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Low concentrations of serum 25-hydroxyvitamin D associated with increased risk for chronic bronchitis among US adults

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Abstract

Increasing evidence suggests that vitamin D benefits both innate and adaptive immunity, thereby eliciting an anti-inflammatory effect and reducing the risk of infectious disease. The present study examined the association between serum 25-hydroxyvitamin D (25(OH)D) levels and the risk of chronic bronchitis among US adults. We analysed data from 6872 US adults aged ≥20 years who participated in the 2003–6 National Health and Nutrition Examination Survey. Prevalence and OR with 95 % CI of having self-reported chronic bronchitis were estimated by quintiles of 25(OH)D or vitamin D-deficiency status after adjustment for potential confounders. The results showed that the adjusted prevalence of chronic bronchitis ranged from 2·4 (95 % CI 1·4, 3·3) % among adults in the highest quintile of 25(OH)D (≥30 ng/ml) to 4·1 (95 % CI 2·5, 5·6) % among adults in the lowest quintile (<15 ng/ml; *P* for trend<0·01). The adjusted OR for chronic bronchitis was 1·85 (95 % CI 1·06, 3·24) in adults with <15 ng/ml 25(OH)D and 1·77 (95 % CI 1·19, 2·65) in those with 15 to <20 ng/ml 25(OH)D compared with adults with ≥30 ng/ml 25(OH)D. Additionally, the adjusted OR for chronic bronchitis was 1·52 (95 % CI 1·03, 2·26) among adults with vitamin D deficiency (<20 ng/ml 25(OH)D) compared with those with ≥20 ng/ml 25(OH)D. For every 1 ng/ml increase in 25(OH)D, the likelihood of having chronic bronchitis fell by 2·6 % (*P*=0·016). In conclusion, low serum 25(OH)D levels are associated with the increased risk of chronic bronchitis among US adults. The present results provide support for continuing research on the role of vitamin D in lung diseases.

Key words: Vitamin D: 25-Hydroxyvitamin D: Chronic bronchitis: National Health and Nutrition Examination Survey

Chronic bronchitis is a disorder characterised by chronic mucus hypersecretion, with clinical symptoms presented as productive cough and phlegm that last at least 3 months every year for at least 2 years[1]. The underlying pathophysiology of chronic bronchitis is inflammation and swelling of the epithelium of the bronchi, which results in the increased risk of lung infections by viral, bacterial and atypical organisms[1]. This causes recurrent episodes of acute exacerbations of chronic bronchitis[2], which often leads to a decline in lung function[3,4], poor quality of life[5], increased risk of chronic obstructive pulmonary disease (COPD – obstruction of the respiratory airways, especially with mucus) and death[6], and a significant economic burden on the health care system and society due to direct costs of hospitalisations[3,4,7].

Vitamin D has received increased attention for its influence on non-skeletal medical conditions, apart from its well-known function in the regulation of Ca and phosphate homeostasis in bone metabolism. Although vitamin D is hydroxylated to 25-hydroxyvitamin D (25(OH)D) and then 1,25-dihydroxyvitamin D ($1,25(OH)_2D$) in the liver and kidneys, respectively, it can also be metabolised by the cells of the immune system[8–10]. In addition, vitamin D receptors are widely expressed in immune cells[11], and vitamin D-binding protein also has immunomodulatory functions relating to macrophage activation and neutrophil chemotaxis in the lung[12]. Thus, the vitamin D axis plays an important role in respiratory health by inhibiting pulmonary inflammatory responses and enhancing the innate antimicrobial response against respiratory pathogens[13,14]. Consequently, a low 25(OH)D level or vitamin D deficiency has been associated with the increased risk of upper-respiratory-tract infections[15] and decreased pulmonary function[16–19], and linked to wheezing illness and asthma exacerbation in both children and adults[20,21], although other studies have reported that

Abbreviations: $1,25(OH)_2D$, 1,25-dihydroxyvitamin D; 25(OH)D, 25-hydroxyvitamin D; COPD, chronic obstructive pulmonary disease; MET, metabolic equivalent; NHANES, National Health and Nutrition Examination Survey.

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serum concentrations of 25(OH)D were not associated with lung function[22,23]. In the present study, we used data from a large, nationally representative survey sample to examine (1) the prevalence of self-reported, physician-diagnosed chronic bronchitis among US adults and (2) the extent to which chronic bronchitis is independently associated with varying concentrations of serum 25(OH)D while controlling for potential confounders.

Methods

Study design

We analysed data from the 2003–6 National Health and Nutrition Examination Survey (NHANES), which uses a multistage stratified sampling design to collect data from a nationally representative sample of the non-institutionalised civilian US population on a 2-year cycle basis. A more detailed description of the NHANES design and methods has been reported elsewhere[24]. Survey participants were initially interviewed at home and then invited to a mobile examination centre, where they received various examinations and provided blood samples for laboratory tests. The present study was conducted according to the guidelines laid down in the Declaration of Helsinki. All procedures involving human subjects were approved by the Research Ethics Review Board of the National Center for Health Statistics, Centers for Disease Control and Prevention. Written informed consent was obtained from all participants.

Participants and measurements

We examined interview and laboratory data from participants aged 20 years or older. Participants' chronic bronchitis (yes, no) was assessed by asking them whether they had ever been told by a doctor or other health professional that they had this condition and still had it during the survey. Self-reported information about chronic respiratory disease has shown to have good or very good agreement with that from general practice medical records[25].

Participants' serum specimens were collected during the medical examination and were frozen and stored at less than −70°C until analysis. Serum concentrations of 25(OH)D were measured in accordance with the DiaSorin RIA procedure (DiaSorin 25(OH)D ^{125}I RIA kit; DiaSorin Corporation, Stillwater, MN, USA), which has been described in detail in laboratory procedure manuals that can be accessed at the NHANES website[24]. Sensitivity for the assay was 1·5 ng/ml, and the CV ranged from 8·9 % for the NHANES 2003–4 participants to 9·9 % for the NHANES 2005–6 participants.

The demographic covariates in the present analyses were participants' age (20–39, 40–59 and ≥60 years), sex, race/ethnicity (non-Hispanic white, non-Hispanic black, Mexican American and other), education (below high school graduate, high school graduate/equivalent and above high school diploma) and family poverty:income ratio (calculated as a ratio of family income:poverty threshold and categorised as <1·0, 1·0 to <3·0 and ≥3·0). Lifestyle-related behaviours included BMI (<25·0, 25·0–29·9 and ≥30·0 kg/m^2, calculated from measured weight and height), smoking (current, former and non-smoking), physical activity (yes, no), excessive alcohol drinking (yes, no) and dietary supplement use (yes, no). Current smoking was defined as having smoked at least 100 cigarettes in one's life and still smoking, former smoking as having smoked at least 100 cigarettes in one's life but stopped and non-smoking as having smoked fewer than 100 cigarettes in one's life. Participants' physical activity was assessed by asking participants whether, over the past 30 d, (1) they had engaged in specific moderate or vigorous leisure-time activities, (2) they had walked or bicycled as part of getting to and from work, or school, or to do errands (transportation physical activity) and (3) they had done any tasks in or around their home or yard for at least 10 min that required moderate or greater physical effort (household physical activity). If a confirmative answer of 'yes' was recorded, they were then asked about how many times and the average duration each time they engaged in the activities over the past 30 d. Based on the metabolic equivalent (MET) score for specific activities, we calculated the average MET-h/week that summed leisure-time, transportation and household physical activity. Participants with a MET-h/week of >0 were considered physically active and those with a MET-h/week of 0 were considered inactive. Alcohol consumption was calculated as the average number of daily drinks. Excessive alcohol drinking was defined as having >2 drinks/d in men and >1 drink/d in women during the previous 12 months. Dietary supplement use was assessed by asking participants whether they had taken any vitamins, minerals or other dietary supplements during the previous month. Covariates on medical conditions included serum concentrations of total cholesterol (< 2000 mg/l, ≥2000 mg/ml), serum concentrations of C-reactive proteins (<3·0 mg/l, ≥3·0 mg/l), systolic blood pressure (<140 mmHg, ≥140 mmHg), physician-diagnosed diabetes (yes, no), physician-diagnosed heart disease including coronary artery disease, angina pectoris and myocardial infarction (yes, no), and current physician-diagnosed asthma (yes, no). Serum concentrations of total cholesterol were measured enzymatically on a Hitachi 717 and 912 (Hitachi Global Storage Technologies, San Jose, CA, USA. Serum concentrations of C-reactive protein were measured by latex-enhanced nephelometry on a Behring Nephelometer (Dade Behring Diagnostics Inc., Somerville, NJ, USA). Mean systolic blood pressure was calculated as the average of the last two readings for participants who had three measurements, as the last reading for those who had two measurements and as the only reading for those who had one measurement. Health insurance status was assessed by asking participants whether they were covered by health insurance or some other kind of health care plan including those obtained through employment or purchased directly as well as government programmes such as Medicare and Medicaid that provide medical care or help pay medical bills (yes, no). Times of health care visit were assessed by asking participants how many times, during the past 12 months, they had seen a doctor or other health care professional about their health at a doctor's office, a clinic, hospital

emergency room, at home or some other place (categorised as 0, 1–3 and ≥4 times). The period of blood sampling was used as a surrogate of potential sun exposure, which was assessed based on the 6-month time period when survey participants' examination was performed; we considered those examined 1 November to 30 April as having low sun exposure and those examined 1 May to 31 October as having high sun exposure.

Statistical analysis

The prevalence with 95 % CI of chronic bronchitis by quintiles of 25(OH)D and by categorical covariates was estimated using the sampling weights and age-adjusted to the 2000 US population. Adjusted prevalence, OR and 95 % CI for having chronic bronchitis were estimated by conducting logistic regression using serum 25(OH)D concentrations (either by quintile or as a continuous variable) as the independent variable while controlling for covariates including sociodemographic characteristics, lifestyle-related behaviours, access to health care, chronic medical conditions and period of blood sampling. Tests for linear trends on the OR across quintiles of 25(OH)D were conducted using the median values for each quintile in logistic regression models. In all analyses, we used SUDAAN (Software for the Statistical Analysis of Correlated Data, Release 9.0; Research Triangle Institute, Research Triangle Park, NC, USA) to account for the complex sampling design.

Results

Of the 9515 survey participants aged ≥20 years who attended the mobile examination centre, we excluded 544 women who reported they were pregnant, as well as thirty-eight participants whose chronic bronchitis status was unknown, and 522 participants whose serum 25(OH)D concentrations were not measured. After further excluding those who had missing values for covariates, 6872 (77 %) eligible participants remained in the present analyses. The mean age of eligible study participants was 46·2 years; 74·0 % were non-Hispanic white, 10·3 % non-Hispanic black, 7·7 % Mexican American and 8·0 % of 'other' race/ethnicity. About 57·1 % attained an educational level above a high school diploma and 52·3 % had a poverty:income ratio of ≥3.

Overall, the unadjusted prevalence of chronic bronchitis was 3·2 (95 % CI 2·7, 3·8) % and the age-adjusted prevalence was 3·1 (95 % CI 2·6, 3·7) %. The prevalence estimates differed significantly by all sociodemographic characteristics except for education, by smoking and physical activity status, by times of health care visit and by some co-existing medical conditions (Table 1). Notably, the prevalence of chronic bronchitis increased significantly with increasing age ($P<0·001$) but decreased with increasing poverty:income ratio ($P<0·05$); the prevalence was lower among men than among women ($P<0·01$); lower among Hispanics than among members of other racial/ethnic groups ($P<0·05$); but higher among current smokers than among former- and non-smokers ($P<0·05$); higher among those who were physically inactive than among those who were active ($P<0·01$); higher among those who had ≥4 times of health care visit than among those who had ≤3 times of health care visit in the previous 12 months ($P<0·001$); and higher among those with elevated C-reactive protein levels ($P<0·001$), diabetes ($P<0·05$), heart disease ($P<0·01$) and current asthma ($P<0·001$) than among their respective counterparts (Table 1).

The age-adjusted prevalence of chronic bronchitis increased linearly from 2·2 (95 % CI 1·4, 3·5) % among adults in the highest 25(OH)D quintile (≥30 ng/ml) to 4·6 (95 % CI 3·2, 6·5) % among those in the lowest quintile (<15 ng/ml; $P<0·001$ for a linear trend). Conversely, the age-adjusted mean concentration of 25(OH)D among adults with chronic bronchitis (20·6 ng/ml, 95 % CI 18·7, 22·5 ng/ml) was significantly lower than that among adults without chronic bronchitis (23·4 ng/ml, 95 % CI 22·6, 24·3 ng/ml, $P<0·001$), which represented a 13·6 % relative difference between the two groups.

After multivariate adjustment for sociodemographic characteristics, lifestyle-related behaviours, access to health care, chronic medical conditions and period of blood sampling, the inverse trend in the prevalence of chronic bronchitis by quintile of 25(OH)D remained statistically significant ($P=0·013$; Table 2). The adjusted OR for chronic bronchitis was 1·85 (95 % CI 1·06, 3·24) among adults with 25(OH)D concentrations of <15 ng/ml and 1·77 (95 % CI 1·19, 2·65) among those with 25(OH)D concentrations of 15 to <20 ng/ml, compared with adults with 25(OH)D concentrations of ≥30 ng/ml. For every 1 ng/ml increase in 25(OH)D, the odds of having chronic bronchitis fell by 2·6 % ($P=0·016$; Table 2).

Alternatively, we conducted sub-analysis by dichotomising participants as having (25(OH)D < 20 ng/ml) and not having (25(OH)D ≥ 20 ng/ml) vitamin D deficiency. The adjusted prevalence of having chronic bronchitis among adults with vitamin D deficiency was significantly higher than among those without vitamin D deficiency (3·9 %, 95 % CI 2·9, 5·0 % *v.* 2·7 %, 95 % CI 2·2, 3·2, $P=0·035$; adjusted OR 1·52, 95 % CI 1·03, 2·26).

Discussion

The present analyses of data from a large, nationally representative survey demonstrated a significant inverse relationship between serum 25(OH)D levels and the risk of chronic bronchitis among adults of the USA. We found that adults with vitamin D deficiency (defined as 25(OH)D < 20 ng/ml based on a commonly used cut-point[26]) were 52 % more likely to have chronic bronchitis than those with 25(OH)D ≥ 20 ng/ml, and 77–85 % were more likely to have the condition than those with 25(OH)D ≥ 30 ng/ml. A significant dose–response relationship was present.

The majority of previous studies have shown that low 25(OH)D levels are associated with a higher risk of COPD[27,28] – a major respiratory health condition constituting the third leading cause of death in 2008 in the USA[29]. However, evidence has shown that the prevalence or the 30-year cumulative incidence of chronic bronchitis was significantly higher than that of COPD in middle-aged Finnish men (42 *v.* 32 % in continuous smokers, 26 *v.* 14 % in former smokers

Table 1. Prevalence* of chronic bronchitis among US adults aged ≥20 years by selected characteristics, National Health and Nutrition Examination Survey 2003–6

(Numbers, percentages and 95 % confidence intervals)

Characteristics	*n*	%	95 % CI	*P*†
Overall				
Unadjusted	6872	3·19	2·67, 3·82	
Age-adjusted	6872	3·11	2·59, 3·72	
Sociodemographic				
Age (years)				<0·001
20–39	2190	1·79	1·26, 2·53	
40–59	2194	3·85	3·01, 4·91	
≥ 60	2488	4·20	3·31, 5·33	
Sex				0·004
Men	3583	2·11	1·57, 2·84	
Women	3289	4·09	3·19, 5·23	
Race/ethnicity				<0·001
Non-Hispanic white	3687	3·30	2·74, 3·96	
Non-Hispanic black	1395	3·09	2·06, 4·62	
Mexican American	1348	0·96	0·59, 1·58	
Other	442	3·29	1·83, 5·86	
Education				0·197
Below high school graduate	1886	4·28	2·65, 6·84	
High school graduate	1688	3·19	2·30, 4·41	
Above high school diploma	3298	2·81	2·27, 3·47	
Poverty:income ratio				0·030
< 1·0	1147	5·48	3·83, 7·78	
1·0–2·9	2909	3·45	2·39, 4·96	
≥ 3·0	2816	2·45	1·91, 3·13	
Lifestyle-related behaviours				
BMI (kg/m^2)				0·282
< 25·0	2045	2·93	2·14, 4·00	
25·0–29·9	2452	2·83	1·99, 4·02	
≥ 30·0	2375	3·56	2·80, 4·52	
Smoking				<0·001
Current smoker	1584	5·76	4·44, 7·46	
Former smoker	1865	3·01	2·03, 4·44	
Never smoked	3423	2·10	1·53, 2·88	
Physical activity				0·003
Yes	4161	2·52	2·05, 3·11	
No	2711	4·24	3·24, 5·52	
Excessive alcohol drinking				0·765
Yes	509	2·73	1·70, 4·37	
No	6363	3·11	2·60, 3·72	
Dietary supplement use				0·441
Yes	3503	3·11	2·48, 3·90	
No	3369	3·21	2·43, 4·23	
Access to health care				
Health insurance				0·524
Yes	5471	2·94	2·41, 3·57	
No	1401	3·89	2·79, 5·41	
Times of health care visit				<0·001
0	1090	1·35	0·71, 2·54	
1–3	3016	1·75	1·23, 2·47	
≥ 4	2766	5·42	4·33, 6·77	
Clinical measurements and medical conditions				
Systolic blood pressure (mmHg)				0·373
≥ 140	1371	3·63	1·92, 6·77	
< 140	5501	3·13	2·45, 3·99	
Serum total cholesterol (mg/l)				0·105
≥ 2000	3902	3·32	2·58, 4·28	
< 2000	2970	2·94	2·33, 3·69	
Serum C-reactive protein (mg/l)				<0·001
≥ 0·3	2721	4·38	3·46, 5·53	
< 0·3	4151	2·31	1·76, 3·02	
Diabetes				0·022
Yes	731	5·88	2·92, 11·48	
No	6141	2·92	2·40, 3·55	
CHD				0·002
Yes	596	11·84	6·34, 21·05	
No	6276	2·79	2·27, 3·43	
Current asthma				<0·001
Yes	509	16·58	12·71, 21·34	
No	6363	1·98	1·59, 2·46	
Period of blood sampling				0·188
May–October	3122	3·68	2·81, 4·80	
November–April	3750	2·73	2·10, 3·54	

* Reported as age-adjusted except for age-specific prevalence.
† *P* values from χ^2 tests.

Table 2. Adjusted prevalence and OR with 95 % CI for having chronic bronchitis among US adults aged ≥20 years, National Health and Nutrition Examination Survey 2003–6

(Odds ratios and 95 % confidence intervals)

				Regression analyses					
				Model 1*		Model 2*		Model 3*	
25(OH)D	*n*	Adjusted prevalence (%)†	95 % CI	OR	95 % CI	OR	95 % CI	OR	95 % CI
Quintile of 25(OH)D‡									
Q1 (<15 ng/ml)	1631	4·05	2·53, 5·57	2·16	1·26, 3·71	1·88	1·16, 3·05	1·85	1·06, 3·24
Q2 (15– < 20 ng/ml)	1373	3·91	2·63, 5·18	1·82	1·16, 2·87	1·74	1·19, 2·55	1·77	1·19, 2·65
Q3 (20– < 25 ng/ml)	1471	3·24	2·10, 4·38	1·47	0·81, 2·66	1·49	0·84, 2·66	1·42	0·72, 2·82
Q4 (25– < 30 ng/ml)	1189	2·51	1·49, 3·54	1·07	0·53, 2·13	1·08	0·55, 2·14	1·07	0·55, 2·07
Q5 (≥30 ng/ml)	1208	2·37	1·42, 3·32	1·00	Ref	1·00	Ref	1·00	Ref
P for trend		0·013			<0·001		0·002		0·007
Continuous 25(OH)D§	6872	–	–						
Regression coefficient					−0·033		−0·028		−0·026
SE					0·010		0·009		0·010
P for trend					0·003		0·006		0·016

25(OH)D, 25-hydroxyvitamin D; Ref, reference.

* Model 1, unadjusted; Model 2, adjusted for sociodemographic characteristics (age, sex, race/ethnicity, education and poverty:income ratio), lifestyle-related behaviours (BMI, smoking, excessive alcohol drinking, physical activity and dietary supplement use), serum concentrations of total cholesterol and C-reactive protein, systolic blood pressure and 6-month period of blood sampling; Model 3, adjusted for variables in Model 2 plus access to health care including health insurance and times of health care visit in the past 12 months, and co-morbidities including diabetes, CHD and current asthma.

† Estimated as predicted marginals after adjustment for all covariates listed in Table 1.

‡ Quintiles of 25(OH)D were entered in the logistic regression models.

§ Continuous 25(OH)D concentrations were entered in the regression models.

and 22 *v.* 12 % in those who had never smoked)[1,3]. In addition, people with chronic bronchitis, regardless of whether they had airflow obstruction, had reduced lung function, increased risk of all-cause mortality[1,3] and increased risk of cardiovascular mortality[6]. Thus, the inverse and dose-dependent relationship that we found between serum 25(OH)D concentrations and the risk of chronic bronchitis potentially has important implications in both clinical practices and public health intervention programmes on respiratory health.

At present, we are not aware of any studies on the association of 25(OH)D specifically with chronic bronchitis. The present results are consistent with the findings of several other studies that have evaluated the relationships between vitamin D deficiency and the risk of other lung diseases. For example, low 25(OH)D levels have been linked to impaired lung function as shown by lowered forced expiratory volume in 1 s and forced vital capacity in the general population[16] and in people with chronic bronchitis, asthma and COPD[3,16,18,30]. However, results of a recent study conducted in continuous smokers with mild-to-moderate COPD showed that baseline 25(OH)D levels were not predictive of the rate of subsequent lung function declining[22]. Other research has also implicated vitamin D in respiratory infections. For example, Ginde *et al.*[15] reported that low 25(OH)D concentrations were inversely associated with upper-respiratory-tract infection in the general population and that the association was even stronger among people with respiratory tract diseases such as asthma and COPD. Liu *et al.*[14,31] further reported that $1,25(OH)_2D_3$ at a concentration of $1/10^8$ M enhanced human antimicrobial activity against mycobacterium tuberculosis in cultured cells. The present results combined with these previous findings suggest that vitamin D may exert beneficial effects on respiratory health.

Low 25(OH)D levels have also been associated with wheezing and asthma severity in children[20,21]. However, evidence concerning the association between asthma or the severity of asthma and serum 25(OH)D concentrations among adults remains controversial[30,32]. In the present study, we did not observe a significant association between serum 25(OH)D concentrations and the risk of asthma (data not shown). In fact, the present results demonstrated that the inverse relationship between serum 25(OH)D concentrations and the risk of chronic bronchitis was independent of asthma status, although chronic bronchitis was highly prevalent in people with asthma. Thus, future studies are needed to further investigate the underlying mechanisms by which vitamin D may be differentially associated with chronic lung conditions.

An inflammatory component, characterised by the presence of numerous cellular elements such as macrophages and neutrophils and their products – pro-inflammatory cytokines, has been shown to be involved in the pathophysiology of chronic bronchitis, resulting in oxidative stress, protease/antiprotease imbalance and tissue damage. Vitamin D has been shown to have immunomodulatory effects[9,10,33,34]. 1-α-Hydroxylase, a 25(OH)D-activating enzyme, is present not only in the kidney but also in activated macrophages and dendritic cells[35,36]. Vitamin D receptors are also expressed in activated inflammatory cells[11]. Previous studies[37,38] have shown that $1,25(OH)_2D_3$ inhibits T-cell activation and proliferation, thereby altering the cytokine expression profile. Vitamin D has also been shown to activate Toll-like receptors in human macrophages, leading to the induction of the antimicrobial peptide cathelicidin and subsequent killing of intracellular bacteria[14,31]. Thus, the immunomodulatory

effects of vitamin D may serve as one of the mechanisms underlying its beneficial effects on chronic lung diseases.

Although the present study demonstrated that low serum 25(OH)D levels were associated with an increased likelihood of having chronic bronchitis, a causal relationship cannot be established from the present cross-sectional study design, which is one of the study limitations. As we have discussed earlier, the vitamin D axis may play an important role in respiratory health through immunomodulatory function such as inhibiting pulmonary inflammatory responses and enhancing the innate antimicrobial response against respiratory pathogens[13,14,31,37,38]. On the other hand, people with chronic respiratory diseases are at high risks for functional limitations, poor capability in physical functioning, unhealthy behaviours and impaired quality of life[39,40]. Consequently, these patients are less likely to go outside for exercise and get sun exposure, thereby at risk of vitamin D deficiency. Thus, it is highly possible that bidirectional associations between low 25(OH)D levels and chronic bronchitis exist in the present study, and the causal relationship deserves further investigation. Second, we are unable to assess pulmonary function in participants who had reported having chronic bronchitis because spirometry was not performed in NHANES 2003–6. Third, although we have included the 6-month period of blood sampling as a surrogate of potential sun exposure, we were unable to adjust for actual seasonality and geographic location due to the lack of data on these variables. Finally, it is unlikely that the variation in serum 25(OH)D measurements between NHANES 2003–4 and 2005–6 affected the present results in a meaningful way[41].

In conclusion, the present results showed that low serum 25(OH)D concentrations were associated with an increased likelihood of chronic bronchitis among US adults; those with 25(OH)D concentrations of <20 ng/ml were at almost twice the risk of the condition as those with 25(OH)D concentrations of ≥ 30 ng/ml. The results add to a growing body of literature on the potential effects of vitamin D on respiratory health and suggest that further research in this area is warranted. Especially, longitudinal studies or vitamin D supplementation trials are needed to further explore whether serum 25(OH)D concentrations are causally linked to the risk of chronic bronchitis. In the meantime, given the high prevalence of vitamin D deficiency/insufficiency in the USA, especially in the African-American population[26], and the emerging data showing that vitamin D may beneficially affect respiratory health, health care providers should consider alerting their patients with chronic bronchitis about the need for adequate intake of vitamin D[42] as well as testing the 25(OH)D concentrations of their patients.

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