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Vitamin D insufficiency and asthma in a U.S. nationwide study

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Abstract

Background—Vitamin D insufficiency (a serum 25(OH)D < 30 ng/ml) has been associated with asthma morbidity.

Objective—To examine vitamin D insufficiency, asthma and lung function among U.S. children and adults.

Methods—Using data from NHANES for 2001–2010, we examined vitamin D insufficiency and: 1) current asthma or wheeze in 10,860 children (6–17 years) and 24,115 adults (18–79 years), and 2) lung function in a subset of participants. Logistic or linear regression was used for the multivariable analysis, adjusting for age, gender, race/ethnicity, income, body mass index, smoking, and C-reactive protein level.

Results—Vitamin D insufficiency was associated with current asthma (odds ratio [OR]=1.35, 95% confidence interval [CI]=1.11–1.64) and current wheeze in children, as well as with current wheeze in adults (OR=1.17, 95%CI=1.04–1.31). After stratifying the analysis by race/ethnicity and (in adults) current smoking, vitamin D insufficiency was associated with current asthma and wheeze in non-Hispanic white children only; in adults, vitamin D insufficiency was associated with current wheeze in non-Hispanic whites and blacks. Vitamin D insufficiency was also associated with lower FEV_1 and FVC in children and adults. When analyzing each NHANES wave separately, vitamin D insufficiency prevalence was 72%–76% from 2001 to 2006, and then decreased from 2007 to 2010 (64%–65%); interestingly, asthma prevalence decreased for the first time from 2007–2008 (8.2%) to 2009–2010 (7.4%).

Conclusions—We show racial/ethnic-specific associations between vitamin D insufficiency and current asthma or wheeze in children and adults. Moreover, we report parallel recent decrements in the prevalence of vitamin D insufficiency and asthma.

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Keywords

Vitamin D insufficiency; Asthma; Wheezing; Lung function; NHANES

INTRODUCTION

Asthma is a common respiratory disease and a significant public health problem worldwide. In the United States (U.S.), the prevalence of asthma increased from 3.1% in 1980 to 8.4% in 2010[1]. The causes of this "asthma epidemic" are unclear but likely to be due to changes in the environment or lifestyle. Vitamin D status, which is assessed by measurement of serum or plasms 25-hydroxyvitamin D (25[OH]D), is key to the metabolism of calcium and phosphorus. While the definition of vitamin D deficiency or insufficiency on the basis of 25(OH)D values is still under debate[2], vitamin D insufficiency, defined as a serum 25-hydroxyvitamin D_3 (25[OH]D) < 30 ng/ml, is now commonly found in children[3] and adults[4] in the U.S., likely due to reduced outdoor activity (and thus sun exposure) over the last few decades. Since vitamin D insufficiency is particularly frequent among members of demographic groups at high risk for asthma, such as African Americans, Puerto Ricans and obese individuals[5,6], there has been considerable recent interest in exploring a potential role of vitamin D in the pathogenesis of asthma.

Experimental findings and results from epidemiologic studies have provided suggestive but inconclusive evidence for vitamin D insufficiency as a cause of asthma or morbidity from asthma, with generally more consistent findings of a possible link in children than in adults[7–16]. Such data provided support for two ongoing randomized clinical trials (RCTs) of prenatal vitamin D for the prevention of childhood asthma[17,18]. In the largest of those two trials (n=876), children born to women who received vitamin D at 4,400 IU/day during pregnancy had a lower incidence of asthma and recurrent wheeze at age 3 years than those born to women who received 400 IU/day of vitamin D during pregnancy (24.3% vs. 30.4%), but this difference (6.1%) was not statistically significant (P=0.05)[17]. However, the study lacked sufficient statistical power to detect an effect ≤20%[17], and longer follow-up of the participating children is ongoing to determine whether the observed effect of vitamin D on asthma is persistent and clinically important. With regard to asthma morbidity, two RCTs have reported that vitamin D did not reduce the rate of first treatment failure or exacerbation among adults with persistent asthma and vitamin D insufficiency[19,20].

However, the larger of those two trials reported that adults in the vitamin D arm received a significantly lower dose of inhaled corticosteroids than those in the placebo arm, suggesting steroid-enhancing effects of vitamin D. Moreover, an exploratory analysis in that trial showed that adults who achieved vitamin D sufficiency while in the intervention arm had a significantly lower risk of severe asthma exacerbations than those in the placebo group[21]. Small clinical trials in children have shown supportive but inconclusive evidence of beneficial effects of vitamin D in preventing asthma exacerbations[21,22] and improving asthma control[23,24], and a larger clinical trial in U.S. school-aged children is ongoing (NCT02687815, PI: Celedón JC).

Given continued controversy and a paucity of large-scale studies, we examined the relationship between vitamin D insufficiency and: current asthma, current wheeze, and lung function among children and adults who participated in the U.S. National Health and Nutrition Examination Survey (NHANES) from 2001 to 2010. Moreover, we examined temporal trends for vitamin D insufficiency and current asthma during the study period.

METHODS

Subject recruitment and study procedures

NHANES is a cross-sectional nationwide survey of a representative sample of the U.S. population. As part of the study design, ethnic minorities (African Americans, Asians and Mexican Americans) and individuals 60 years and older are over-sampled, to achieve adequate statistical power for data analysis in these groups.

Serum 25(OH)D level was measured in study participants at the National Center for Environmental Health, using the DiaSorin RIA kit (Stillwater MN) for NHANES 2001–2006, and liquid chromatography-tandem mass spectrometry (LC-MS/MS) for the NHANES 2007–2010 data. In order to allow comparison of standardized 25(OH)D levels across the two study periods, a variety of regression equations were developed to convert NHANES 2001–2006 RIA measurements to a standardized LC-MS/MS-equivalent 25(OH)D level[25]. Serum total 25(OH)D (in SI units of nmol/L) was defined as the sum of $25(OH)D_3$ and $25(OH)D_2$ and then converted to conventional units (ng/mL) using the suggested conversion factors: 1 nmol/L = 0.40066 ng/mL[25].

Spirometry was available in NHANES 2007–2008 and 2009–2010. Participants were not eligible for spirometry if they were on supplemental oxygen or had painful ear infections, current chest pain or a physical problem with forceful expiration, surgery (of the eye, chest or the abdomen) in the prior 3 months, heart disease, history of an aneurysm or a detached retina, hemoptysis, or history of a collapsed lung or tuberculosis exposure. Eligible participants performed spirometry following American Thoracic Society (ATS) recommendations[26]. The best forced expiratory volume in 1 second (FEV_1) and forced vital capacity (FVC) were selected for analysis. Participants whose baseline FEV_1/FVC ratio was below the lower limit of normal (LLN)[27,28] and/or whose baseline FEV_1 was below 70% of the predicted value for their demographic characteristics underwent a repeat spirometry, 15 minutes after inhalation of albuterol. Participants were excluded from bronchodilator administration if they had recently used a short-acting inhaled β_2-agonist or had a previous adverse reaction to albuterol; had a history of congenital heart disease, hypertension, major arrhythmia or an implanted defibrillator; or were pregnant or breastfeeding. Age-, gender-, and race/ethnicity-specific percent predicted (%predicted) values of FEV_1, FVC, and FEV_1/FVC were calculated adopting normal equations for spirometric parameters of the general US population[27].

Informed consent was obtained from all study participants. NHANES was approved by the institutional review board of the National Center for Health Statistics of the Center for Disease Control and Prevention (CDC). Further details on study measurements and procedures may be found in the NHANES website (http://www.cdc.gov/nchs/nhanes.htm);

specific details on spirometry and bronchodilator administration can be found in the NHANES spirometry procedures manual[29].

Statistical analysis

Vitamin D insufficiency was defined as a serum 25(OH)D <30 ng/ml. Current asthma was defined by a positive answer to both of the following questions: “Has a doctor or other health professional ever told you that you have asthma?”, and “Do you still have asthma?”. Participants who answered no to both questions were selected as controls. Current wheeze was defined by a positive answer to the question “In the past 12 months, have you had wheezing or whistling in your chest?”. Bronchodilator response (BDR) was defined as: ([post-bronchodilator FEV_1 − pre-bronchodilator FEV_1]/pre-bronchodilator FEV_1) × 100.

Sampling weights, stratification, and clusters provided in the NHANES dataset were incorporated into the analysis, in order to account for the complex NHANES survey design and obtain proper estimates and their standard errors. Wald chi-square tests and *t*-tests were used for bivariate analyses of binary and continuous variables, respectively. In children, body mass index (BMI) z-scores were calculated based on the 2000 U.S. CDC growth charts[30]. Logistic regression was used for the multivariable analysis of vitamin D insufficiency and current asthma, current wheeze and BDR. Linear regression was used for the multivariable analysis of vitamin D insufficiency and lung function measures (FEV_1, FVC, and FEV_1/FVC). All multivariable models were adjusted for age, gender, race/ethnicity (non-Hispanic white, non-Hispanic black, Hispanic, or other), household income (<$20,000/year or ≥$20,000/year), BMI (for adults) or BMI z-score (for children), and serum levels of cotinine and C-reactive protein (CRP). Multivariable models of BDR were additionally adjusted for baseline (pre-bronchodilator) FEV_1. All statistical analyses were conducted using the SAS SURVEY procedure and SAS 9.3 software (SAS Institute Inc., Cary, NC).

RESULTS

During the study period (2001 to 2010), a total of 10,860 children aged 6 to 17 years and 24,115 adults aged 18 to 79 years who had serum vitamin D measures and information on asthma status were included in the current analysis. Of these participants, 3,001 children and 8,347 adults from NHANES 2007–2010 also had baseline spirometry data; 234 (7.8%) of these children and 744 (8.9%) of these adults had a BDR measurement.

The overall prevalence of current asthma among study participants was 10.9% in children and 7.6% in adults. The main characteristics of participants are shown in Table 1. Compared to children without asthma (n=9,668), those with asthma (n=1,192) were more likely to be non-Hispanic Black and to have health insurance coverage, a higher BMI z-score, a lower serum vitamin D level and a higher prevalence of vitamin D insufficiency, lower FEV_1/FVC, and higher BDR. Compared to adults without asthma (n=22,286), those with asthma (n=1,829) were more likely to be female and non-Hispanic white or black, and to have: health insurance coverage, an annual household income <$20,000, higher BMI, higher levels of serum cotinine and C-reactive protein, lower FEV_1 and FVC, lower FEV_1/FVC, and higher BDR. Vitamin D insufficiency was common in both children and adults (68% to

75%), and most common in non-Hispanic blacks (94% to 97%). Figure 1 shows vitamin D levels by race/ethnicity for each NHANES study wave (2001–2002 to 2009–2010). Overall, non-Hispanic blacks had lower vitamin D level (mean = 16.0–18.6 ng/ml) than other racial or ethnic groups. Moreover, an upward trend of increased vitamin D levels, specifically in the periods 2007–2008 and 2009–2010, was seen in the U.S. population.

The multivariable analysis of vitamin D insufficiency and current asthma or current wheeze is shown in Table 2. After adjusting for age, gender, race/ethnicity, household income, BMI, and serum cotinine and CRP levels, vitamin D insufficiency was significantly associated with increased odds of current asthma and current wheeze in children, as well as with current wheeze in adults. After stratification by race or ethnicity, vitamin D insufficiency remained significantly associated with current wheeze in non-Hispanic white children and adults, as well as with current asthma in non-Hispanic white adults. However, there was no significant association between vitamin D insufficiency and current wheeze or current asthma in children or adults in other racial or ethnic groups. We obtained similar results to those shown in Table 2 when the multivariable analyses were adjusted for health insurance coverage instead of household income (data not shown).

In a secondary analysis, we repeated the multivariable analysis in adults after stratification by current smoking, in order to minimize potential misclassification of chronic obstructive pulmonary disease (COPD) as current asthma or current wheeze (Supplementary Table 1). In this analysis, vitamin D insufficiency was significantly associated with current wheeze among non-smoking non-Hispanic white and black adults. We found no significant association between vitamin D insufficiency and current asthma (regardless of current smoking) or current wheeze in current smokers.

Table 3 shows the results of the multivariable analysis of vitamin D insufficiency and lung function measures among participants in NHANES 2007–2010. In children, vitamin D insufficiency was significantly associated with 110 ml to 129 ml decrements in FEV_1 and FVC. In adults, vitamin D insufficiency was significantly and inversely associated with FEV_1 (−70 mL) and FVC (−118 mL), but significantly and positively associated with FEV_1/FVC (0.45%, 95% CI=0.05%–0.85%). Similar results were obtained when the analysis was repeated using %predicted values of FEV_1, FVC and FEV_1/FVC (supplemental Table 2) and after stratification by current asthma (Supplemental Table 3). Vitamin D insufficiency was not associated with BDR in either children or adults.

We next examined estimates of the prevalence of vitamin D insufficiency and current asthma for each NHANES study wave from 2001 to 2010 (Figure 2). In this analysis, the estimated prevalence of vitamin D insufficiency was 72% to 76% in 2001–2006, and then decreased to 64%–65% in 2007–2010. Of interest, the estimated prevalence of current asthma decreased from 8.2% in 2007–2008 to 7.4% in 2009–2010, in parallel with the reduction in the estimated prevalence of vitamin D insufficiency for the same period.

DISCUSSION

To our knowledge, this is the first study to examine the relation between vitamin D insufficiency and current asthma or current wheeze in a large sample of U.S. children and adults. Vitamin D insufficiency was common, being present in two thirds of study participants. Vitamin D insufficiency was associated with current asthma and current wheeze in non-Hispanic white children, as well as with current wheeze in non-Hispanic white and black adults without history of current smoking. Vitamin D insufficiency was not associated with current asthma or current wheeze in non-white (black or Mexican) children or Mexican adults. Temporal trends in NHANES showed that a decrement in the estimated prevalence of vitamin D insufficiency was followed by decreased prevalence of current asthma.

Consistent with our findings in the U.S. NHANES, vitamin D insufficiency or vitamin D deficiency (a serum 25[OH]D <20 ng/ml) has been associated with asthma or wheeze in population-based studies of Peruvian[8], Australian[31] and Canadian children[32], but not significantly associated with asthma in a large study of Israeli adults[12]. Although two recent RCTs of vitamin D supplementation (with 2800 IU/day[17] or 4000 ID/day[18]) during pregnancy failed to show a significant effect on asthma or wheeze (recurrent or persistent) in the first 3 years of life, the RCT using the larger dose of vitamin D reported a non-statistically significant trend (P=0.05) for a protective effect against asthma or recurrent wheeze, as well as a significant protective effect against degree of allergic sensitization (i.e. fewer positive IgE tests to allergens) in a secondary analysis[18]. Both trials had insufficient statistical power to detect small to moderate effects on asthma or wheeze, and continued follow up of participating children is needed to determine potential effects of vitamin D supplementation on asthma *per se* (as this disease cannot be confidently diagnosed in children younger than 6 years).

Growing evidence indicates that vitamin D affects innate and adaptive immune responses relevant to childhood asthma. In murine models, vitamin D deficiency is associated with airway hyper-responsiveness (AHR), as well as with increased pro-inflammatory cytokines and reduced T-regulatory (T-reg) cells in bronchoalveolar lavage fluid (BALF)[33]. Moreover, vitamin D supplementation attenuates allergen-induced inflammation and AHR in sensitized mice[33,34]. Among children, three common genetic variants in the class I MHC–restricted T cell–associated molecule gene (CRTAM) have been associated with asthma exacerbations in those with vitamin D deficiency[35], and polymorphisms in the gene for the vitamin D receptor have been associated with asthma[365]. Whether gene-by-vitamin D interactions explain inconsistent results across observational studies of asthma is uncertain.

We found a significant association between vitamin D insufficiency and decreased FEV_1 or FVC in children and adults, regardless of co-existing asthma. Our results for lung function are thus consistent with those of prior reports in children[37,3839] and adults[40]. In a study of adults followed for 11 years, those with asthma and low serum 25(OH)D (<20 ng/mL) at baseline had larger declines in FEV_1, FVC and FEV_1/FVC than those with a serum 25(OH)D ≥20 ng.ml). In general agreement with our results, that study showed that the inverse association between vitamin D deficiency and lung function was more pronounced among adults who were non-smokers and did not use inhaled corticosteroids[14]. In contrast to

our results, serum or plasma 25(OH)D was not associated with lung function in a Danish population-based study of 4999 adults[15] or in a Canadian Health Measure Survey that included 1,421 children[41]. Moreover, the VIDA (Vitamin D Add-on Therapy Enhances Corticosteroid Responsiveness in Asthma) trial found no significant effects of vitamin D on lung function (a secondary outcome) in adults with persistent asthma and vitamin D insufficiency[19]. The discrepant findings for vitamin D and lung function may be explained by differences in age, race/ethnicity, number of participants, or degree of residual confounding across studies.

In our study, vitamin D insufficiency was significantly associated with asthma or wheeze in non-Hispanic white children, but not in non-Hispanic black or Mexican children. We found similarly negative results for asthma or wheeze in non-Hispanic black children when lower cut points for vitamin D (e.g., <20 ng/ml or <25 ng/ml) were used (data not shown). Such negative findings may be explained by lack of variability in vitamin D status. Among non-Hispanic black children, >90% had a vitamin D level <30 ng/ml and >50% had a vitamin D level <20 ng/ml. In contrast to our results in children, vitamin D insufficiency was significantly associated with current wheeze among non-smoking white and black adults, suggesting that age may modify the effect of vitamin D on wheeze in non-Hispanic blacks. Similarly, Mexican ethnicity may modify the effects of vitamin D insufficiency on asthma, given null results among Mexican children and adults in our study.

A recent study reported that trends in overall childhood asthma prevalence plateaued in 2008, and then declined significantly in 2013[42]. Although our finding of parallel decrements in asthma and vitamin D insufficiency must be cautiously interpreted due to inherent limitations of ecological results, they are both intriguing and worth exploring in future longitudinal studies.

Our study has considerable strengths, including large and ethnically diverse cohorts of both children and adults, and ability to adjust for potential confounders such as cigarette smoking (measured by serum cotinine), low-grade systematic inflammation (measured by CRP), and obesity. We also acknowledge several limitations of our findings. First, we cannot determine a temporal relationship between vitamin D insufficiency and asthma or lung function in a cross-sectional study. Second, we cannot exclude residual confounding by unmeasured variables, including atopy, use of asthma medications, outdoor activities, seasonal variation in vitamin D measurements, and dietary intake of other nutrients. Third, we cannot stratify the analysis of vitamin D insufficiency and lung function by race or ethnicity, due to small sample size. Finally, the cut points for serum vitamin D levels associated with optimal general (non-musculoskeletal) health are uncertain and under study[2,43]. The potential effects of vitamin D on asthma and lung health and what adequate levels should be recommended require further investigation.

In summary, vitamin insufficiency was highly prevalent among children and adults who participated in a large U.S. survey (NHANES). In NHANES, vitamin D insufficiency was associated with current asthma or current wheeze in non-Hispanic white children, as well as with current wheeze in non-smoking non-Hispanic white and black adults. Moreover, vitamin D insufficiency was associated with reduced FEV_1 and FVC in children and adults.

Ongoing RCTs should help determine whether vitamin D supplementation prevents asthma or severe asthma exacerbations during childhood.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Abbreviations

25(OH)D	25-hydroxy vitamin D
BDR	bronchodilator response
BMI	body mass index
CRP	C-reactive protein
FEV_1	forced expiratory volume in 1 second
FVC	forced vital capacity
NHANES	National Health and Nutrition Examination Survey
RCTs	randomized clinical trials

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Highlights

What is already known about this topic?

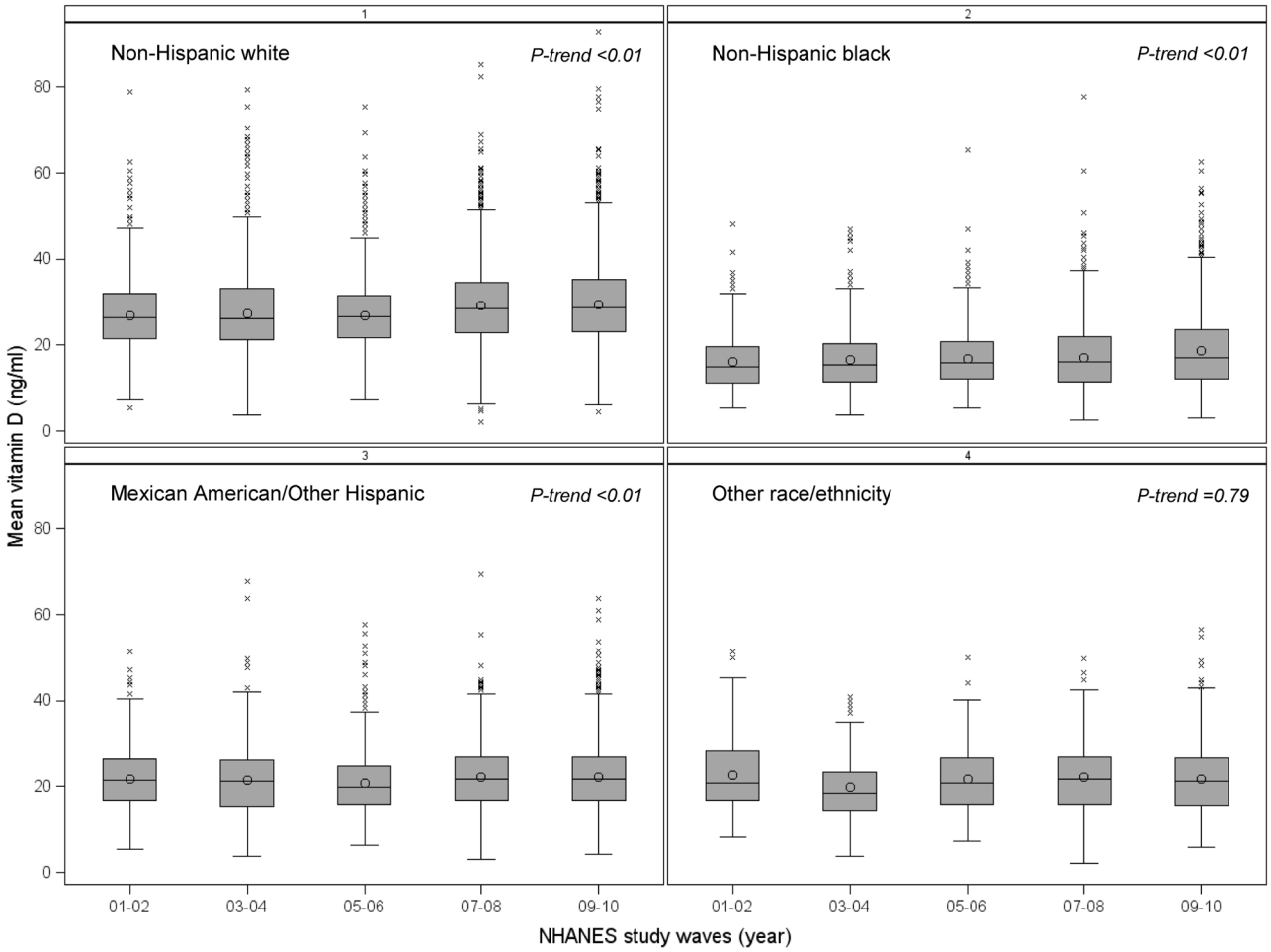
Vitamin D deficiency or insufficiency may increase the risk of asthma or morbidity from asthma, particularly in children.

What does this article add to our knowledge?

We show racial/ethnic-specific effects of vitamin D insufficiency on current asthma or wheeze. Moreover, we show parallel recent decrements in the prevalence of vitamin D insufficiency and asthma among participants in different study waves.

How does this study impact current management guidelines?

At this time, vitamin D cannot be recommended for asthma treatment. Clinicians should consider screening for vitamin D deficiency (which causes musculoskeletal problems) in high-risk groups (e.g., Blacks, Puerto Ricans, institutionalized individuals and the obese).



P for linear trend calculated using generalized linear models

Figure 1.

Vitamin D level (25[OH]D, ng/ml) by race/ethnicity and NHANES study waves (2001–2002 to 2009–2010)

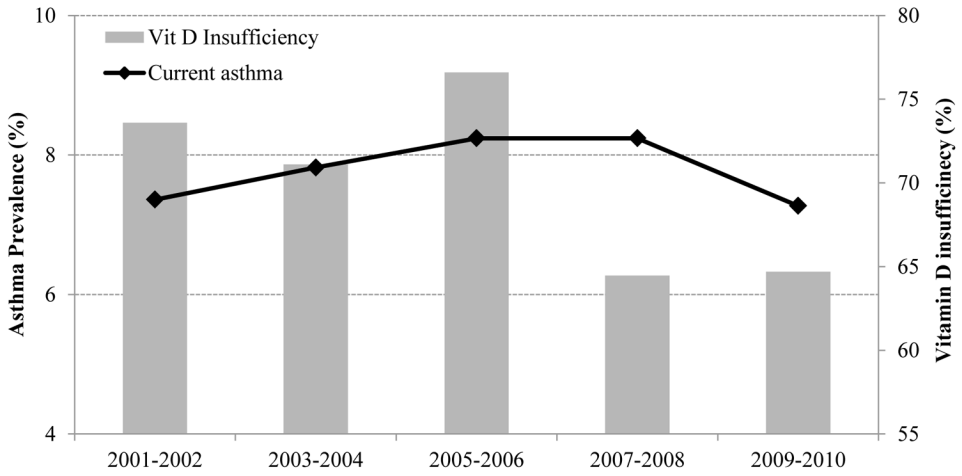


Figure 2.

Prevalence of current asthma and vitamin D insufficiency (25[OH]D <30 ng/ml) by NHANES study waves (2001–2002 to 2009–2010), in all participants

Table 1

Characteristics of participants in NHANES 2001–2010, by current asthma status

Characteristics	Children 6–17 years		Adults 18–79 years	
	Current asthma			
	No n=9,668	Yes n=1,192	No n=22,286	Yes n=1,829
Age (years)	11.7 ± 0.1	12.1 ± 0.1	44.1 ± 0.2	44.2 ± 0.5
Male gender	4833 (51.2)	655 (53.9)	11046 (49.8)	662 (36.3)‡
Race/ethnicity				
Non-Hispanic white	2779 (60.1)	316 (56.0)‡	10327 (70.1)	967 (74.2)‡
Non-Hispanic Black	2737 (13.6)	465 (20.8)	4560 (10.8)	433 (12.4)
Mexican American/other Hispanic	3685 (19.6)	352 (17.7)	4619 (13.4)	349 (8.4)
Other	467 (6.6)	59 (5.1)	980 (5.7)	80 (5.0)
Health insurance coverage (yes)	8041 (88.0)	1083 (94.0)‡	16672 (80.1)	1507 (85.5)‡
Annual household income < $20,000	2169 (16.3)	288 (17.1)	4680 (14.8)	518 (21.1)‡
Body mass index (kg/m^2)	20.8 (0.1)	22.2 (0.2)‡	28.2 ± 0.1	30.5 ± 0.3‡
BMI z-score	0.58 (0.02)	0.88 (0.04)‡	-	-
Serum cotinine level (ng/ml)	6.7 ± 0.5	9.5 ± 2.0	63.2 ± 2.1	72.0 ± 4.0‡
Current smoker	-	-	4723 (23.8)	453 (26.8)
Serum C-reactive protein (mg/dl)	0.14 ± 0.01	0.18 ± 0.02	0.39 ± 0.01	0.53 ± 0.02‡
Serum vitamin D level (ng/ml)	26.9 ± 0.1	25.7 ± 0.4†	25.7 ± 0.2	25.0 ± 0.3
Vitamin D insufficiency (<30 ng/ml)	7685 (67.7)	995 (75.9)‡	7052 (69.9)	1046 (72.3)
Non-Hispanic White	1527 (54.6)	199 (64.6)	6379 (61.8)	621 (65.5)
Non-Hispanic Black	2584 (93.8)	440 (94.4)	4287 (94.4)	416 (96.5)
Mexican American/other Hispanic	3183 (84.1)	308 (88.0)	5552 (86.3)	299 (87.8)
Other	391 (83.6)	48 (82.4)	834 (85.3)	70 (86.5)
Pre-bronchodilator FEV_1 (L)[1]	2.73 ± 0.03	2.76 ± 0.07	3.28 ± 0.02	2.82 ± 0.03‡
Pre-bronchodilator FVC, (L)[1]	3.14 ± 0.03	3.28 ± 0.08	4.18 ± 0.02	3.77 ± 0.05‡
Pre-bronchodilator FEV_1/FVC (%)[1]	86.5 ± 0.2	83.4 ± 0.5‡	78.5 ± 0.2	74.5 ± 0.4‡
Bronchodilator response as a percent of baseline FEV_1 (BDR, %)[1]	9.0 ± 0.6	13.2 ± 1.5‡	5.5 ± 0.2	10.9 ± 1.1‡

Results are shown as mean ± standard error (SE) for continuous variables, and as N (%) for binary variables.

†P<0.05 or

‡P<0.01 for current asthma vs no current asthma (within each age group).

[1]Data are only available in NHANES 2007–2010.

Table 2

Multivariable analysis * of vitamin D insufficiency and current asthma or current wheeze by race/ethnicity, NHANES 2001–2010

Outcomes	Children (total=10,860)		Adults (total=24,115)	
	N[1]	Odds ratio, (95% confidence interval), P-value	N[1]	Odds ratio, (95% confidence interval), P-value
Current asthma				
All participants	995	**1.35 (1.11, 1.64), <0.01**	1046	1.06 (0.93, 1.21), 0.39
Non-Hispanic whites	199	**1.41 (1.12, 1.77), <0.01**	621	1.07 (0.93, 1.24), 0.36
Non-Hispanic blacks	440	1.11 (0.69, 1.79), 0.68	416	1.53 (0.91, 2.58), 0.11
Mexican American/other Hispanic	308	1.35 (0.85, 2.14), 0.20	299	0.95 (0.61, 1.48), 0.83
Current wheeze				
All participants	978	**1.24 (1.02, 1.52), 0.03**	2597	**1.17 (1.04, 1.31), <0.01**
Non-Hispanic whites	228	**1.40 (1.11, 1.75), <0.01**	1264	**1.22 (1.08, 1.38), <0.01**
Non-Hispanic blacks	383	0.71 (0.47, 1.06), 0.10	660	1.29 (0.91, 1.81), 0.15
Mexican American/other Hispanic	316	0.91 (0.63, 1.32), 0.61	561	1.00 (0.72, 1.38), 0.98

* All multivariable models were adjusted for age, gender, household income, cotinine, C-reactive protein, BMI (in adults) and BMIZ (in children). The model for all participants was additionally adjusted for race/ethnicity

[1] N = participants with vitamin D insufficiency and current asthma (or current wheeze). See Table 1 for the number of participants with vitamin D insufficiency but no current asthma or current wheeze.

Table 3

Multivariable analysis* of vitamin D insufficiency and lung function measures, NHANES 2007–2010

	Children (n=3,001)	Adults (n=8,347)
Lung Function Measures	**β (95% confidence interval), P-value**	
Pre-bronchodilator FEV_1 (mL)[1]	**−110.17 (−146.79, −75.54), <0.01**	**−69.68 (−94.17, −45.18), <0.01**
Pre-bronchodilator FVC, (mL)[1]	**−129.13 (−176.09, −82.19), <0.01**	**−118.11 (−150.43, −85.79), <0.01**
Pre-bronchodilator FEV_1/FVC (%)	−0.06 (−0.84, 0.72), 0.88	**0.45 (0.05, 0.85), 0.03**
Bronchodilator response (BDR,%)[2,3]	0.50 (0.20, 1.21), 0.12	0.69 (0.36, 1.36), 0.29

*All models were adjusted for age, gender, race/ethnicity, household income, current asthma, cotinine, C-reactive protein, BMI (in adults) or BMIZ (in children).

[1]Additionally adjusted for height and height square

[2]The model for bronchodilator response were additionally adjusting for baseline (pre-bronchodilator) FEV_1.

[3]Bronchodilator response defined as ≥ 12% increment from baseline FEV_1 in children, and as ≥12% and ≥ 200ml increment from baseline in adults P for linear trend calculated using generalized linear models