); Phosphorus (mg/dL); Vitamin D (nmol/L). *BMD* bone mineral density, *RAE* retinol activity equivalents.

	Vitamin A ( $\beta$ )	95%CI	P value
Thoracic Spine BMD (g/cm <sup>2</sup> )	< 52.7	0.001 (0.001, 0.001)	<0.0001
	> 52.7	−0.000 (−0.001, 0.000)	0.5823
	Log likelihood ratio test		<0.001
Lumbar Spine BMD (g/cm <sup>2</sup> )	< 53.62	0.001 (0.001, 0.002)	<0.0001
	> 53.62	−0.000 (−0.001, 0.000)	0.2854
	Log likelihood ratio test		<0.001
Pelvis BMD (g/cm <sup>2</sup> )	< 53.4	0.003 (0.003, 0.004)	<0.0001
	> 53.4	0.001 (−0.000, 0.002)	0.0541
	Log likelihood ratio test		<0.001
Trunk Bone BMD (g/cm <sup>2</sup> )	< 53.4	0.001 (0.001, 0.002)	<0.0001
	> 53.4	0.000 (−0.001, 0.001)	0.9901
	Log likelihood ratio test		<0.001
Total BMD (g/cm <sup>2</sup> )	< 66	0.001 (0.001, 0.001)	<0.0001
	> 66	−0.001 (−0.001, 0.000)	0.2841
	Log likelihood ratio test		0.002

**Table 3.** Threshold effect analysis of serum vitamin A and BMD using piece-wise linear regression.

Model	Male [ $\beta$ (95% CI)]	P-value	Female [ $\beta$ (95% CI)]	P-value	P interaction
Thoracic Spine BMD (g/cm <sup>2</sup> )					
Crude	0.0030 (0.0026, 0.0033)	<0.0001	0.0004 (0.0000, 0.0007)	0.0428	<0.0001
Model 1	0.0017 (0.0014, 0.0020)	<0.0001	−0.0001 (−0.0004, 0.0002)	0.4311	<0.0001
Model 2	0.0011 (0.0008, 0.0014)	<0.0001	0.0001 (−0.0002, 0.0004)	0.4752	<0.0001
Lumbar Spine BMD (g/cm <sup>2</sup> )					
Crude	0.0037 (0.0032, 0.0041)	<0.0001	0.0006 (0.0000, 0.0011)	0.0380	<0.0001
Model 1	0.0022 (0.0018, 0.0027)	<0.0001	0.0001 (−0.0003, 0.0006)	0.5949	<0.0001
Model 2	0.0012 (0.0008, 0.0016)	<0.0001	0.0003 (−0.0002, 0.0007)	0.2037	0.0017
Pelvis BMD (g/cm <sup>2</sup> )					
Crude	0.0052 (0.0046, 0.0058)	<0.0001	0.0012 (0.0005, 0.0019)	0.0007	<0.0001
Model 1	0.0040 (0.0034, 0.0046)	<0.0001	0.0010 (0.0004, 0.0016)	0.0022	<0.0001
Model 2	0.0030 (0.0024, 0.0036)	<0.0001	0.0019 (0.0013, 0.0024)	<0.0001	0.0034
Trunk Bone BMD (g/cm <sup>2</sup> )					
Crude	0.0035 (0.0031, 0.0039)	<0.0001	0.0006 (0.0001, 0.0010)	0.0108	<0.0001
Model 1	0.0023 (0.0019, 0.0027)	<0.0001	0.0002 (−0.0002, 0.0006)	0.3648	<0.0001
Model 2	0.0014 (0.0010, 0.0017)	<0.0001	0.0005 (0.0001, 0.0008)	0.0122	0.0001
Total BMD (g/cm <sup>2</sup> )					
Crude	0.0034 (0.0030, 0.0038)	<0.0001	0.0005 (0.0001, 0.0009)	0.0161	<0.0001
Model 1	0.0022 (0.0018, 0.0025)	<0.0001	0.0002 (−0.0001, 0.0006)	0.2326	<0.0001
Model 2	0.0014 (0.0011, 0.0017)	<0.0001	0.0004 (0.0001, 0.0007)	0.0171	<0.0001

**Table 4.** Stratified analyses of the association between vitamin A concentrations and bone mineral density by gender. Model 1 adjusts for Age, Race, Poverty Income Ratio. Model 2 adjusts for Age, Race, Poverty Income Ratio, Standing Height (cm), Protein (gm), Carbohydrate (gm), Vitamin A, RAE (mcg), Total calcium (mg/dL), Phosphorus (mg/dL), Vitamin D (nmol/L).

Conclusion

Based to our research, serum vitamin A and BMD in adolescents aged 12 to 19 have a beneficial relationship, with the impact being stronger in males. Future prospective studies are required to confirm our findings, and more research is required to examine how gender variations affect the relationship between serum vitamin A and BMD.

Data availability

Data Availability Statement: There is public access to the data described in this study through the NHANES website (<https://www.cdc.gov/nchs/nhanes/index.htm>).

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## Author contributions

L.L.contributed to the study conception, design, material preparation, data collection and analysis.

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## Declarations

## Competing interests

The authors declare no competing interests.

## Additional information

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