Vitamin D Deficiency is Associated With Elevated Blood Concentrations of Ethylene Oxide

Mengli Chen
Jiangsu Province Hospital and Nanjing Medical University First Affiliated Hospital
Xiangying Kong
Jiangsu Province Hospital and Nanjing Medical University First Affiliated Hospital
Xinyi Lu
Jiangsu Province Hospital and Nanjing Medical University First Affiliated Hospital
Shengen Liao
Jiangsu Province Hospital and Nanjing Medical University First Affiliated Hospital
Xiaosu Tang
JXAES: Jiangxi Academy of Environmental Sciences
Haifeng Zhang
Jiangsu Province Hospital and Nanjing Medical University First Affiliated Hospital
Xinli Li (xinli3267@njmu.edu.cn)
Jiangsu Province Hospital and Nanjing Medical University First Affiliated Hospital
https://orcid.org/0000-0002-7889-6359

Research Article

Keywords: Vitamin D, Ethylene oxide, Concentration, Deficiency, NHANES, Nonlinear

Posted Date: December 21st, 2021

DOI: https://doi.org/10.21203/rs.3.rs-1135102/v1

Abstract

Ethylene oxide has been associated with increased oxidative stress and related disorders in recent studies, while vitamin D is a widely recognized antioxidant. Whether vitamin D deficiency is related to elevated blood concentrations of ethylene oxide is still unknown. We aimed to explore the relationship between vitamin D deficiency and blood concentrations of ethylene oxide in the general population. A total of 4125 adults who participated in the National Health and Nutrition Examination Survey (NHANES) 2013–2016 were analyzed. Participants were divided into 3 groups: vitamin D sufficiency (≥75.0 nmol/L), insufficiency (50–74.9 nmol/L), and deficiency (<50.0 nmol/L). Adjusted linear and restricted cubic spline regression models were performed to evaluate the associations between vitamin D levels and blood concentrations of ethylene oxide. Compared with participants with vitamin D sufficiency, the adjusted mean ethylene oxide level was approximately 0.08 and 0.23 log2-units higher in the presence of vitamin D insufficiency and vitamin D deficiency (P for trend <0.001). The adjusted percent difference with a 95% confidence interval in ethylene oxide per interquartile range increase in vitamin D was -1.13 (-1.68, -0.57). A restricted cubic spline model demonstrated that vitamin D levels are nonlinearly and inversely associated with blood concentrations of ethylene oxide (P for nonlinearity =0.021). Further research is warranted to understand how vitamin D may have a role in reducing blood concentrations of ethylene oxide.

Introduction

Vitamin D is a widely recognized fat-soluble vitamin and is mainly derived from synthesis in the body by the skin when exposed to sunlight. Other sources of vitamin D include the diet and dietary supplements. Regular sunlight can provide sufficient vitamin D, which can be stored in body fat and released in the winter, when the intensity and utilization of sunlight are too low to produce enough vitamin D in the skin (Holick 2007; Skaaby et al. 2017). Vitamin D insufficiency and deficiency are common all over the world; the prevalence of vitamin D insufficiency and deficiency among US adults was 41.4 and 28.9%, respectively (Liu et al. 2018). Vitamin D deficiency has been traditionally linked to skeletal health (Holick 2007), cardiovascular events (Judd and Tangpricha 2009), cancer incidence and decreased cancer-related mortality (Freedman et al. 2007), hypertension (Judd et al. 2008), diabetes (Holick 2005), and autoimmune conditions(Merlino et al. 2004).

Ethylene oxide was classified as a Group 1 carcinogen by the International Agency for Research on Cancer and as a Class 2 carcinogen by the German MAK commission (Jinot and Fritz 2018). Ethylene oxide has been detected in food, tobacco, and automobile exhaust. Given its widespread occurrence and adverse health effects, exposure to ethylene oxide is a major concern worldwide. Recently, ethylene oxide exposure has been associated with increased oxidative stress and health-related disorders in humans (Guo et al. 2021; Jain 2020; Zeng et al. 2021).

Vitamin D may alter and reduce the exposure level of environmental pollutants, including perfluoroalkyl substances (Etzel et al. 2019), acrylamide hemoglobin biomarkers (Yin et al. 2021), bisphenol A (Johns et al. 2016) and phthalates (Johns et al. 2017). In a recent study using data from the National Health and Nutrition Examination Survey (NHANES), the significant association of ethylene oxide with blood inflammation parameters was 0.05 *10^9/L per pmol/g Hb of ethylene oxide in the blood for white blood cells (Zeng et al. 2021). Since the influence of vitamin D on inflammation is well recognized (Mangin et al. 2014), we hypothesized that an elevated vitamin D level is linked to reduced blood concentrations of ethylene oxide. The objective of the study was to test the relationship between vitamin D levels and blood concentrations of ethylene oxide using data from the National Health and Nutrition Examination Survey (NHANES).

Methods

Study population

The NHANES, conducted by the National Center for Health Statistics (NCHS) at the Centers for Disease Control and Prevention (CDC), is a large-scale, multistage, ongoing, nationally representative health survey to represent the civilian noninstitutionalized population in the U.S. We used publicly available data on the blood ethylene oxide concentrations of 20,146 individuals from the 2013–2016 NHANES cycles (n=5,446). We excluded individuals who lacked a vitamin D measurement (n=63). Given that the metabolism of ethylene oxide may be abnormal in teenagers and pregnant women due to hormonal alterations, we excluded individuals aged < 18 years (n=1,216) and pregnant women (n=25). Finally, a total of 4,125 individuals were left for our analysis (Fig. 1). The NCHS Research Ethics Review Board approved the study protocol, and written informed consent was obtained from each participant.

Ethylene oxide exposure assessment

Red blood cell specimens were processed and stored until shipped to the CDC's National Center for Environmental Health for laboratory testing. Ethylene oxide was detected by high-performance liquid chromatography coupled with tandem mass spectrometry (HPLC–MS/MS) as described in detail elsewhere (Zeng et al. 2021). Undetectable concentrations were substituted with the respective detection limit divided by the square root of two.

Vitamin D measurements

The standardized liquid chromatography-tandem mass spectrometry (LC–MS/MS) method was used to measure serum 25-hydroxyvitamin D (25(OH)D) in serum sample data from the NHANES. In addition to the quantitative analyses of vitamin D as a continuous variable, we also considered individuals with a measured 25(OH)D level of ≥75.0 nmol/L as having vitamin D sufficiency, individuals with a measured 25(OH)D level of 50-74.9 nmol/L as having vitamin D insufficiency, and individuals with a measured 25(OH)D level of <50.0 nmol/L as having vitamin D deficiency (Liu et al. 2018).

Assessment of covariates

Information on age, sex, race/ethnicity, family income, education level, and physical activity was obtained from the household interview using demographic questionnaires. Race/ethnicity was recorded as non-Hispanic white, non-Hispanic black, Mexican American, other Hispanic, or other. The family income-to-poverty ratio was positively correlated with family income status. The self-reported education level was segmented into below high school, high school, and above high school. Physical activity, described as leisure time moderate-to-vigorous exercise, comprised the inactive group (indicating fewer than 150 minutes per week), insufficiently active group (indicating 150 to 300 minutes per week), and active group (indicating more than 300 minutes per week). Data on smoking status and alcohol intake were collected from the health questionnaire. In compliance with the NCHS classifications, the participants were categorized as never smokers and smokers based on their responses about smoking more than 100 cigarettes. Alcohol intake was grouped into drinkers or nondrinkers by having at least 12 alcoholic drinks per year or not. Body weight and height were measured by certified examiners to calculate the body mass index (BMI) as the ratio of weight in kilograms to height in meters squared (kg/m^2). Additionally, chronic health conditions (hypertension, diabetes) were defined using the participants' self-reported answers to whether a doctor or other health professional had ever informed that they had a certain chronic condition.

Statistical analysis

The baseline characteristics were described across three levels of vitamin D. Log2 transformation was performed due to the skewed distribution of ethylene oxide levels. We modeled differences in blood ethylene oxide levels across the three levels of vitamin D using linear regression. We developed three models by sequential adjustment for three groups of covariates. Model 1 included age and sex; Model 2 was further adjusted for education level, race, smoking status, alcohol use, diabetes, hypertension and body mass index; and Model 3 additionally included the poverty-income ratio, energy intake, and physical activity. Our results are also presented as the average percent difference and 95% confidence interval (CI). The interquartile range (IQR) of the vitamin D concentration was calculated. Then, the formula % = (IQR ^ beta-1)*100% was calculated. In addition, we assessed the potential nonlinear relationships between serum vitamin D concentrations and blood ethylene oxide levels using restricted cubic splines with three knots located at the 10^{th}, 50^{th}, and 90^{th} percentiles. All analyses were conducted using R software version 4.0.5 (R Foundation for Statistical Computing, Vienna, Austria). A two-sided *P* value < 0.05 was considered statistically significant.

Results

Characteristics

In our study, as shown in Table 1, the average age of the individuals was 47.5 years, and 50.0% were male. The mean vitamin D concentration in our sample was 63.9 nmol/L. Serum vitamin D concentrations were lower among younger individuals, males, non-Hispanic blacks, individuals with a higher body mass index, individuals with a lower family income-to-poverty ratio, and individuals who had no physical activity (Table 1). Furthermore, individuals with vitamin D deficiency had a higher probability of hypertension and were less likely to have a history of diabetes.

Table 1
Characteristics of the study population.

Variables	Overall (n=4125)	Vitamin D sufficiency (n=1243)	Vitamin D insufficiency (n=1490)	Vitamin D deficiency (n=1392)	*P* value
Age, years	47.5 (17.8)	54.7 (18.0)	45.9 (17.1)	42.7 (16.2)	<0.001
Male, %	2063 (50.0%)	550 (44.2%)	788 (52.9%)	725 (52.1%)	<0.001
Education level, %					<0.001
<9th grade	395 (9.6%)	105 (8.4%)	166 (11.1%)	124 (8.9%)	
9–11th grade	565 (13.7%)	131 (10.5%)	197 (13.2%)	237 (17.0%)	
High school	982 (23.8%)	278 (22.4%)	366 (24.6%)	338 (24.3%)	
College	1237 (30.0%)	378 (30.4%)	431 (28.9%)	428 (30.7%)	
Graduate	946 (22.9%)	351 (28.2%)	330 (22.1%)	265 (19.0%)	
Race/ethnicity, %					<0.001
Mexican American	599 (14.5%)	100 (8.0%)	227 (15.2%)	272 (19.5%)	
Other Hispanic	427 (10.4%)	92 (7.4%)	209 (14.0%)	126 (9.1%)	
Non-Hispanic White	1681 (40.8%)	758 (61.0%)	627 (42.1%)	296 (21.3%)	
Non-Hispanic Black	846 (20.5%)	135 (10.9%)	220 (14.8%)	491 (35.3%)	
Other race	572 (13.9%)	158 (12.7%)	207 (13.9%)	207 (14.9%)	
Hypertension, %	1434 (34.8%)	545 (43.8%)	450 (30.2%)	439 (31.5%)	<0.001
Diabetes	521 (12.6%)	203 (16.3%)	155 (10.4%)	163 (11.7%)	<0.001

Data are presented as mean (standard deviation, SD) or n (%).

Variables	Overall (n=4125)	Vitamin D sufficiency (n=1243)	Vitamin D insufficiency (n=1490)	Vitamin D deficiency (n=1392)	*P* value
Body mass index, kg/m2	29.1 (7.2)	28.0 (6.6)	28.9 (6.6)	30.3 (8.1)	<0.001
Smoker, %	2080 (50.4%)	624 (50.2%)	753 (50.5%)	703 (50.5%)	0.982
Alcohol user, %	521 (12.6%)	203 (16.3%)	155 (10.4%)	163 (11.7%)	0.476
Energy intake, kcal/day	2050 (875)	2020 (893)	2060 (851)	2070 (885)	0.353
Poverty-income ratio	2.18 (1.54)	2.50 (1.59)	2.14 (1.52)	1.92 (1.45)	<0.001
Physical activity					0.043
Never	2444 (59.2%)	715 (57.5%)	882 (59.2%)	847 (60.8%)	
Moderate	823 (20.0%)	278 (22.4%)	274 (18.4%)	271 (19.5%)	
Vigorous	858 (20.8%)	250 (20.1%)	334 (22.4%)	274 (19.7%)	
Ethylene oxide, pmol/g Hb	36.7(24.6-157)	33.0(23.2-111.5)	36.3(24.7-147.8)	41.5(26.0-205.0)	<0.001
Data are presented as mean (standard deviation, SD) or n (%).					

Association between serum vitamin D and the blood concentration of ethylene oxide.

After adjusting for cofounding factors, including age, sex, education level, race, smoking status, alcohol use, diabetes, hypertension, body mass index, poverty-income ratio, energy intake, and physical activity, compared with individuals with vitamin D sufficiency, the adjusted mean ethylene oxide (log2 transformed) levels with 95% confidence intervals (CIs) were 0.08 (-0.02, 0.18) and 0.23 (0.12, 0.33) units higher in the presence of vitamin D insufficiency and vitamin D deficiency (*P* for trend<0.001). The adjusted percent difference with a 95% confidence interval in ethylene oxide per interquartile range increase in vitamin D was -1.13 (-1.68, -0.57) (Table 2). When examining nonlinear relationships across the three levels of vitamin D, there was a nonlinear and negative relationship between serum vitamin D and the blood concentration of ethylene oxide (Fig. 2).

Table 2
Association between serum vitamin D and blood concentration of ethylene oxide.

Vitamin D	Model 1	Model 2	Model 3
	β (95% CI)	β (95% CI)	β (95% CI)
Vitamin D sufficiency(≥75.0 nmol/L)	Ref.	Ref.	Ref.
Vitamin D insufficiency (50.0-74.9 nmol/L)	0.07 (-0.05, 0.20)	0.09 (-0.01, 0.19)	0.08 (-0.02, 0.18)
Vitamin D deficiency (<50.0 nmol/L)	0.30 (0.17, 0.43)***	0.25 (0.14, 0.36)***	0.23 (0.12, 0.33)***
P for trend	<0.001	<0.001	<0.001
Percent change, %	-1.41(-2.07, -0.75)***	-1.21(-1.76, -0.66)***	-1.13(-1.68, -0.57)***
Model 1 was adjusted for age and sex.			
Model 2 was adjusted for age, sex, education level, race, smoking status, alcohol use, diabetes, hypertension and body mass index.			
Model 3 was adjusted for age, sex, education level, race, smoking status, alcohol use, diabetes, hypertension, body mass index, poverty-income ratio, energy intake, and physical activity.			
Blood concentration of ethylene oxide was log2-transformed to fit the linear regression model. ****P*< 0.001.			

Subgroup analysis for the association between serum vitamin D and the blood concentration of ethylene oxide

To determine whether there were any differences in the association between serum vitamin D and the blood concentration of ethylene oxide among the different covariate groups, we conducted a stratified analysis according to the covariate groups. Subgroup analysis demonstrated that individuals who were elderly, female, had a history of diabetes or hypertension, were non-obese, and had no physical activity were more susceptible to the association between serum vitamin D and the blood concentration of ethylene oxide (Table 3).

Table 3
Subgroups analysis for the associations between serum vitamin D and blood concentration of ethylene oxide.

	Vitamin D sufficiency	Vitamin D insufficiency	Vitamin D deficiency	*P* for trend	*P* for interaction
	β	β(95% CI)	β(95% CI)		
Age					0.021
>60 years, n=1140	1.00	0.16(-0.03, 0.34)	0.50(0.28, 0.71)***	<0.001	
≤60 years, n=2985	1.00	0.03(-0.08, 0.15)	0.17(0.04, 0.29) **	0.007	
Sex					0.822
Male, n=2063	1.00	0.02(-0.13, 0.16)	0.20(0.04, 0.36)*	0.013	
Female, n=2062	1.00	0.13(0.00, 0.27)	0.25(0.10, 0.39) **	0.001	
Diabetes					0.355
Yes, n=521	1.00	0.05(-0.24, 0.34)	0.29(0.00, 0.58) *	0.058	
No, n=3604	1.00	0.08(-0.03, 0.18)	0.21(0.10, 0.33) ***	<0.001	
Hypertension					0.407
Yes, n=1434	1.00	0.06(-0.12, 0.23)	0.25(0.07, 0.44) **	0.009	
No, n=2691	1.00	0.08(-0.04, 0.20)	0.20(0.07, 0.34) **	0.003	
Obesity					0.386
BMI>30 kg/m^2, n=1543	1.00	0.12(-0.06, 0.30)	0.16(-0.02, 0.34)	0.094	
BMI≤30 kg/m^2, n=2582	1.00	0.03(-0.09, 0.15)	0.22(0.08, 0.35)**	0.003	
Physical activity					0.884

Analyses was adjusted for age, sex, education level, race, smoking status, alcohol use, diabetes, hypertension, body mass index, poverty-income ratio, energy intake, and physical activity when they were not the strata variables. OR, Odd ratio; CI, confidence interval. ** *P*<0.05, ** *P*<0.01, *** *P* < 0.001

	Vitamin D sufficiency	Vitamin D insufficiency	Vitamin D deficiency	*P* for trend	*P* for interaction
	β	β(95% CI)	β(95% CI)		
Never, n=2444	1.00	0.05(-0.08, 0.18)	0.22(0.09, 0.36)**	0.001	
Moderate, n=823	1.00	0.08(-0.15, 0.31)	0.19(-0.06, 0.44)	0.140	
Vigorous, n=858	1.00	0.21(-0.02, 0.43)	0.25(-0.01, 0.51)	0.059	

Analyses was adjusted for age, sex, education level, race, smoking status, alcohol use, diabetes, hypertension, body mass index, poverty-income ratio, energy intake, and physical activity when they were not the strata variables. OR, Odd ratio; CI, confidence interval. $^{**}P<0.05$, $^{**}P<0.01$, $^{***}P < 0.001$

Discussion

Our study is the first to demonstrate that vitamin D deficiency is associated with an elevated blood concentration of ethylene oxide in a nationally representative sample of the United States population. Vitamin D may reduce the production of ethylene oxide.

Previous studies have suggested that endocrine vitamin D may disrupt the metabolism of environmental pollutants, and our results are consistent with previous studies investigating the associations of endocrine vitamin D with other environmental pollutants including perfluoroalkyl substances (Etzel et al. 2019), acrylamide hemoglobin biomarkers (Yin et al. 2021), di(2-ethylhexyl) phthalate (DEHP) metabolite and bisphenol A (Johns et al. 2016) In a cross-sectional study of NHANES participants, Etzel et al. found that elevated serum perfluoroalkyl substance levels were associated with lower total 25(OH)D concentrations (Etzel et al. 2019). Additionally, using data from NHANES participants, Yin et al. found that vitamin D was inversely and nonlinearly associated with acrylamide hemoglobin biomarkers (Yin et al. 2021). In another study also using data from the NHANES, higher urinary levels of di(2-ethylhexyl) phthalate (DEHP) metabolites and bisphenol A (BPA) were inversely related to lower serum total 25(OH)D (Johns et al. 2016).

The potential mechanism behind the vitamin D relationship with the blood concentration of ethylene oxide has not been explored. As noted earlier, a previous epidemiological study observed that an increase in the blood concentration of ethylene oxide was associated with an increased white blood cell count and neutrophils in the general population, and there was a positive correlation between the blood concentration of ethylene oxide and cardiovascular diseases (Zeng et al. 2021). These results demonstrated that ethylene oxide may activate the inflammatory response. Furthermore, experimental study confirmed that macrophage with impaired vitamin D receptor have directly impact on the secretion of miR-106b-5p, thus leading to the production of inflammation (Oh et al. 2020). Given the anti-inflammatory properties of vitamin D (Mangin et al. 2014), the possible mechanism underlying this phenomenon is that the level of oxidative stress increases when a vitamin D deficiency occurs, and the mediating effect of the white blood cell count is activated. Nevertheless, further studies are warranted to investigate the mechanism of vitamin D deficiency-induced blood ethylene oxide increases.

Our results demonstrated a negative association between the blood concentration of ethylene oxide and serum total 25(OH)D levels. This investigation has certain practical significance, and vitamin D supplementation may reduce the blood concentrations of ethylene oxide to reduce the carcinogenic effects of ethylene oxide.

Our study is the first to investigate the potential ethylene oxide reduction effect of vitamin D in adults. There are some limitations in our study. First, given that the study had a cross-sectional design, we cannot determine a causal relationship between serum total 25(OH)D levels and blood concentrations of ethylene oxide. Second, information on some cofounding factors of interest was sparse. In particular, data on complete daily sunlight exposure time assessment and time spent outdoors were not available for the examined patients. Finally, reverse causation, that is, ethylene oxide, may be associated with altered endocrine hormones that may also affect vitamin D metabolism, must also be considered.

Conclusion

In summary, vitamin D deficiency has an effect on elevated blood concentrations of ethylene oxide in the general adult population. The white blood cell count may be the intermediate pathway for blood concentrations of ethylene oxide incremental changes caused by vitamin D deficiency. Further laboratory and prospective epidemiological studies are warranted to confirm our findings.

Declarations

Funding

None.

Affiliations

The First Affiliated Hospital of Nanjing Medical University, Jiangsu Province Hospital, Nanjing, 210029, China.

Mengli Chen, Xiangying Kong, Xinyi Lu, Shengen Liao, Haifeng Zhang and Xinli Li

Jiangxi Environmental Engineering Vocational College, Ganzhou, 341000, China.

Xiaosu Tang

Author contribution

Mengli Chen, Xiangying Kong and Xinyi Lu: conceptualization, methodology and software. Shengen Liao, Xiaosu Tang, Haifeng Zhang and Xinli Li: investigation, data curation, and writing (reviewing and editing).

Corresponding author

Correspondence to Xinli Li.

Data availability

The data is available on request from the corresponding author.

Ethics declarations

Ethics approval and consent to participate

The National Center for Health Statistics (NCHS) Research Ethics Review Board approved the study protocol, and written informed consent was obtained from each participant.

Consent for publication

Not applicable.

Competing interest

The authors declare no conflicts of interest.

References

1. Etzel TM, Braun JM, Buckley JP (2019) Associations of serum perfluoroalkyl substance and vitamin D biomarker concentrations in NHANES, 2003-2010. Int J Hyg Environ Health 222:262–269. doi:10.1016/j.ijheh.2018.11.003
2. Freedman DM, Looker AC, Chang SC, Graubard BI (2007) Prospective study of serum vitamin D and cancer mortality in the United States. J Natl Cancer Inst 99:1594–1602. doi:10.1093/jnci/djm204
3. Guo J, Wan Z, Cui G, Pan A, Liu G (2021) Association of exposure to ethylene oxide with risk of diabetes mellitus: results from NHANES 2013-2016. Environ Sci Pollut Res Int. doi:10.1007/s11356-021-15444-7
4. Holick MF (2005) Vitamin D: important for prevention of osteoporosis, cardiovascular heart disease, type 1 diabetes, autoimmune diseases, and some cancers. South Med J 98:1024–1027. doi:10.1097/01.smj.0000140865.32054.db
5. Holick MF (2007) Vitamin D deficiency. N Engl J Med 357:266–281. doi:10.1056/NEJMra070553
6. Jain RB (2020) Associations between observed concentrations of ethylene oxide in whole blood and smoking, exposure to environmental tobacco smoke, and cancers including breast cancer: data for

US children, adolescents, and adults. Environ Sci Pollut Res Int 27:20912–20919. doi:10.1007/s11356-021-15444-7

7. Jinot J, Fritz JM (2018) Carcinogenicity of ethylene oxide: key findings and scientific issues. Toxicol Mech Methods 28:386–396. doi:10.1080/15376516.2017.1414343
8. Johns LE, Ferguson KK, Cantonwine DE, McElrath TF, Mukherjee B, Meeker JD (2017) Urinary BPA and Phthalate Metabolite Concentrations and Plasma Vitamin D Levels in Pregnant Women: A Repeated Measures Analysis. Environ Health Perspect 125:087026. doi:10.1289/ehp1178
9. Johns LE, Ferguson KK, Meeker JD (2016) Relationships Between Urinary Phthalate Metabolite and Bisphenol A Concentrations and Vitamin D Levels in U.S. Adults: National Health and Nutrition Examination Survey (NHANES), 2005-2010. J Clin Endocrinol Metab 101:4062–4069. doi:10.1210/jc.2016-2134
10. Judd SE, Nanes MS, Ziegler TR, Wilson PW, Tangpricha V (2008) Optimal vitamin D status attenuates the age-associated increase in systolic blood pressure in white Americans: results from the third National Health and Nutrition Examination Survey. Am J Clin Nutr 87:136–141. doi:10.1093/ajcn/87.1.136
11. Judd SE, Tangpricha V (2009) Vitamin D deficiency and risk for cardiovascular disease. Am J Med Sci 338:40–44. doi:10.1097/MAJ.0b013e3181aaee91
12. Liu X, Baylin A, Levy PD (2018) Vitamin D deficiency and insufficiency among US adults: prevalence, predictors and clinical implications. Br J Nutr 119:928–936. doi:10.1017/s0007114518000491
13. Mangin M, Sinha R, Fincher K (2014) Inflammation and vitamin D: the infection connection. Inflamm Res 63:803–819. doi:10.1007/s00011-014-0755-z
14. Merlino LA, Curtis J, Mikuls TR, Cerhan JR, Criswell LA, Saag KG (2004) Vitamin D intake is inversely associated with rheumatoid arthritis: results from the Iowa Women's Health Study. Arthritis Rheum 50:72–77. doi:10.1002/art.11434
15. Oh J, Matkovich SJ, Riek AE, Bindom SM, Shao JS, Head RD, Barve RA, Sands MS, Carmeliet G, Osei-Owusu P, Knutsen RH, Zhang H, Blumer KJ, Nichols CG, Mecham RP, Baldán Á, Benitez BA, Sequeira-Lopez ML, Gomez RA, Bernal-Mizrachi C (2020) Macrophage secretion of miR-106b-5p causes renin-dependent hypertension. Nat Commun 11:4798. doi:10.1038/s41467-020-18538-x
16. Skaaby T, Thuesen BH, Linneberg A (2017) Vitamin D, Cardiovascular Disease and Risk Factors. Adv Exp Med Biol 996:221–230. doi:10.1007/978-3-319-56017-5_18
17. Yin T, Xu F, Shi S, Liao S, Tang X, Zhang H, Zhou Y, Li X (2021) Vitamin D mediates the association between acrylamide hemoglobin biomarkers and obesity. Environ Sci Pollut Res Int. doi:10.1007/s11356-021-16798-8
18. Zeng G, Zhang Q, Wang X, Wu KH (2021) Association between blood ethylene oxide levels and the risk of cardiovascular diseases in the general population. Environ Sci Pollut Res Int. doi:10.1007/s11356-021-15572-0

Figures

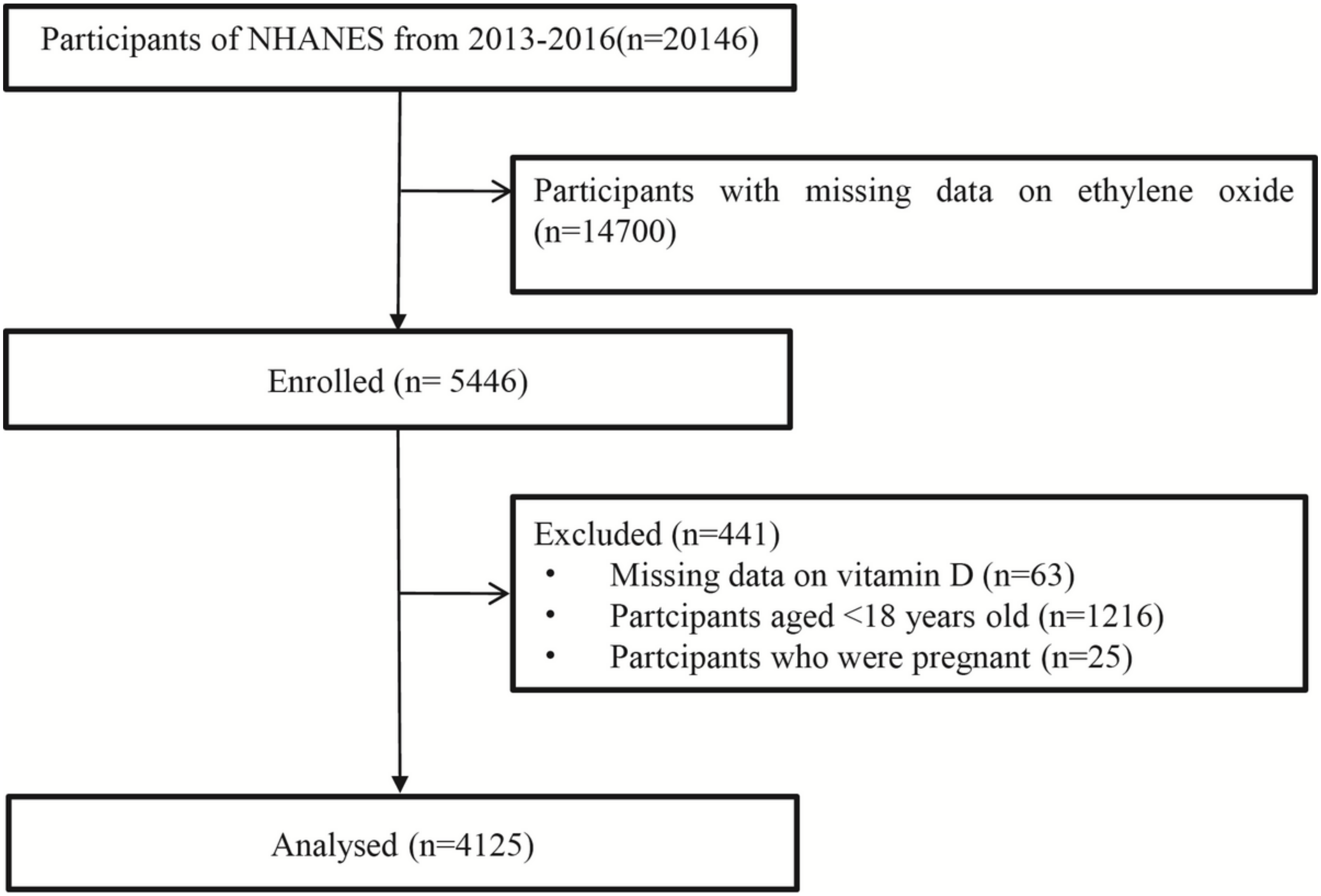

Figure 1

Study flow chart.

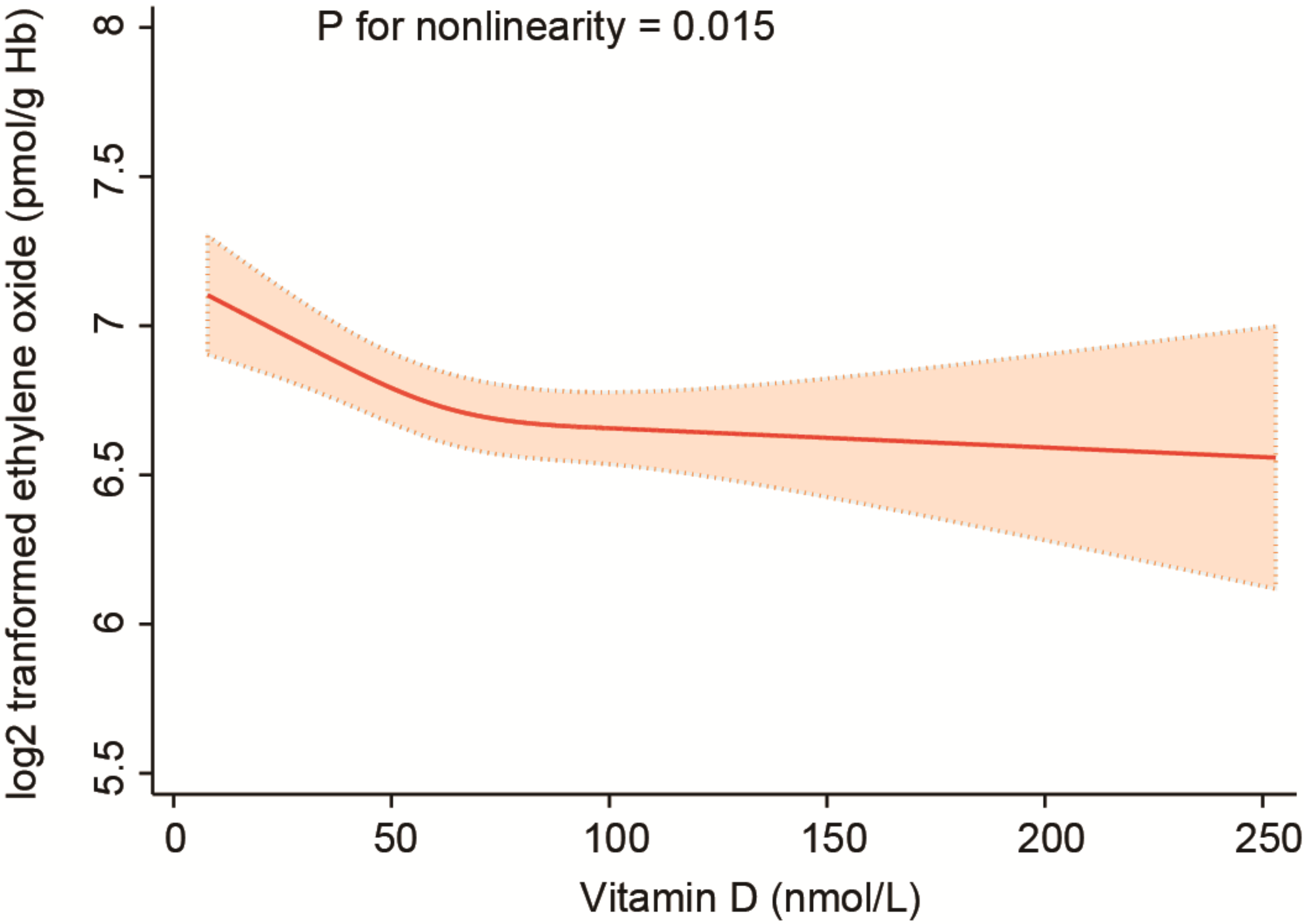

Figure 2

Restricted cubic spline plots of the associations between serum vitamin D and the blood concentration of ethylene oxide. Analyses were adjusted for age, sex, education level, race, smoking status, alcohol use, diabetes, hypertension, body mass index, poverty-income ratio, energy intake, and physical activity. The solid line and dashed line represent the predicted values of log2 transformed blood concentrations of ethylene oxide and the corresponding 95% confidence intervals.