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# Association between dietary niacin intake and lung function among American adults: A cross-sectional analysis from national health and nutrition examination survey, 2007–2012

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#### ABSTRACT

*Background:* The pathogenesis of pulmonary senescence involves immune system dysregulation, oxidative stress, and mitochondrial dysfunction. The effects on lung function of niacin, an essential coenzyme involved in mitochondrial energy metabolism with known antioxidant properties, are poorly understood.

*Methods:* This cross-sectional study used data from the 2007–2012 National Health and Nutrition Examination Survey, including spirometry data and niacin intake information of 9706 adults. This study investigated various spirometry measures, such as forced expiratory volume in 1 s, forced vital capacity, pulse expiratory flow, (forced expiratory volume in 1 s)/(forced vital capacity) ratio, and predicted forced expiratory volume in 1 s and forced vital capacity percentages. Additionally, a secondary analysis was conducted using Global Initiative for Chronic Obstructive Lung Disease and chronic obstructive pulmonary disease. Foundation Spirometry Grade criteria to assess the relationship between niacin intake, airflow limitation, and obstruction. Multivariate regression models were used to adjust for relevant covariates.

*Results*: The study included 9706 U S. adults (4788 men and 4918 women) with a median age of 46.2 years. After adjusting for relevant factors, a positive correlation was observed between niacin intake and lung function. Compared to the lowest quintile of niacin intake (Q1,  $\leq$ 14.5 mg/ day), individuals in the highest quintile (Q5, >34.5 mg/day) exhibited significant increases in lung function parameters, including forced expiratory volume in 1s (69.84 mL, p = 0.003), pulse expiratory flow (254.48 mL, p < 0.001), (forced expiratory volume in 1 s)/(forced vital capacity) (0.01, p = 0.041), percent predicted forced expiratory volume in 1 s(2.05, p = 0.002), and percent predicted forced vital capacity(1.29, p = 0.042).

*Abbreviations*: NHANES, National Health and Nutrition Examination Survey; PIR, poverty-income ratio; BMI, body mass index; FEV1, forced expiratory volume in 1 s; FVC, forced vital capacity; PEF, peak expiratory flow; GOLD, Global Initiative for Chronic Obstructive Lung Disease classification of COPD; COPD, chronic obstructive pulmonary disease; ATS, American Thoracic Society; Akt, threonine kinase.

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Subset analyses of individuals with spirometry-defined airflow obstruction showed associations of high niacin intake with significantly improved forced expiratory volume, pulse expiratory flow, and percent predicted pulse expiratory flow and an interaction among race, education, and smoking status with respect to the relationship between niacin intake and lung function parameters.

*Conclusions*: Higher niacin intake was associated with increased measures of lung function. A diet rich in niacin-containing foods may play a role in improving lung health.

# 1. Background

Lung disease is a major public health issue and chronic obstructive pulmonary disease (COPD) now the third leading cause of death in the world [1]. According to current evidence, patients' lungs may be irreversibly damaged before the onset of severe respiratory symptoms. As the disease progresses, symptoms gradually worsen, and later interventions have limited effect [2,3]. The worldwide impact of lung diseases, specifically chronic respiratory disease (CRD), is evident through the substantial economic costs and premature mortality among diagnosed individuals [4,5]. Furthermore, the profound repercussions of the coronavirus disease 2019 (COVID-19) pandemic throughout the previous year are anticipated to contribute to a sustained increase in the prevalence of chronic respiratory diseases, specifically owing to the development of irreversible pulmonary fibrosis [6]. Maintaining lung function is crucial for preventing lung-related diseases and is a public health priority. Studies have shown that lung function is a prognostic indicator for people with lung disease and for the general population [7]. Therefore, early prevention is crucial in controlling lung-related diseases, which can effectively slow down the rate of lung function decline and improve prognosis. However, few preventive interventions have been identified beyond smoking cessation. While smoking is a significant risk factor, other factors also contribute to the risk of lung disease. There is evidence to indicate that diet may have a significant impact on maintaining lung health [8–13]. Therefore, it is necessary to investigate other dietary nutrients that may improve lung function.

Niacin is a nutritional precursor of nicotinamide adenine dinucleotide and nicotinamide adenine dinucleotide phosphate, which are critical cofactors for mitochondrial energy metabolism [14]. Dietary niacin deficiency hinders oxidative phosphorylation and disrupts mitochondrial respiration [15]. Previous clinical studies have indicated that age-related mechanisms of pulmonary disease can be attributed to immune system dysregulation, oxidative stress, and mitochondrial dysfunction [16,17]. Previous clinical studies have shown a significant association between niacin intake and better mean FEV1 among Hispanic and non-Hispanic white smokers in New Mexico [18]. However, research on the association between dietary niacin intake and lung function in the general population is scarce.

The National Health and Nutrition Examination Surveys (NHANES) include spirometry measures and dietary intake information in a representative sample of US adults, allowing evaluation of the relationship between niacin intake and lung function parameters. Therefore, the purpose of this study was to examine if dietary intake of niacin is associated with measures of lung function in a generalizable adult population, as well as in patients with chronic obstructive pulmonary disease (COPD).

# 2. Methods

## 2.1. Study population

This cross-sectional study utilized data from the NHANES between 2007 and 2012. This survey is conducted by the Centers for Disease Control and Prevention [19] and aims to evaluate the health and nutritional status of non-institutionalized Americans through a stratified multistage probability survey approach [20]. The NHANES collects comprehensive demographic and health data via home visits, screening, and laboratory testing at a mobile examination center. The NCHS research ethics review board approved the NHANES study protocol, and participants provided written informed consent at enrollment (the website is https://www.cdc.gov/nchs/nhanes/irba98.htm). Ethical approval and consent were not required as this study was based on publicly available deidentified data. As a secondary analysis, the present study did not require approval from additional institutional review boards [21]. Our study involved interviews with individuals aged  $\geq$ 20 years. Pregnant women and individuals with missing data on dietary niacin intake, lung function, and other covariates were excluded. This study adhered to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guidelines [22].

## 2.2. Dietary niacin intake

The NHANES dietary survey utilized the United States Department of Agriculture's Automated Multiple Pass Method to evaluate the types and quantities of food and beverages consumed by participants within a 24-h period. Data from 2007 to 2012 were used to accurately calculate the nutrient values for each participant based on their individual consumption patterns [23]. The NHANES Dietary Interviewers Procedure Manuals provide a comprehensive description of the methodologies used in the dietary survey [24]. Despite limitations in reliability and validity, the 24-h dietary recall method provides a more comprehensive portrayal of the food types and quantities consumed, in contrast to the food frequency questionnaire [25,26]. The participants were categorized into quintiles (Q1–Q5) according to their dietary niacin intake.

#### 2.3. Lung function parameters

Between 2007 and 2012, pre-bronchodilator spirometry was performed using an Ohio 822/827 dry-roll volume spirometer according to the guidelines established by the American Thoracic Society (ATS) and European Respiratory Society (ERS) [27]. The variables obtained from spirometry and used in this study included forced expiratory volume in 1 s (FEV1), forced vital capacity (FVC), peak expiratory flow (PEF), FEV1/FVC ratio, and percent predicted values of FEV1 and FVC. Spirometry was graded from A to F according to the acceptability and reproducibility criteria outlined by ATS/ERS. Grades A–B indicated that the spirometry findings met or surpassed the ATS criteria; grade C remained potentially useful; and grades D–F were unlikely to yield valuable information [28]. Only FEV1 and FVC measurements with quality grades A and B were included in this study to ensure accuracy; measurements with grades C, D, and F were excluded. Lung function was assessed as a predicted percentage, considering age, sex, height, and race (white, black, or Mexican/Hispanic) based on the third NHANES reference value [29]. Reference values for lung function have been established for non-Hispanic white, black, and Mexican-American populations. However, we applied a correction factor of 0.88 was applied to the "other" race category based on data that specifically accounts for Asian participants [30]. For the "other Hispanic" group, we utilized predicted values specifically developed for Mexican Americans [31]. Due to the limited completion rate of post-bronchodilator spirometry among a small number of individuals, our analyses primarily relied on pre-bronchodilator values.

# 2.4. Respiratory phenotype determination

The respiratory phenotype of obstructive lung disease was determined using the Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines and COPD Foundation Spirometry Grade (SG) classifications to assess airflow obstruction [32,33]. Our analysis involved three comparison groups: individuals with a normal spirometry pattern (FEV1/FVC  $\geq$ 0.70, FEV1  $\geq$ 80 % predicted), those with a "restrictive" spirometry pattern (FEV1/FVC  $\geq$ 0.70, FEV1 <80 % predicted), and individuals with airflow obstruction (FEV1/FVC <0.70), categorized into the GOLD normal and airflow obstruction stages based on FEV1% prediction.

# 2.5. Other covariates

We comprehensively examined potential covariates including age, sex, race/ethnicity, education level, family income, insurance status, body mass index (BMI), smoking habits, recreational and work activities, hypertension, diabetes, stroke, coronary heart disease, and respiratory illnesses (e.g. asthma, emphysema, and Chronic bronchitis) by reviewing the available literature [34–38]. We also considered dietary factors, specifically caloric, protein, carbohydrate, and fat intakes. We also considered the white blood cell counts. Educational attainment was categorized as primary school or lower, middle school and high school, or college or higher [39]. BMI categories were determined using the World Health Organization classifications as underweight (<18.5 kg/m<sup>2</sup>), normal weight (18.5–25.0 kg/m<sup>2</sup>), overweight (25.0–30.0 kg/m<sup>2</sup>), and obese (>30.0 kg/m<sup>2</sup>). Based on a US government report, the poverty income ratio (PIR) was utilized to categorize family income into three groups: low (PIR  $\leq$ 1.3), medium (PIR >1.3–3.5), and high (PIR >3.5) [40]. Smoking status was classified into three categories based on definitions in the literature: never smoker (smoked 100 cigarettes), current smoker, and former smoker (quit smoking after having smoked >100 cigarettes) [38]. We determined previous medical conditions (chronic bronchitis, asthma, hypertension, diabetes, stroke, and coronary heart disease) through participant self-reports of these conditions. A dietary recall interview, conducted before the interview at the mobile examination center, aimed to collect participants' 24-h nutritional information [41] encompassing dietary calorie, protein, carbohydrate, and fat intakes [37]. The intake of niacin dietary supplements was determined by the participants' responses to a question about their consumption of nutritional supplements within the past month [41].

## 2.6. Statistical analysis

We performed a secondary analysis of publicly available datasets to investigate the association between dietary niacin intake and lung function. We applied chi-square and analysis of variance (ANOVA) to assess the characteristics of demographic variables and risk factors associated with pulmonary function. Proportions were used to express categorical variables, while appropriate measures such as mean (standard deviation) or median (interquartile range) were employed to describe continuous variables. A multivariable linear regression model was used to investigate the association between niacin intake and lung function. The model estimated the coefficients ( $\beta$ ) and 95 % confidence intervals (CIs). The participants were categorized into five groups based on quintiles of niacin intake: Q1 ( $\leq$ 14.5 mg/d; n = 1940), Q2 (14.5–19.85 mg/d; n = 1941), Q3 (19.85–25.8 mg/d; n = 1943), Q4 (25.8–34.5 mg/d; n = 1940), and Q5 ( $\geq$ 34.283 mg/d; n = 1942), with Q1 serving as the reference group. We constructed three regression models: an unadjusted model, a minimally adjusted model considering sociodemographic variables, and a fully adjusted model incorporating multiple factors. The fully adjusted model accounted for variables such as smoking status, work and recreational activity, medical conditions (hypertension, diabetes, stroke, coronary heart disease, emphysema, chronic bronchitis, and asthma), dietary factors (energy, protein, carbohydrate, and fat consumption), dietary supplement use, and white blood cell count.

Restricted cubic splines (RCSs) were used to assess the relationship between niacin levels and lung function. A smooth curve-fitting graph was generated by adjusting for the covariates included in the fully adjusted model. Four knots were placed at specific percentiles (5th, 35th, 65th, and 95th percentiles) of the niacin level distribution.

Interaction and subgroup analyses were conducted using multivariable linear regression models to explore factors such as age (20–60 vs. >60 years), sex, race/ethnicity, education level ( $\leq$ 12 years vs. >12 years), and smoking status. To ensure

the reliability of the results and account for gender differences in energy intake, we excluded participants with extreme levels of energy intake (<600 or >6000 kcal/day for women and <800 or >6000 kcal/day for men) from the sensitivity analyses. This approach is consistent with previous diet-related studies [34,38,41]. Supplements are an important source of niacin in addition to dietary intake. To investigate the impact of niacin supplementation on lung function, we performed a sensitivity analysis on participants who completed the Niacin Supplementation Survey.

The sample size was determined solely based on the available data, without prior estimation of statistical power. However, we verified the adequacy of the sample size of 9706 populations using the statistical software G\*Power and the R package 'pwr', which showed a statistical power of over 99 % with a significance level (p value) of less than 0.05. All analyses utilized R 4.2.2 and Free Statistics software version 1.8 [42]. A descriptive study was conducted on all participants, and statistical significance was determined by a two-tailed test with p < 0.05.

# 3. Results

## 3.1. Study population

A total of 30,442 participants completed the interview, including 12,729 aged <20 years. We excluded pregnant women (n = 182) and those with missing data on FVC, FEV1, PEF, FVC, and FEV1 quality grades C/D/F (n = 4780); dietary niacin intake (n = 1720); and other covariates (n = 1325). Finally, this cross-sectional study analyzed data from 9706 NHANES participants between 2007 and 2012. The inclusion and exclusion processes are illustrated in Fig. 1.

# 3.2. Baseline characteristics

Table 1 presents the baseline characteristics of the 9706 participants. The average age was 46.2 years, with a sex distribution of 49.3 % male and 50.7 % female participants. Individuals with higher niacin consumption exhibited characteristics such as younger age (mean ages in Q1 to Q5 groups were 49, 47.3, 46.8, 45.6, and 42.1 years, respectively); male sex (males accounted for 77.1 % of the Q5 group); marital or partnered status; non-Hispanic white ethnicity; non-smoking status; higher levels of education and family income; and lower incidence rates of hypertension, diabetes, stroke, and coronary heart disease, as detailed in Table 1. Additionally, individuals with higher niacin consumption had higher intakes of energy, proteins, carbohydrates, and fats. Furthermore, an increased percentage of participants displayed normal lung function, while a significantly lower proportion of individuals experienced airflow restriction and airflow obstruction.

# 4. Association of dietary niacin intake with lung function

## 4.1. Univariable and multivariable regression analyses

The findings from the multivariable linear regression analysis of the association between dietary niacin intake and lung function parameters are shown in Table 2. When niacin was analyzed as a continuous variable, we observed a significant independent positive association between niacin and FVC ( $\beta = 23.72$ , p < 0.001), FEV1 ( $\beta = 18.31$ , p < 0.001), PEF ( $\beta = 42.85$ , p < 0.001), percent predicted FVC ( $\beta = 0.04$ , p = 0.001), and percent predicted FVC ( $\beta = 0.04$ , p = 0.011) in the non-adjusted crude model. Further adjustment did



Fig. 1. The study's flow diagram.

## Table 1

Population characteristics by categories of dietary niacin intake.

Characteristic	Niacin Intake, mg/d									
	Total	Q1 (≦14.5))	Q2 (14.5–19.8)	Q3 (19.8–25.8)	Q4 (25.8–34.5)	Q5 (>34.5)	p-value			
NO.	9706	1940	1941	1943	1940	1942				
Demographic										
Sex, n (%):Male	4788 (49.3)	545 (28.1)	689 (35.5)	903 (46.5)	1153 (59.4)	1498 (77.1)	< 0.001			
Age, Mean(SD)	$46.2\pm16.0$	$49.0\pm16.8$	$47.3 \pm 15.9$	$46.8 \pm 16.0$	$45.6\pm15.6$	$42.1\pm14.7$	< 0.001			
Race, n (%)							< 0.001			
Mexican American	1507 (15.5)	315 (16.2)	293 (15.1)	293 (15.1)	293 (15.1)	313 (16.1)				
Other-Hispanic	987 (10.2)	224 (11.5)	211 (10.9)	183 (9.4)	169 (8.7)	200 (10.3)				
Non-Hispanic White	4546 (46.8)	819 (42.2)	895 (46.1)	930 (47.9)	974 (50.2)	928 (47.8)				
Non-Hispanic Black	1919 (19.8)	433 (22.3)	390 (20.1)	376 (19.4)	344 (17.7)	376 (19.4)				
Other Race	747 (7.7)	149 (7.7)	152 (7.8)	161 (8.3)	160 (8.2)	125 (6.4)				
BMI, Mean ± SD Education, n (%)	$29.1 \pm 6.8$	$29.4\pm 6.9$	$29.3\pm 6.9$	$29.2 \pm 6.8$	$29.0\pm 6.6$	$\textbf{28.8} \pm \textbf{6.5}$	0.028 < 0.001			
Primary school and less	809 (8.3)	234 (12.1)	187 (9.6)	131 (6.7)	132 (6.8)	125 (6.4)				
Middle and high school	3579 (36.9)	782 (40.3)	725 (37.4)	685 (35.3)	646 (33.3)	741 (38.2)				
College and higher	5318 (54.8)	924 (47.6)	1029 (53)	1127 (58)	1162 (59.9)	1076 (55.4)				
Marital, n (%)							< 0.001			
Married/living with partner	5930 (61.1)	1076 (55.5)	1151 (59.3)	1228 (63.2)	1269 (65.4)	1206 (62.1)				
Widowed/divorced/ separated	1899 (19.6)	485 (25)	451 (23.2)	357 (18.4)	304 (15.7)	302 (15.6)				
Never married	1877 (19.3)	379 (19.5)	339 (17.5)	358 (18.4)	367 (18.9)	434 (22.3)				
PIR, Mean (SD)	$2.6\pm1.7$	$2.3\pm1.6$	$2.5\pm1.6$	$2.7\pm1.7$	$\textbf{2.8} \pm \textbf{1.7}$	$2.7\pm1.7$	< 0.001			
Insurance, n (%):Yes	2490 (25.7)	502 (25.9)	503 (25.9)	456 (23.5)	457 (23.6)	572 (29.5)	< 0.001			
Smoking status, n (%)							< 0.001			
Never	5267 (54.3)	1089 (56.1)	1061 (54.7)	1071 (55.1)	1056 (54.4)	990 (51)				
Former	2237 (23.0)	402 (20.7)	444 (22.9)	476 (24.5)	486 (25.1)	429 (22.1)				
Current	2202 (22.7)	449 (23.1)	436 (22.5)	396 (20.4)	398 (20.5)	523 (26.9)				
Work activity, n (%)							< 0.001			
Other	5425 (55.9)	1231 (63.5)	1111 (57.2)	1103 (56.8)	1004 (51.8)	976 (50.3)				
Vigorous	2294 (23.6)	422 (21.8)	486 (25)	468 (24.1)	482 (24.8)	436 (22.5)				
Moderate	1987 (20.5)	287 (14.8)	344 (17.7)	372 (19.1)	454 (23.4)	530 (27.3)				
Recreational activity, n (%)							< 0.001			
Other	4702 (48.4)	1044 (53.8)	1014 (52.2)	962 (49.5)	858 (44.2)	824 (42.4)				
Vigorous	2660 (27.4)	556 (28.7)	546 (28.1)	556 (28.6)	539 (27.8)	463 (23.8)				
Moderate	2344 (24.2)	340 (17.5)	381 (19.6)	425 (21.9)	543 (28)	655 (33.7)				
Comorbidity(Yes)	0005 (045)	FF1 (00 4)	500 (05 0)	511 (0( 0)	(50 (00 0)	000 (10 7)	0.001			
HBP, ft (%):	2397 (24.7)	551 (28.4)	500 (25.8)	511 (26.3)	452 (23.3)	383 (19.7)	< 0.001			
Diabetes, ii (%):	973 (10.0)	210 (11.1)	231 (11.9)	201 (10.3)	180 (9.0)	139 (7.2)	< 0.001			
Chronia bronchitic n (%):	109 (1.1)	29 (1.5)	27 (1.4) 127 (6 E)	24 (1.2)	17 (0.9)	12(0.6)	<0.001			
Asthma n (%):	467 (3.0)	286 (147)	201 (15)	93 (4.9) 278 (14 3)	04 (4.3) 256 (13.2)	267(13.7)	<0.001 0.401			
CHD $p(%)$ :	246 (2 5)	200 (14.7) 51 (2.6)	64 (3 3)	43 (2 2)	49 (2 5)	207 (13.7)	0.491			
Stroke n (%):	290(2.3)	60(31)	39 (2)	44 (2.3)	33(1.7)	26 (1.3)	0.002			
Dietary	202 (2.1)	00 (011)	0, (1)	11 (210)	00(11))	20 (110)	0.002			
Niacin supplement, n (%):	2935(30.2)	537(27.7)	561(28.9)	640(32.9)	618(31.9)	579(29.8)	0.002			
Carbohydrate(g/d),Mean	$\textbf{263.5} \pm \textbf{128.2}$	$\textbf{176.0} \pm \textbf{81.3}$	$\textbf{224.7} \pm \textbf{91.8}$	$\textbf{256.6} \pm \textbf{93.7}$	$\textbf{295.1} \pm \textbf{112.8}$	$\textbf{365.2} \pm \textbf{158.3}$	< 0.001			
Eat (g/d) Mean (SD)	$81.2 \pm 47.0$	$48.1 \pm 25.7$	$66.4 \pm 20.3$	$795 \pm 348$	$93.1 \pm 41.4$	$118.7 \pm 61.2$	<0.001			
Calorie(kcal/d), Mean (SD)	2171.0+	$1323.0 \pm$	1773.9+	2099.3+	2467.3+	3190.6+	< 0.001			
	1004.9	512.9	570.5	631.8	757.4	1216.1				
Protein (g/d), Mean (SD)	$83.5\pm42.6$	$43.8\pm17.4$	$63.3 \pm 18.8$	$\textbf{79.3} \pm \textbf{21.8}$	$\textbf{96.4} \pm \textbf{26.1}$	$134.5\pm49.9$	< 0.001			
FVC (mL), Mean (SD)	3952.8 +	$3466.1 \pm 950.1$	$3706.6 \pm 977.3$	3887.0 +	4173.9 +	4529.9 +	< 0.001			
	1075.7		0/0010 ± 3//10	1017.6	1049.2	1053.2	0.001			
FEV1 (mL), Mean (SD)	$3091.9 \pm 890.7$	$2714.1 \pm 801.5$	$2898.9 \pm 822.6$	$3040.8 \pm 848.8$	$3254.9 \pm 870.0$	$3550.6 \pm 867.1$	< 0.001			
PEF (mL), Mean (SD)	8136.9 ±	7213.0 $\pm$	7636.7 ±	8049.8 ±	8591.1 ±	9193.1 ±	< 0.001			
	2190.6	1970.0	2085.1	2086.1	2150.4	2089.2				
FEV1/FVC, Mean (SD)	$0.8\pm0.1$	$0.8\pm0.1$	$0.8\pm0.1$	$0.8\pm0.1$	$0.8\pm0.1$	$0.8\pm0.1$	0.441			
FEV1 predicted(%)	$96.7 \pm 15.3$	$95.6 \pm 16.4$	$96.3 \pm 16.1$	$96.7 \pm 15.2$	$97.3 \pm 14.6$	$\textbf{97.3} \pm \textbf{13.9}$	< 0.001			
FVC predicted (%)	$100.4 \pm 14.4$	$99.9 \pm 15.5$	$100.5\pm14.9$	$100.4 \pm 14.4$	$100.7 \pm 13.8$	$100.3\pm13.1$	0.527			
WBC, Mean (SD)	$\textbf{7.1} \pm \textbf{2.3}$	$\textbf{7.2} \pm \textbf{3.0}$	$\textbf{7.2} \pm \textbf{2.1}$	$\textbf{7.1} \pm \textbf{2.3}$	$\textbf{7.1} \pm \textbf{2.0}$	$\textbf{7.0} \pm \textbf{2.1}$	0.066			
SG, classification n (%)							0.045			
Normal	7812 (80.5)	1527 (78.7)	1556 (80.2)	1572 (80.9)	1568 (80.8)	1589 (81.8)				
Airflow restriction	629 (6.5)	161 (8.3)	128 (6.6)	112 (5.8)	116 (6)	112 (5.8)				
Airflow obstruction	1265 (13.0)	252 (13)	257 (13.2)	259 (13.3)	256 (13.2)	241 (12.4)				
GOLD, classification (%)							0.919			
Normal	8441 (87.0)	1688 (87)	1684 (86.8)	1684 (86.7)	1684 (86.8)	1701 (87.6)				
Airflow obstruction	1265 (13.0)	252 (13)	257 (13.2)	259 (13.3)	256 (13.2)	241 (12.4)				

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Abbreviations: Q1–Q5:quintiles based on dietary niacin consumption; BMI: Body Mass Index; HBP:hypertension; CHD:coronary heart disease; PIR: Family income; BMI: Body Mass Index; FEV1: Forced Expiratory Volume 1st Second; FVC: Forced Vital Capacity; FEV1/FVC: 1-s rate; PEF: Peak expiratory flow; White blood cell; WBC:white blood cell; SG: The COPD Foundation Spirometry Grade (SG) classification; GOLD: The Global Initiative for Chronic Obstructive Lung Disease classification of COPD.

not significantly affect these results. With increased quintiles of niacin levels, the lung function parameters increased, and the  $\beta$  of Q5 was higher than that of Q1 (FVC (56.75, p = 0.052), FEV1 (69.84 mL, p = 0.003), PEF (254.48 mL, p < 0.001), FEV1/FVC (0.01, p = 0.041), percent predicted FEV1 (2.05, p = 0.002), and percent predicted FVC (1.29, p = 0.042)) in the fully adjusted model. A subset of participants diagnosed with airway obstruction by spirometry (n = 1265) showed a significant correlation between niacin intake and lung function parameters (Table 3). Compared to Q1, Q5 exhibited significant increases in FVC ( $\beta$  = 150.08, p = 0.214), FEV1 ( $\beta$  = 165.09, p = 0.017), PEF ( $\beta$  = 624.01, p = 0.003), percent predicted PEV1 ( $\beta$  = 5.23, p = 0.015), and percent predicted FVC ( $\beta$  = 4.12, p = 0.055) after adjusting for pertinent confounders. Although statistically insignificant positive correlations between niacin intake and FVC were observed in both primary and secondary outcomes in the fully adjusted model, the direction of the association remained reasonable.

## 4.2. Restricted cubic splines analyses

The RCSs of the association between niacin and lung function are shown in Figure S1. Niacin levels and lung function parameters (FVC, PEF, and FEV1) were positively associated with all potential confounders considered (nonlinearity, p > 0.05).

## 4.3. Sensitivity analyses

Sensitivity analyses were performed to assess the stability and robustness of statistical analyses. After excluding individuals with energy intakes outside a plausible range (women: <600 or >6000 kcal/day; men: <800 or >8000 kcal/day), the analysis included 9551 individuals. The associations between dietary niacin intake and lung function parameters remained stable in this reduced set of samples (Table S1). The fully adjusted model analyzing niacin as a continuous variable revealed significant associations with FVC ( $\beta$  = 2.36, 95 % CI: 1.04–3.67; p < 0.001), FEV1 ( $\beta$  = 1.81, 95 % CI: 0.74–2.83; p = 0.001), and PEF ( $\beta$  = 6.26, 95 % CI: 3.1–9.42; p < 0.001). Participants in the highest quartile of niacin intake had higher mean percent predicted FEV1 and FVC by averages of 2.05 (p = 0.003) and 1.33 (p = 0.039), respectively, than those in the lowest quartile. However, we observed no significant relationship between niacin intake and FEV1/FVC ratio.

Out of the 9706 participants, 6696 completed the niacin supplement survey. Among them, 2607 reported using niacin supplements. When niacin supplementation was analyzed as a continuous variable, fully adjusted models showed no association between niacin supplementation and FVC ( $\beta = -0.01$ , 95 % CI: 0.22–0.2; p = 0.938), FEV1 ( $\beta = 0$ , 95 % CI: 0.17–0.17; p = 0.965), and PEF ( $\beta = 0.18$ , 95 % CI: 0.32–0.68; p = 0.965). (Table S2).

#### 4.4. Subgroup analyses by adjusted potential effect confounders

Fig. 2 presents the results of the interaction analyses of niacin intake on FEV1, FVC, and PEF within different subgroups. We observed a significant interaction (p < 0.05) among race, education, smoking status, and lung function. The results indicated a weaker association among non-Hispanic black individuals, with a 0.74 mL increase in FVC and a 1.28 mL increase in FEV1 per unit increment in niacin levels. Similarly, individuals with a low education level also showed a weaker association, with 1.32 mL, 0.33 mL, and 1 mL increases in FVC, FEV1, and PEF, respectively. Current smokers showed a weaker association, with a 2.28 mL increase in PEF. We observed no significant interactions in the remaining subgroups.

#### 5. Discussion

In this cross-sectional study utilizing NHANES data obtained from the US population, we observed significant positive associations between dietary niacin intake and lung function parameters in adults and individuals with spirometry-defined airflow obstruction. Moreover, a higher niacin intake was associated with significantly higher FEV1, FVC, PEF, and percent predicted FEV1. Sensitivity analyses revealed a robust association between dietary niacin intake and lung function in adults in the US. Subgroup analysis revealed an interaction between race, education, smoking status, and lung function (p < 0.05).

Few studies have reported the effects of niacin on lung function. Leng et al. examined whether nutrient intake accounted for ethnic differences in FEV1 decline between Hispanic and non-Hispanic white smokers. They reported that niacin was consistently and significantly associated with a better average FEV1 [18]. Kim et al. observed a significant association between niacin intake and the severity of airway compromise in elderly patients with COPD in South Korea [43]. However, no studies have specifically examined the association between dietary niacin and lung function in the general population. Our findings indicated a positive association between higher niacin levels and increased lung function across all indices, which is partly consistent with previous findings. This association may be influenced by factors such as variations in participant demographics including country, age, and target population.

Additionally, subgroup analyses revealed race, education, and smoking as interaction factors. Specifically, increased dietary niacin intake was associated with higher FVC and FEV1 in non-Hispanic Black adults. This finding may be attributed to variations in the factors influencing lung function across different races and regions [44–46]. The same niacin level appeared to show a weaker effect on

able 2
association between dietary niacin intake and lung function of univariable and multivariable linear regression analysis.

Variable		Niacin mg/d	Q1 (≦14.5)	Q2 (14.5–19.8)	Q3 (19.8–25.8)	Q4 (25.8–34.5)	Q5 (>34.5)	P for trend
FVC	model1	23.73(22.4–25.07) <sup>c</sup>	0(Ref)	240.55(176.98-304.13) <sup>c</sup>	420.94(357.38-484.49) <sup>c</sup>	707.77(644.19–771.35) <sup>c</sup>	1063.79(1000.22–1127.35) <sup>c</sup>	< 0.001
	model2	4.21(3.31–5.11) <sup>c</sup>	0(Ref)	58.83(18.4–98.66) <sup>b</sup>	57.05(16.48–97.63) <sup>b</sup>	120.25(78.89–161.61) <sup>c</sup>	165.43(122.61-208.26) <sup>c</sup>	< 0.001
	model3	2.18(0.88-3.49) <sup>c</sup>	0(Ref)	41.74(1.25-82.23) <sup>a</sup>	17.758(-25.03-60.53)	56.97(10.42-103.53) <sup>a</sup>	56.75(-0.56-114.06)	0.05
FEV <sub>1</sub>	model1	18.31(17.2–19.43) <sup>c</sup>	0(Ref)	184.81(131.8–237.82) <sup>c</sup>	326.79(273.79-379.78) <sup>c</sup>	540.86(487.85–593.88) <sup>c</sup>	836.56(783.56-889.56) <sup>c</sup>	< 0.001
	model2	2.69(1.95-3.42) <sup>c</sup>	0(Ref)	37.04(4.14–69.95) <sup>a</sup>	39.88(6.61–73.15) <sup>a</sup>	80.74(46.82–114.66) <sup>c</sup>	119.74(84.62–154.86) <sup>c</sup>	< 0.001
	model3	$1.65(0.59-2.71)^{b}$	0(Ref)	32.64(-0.23-65.5)	21.47(-1326-56.2)	48.63(10.84-86.42) *	69.84(23.31–116.36) <sup>b</sup>	0.006
PEF	model1	42.85(40.09–45.6) <sup>c</sup>	0(Ref)	423.76(293.07–554.45) <sup>c</sup>	836.85(706.19-967.51) <sup>c</sup>	1378.11(1247.4–1508.82) <sup>c</sup>	$1980.14(1849.46-2110.81)^{\circ}$	< 0.001
	model2	6.75(4.58–8.92) <sup>c</sup>	0(Ref)	89.69(-7.38-186.71)	133.83(35.7–231.95) <sup>b</sup>	263.66(163.63-363.69) <sup>c</sup>	304.16(200.59–407.73) <sup>c</sup>	< 0.001
	model3	5.88(2.74–9.01) <sup>c</sup>	0(Ref)	87.06(-10.84-183.61)	110.13(7.38-212.89) <sup>a</sup>	216.7(104.88-328.51) <sup>c</sup>	254.48(116.83–392.13) <sup>c</sup>	< 0.001
FEV <sub>1</sub>	model1	0(0–0)	0(Ref)	0(-0.01–0)	0(0~0.01)	0(-0.01~0)	0(0~0.01)	0.333
/FVC	model2	0(0–0)	0(Ref)	0(-0.01–0)	0(0-0)	0(-0.01–0)	0(-0.01–0)	0.849
	model3	0(0–0)	0(Ref)	0(0–0)	0(0-0.01)	0(0-0.01)	0.01(0–0.01) <sup>a</sup>	0.083
FEV <sub>1</sub> , %Predicted	model1	0.03(0.01–0.05) <sup>c</sup>	0(Ref)	0.76(-0.2-1.72)	$1.19(0.23-2.15)^{a}$	$1.75(0.79-2.71)^{c}$	$1.77(0.81-2.73)^{c}$	< 0.001
	model2	0.03(0.01–0.06) <sup>c</sup>	0(Ref)	0.61(0.38-1.49)	$0.96(0.01-1.91)^{a}$	$1.56(0.59-2.52)^{b}$	$1.78(0.78-2.78)^{\circ}$	< 0.001
	model3	$0.04(0.01-0.07)^{a}$	0(Ref)	0.91(-0.02-1.83)	$1.13(0.15-2.12)^{a}$	$1.64(0.57-2.71)^{b}$	$2.05(0.73-3.37)^{b}$	0.001
FVC, %Predicte	model1	0.01(-0.01-0.03)	0(Ref)	0.57(0.34-1.48)	0.46(-0.44-1.37)	0.79(-0.11-1.7)	0.37(-0.53-1.28)	0.347
	model2	0.05(0.03–0.07) <sup>c</sup>	0(Ref)	0.79(0.08-1.59)	1.04(0.136–1.93) <sup>a</sup>	1.79(0.86–2.69) <sup>c</sup>	$1.88(0.95-2.82)^{\circ}$	< 0.001
	model3	$0.04(0.01-0.07)^{a}$	0(Ref)	0.88(-0.01–1.76)	0.94(0.01–1.87) <sup>a</sup>	$1.48(0.47-2.49)^{b}$	$1.29(0.05-2.54)^{a}$	0.018

*Note:*Q1–Q5: quintiles based on dietary niacin consumption; FEV1: Forced Expiratory Volume 1st Second; FVC: Forced Vital Capacity; PEF: Peak expiratory flow CI: confidence interval. Model 1: Non adjusted model was adjusted for age, sex, race/ethnicity, marital status education level, family income, BMI, insurance). Model 3: Fully adjusted model was adjusted for Model 2+ smoking status, work activity, recreational activity, hypertension, diabetes, stroke, coronary heart disease, emphysema, chronic bronchitis, asthma, energy consumption, protein consumption, carbohydrate consumption and White blood cell count.

P-value.

 $\checkmark$ 

 $^{a}_{.} p < 0.05.$ 

<sup>b</sup> p < 0.01.

 $^{c}~p \leq 0.001_{\circ}$  .

## Table 3

Results of multivariable regres	sion models for niacin intake a	and lung function in adults v	with airflow obstruction ( $n = 1265$ ).

Outcome	Q1	Q2 14.5–19.8 mg/d		Q3 Q4   19.8-25.8 mg/d 25.8-		Q4	Q4		Q5	
	≦14.5 mg/d					25.8–34.5 mg/d		≧34.5 mg/d		
		β	Р	β	Р	β	Р	β	Р	
FVC(ml)	Ref	79.54	0.214	90.08	0.182	209.12	0.005	150.08	0.109	0.022
FEV1(ml)	Ref	47.23	0.318	101.13	0.043	159.81	0.004	165.09	0.017	0.003
PEF(ml)	Ref	156.14	0.272	410.21	0.006	515.34	0.002	624.01	0.003	< 0.001
FEV1/FVC (ml)	Ref	0	0.675	0.01	0.154	0.01	0.411	0.02	0.054	0.052
FEV1 predicted (%)	Ref	1.01	0.49	3.38	0.029	5.24	0.001	5.23	0.015	0.001
FVC predicted (%)	Ref	1.98	0.176	3.17	0.04	6.18	< 0.001	4.12	0.055	0.003

Note:Adjusted for all other variables age, sex, marital status, race/ethnicity, education level, family income, BMI:body mass index, insurance, smoking status, work activity, recreational activity, hypertension, diabetes, stroke, coronary heart disease, emphysema, chronic bronchitis, asthma, energy consumption, protein consumption, carbohydrate consumption, fat consumption and White blood cell count. Q1–Q5: quintiles based on dietary niacin consumption; FEV1: Forced Expiratory Volume 1st Second; FVC: Forced Vital Capacity; PEF: Peak expiratory flow.





Values are presented as  $\beta$  (95 % confidence interval) and P for interaction.

the PEF of current smokers. As an initial defense against inhaled particulates and pathogens, alveolar macrophage function is dysregulated after exposure to cigarette smoke [47]. This dysregulation may explain the reduced increase in PEF observed in current smokers. Similar to previous studies [48,49], our results indicate that individuals with higher levels of education exhibited higher FVC and FEV1. This may be due to the fact that lower levels of education are associated with the complex effects of low socioeconomic status, which can have negative impacts on respiratory health beginning early in life, such as intrauterine dysplasia and childhood respiratory infections [50]. However, another study found no significant correlation between educational factors and lung function [51]. Due to differences in education systems, the education level categories used in this study are broadly comparable but not directly corresponding. Therefore, it is necessary to investigate specific underlying factors in the future.

Although the underlying mechanisms underlying the positive association of niacin intake with lung function remain to be further investigated, our findings are consistent with the available evidence and are biologically plausible. First, immune system involvement may help explain this phenomenon. Previous studies demonstrated a negative association among levels of circulating inflammatory biomarkers, lung function, and respiratory morbidity [52]. In animal models, activation of the threonine kinase (Akt) pathway reduced inflammation, reactive oxygen species production, and apoptosis, thereby mitigating immunosuppression and lung inflammation [53]. Moreover, various studies have demonstrated that niacin activates the Akt pathway [54–56]. Furthermore, mitochondrial dysfunction is a potential mechanism underlying lung aging [16,17]. Insufficient niacin, an essential cofactor in mitochondrial oxidative phosphorylation reactions [14], can impair mitochondrial function, thus contributing to a decline in lung function. Finally, oxidative stress is closely associated with pulmonary senescence [17]. Niacin alleviates oxidative stress in endothelial cells by increasing NADP content, reducing glutathione levels, and inhibiting reactive oxygen species generation [57]. Increased niacin intake has been linked to elevated threonine kinase levels, reduced lung inflammation, and potent antioxidant properties. These biological mechanisms may explain the positive effects of niacin on lung function. However, further prospective investigations are required to substantiate the preventive effects of niacin on lung function and its potential as a therapeutic agent.

## 5.1. Strength and limitations

Our study has several strengths. First, we benefited from a large and diverse cohort of US adults; second, the substantial sample size allowed for the robust adjustment of numerous covariates, thereby enhancing the precision and reliability of our analyses. Third, a significant strength of our study lies in the utilization of spirometry measurements to accurately identify airflow obstruction, surpassing the reliance on self-reported COPD diagnoses that are prevalent in many epidemiological studies. Our investigation encompassed a comprehensive evaluation of multiple lung function parameters, subgroup analyses, interaction tests, and potential nonlinear relationships. The results of these subgroup analyses revealed race, education, and smoking status as relevant interaction factors, underscoring the need for targeted attention on the Hispanic population and smokers. These findings offer valuable guidance for future studies aimed at elucidating the underlying mechanisms of these relationships.

This study also has several limitations. First, the inherent limitations of the cross-sectional design prevented us from establishing a causal relationship between increased dietary niacin intake and improved pulmonary function. Therefore, prospective cohort studies are required to investigate this potential causal relationship. Second, the reliance on participant questionnaires to assess dietary niacin intake introduced the possibility of self-reporting or courtesy bias. However, questionnaires remain the least biased method for describing dietary intake at the population level [45]. Furthermore, the lung function measurements in our study were based on pre-bronchodilator rather than post-bronchodilator values. Caution is required when generalizing our findings regarding dietary niacin intake and its impact on lung function in individuals with COPD. Despite this limitation, we applied the GOLD criteria instead of the lower limit of normal (LLN) classification to minimize false-negative findings, especially in the elderly population, which is more susceptible to COPD [58]. Finally, despite thorough adjustment for established confounding factors based on professional knowledge and prior literature, the potential influence of unidentified confounders cannot be completely ruled out. Hence, extensive prospective studies with large sample sizes are imperative to conclusively validate our findings.

## 6. Conclusions

This study demonstrated a positive correlation between dietary niacin intake and lung function in an adult American population. Our findings indicate that niacin is a crucial nutrient that affects lung function.

#### Ethics approval and consent to participate

Ethical review and approval were waived for this study, because no additional institutional review board approval was required for the secondary analysis.

## Data availability statement

All the questionnaires used in this study can be obtained from the official website of NHANES at ".https://www.cdc.gov/nchs/nhanes/index.htm.

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## CRediT authorship contribution statement

Xiaoli Xu: Writing – review & editing, Writing – original draft, Software, Formal analysis, Data curation, Conceptualization. Qiong Han: Writing – review & editing, Writing – original draft, Methodology, Conceptualization. Xiaoying Lin: Conceptualization. Jianping Lin: Validation, Supervision, Project administration. Shizhong Wang: Writing – review & editing, Supervision, Project administration.

## Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

# Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2024.e33482.

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