Chen *et al. Nutrition & Metabolism* (2024) 21:57
https://doi.org/10.1186/s12986-024-00830-y

Nutrition & Metabolism

RESEARCH Open Access

The association between vitamin E intake and hepatic steatosis in general and obese populations

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Abstract

Purpose Using data from the National Health and Nutrition Examination Survey (NHANES) and employing Controlled Attenuation Parameter (CAP) measures, this study explores the correlation between vitamin E (VE) intake and hepatic steatosis and its impact on different subsets.

Materials and methods We selected 5757 participants with CAP data from the 2017–2020 NHANES dataset. Daily VE intake was assessed by a 24-hour dietary recall. Hepatic fat content was quantified using transient elastography to measure CAP. Stratified multivariable regression analysis investigated relationships in different subsets, and a generalized additive model identified nonlinear relationships and thresholds.

Results After adjusting for confounders, higher VE intake correlated with lower CAP levels. Subgroup analyses and tests for interaction revealed a significantly stronger negative correlation between VE intake and CAP in obese individuals. Further analysis indicated a curvilinear relationship between VE intake and the severity of liver fat degeneration in both the general study population and the obese subgroup, demonstrating a threshold effect. In the general population, VE intake below the threshold (6.58 mg/day) is positively correlated with CAP levels, whereas intake above this threshold shows a negative correlation. For obese individuals, the threshold is set at 7.37 mg/day, above which the negative correlation with CAP is even more pronounced.

Conclusion Our study revealed a negative correlation between VE intake and hepatic fat content, highlighting the potentially crucial role VE plays in obese fatty liver patients. Importantly, we identified threshold effects of VE intake in both general and obese populations. Our results support clinical nutritional interventions, personalized dietary guidance, and the development of drugs to combat fatty liver.

Keywords VE, Hepatic Steatosis, Obesity, Threshold, NHANES

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Introduction

The global prevalence of fatty liver disease has risen in sync with the obesity epidemic, affecting an estimated 25% of the global population [1]. Fatty liver is characterized by the accumulation of fat droplets within liver cells, known as hepatic steatosis (HS) [2]. HS can progress to liver cirrhosis, liver cancer, or liver failure, depending on various factors, inflammation, and fibrosis resulting from this condition [3]. Therefore, early diagnosis and prevention of hepatic steatosis are crucial.

Non-invasive methods for diagnosing and quantifying hepatic steatosis have become increasingly important in clinical practice due to the limitations and risks associated with liver biopsy [4]. Certain biomarkers provide valuable information about liver function and damage, with levels typically elevated in individuals with fatty liver disease [5]. However, these biomarkers are not specific. Additionally, non-invasive imaging techniques such as liver ultrasound, computed tomography (CT), and magnetic resonance imaging (MRI) are widely used for detecting hepatic steatosis [6, 7], but they cannot provide quantifiable indicators. Controlled Attenuation Parameter (CAP) stands out as another non-invasive method in assessing hepatic steatosis. Integrated into transient elastography, CAP measures liver stiffness while quantifying liver fat content, offering an early, reliable, and effective assessment of hepatic steatosis without the need for a liver biopsy [7, 8].

Currently, there are no approved drugs for directly treating fatty liver disease. Research indicates that lifestyle changes, such as weight loss and a healthy diet, are effective interventions [9–11]. However, successful weight loss is challenging and even more difficult to maintain, with only about 20% of obese individuals achieving long-term weight loss [12]. Because it is difficult to change the lifestyle and diet of most patients, pharmacological approaches to reversing hepatic steatosis are being hotly discussed. The fat-soluble vitamin E (VE) shows potential in treating non-alcoholic steatohepatitis (NASH) and non-alcoholic fatty liver disease (NAFLD) due to its anti-inflammatory, anti-apoptotic, and antioxidant properties [13–15]. VE supplementation is advised for NASH patients without diabetes that has been biopsy-verified according to guidelines from the American Association for the Study of Liver Diseases [16] and the European Association for the Study of the Liver [17]. However, there is currently a lack of evidence supporting the link between VE and early hepatic steatosis, as well as its role in other subgroups of fatty liver patients, particularly in obese populations.

Therefore, this study's design is based on utilizing data from the National Health and Nutrition Examination Survey (NHANES) from 2017 to 2020, a large nationally representative sample. The study aims to investigate the correlation between vitamin E intake and hepatic steatosis using controlled attenuation parameter measures and its impact on different subsets.

Materials and methods

Statement of ethics

This study received approval from the National Center for Health Statistics Research Ethics Review Board, with each participant providing consent.

Study population

To ensure nationwide representation, NHANES, an extensive, continuous cross-sectional survey in the US, employs stratified, multistage, clustered random sampling to gather diet and health data from the entire population [18]. Of the 15,560 participants in the 2017–2020 NHANES cycle, 9698 had available CAP data. We excluded 2451 participants who tested positive for hepatitis B antigen, hepatitis C antibody, or hepatitis C RNA, 799 with significant alcohol consumption (4 or more drinks daily), 514 lacking VE intake data, and 117 participants with unreliable dietary intake (total energy <800 or >4200 kcal/day in men and <600 or >3500 kcal/day in women). Ultimately, the study included 5757 participants. Figure 1 presents the flowchart of sample selection.

Variables

This study focused on VE intake as the exposure variable. Daily dietary intake data were gathered via 24-hour recall interviews and a 30-day dietary supplement questionnaire. For each NHANES 2017–2020 participant, two 24-hour recalls were conducted. The first dietary recall was performed in person at the NHANES Mobile Examination Centers (MEC), and the second via telephone by trained interviewers 3–10 days post-MEC interview. The United States Department of Agriculture's Food and Nutrient Database for Dietary Studies was the source of information on nutrient intakes, including VE [19]. The total amount of VE consumed per day from food and dietary supplements was determined.

The outcome variable, CAP, was measured using the FibroScan® 502 V2 Touch, equipped with liver ultrasonography transient elastography. This device measures CAP by recording ultrasonic attenuation, indicative of hepatic steatosis and liver fat content.

We primarily referred to previous research literature [20–23] and data from the NHANES database to include potential confounding variables that may affect the exposure variables and outcome variables. Categorical variables such as gender, race/ethnicity, education level, marital status, smoking habit, diabetes, hypertension, and cholesterol levels were included in our study. Age, income to poverty ratio, body mass index (BMI), γ-glutamyl transpeptidase (GGT), aspartate aminotransferase

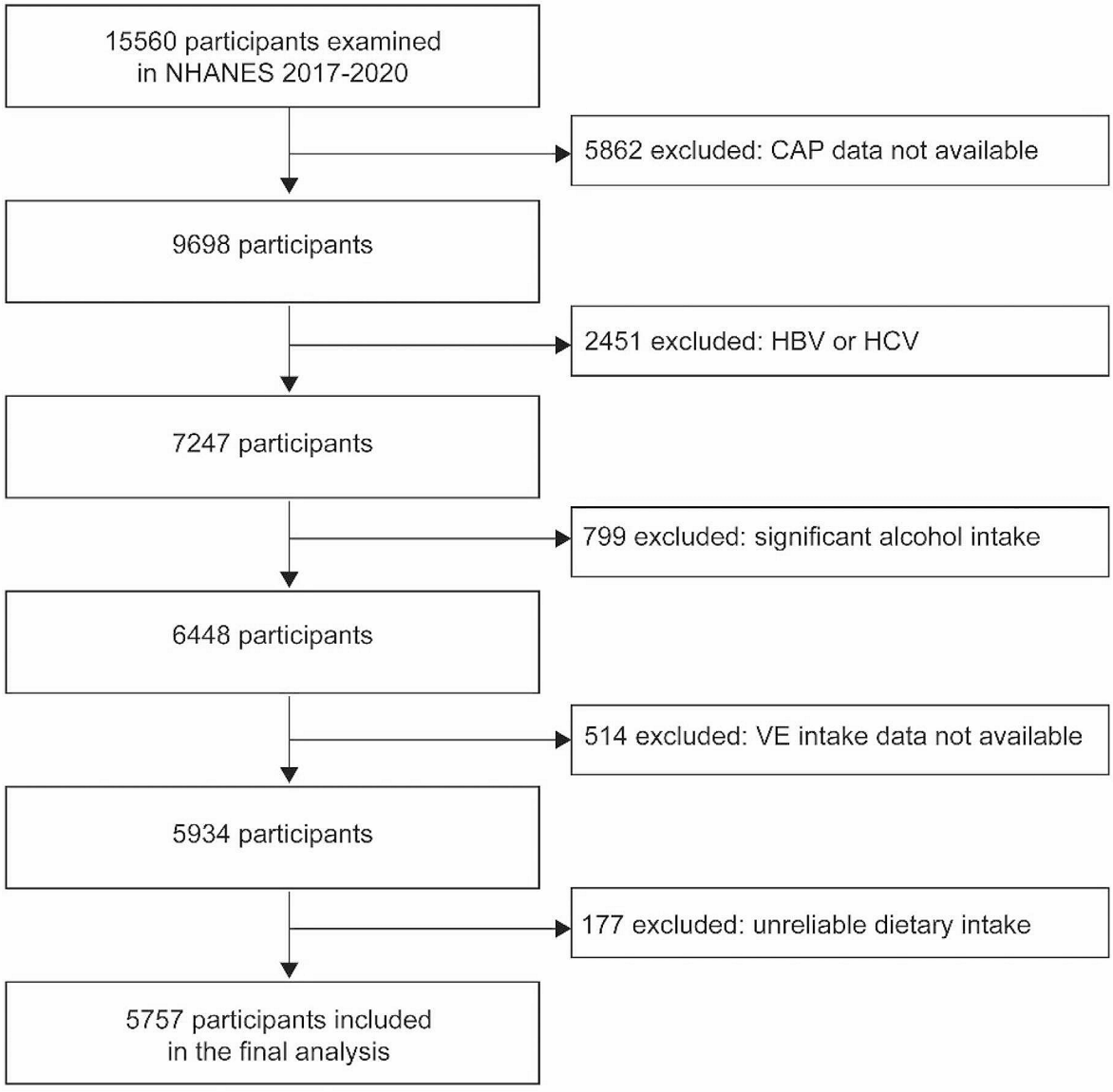

Fig. 1 Flowchart of participant selection. NHANES, National Health and Nutrition Examination Survey; CAP, controlled attenuation parameter; VE, vitamin E

(AST), alanine aminotransferase (ALT), serum albumin, serum creatinine, and uric acid were among the continuous factors in our study. Other nutrients as confounding factors including vitamin A, alpha-carotene, beta-carotene, beta-cryptoxanthin, lycopene, lutein, vitamin C, vitamin D, vitamin K, protein, total sugar, dietary fiber, total fat and moisture. You may find detailed information about CAP, VE intake, and other variables at http://www.cdc.gov/nchs/nhanes/.

Statistical analysis

We utilized a weighted variance estimation technique to tackle notable fluctuations in our dataset. A weighted multivariate linear regression model was employed to investigate the correlation between VE intake and CAP. For categorical data, the weighted $\chi 2$ test was utilized to evaluate group differences, and for continuous variables, the weighted linear regression model was employed. The subgroup analysis involves using stratified multiple regression analysis. Furthermore, we conduct interaction analysis to examine their interplay, where *P* for interaction below 0.05 indicates statistically significant

differences between subgroups. The data were categorized into subgroups based on various classification variables. Continuous variables were converted into categorical ones. For instance, age (<45 years; 45–60 years; >60 years), income to poverty ratio (<2; ≥2), BMI (Non-obesity < 30 kg/m^2; obesity ≥ 30 kg/m^2). A combination of smooth curve fits and generalized additive models were utilized to investigate the nonlinear relationship between CAP and VE intake. After nonlinearity was identified, we used a recursive method to identify the inflection point in the connection between VE intake and CAP, and on either side of this point, we applied a two-piecewise linear regression model. All analyses were conducted using R (http://www.Rproject.org) and EmpowerStats (http://www.empowerstats.com), considering a *P* value < 0.05 as statistically significant.

Results

A total of 5757 participants were included in our analysis, with the weighted characteristics of the participants subclassified based on VE intake quartiles (Q1: <4.43 mg/day; Q2: 4.44–6.83 mg/day; Q3: 6.83–9.99 mg/day; and Q4: >10.00 mg/day), as shown in Table 1. Those in the highest quartile (Q4) tended to be older, more often male, non-Hispanic White, more educated, married/partnered, and had a higher income-to-poverty ratio compared to those in the lowest quartile (Q1). Several biomarkers and nutrients differ across various quartile groups, with higher intake groups typically showing increased levels. A few characteristics like BMI, hypertensive state, GGT, serum albumin and CAP did not differ significantly by quartile.

Table 2 shows the results of multivariable linear regression analyses examining the association between dietary VE intake and controlled attenuation parameter (CAP). Three models were tested with progressive adjustment for potential confounders. In Model 1 without adjustment, a higher VE intake was associated with higher CAP levels, though not significantly. In Model 2 adjusting for demographics, every 1 mg/day increase in VE intake was associated with a 0.59 dB/m lower CAP (95% CI: -0.93 to -0.25, *P* = 0.0006). Further adjusting clinical factors in Model 3 slightly strengthened this negative correlation, with every 1 mg/day linked to a 0.85 dB/m lower CAP (95% CI: -1.30 to -0.40, *P* = 0.0002). After converting VE intake from a continuous variable to a categorical variable, compared to the reference lowest intake quartile Q1, Q4 showed a significant lower CAP in Model 3 (-9.59 dB/m, 95% CI: -16.87 to -2.31, *P* = 0.0099).

Figure 2 details stratified analyses of the association between dietary VE intake and CAP. After adjusting for confounding factors in the study, in the non-obese group, there is no significant correlation between increased VE intake and fatty liver as defined by CAP values. In contrast, among obese individuals, a significant inverse relationship exists between VE intake and hepatic steatosis. Additionally, the relationship between VE intake and CAP varies significantly across different BMI categories (*P* for interaction = 0.0436). This implies that for every 1 mg/day increase in VE intake, CAP decreases by 0.64 dB/m more in the obesity group (β=-0.89) compared to the non- obesity group(β=-0.25).

Figures 3 and 4 use smooth curve fitting and generalized additive models to show the non-linear relationship between VE intake and CAP in both the general study population and the obese subgroup. In these groups, the relationship between VE intake and CAP exhibits a threshold effect. As shown in Tables 3 and 4, We used a two-part linear regression model to identify these thresholds, found at 6.58 mg/day and 7.37 mg/day for the general and obese populations, respectively. Statistical tests comparing standard linear models with the two-part models confirm the presence of these thresholds (*P*-values are 0.023 and 0.006, respectively). In the general study population, when VE intake is below 6.58 mg/day, there is no significant correlation with CAP (β = 0.79, 95% CI: -0.45 to 2.04, *P* = 0.2110). Above this threshold, however, increasing VE intake correlates negatively with CAP; for every additional 1 mg/day of VE, CAP decreases by 0.86 dB/m (95% CI: -1.24 to -0.49, *P* < 0.0001) (Table 3). In the obese subgroup, VE intake shows no significant correlation with CAP when below 7.37 mg/day (β = 1.41, 95% CI: -0.36 to 3.18, *P* = 0.1175). Above this level, a strong negative correlation emerges, with a greater effect than in the general population. Here, each additional 1 mg/day of VE intake results in a CAP decrease of 1.57 dB/m (95% CI: -2.26 to -0.89, *P* < 0.0001) (Table 4).

Discussion

This study utilized data from the National Health and Nutrition Examination Survey in the United States, employing controlled attenuation parameters to quantitatively measure liver fat content. It examined the relationship between VE intake and liver steatosis, including its impact across different demographic subgroups. After adjusting for various potential confounding factors, the research, using a weighted multivariable regression model, found a significant correlation between high VE intake and reduced liver fat accumulation. Further analysis showed a threshold effect of VE on liver steatosis in the general population, identified at 6.58 milligrams per day. Below this threshold, VE intake was positively correlated with fatty liver; above it, the correlation was negative. Notably, in the obese population, this threshold was higher, at 7.37 milligrams per day, with a stronger negative correlation with fatty liver above this threshold.

Our findings align with previous research, suggesting VE's protective effect against liver steatosis. A study

Table 1 Weighted characteristics of the study population based on dietary VE intake quartiles

VE intake (mg/day)	Total (*N* = 5757)	Q1 (< 4.43, *N* = 1376)	Q2 (4.44–6.83, *N* = 1482)	Q3 (6.83–9.99, *N* = 1477)	Q4 (> 10.00, *N* = 1422)	*P* value
Age (years)	44.98 ± 20.14	42.36 ± 20.97	44.71 ± 20.54	44.94 ± 20.26	47.29 ± 18.71	< 0.0001
Gender (%)						< 0.0001
Men	47.26	37.03	46.00	48.57	55.01	
Women	52.74	62.97	54.00	51.43	44.99	
Race/Ethnicity (%)						< 0.0001
Mexican American	9.73	10.95	10.88	9.32	8.12	
Other Hispanic	7.44	10.44	7.06	6.84	6.06	
Non-Hispanic White	62.82	59.07	60.86	63.33	67.00	
Non-Hispanic Black	11.13	11.27	11.23	12.65	9.43	
Other Race	8.90	8.28	9.97	7.86	9.39	
Education level (%)						< 0.0001
Less than high school	10.24	15.45	11.13	8.79	7.43	
High school	27.92	33.87	29.02	30.26	20.78	
More than high school	61.79	50.68	59.86	60.95	71.79	
Marital status (%)						< 0.0001
Married/Living with Partner	64.24	55.83	64.61	64.19	69.70	
Widowed/Divorced/Separated	18.93	24.14	19.03	17.55	16.60	
Never married	16.82	20.03	16.35	18.26	13.69	
Income to poverty ratio	3.16 ± 1.63	2.68 ± 1.63	3.09 ± 1.62	3.21 ± 1.63	3.52 ± 1.56	< 0.0001
BMI (kg/m^2)	29.29 ± 7.44	28.86 ± 7.63	29.13 ± 6.89	29.58 ± 7.62	29.50 ± 7.60	0.0406
Smoked at least 100 cigarettes in life (%)						0.0019
Yes	38.63	43.25	39.60	36.13	36.91	
No	61.37	56.75	60.40	63.87	63.09	
Diabetes (%)						0.0009
Yes	10.84	10.90	12.85	8.18	11.55	
No	86.73	86.65	84.87	88.68	86.58	
Borderline	2.43	2.45	2.27	3.14	1.88	
Hypertension (%)						0.0966
Yes	32.00	30.69	34.77	30.96	31.53	
No	68.00	69.31	65.23	69.04	68.47	
High cholesterol level (%)						0.0068
Yes	34.40	31.39	34.44	33.23	37.64	
No	65.60	68.61	65.56	66.77	62.36	
AST (IU/L)	21.00 ± 10.34	20.40 ± 12.18	20.74 ± 10.72	20.76 ± 8.49	21.92 ± 10.07	0.0008
ALT (IU/L)	21.52 ± 14.66	20.01 ± 15.42	20.96 ± 14.42	21.70 ± 14.56	22.98 ± 14.21	< 0.0001
GGT (IU/L)	26.18 ± 29.75	26.26 ± 34.36	26.35 ± 32.84	26.36 ± 27.17	25.80 ± 25.25	0.9535
Serum albumin (g/L)	41.22 ± 3.22	41.26 ± 3.39	41.18 ± 3.26	41.29 ± 3.14	41.15 ± 3.11	0.6429
Serum creatinine (mg/dl)	0.85 ± 0.30	0.81 ± 0.28	0.86 ± 0.26	0.86 ± 0.35	0.87 ± 0.28	< 0.0001
Uric acid (mg/dl)	5.28 ± 1.37	5.10 ± 1.35	5.36 ± 1.45	5.32 ± 1.35	5.32 ± 1.32	< 0.0001
Vitamin A (mcg/day)	554.70 ± 465.11	322.30 ± 526.27	462.50 ± 305.54	576.85 ± 345.92	796.21 ± 519.71	< 0.0001
Alpha-carotene (mcg/day)	353.23 ± 829.38	157.57 ± 350.65	269.98 ± 536.30	380.76 ± 766.72	537.06 ± 1212.47	< 0.0001
Beta-carotene (mcg/day)	2024.97 ± 3141.63	879.33 ± 1321.91	1470.26 ± 2017.14	2185.63 ± 2838.53	3258.08 ± 4516.16	< 0.0001
Beta-cryptoxanthin(mcg/day)	75.10 ± 148.16	43.05 ± 118.12	67.58 ± 138.59	82.67 ± 145.08	98.22 ± 172.81	< 0.0001
Lycopene(mcg/day)	4878.15 ± 6232.33	2504.66 ± 2882.05	4081.35 ± 5030.96	5177.68 ± 5839.07	6874.70 ± 8211.04	< 0.0001
Lutein (mcg/day)	1354.49 ± 2277.94	546.61 ± 659.79	972.52 ± 1340.01	1437.37 ± 1939.12	2245.52 ± 3454.53	< 0.0001
Vitamin C(mg/day)	66.99 ± 62.35	36.30 ± 39.62	54.91 ± 48.78	70.65 ± 58.89	97.94 ± 75.06	< 0.0001
Vitamin D(mcg/day)	3.87 ± 3.74	2.43 ± 2.39	3.39 ± 3.03	3.92 ± 3.28	5.34 ± 4.89	< 0.0001
Vitamin K(mcg/day)	108.66 ± 121.73	46.49 ± 40.50	82.06 ± 71.68	118.08 ± 107.57	171.69 ± 171.39	< 0.0001
Protein (g/day)	72.19 ± 32.04	46.08 ± 22.35	64.12 ± 22.93	77.23 ± 26.54	94.73 ± 33.06	< 0.0001
Total sugar (g/day)	91.61 ± 55.32	63.84 ± 43.64	83.85 ± 51.41	99.50 ± 56.27	112.34 ± 55.59	< 0.0001
Dietary fiber (g/day)	14.87 ± 8.28	8.34 ± 4.46	12.29 ± 5.37	15.75 ± 6.41	21.39 ± 9.34	< 0.0001
Total fat (g/day)	77.82 ± 35.51	43.46 ± 17.10	66.44 ± 21.92	84.85 ± 24.98	107.83 ± 37.08	< 0.0001

Table 1 (continued)

VE intake (mg/day)	Total (*N* = 5757)	Q1 (< 4.43, *N* = 1376)	Q2 (4.44–6.83, *N* = 1482)	Q3 (6.83–9.99, *N* = 1477)	Q4 (> 10.00, *N* = 1422)	*P* value
Moisture (g/day)	2514.34 ± 1186.16	1882.96 ± 1016.96	2382.18 ± 1129.46	2577.97 ± 1098.25	3058.73 ± 1178.52	< 0.0001
CAP (dB/m)	261.47 ± 63.70	257.69 ± 62.82	262.46 ± 63.94	263.70 ± 65.62	261.27 ± 62.08	0.0900

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

Table 2 Multivariable regression to assess the association of dietary VE intake (mg/day) with controlled attenuation parameter (dB/m)

	Model β (95% CI) *P* value	Model 2 β (95% CI) *P* value	Model 3 β (95% CI) *P* value
VE intake (mg/day)	-0.08 (-0.40, 0.24) 0.6396	-0.59 (-0.93, -0.25) 0.0006	-0.85 (-1.30, -0.40) 0.0002
VE intake categories			
Q1 (< 4.43 mg/day)	Reference	Reference	Reference
Q2 (4.44–6.83 mg/day)	4.77 (-0.10, 9.64) 0.0548	0.83 (-4.62, 6.28) 0.7657	-0.60 (-6.30, 5.09) 0.8362
Q3 (6.83–9.99 mg/day)	6.01 (1.21, 10.81) 0.0142	1.89 (-3.38, 7.16) 0.4814	-1.72 (-7.70, 4.25) 0.5722
Q4 (> 10.00 mg/day)	3.58 (-1.20, 8.36) 0.1422	-5.04 (-10.35, 0.28) 0.0636	-9.59 (-16.87, -2.31) 0.0099

Model 1: no covariates were adjusted

Model 2: age, gender, and race/ethnicity were adjusted

Model 3: age, gender, race/ethnicity, education level, marital status, income to poverty ratio, body mass index, smoking behavior, and the existence of diabetes, hypertension, and high cholesterol level, aspartate aminotransferase, alanine aminotransferase, γ- glutamyl transpeptidase, serum albumin, serum creatinine, uric acid, vitamin A, alpha-carotene, beta-carotene, beta-cryptoxanthin, lycopene, lutein, vitamin C, vitamin D, vitamin K, protein, total sugar, dietary fiber, total fat and moisture were adjusted

using medical phenotype (PheCodes) from the UK Biobank (UKB) indicated that increased dietary VE might protect against NAFLD and other diseases [24]. Experimental studies have shown that supplementing with VE can reduce oxidative stress in NASH model mice, lower serum transaminase levels, and mitigate liver steatosis [25, 26]. In humans, VE has been used as a standalone treatment or in combination with other drugs for NAFLD or NASH. Some studies have shown its effectiveness in reducing serum alanine transaminase levels and NASH, though it has not shown improvement in fibrosis. Our study sheds light on VE's role in early-stage liver steatosis in chronic liver diseases and suggests its potential in preventing and treating liver diseases [13, 14, 27, 28].

Vitamin E, a natural antioxidant, primarily works by alleviating oxidative stress in fatty liver disease, thereby reducing liver steatosis [28, 29]. It also has lipid peroxidation repair and anti-apoptotic effects, mitigating cell damage caused by peroxidized lipids in fatty acids [30]. Studies indicate that fatty liver patients exhibit reduced expression of hepatic lipid transport proteins, such as CD36 and triglyceride transport proteins. VE can rectify this aberrant expression, thus aiding in the secretion and clearance of hepatic fatty acids [31]. Moreover, VE increases the expression of hepatic inositol phospholipids, promoting the production and secretion of very low-density lipoprotein (VLDL) and alleviating fatty liver disease [32].

Interestingly, our study found that VE's protective effect is most pronounced in obese populations. Similar results were observed in another study examining VE intake's impact on NAFLD development in high-risk subpopulations [24]. It was found that in cases with Type 2 Diabetes (T2D), increased VE intake had a more significant protective effect against NAFLD, especially in overweight patients. This suggests that VE works synergistically with obesity and fatty liver, enhancing its efficacy. These findings offer new insights for developing treatments for fatty liver in different populations and suggest new hypotheses for future research in various subgroups.

To our knowledge, our study might be the first to propose a threshold effect of VE on liver steatosis. Threshold points were identified in both the general and specific populations (obese individuals), at 6.58 milligrams/day and 7.37 milligrams/day, respectively. This indicates that, in clinical interventions, a certain threshold of VE intake might be necessary to maximize its protective effect on the liver.

This study has several strengths. First, we used nationally representative and reliable data from the National Health and Nutrition Survey. Second, we employed a non-invasive early quantification indicator called CAP to assess liver fat content, enhancing measurement accuracy and clinical reproducibility. Additionally, we conducted a stratified multivariable regression analysis to explore relationships between different subgroups, contributing to a more comprehensive understanding of the research findings. Most importantly, we identified a nonlinear relationship and threshold effect between vitamin E intake and the severity of liver fat degeneration using generalized additive models. This study proposed a threshold effect of vitamin E intake on hepatic steatosis, offering crucial guidance for clinical nutrition

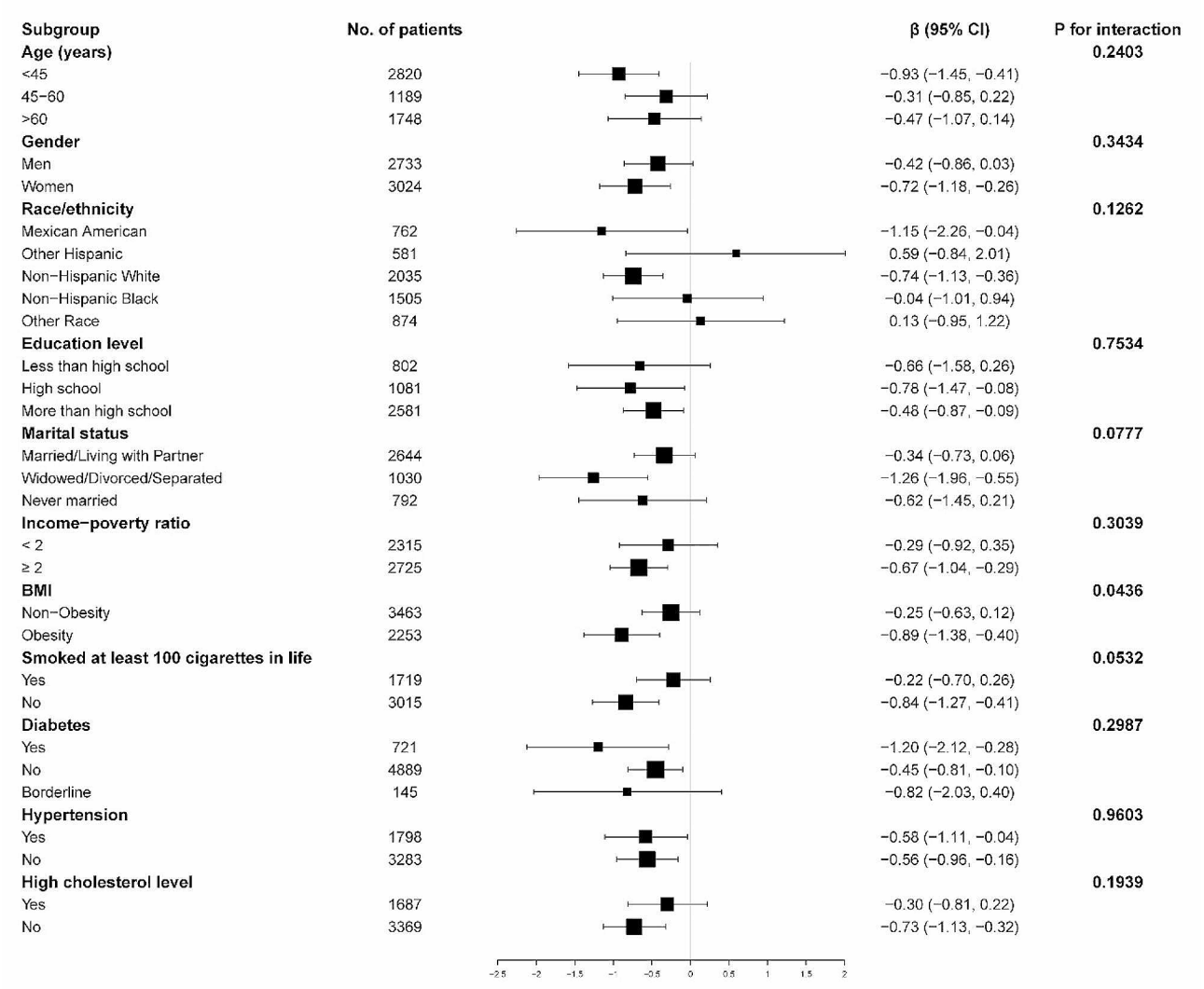

Fig. 2 Subgroup analysis of the association between dietary VE intake (mg/day) with controlled attenuation parameter (dB/m). Age, gender, race/ethnicity, education level, marital status, income to poverty ratio, body mass index, smoking behavior, and the existence of diabetes, hypertension, and high cholesterol level, aspartate aminotransferase, alanine aminotransferase, γ- glutamyl transpeptidase, serum albumin, serum creatinine, uric acid, vitamin A, alpha-carotene, beta-carotene, beta-cryptoxanthin, lycopene, lutein, vitamin C, vitamin D, vitamin K, protein, total sugar, dietary fiber, total fat and moisture were adjusted. In the subgroup analyses, the model is not adjusted for the stratification variable itself

interventions and personalized dietary recommendations. Furthermore, we observed a more significant negative correlation in the obese population, yielding more specific research results for this particular group.

Nevertheless, our study has limitations. Firstly, its cross-sectional design precludes establishing causality, only allowing for the identification of correlations. Secondly, VE intake data, based on 24-hour dietary recall, may be subject to reporting bias and doesn't capture the long-term effects of VE intake. Additionally, due to the absence of dietary follow-up information in the NHANES database, we are unable to investigate how changes in dietary patterns might impact study outcomes. Moreover, liver steatosis was defined using CAP values in transient elastography, not through biologically proven fatty liver, potentially introducing bias in assessing the degree of liver steatosis. Finally, as our sample exclusively comprises American participants, this might limit the generalizability of our findings to international populations. Furthermore, it is important to note that while our study includes several secondary analyses that provide valuable insights, we advise readers to interpret these results with caution. These secondary analyses should not be overgeneralized or considered universally applicable. Further research is required to validate their reliability and generalizability.

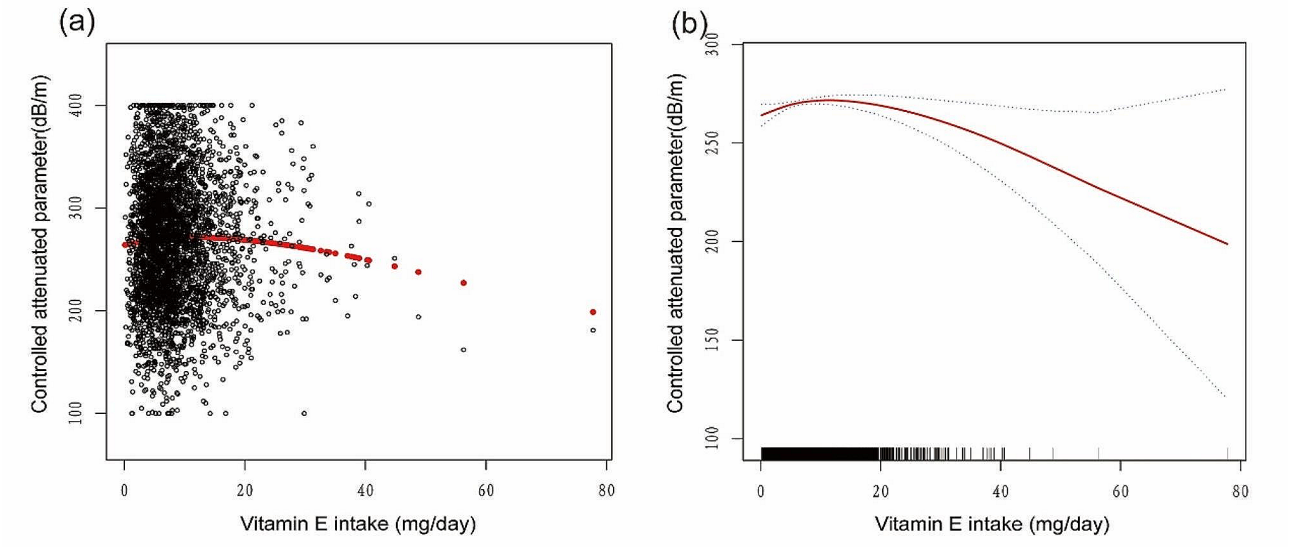

Fig. 3 The association between vitamin E intake and controlled attenuation parameter. (**a**) Each black point represents a sample. (**b**) Solid rad line represents the smooth curve fit between variables. Blue bands represent the 95% of confidence interval from the fit. Age, gender, race/ethnicity, education level, marital status, income to poverty ratio, body mass index, smoking behavior, and the existence of diabetes, hypertension, and high cholesterol level, aspartate aminotransferase, alanine aminotransferase, γ- glutamyl transpeptidase, serum albumin, serum creatinine, uric acid, vitamin A, alpha-carotene, beta-carotene, beta-cryptoxanthin, lycopene, lutein, vitamin C, vitamin D, vitamin K, protein, total sugar, dietary fiber, total fat and moisture were adjusted

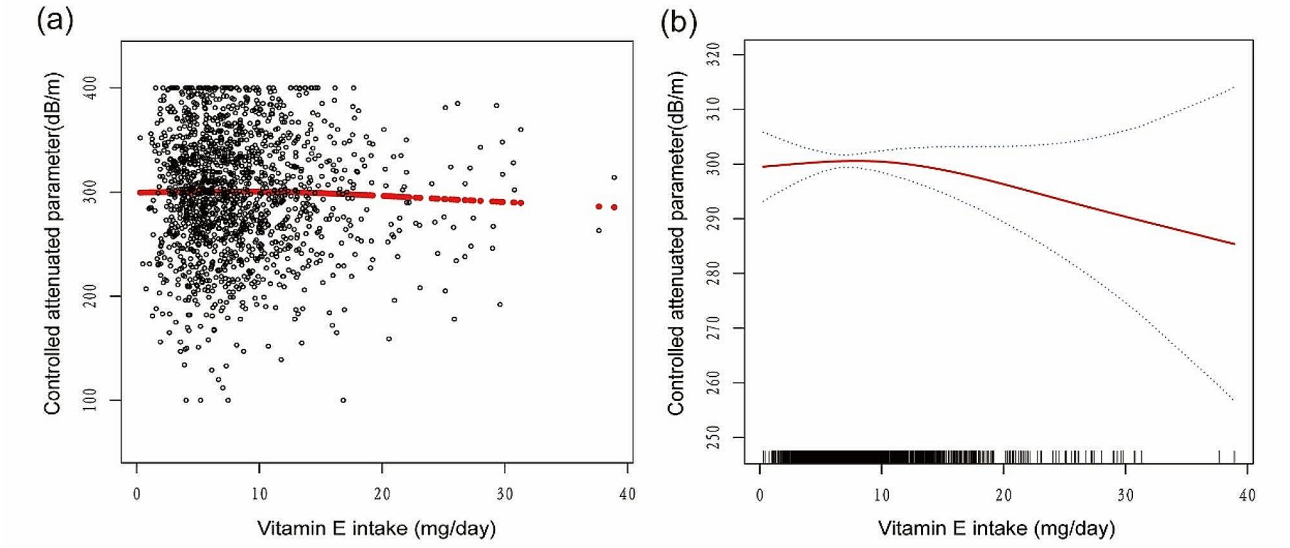

Fig. 4 The association between vitamin E intake and controlled attenuation parameter in Obesity. (**a**) Each black point represents a sample. (**b**) Solid rad line represents the smooth curve fit between variables. Blue bands represent the 95% of confidence interval from the fit. Age, gender, race/ethnicity, education level, marital status, income to poverty ratio, smoking behavior, and the existence of diabetes, hypertension, and high cholesterol level, aspartate aminotransferase, alanine aminotransferase, γ- glutamyl transpeptidase, serum albumin, serum creatinine, uric acid, vitamin A, alpha-carotene, beta-carotene, beta-cryptoxanthin, lycopene, lutein, vitamin C, vitamin D, vitamin K, protein, total sugar, dietary fiber, total fat and moisture were adjusted

Conclusions

Our study offers fresh insights into the relationships between VE intake and hepatic steatosis. Leveraging a large, nationally representative dataset and quantitative CAP measures, we demonstrated a negative correlation between VE intake and hepatic fat content. Importantly, we identified a threshold effect of VE intake in both the general population and obese subsets. This indicates that a certain level of VE intake is necessary for maximizing its protective effect on the liver. Notably, our findings suggest VE's role may be particularly significant in obese patients with fatty liver. Overall, these results can assist in clinical nutritional interventions, personalized dietary guidance, and the development of drugs to reverse fatty

Table 3 Threshold effect analysis of dietary VE intake (mg/day) on controlled attenuation parameter (dB/m) using the two-piecewise linear regression model

controlled attenuation parameter	Adjusted β (95% CI), *P* value
Fitting by the standard linear model	-0.85 (-1.30, -0.40) 0.0002
Fitting by the two-piecewise linear model	
Inflection point	6.58
VE intake < 6.58 (mg/day)	0.79 (-0.45, 2.04) 0.2110
VE intake > 6.58 (mg/day)	-0.86 (-1.24, -0.49) < 0.0001
Log likelihood ratio	0.023

Age, gender, race/ethnicity, education level, marital status, income to poverty ratio, body mass index, smoking behavior, and the existence of diabetes, hypertension, and high cholesterol level, aspartate aminotransferase, alanine aminotransferase, γ- glutamyl transpeptidase, serum albumin, serum creatinine, uric acid, vitamin A, alpha-carotene, beta-carotene, beta-cryptoxanthin, lycopene, lutein, vitamin C, vitamin D, vitamin K, protein, total sugar, dietary fiber, total fat and moisture were adjusted

Table 4 Threshold effect analysis of dietary VE intake (mg/day) on controlled attenuation parameter (dB/m) **in obesity** using the two-piecewise linear regression model

controlled attenuation parameter	Adjusted β (95% CI), *P* value
Obesity	
Fitting by the standard linear model	-0.95 (-1.47, -0.42) 0.0004
Fitting by the two-piecewise linear model	
Inflection point	7.37
VE intake < 7.37 (mg/day)	1.41 (-0.36, 3.18) 0.1175
VE intake > 7.37(mg/day)	-1.57 (-2.26, -0.89) < 0.0001
Log likelihood ratio	0.006

Age, gender, race/ethnicity, education level, marital status, income to poverty ratio, smoking behavior, and the existence of diabetes, hypertension, and high cholesterol level, aspartate aminotransferase, alanine aminotransferase, γ- glutamyl transpeptidase, serum albumin, serum creatinine, uric acid, vitamin A, alpha-carotene, beta-carotene, beta-cryptoxanthin, lycopene, lutein, vitamin C, vitamin D, vitamin K, protein, total sugar, dietary fiber, total fat and moisture were adjusted

liver. Future research should validate these findings and clarify VE's role in the pathogenesis of NAFLD, as well as its potential as an adjunctive treatment strategy, especially for high-risk obese populations.

Abbreviations

NHANES	National Health and Nutrition Examination Survey
CAP	Controlled Attenuation Parameter
VE	Vitamin E
HS	hepatic steatosis
CT	computed tomography
MRI	magnetic resonance imaging
NAFLD	Non-alcoholic fatty liver disease
NASH	Non-alcoholic steatohepatitis
MEC	Mobile Examination Centers
BMI	Body mass index
GGT	γ-glutamyl transpeptidase
AST	Aspartate aminotransferase
ALT	Alanine aminotransferase
UKB	United Kingdom Biobank
VLDL	Very low-density lipoprotein
T2D	Type 2 Diabetes

Acknowledgements
We thank all the participants in NHANES for their selfless contributions to this study.

Author contributions
BC and XC participated in the conception and design of the experiments; XC and LH performed most of the experiments; BC and LH analyzed and interpreted the data; XC and BC drafted the paper and critically revised it for intellectual content. All authors read and approved the final manuscript. And that all authors agree to be accountable for all aspects of the work.

Funding
No funding was received.

Data availability
Publicly available datasets were analyzed in this study. This data and materials can be found here: https://www.cdc.gov/nchs/nhanes/.

Declarations

Ethics approval and consent to participate
The studies involving human participants were reviewed and approved by The National Center for Health Statistics Research Ethics Review Board. Written informed consent to participate in this study was provided by the participants' legal guardian/next of kin.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

Received: 20 February 2024 / Accepted: 22 July 2024
Published online: 30 July 2024

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