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Vitamin D levels and food and environmental allergies in the United States: Results from NHANES 2005–2006

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Abstract

Background—Previous research supports a possible link between low vitamin D levels and atopic disease. However, the association between low vitamin D levels and total and allergen-specific IgE levels has not been studied.

Objective—To test the association between serum 25-hydroxyvitamin D (25(OH)D) deficiency (<15 ng/ml) and insufficiency (15–29 ng/ml), and allergic sensitization measured by serum IgE levels in a US nationally representative sample of 3136 children and adolescents and 3454 adults in the National Health and Nutrition Examination Survey (NHANES) 2005–2006.

Methods—The association of 25(OH)D deficiency with 17 different allergens was assessed after adjustment for potential confounders including age, sex, race/ethnicity, obesity, low socioeconomic status, frequency of milk intake, daily hours spent watching television, playing videogames or using a computer, serum cotinine levels and vitamin D supplement use.

Results—In children and adolescents, allergic sensitization to 11 of 17 allergens was more common in those with 25(OH)D deficiency. Compared with sufficient vitamin D levels of >30 ng/mL, after multivariate adjustment, 25(OH)D levels <15 ng/mL were associated with peanut (odds ratio OR 2.39, 95% CI: 1.29, 4.45), ragweed (OR: 1.83, 95% CI: 1.20, 2.80) and oak (OR: 4.75, 95% CI: 1.53, 4.94) allergies ($p < 0.01$ for all). Eight other allergens were associated with 25(OH)D deficiency with p -values < 0.05 but > 0.01 . There were no consistent associations seen between 25(OH)D levels and allergic sensitization in adults.

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Clinical Implications: We found an association between vitamin D deficiency and the prevalence of IgE sensitization. Low vitamin D levels may be a risk factor for allergies and patients with allergies may be at risk for low vitamin D levels.

None of the authors have financial conflicts of interest

Conclusion—Vitamin D deficiency is associated with higher levels of IgE sensitization in children and adolescents. Further research is needed to confirm these findings.

Keywords

Atopy; allergic sensitization; Vitamin D

INTRODUCTION

The non-calcemic effects and immunologic significance of vitamin D have recently been an area of much research [1]. Its immune-modulatory role has been implicated in diseases mediated by both Th1 and Th2 mechanisms including transplantation [2], autoimmune conditions such as rheumatoid arthritis [3], and multiple sclerosis [4,5]. Chronically low 25 hydroxyvitamin D (25(OH)D) levels, the most commonly measured indicator of vitamin D status, or vitamin D deficiency, defined as levels <15 ng/mL, result in bone changes that are consistent with rickets [6] and levels of 15 to 29 ng/mL are considered insufficient. Recent analysis of the National Health and Nutrition Examination Survey (NHANES) 2001–2004 data suggest that a substantial proportion of children [7] and adults [8,9] have 25 hydroxyvitamin D (25(OH) D) levels <15 ng/ml. Vitamin D deficiency is increasing in the United States [6,10,11] as is the prevalence of food allergies [12,13].

There has been a link reported between the supplementation of vitamins A and D, and food hypersensitivity and asthma in children with multivitamin use in the first 6 months of life [14,15]. Camargo et. al reported more epinephrine auto-injector (filled and refilled) prescriptions in northern versus southern states [16]. Vitamin D levels accordingly are lower in northern states, suggesting a possible link between vitamin D deficiency and atopic sensitization. However, the association between 25(OH)D levels and food hypersensitivities and other allergies remains unknown. To test a possible association between low 25(OH)D levels and allergies, we examined the relation of 25(OH) D deficiency and insufficiency in US children, adolescents and adults and the prevalence of food and environmental allergies as measured by serum IgE levels in the National Health and Nutrition Examination Survey (NHANES) 2005–2006.

METHODS

Study Population

The population of NHANES 2005–2006 is the civilian, non-institutionalized population of the United States. The survey used a complex, multistage, clustered and stratified probability sample design to select participants. Non-Hispanic blacks and Mexican-Americans were over-sampled [17] to obtain accurate estimates in these sub-populations. Data from the survey and details of the plan and operation of NHANES 2005–2006 are publicly available on the Centers for Disease Control/ National Center for Health Statistics (CDC/NCHS) website <http://www.cdc.gov/nchs/nhanes.htm>. All data is completely de-identified on the NCHS web-site and publicly available. All participants and/or their parents signed informed consent and the Albert Einstein College of Medicine Committee on Clinical Investigations found this analysis to qualify as exempt.

For this analysis, inclusion criteria included all participants ≥ 1 year of age with available 25(OH)D levels and allergy testing results. Participants missing covariables included in the multivariable adjusted model, as described below, were excluded; 8290 participants had 25(OH)D and allergy testing, of these 1700 were excluded due to missing data for covariables resulting in a final sample of 3136 children and adolescents and 3454 adults

(>21 years old). The 6590 participants that were included in the analysis represent 71 million people in the United States.

Data collection

Trained interviewers administered a detailed questionnaire to collect information on demographics including age, sex, self-identified race/ethnicity and the poverty to income ratio (PIR) with values of less than 1.00 being below the poverty threshold and defining low socioeconomic status (SES) in this analysis. Other data collected include use of vitamin D supplements, milk intake in the last 30 days (including milk poured on cereal or chocolate milk drinks) coded as daily, less than daily but more than once weekly and once weekly or less. Television (TV), videogame and computer use was assessed in the interviews and coded in hours per day and categorized as no use, <2h/day, 2–4 h/day and >4h/day and was used as a surrogate for physical activity. Physical examinations were conducted and obesity was defined as a BMI >30 kg/m² in adults and in children in two ways: weight was used in 1 year olds and obesity was defined as levels exceeding the 95th percentile of the weight distribution on the basis of gender-specific weight curves. In 2 to 21 year-olds, obesity was defined by using age and gender-specific centile curves on the basis of pooled international data and linked to the widely used adult obesity cutoff point of 30 kg/m² as defined by Cole et. al. [18].

Details of lab protocol and measurements are found on the NHANES website: (http://www.cdc.gov/nchs/nhanes/nhanes2005-2006/lab05_06.htm). Serum cotinine levels, a measure of smoking exposure were measured using an isotope dilution-high performance liquid chromatography / atmospheric pressure chemical ionization tandem mass spectrometry. Serum cotinine was categorized as values of <2.0, 2.0–20 and >20 ng/mL [19]. During the 2005–2006 survey, serum 25(OH)D levels were measured using the two step procedure using the Diasorin (formerly Incstar) 25-OH-Vitamin D assay. The assay was designed to detect serum 25(OH)D values from 5 to 100 ng/mL. Values <5.0 and >70 ng/mL were verified by re-assay, including re-extraction. Any sample batches with coefficients of variation (CVs) >10% were also re-assayed.

Allergy was determined in 2 ways: a questionnaire about allergy symptoms and measurement of total serum IgE and antigen-specific IgE levels. The NHANES 2005–2006 questionnaire assessed allergic symptoms divided into: allergies, hay fever, eczema, and pet avoidance due to allergic symptoms. The questions were asked of the participant or parent for children who could not answer and the responses coded as follows: the occurrence of allergy symptoms or attacks within the past year (yes/no), occurrence of hay fever symptoms in the past year (yes/no), and eczema (itchy rash coming and going for ≥ 6 months in the past year, (yes/no), and avoidance of pets due to allergic symptoms in the past year (yes/no).

Participants 1 year and older were tested for total and allergen-specific serum IgE by using the Pharmacia Diagnostics ImmunoCAP 1000 System (Kalamazoo, Mich). Children aged 1 to 5 years were tested for total IgE and specific IgE to dust mites (*Dermatophagoides farinae* (Mite) and *Dermatophagoides pteronyssinus* (Mite 2)), cat, dog, *Alternaria* species, peanut, egg and milk. Children aged 6 years and older and adults also had specific IgE measurements for German cockroach, short ragweed, perennial ryegrass, Bermuda grass, Russian thistle, white oak, birch and shrimp. Those 6 years and older were also tested for IgE specific to mouse and rat but positive results were in present in <2.5% of the population, therefore the models were not reliable and results are not reported. We defined a positive allergy as an IgE response of ≥0.35kU/L to any allergen. High elevated IgE level was defined as the top quintile of the distribution (>191 kU/L). We separately defined a pollen allergy as a positive reaction to any of the following: short ragweed, perennial ryegrass,

Bermuda grass, Russian thistle, white oak and birch. We also defined a perennial allergy as a positive reaction to any of the following: dust mite (*Dermatophagoides farinae*) and dust mite 2 (*Dermatophagoides pteronyssinus*), cat, dog, *Alternaria* species, German cockroach, *Aspergillus*, mouse and rat. Total allergy was defined as a positive reaction to any of the above allergens.

Statistical analyses

Participant characteristics were calculated for children/adolescents and adults, separately, by vitamin D level (≥ 30 ng/mL (sufficient), 15–29 ng/mL (insufficient), < 15 ng/mL (deficient)) with the statistical significance of trends across levels calculated via linear and logistic regression as appropriate. The prevalence of total serum and antigen-specific IgE levels were calculated by 25(OH)D levels. Potential confounders of the association between 25(OH)D levels and allergic sensitization were first examined by looking at the strength of the univariate associations between available confounders and the exposure and outcome. Age, sex, race/ethnicity, low SES (PIR < 1.0), obesity, milk drinking, number of hours watching TV, playing videogames and using a computer, vitamin D supplement use and smoking exposure (as measured by serum cotinine levels) were retained in the adjusted models based on these associations and findings from previous studies. No covariates were included in the models with a correlation > 0.52 to avoid issues of multicollinearity. Because milk intake and vitamin D supplement use may be over-adjusting, we performed a sensitivity analysis taking these variables out of the multivariable model.

Logistic regression was used to determine the odds ratio (OR) associated with 25(OH)D levels < 15 ng/mL and 15–29 ng/mL compared to a level ≥ 30 ng/mL. We analyzed positive test results for each allergen separately, total allergy, pollen allergy and perennial allergy. In addition, we used 25(OH)D levels as a continuous variable in a linear model to assess associations with continuous log transformed total and allergen specific IgE levels. Additionally a separate analysis was performed assessing the association of 25(OH)D status and positive responses to the allergic symptom questions on the allergy questionnaire. We also created another category of participants who reported any allergy symptoms and were in the highest quintile of total IgE levels and tested associations with 25(OH)D status. In another sensitivity analysis, we created a variable consisting of the number of positive IgE sensitization for each participant. We then analyzed the association between 25(OH)D categories and the number of positive allergens using poisson regression. Interactions by race and gender were tested by including a multiplicative term in the model. When an interaction was detected (< 0.05 significance level) stratified models were performed and reported. A Bonferroni corrected p-value for the analysis of individual allergens is < 0.003 . All analyses used survey command (svy) in Stata 10.1 to account for the complex, multistage probability sample survey design used in NHANES 2005–2006.

RESULTS

Participant characteristics

In children and adolescents and adults, 25(OH)D levels < 15 ng/mL were associated being non-Hispanic black and Mexican-American, having a low SES, TV, videogame or computer use > 4 h per day, a lower frequency of milk drinking and not taking vitamin D supplements (Tables 1 and 2). Additionally, in children and adolescents, older age and female sex were also associated with lower 25(OH)D levels.

Prevalence of positive IgE testing by 25(OH)D levels

Overall IgE sensitization was more common in children and adolescents than in adults (Figures 1 and 2). The most common allergen sensitization overall in children and

adolescents and adults was ryegrass; 22.9% of children and adolescents and 18.7% of adults. In children and adolescents, lower 25(OH)D levels were associated with a higher prevalence of sensitization to most allergens (Figures 1 and 2). These trends were not present in adults.

Associations between IgE testing and 25(OH)D levels

Lower levels of 25(OH)D were associated with allergic sensitization to various allergens, both food and environmental in children and adolescents (Table 3). An association was present for 25(OH)D levels of 15–29 ng/mL and oak allergy (OR 2.29, 95% CI: 1.51, 3.48). Strong associations were also seen between 25(OH)D levels <15 ng/mL and peanut (OR 2.39, 95% CI: 1.29, 4.45) (p-trend=0.005), ragweed (OR: 1.83, 95% CI: 1.20, 2.80) (p-trend=0.005) and oak allergies (OR: 4.75, 95% CI: 1.53 – 4.94) (p-trend=0.001). Associations were also found for 25(OH)D deficiency and the following allergens: dog, cockroach, *Alternaria*, shrimp, ryegrass, Bermuda grass, birch, and thistle with a p-value <0.05 but >0.01. Among the composite allergy categories, 25(OH)D levels <15 ng/mL were associated with a higher prevalence of sensitization to perennials (OR 1.80, 95% CI: 1.08, 3.00) (p-trend = 0.03). Using linear regression to find unadjusted and multivariable adjusted associations between continuous 25(OH)D levels and log-transformed total and antigen specific IgE levels many of the associations found in the earlier analysis persisted (Table 3, second and third columns). In children and adolescents, the incidence rate ratio (IRR) for the association between 25(OH)D levels and the number of positive allergen specific IgE levels was 1.46 (1.15, 1.83) (p-value = 0.004) and 1.72 (1.24 to 2.39) (p-value=0.003) for 25(OH)D levels 15–29 ng/mL and <15 ng/mL, respectively.

In adults, fewer significant associations were observed between 25(OH)D levels and IgE allergen sensitization (Table 4). However, 25(OH)D levels 15–29 ng/mL had protective associations with dog sensitization (OR 0.71, 95% CI: 0.53, 0.96) and cockroach allergens (OR 0.64, 95% CI: 0.43, 0.94) and levels <15 ng/mL showed a protective association with ragweed allergy (OR: 0.60, 95% CI: 0.40, 0.89). In continuous analysis, there was an inverse association between 25(OH)D levels and log-transformed total IgE levels. But this association disappeared after multivariable adjustment. In adults, the IRR for the association between 25(OH)D levels and the number of positive allergen specific IgE levels was 0.84 (0.70 to 1.02) (p-value = 0.07) and 0.80 (0.58 to 1.12) (p-value=0.18) for 25(OH)D levels 15–29 ng/mL and <15 ng/mL, respectively. Analyses without including milk intake and vitamin D supplementation in the multivariable models did not change the observed associations in children/adolescents or adults (data not shown).

25(OH)D levels and allergy symptoms

Questionnaire data showed an association between 25(OH)D levels of 15–29 ng/mL and <15 ng/mL and allergic symptoms in children and adolescents (OR: 1.50, 95% CI: 1.04 – 2.17 and 1.79, 95% CI: 1.10 – 2.93, respectively) but not to specific symptoms of hay fever, eczema or pet avoidance. In adults, no significant associations were seen for any of these self-reported symptoms. Associations were stronger when we created a separate category of having allergy symptoms and being in the highest quintile of total IgE levels. Children with 25(OH)D levels 15 to 29 ng/mL and <15 ng/mL had odds ratios of 1.92 (1.38 to 1.66) and 2.48 (1.45 to 4.25) respectively, for being in the highest IgE quintile and having any allergy symptoms (hay fever, allergy, avoidance of pets or eczema). Adults in these two vitamin D categories had odds ratios of 0.96 (0.57 to 1.63) and 0.98 (0.52 to 1.85), respectively.

Interactions

There were no significant interactions found in children and adolescents. In adults, significant interactions were seen between vitamin D levels and sex for birch allergy with a p-interaction of 0.04. In women, 25(OH)D levels of <15 ng/mL had an OR of 1.26 (95% CI:

0.38, 4.07) whereas in men the OR was 0.42 (95% CI: 0.18, 0.94). An interaction was also seen in adults for peanut allergy between vitamin D levels and race with a p-interaction of 0.04. The odds ratio in non-Hispanic blacks was 0.16 (95% CI: 0.07, 0.38) whereas in whites the OR was 0.88 (95% CI: 0.32, 2.43).

DISCUSSION

We found consistent associations between vitamin D deficiency and the presence of allergies in children and adolescents. While there were some protective associations between 25(OH)D deficiency and allergic sensitization in adults, these were not as consistent as in children. This is the first large study evaluating a relationship between 25(OH) D levels and allergic sensitization.

Vitamin D and its immunologic functions have been implicated in a variety of inflammatory and allergic diseases. The anti-inflammatory mechanism of its action has been thought to be due to the suppression of antigen-dendritic cell mediated Th1 response and proliferation [20], macrophage activation [21,22] and cytokine expression such as IL-2 [23]. An analysis of birth month in patients presenting to the emergency department showed that birth in the fall or winter, when vitamin D levels are lowest, was associated with a higher risk of presenting with food-related acute allergic symptoms.[24] In a recent study, Sidbury et. al. randomized 11 patients with atopic dermatitis to ergocalciferol 1000 IU or placebo daily for 1 month and found that more children on vitamin D had an improvement in their Investigator's Global Assessment score [25]. The same investigators found an association between vitamin D deficiency and atopic dermatitis in obese individuals [26]. The active form of vitamin D, 1,25-dihydroxyvitamin D3, induces expression of antimicrobial peptides like cathelicidin that may prevent skin infection [27]. Additionally, vitamin D also down-regulates effector T cell activity and inhibits T cell proliferation and IL-2 production as referred to earlier. Furthermore, topical Vitamin D application has been observed to lead to the expansion of antigen-specific T regulatory cells [28]. Recent studies have suggested a link between asthma and low vitamin D levels [29–31] although further work is necessary in order to provide more evidence. There are currently several ongoing clinical trials (clinicaltrials.gov identifiers: [NCT00856947](#), [NCT00920621](#)) that are investigating the use of vitamin D to improve asthma and allergies, and thus trial data should be forthcoming in the next few years.

The current study assessed whether serum levels of 25(OH)D were related to the prevalence of allergic sensitization. Past studies have shown a non-linear, U-shaped association between low and high vitamin D with increased serum total IgE levels [32]. We found that in children and adolescents, there was a trend towards higher IgE levels in those with 25(OH)D levels <15 ng/mL compared to ≥30 ng/mL. There are not many participants of NHANES 2005–2006 with high (>40 ng/mL) 25(OH)D levels which may be the reason we did not see a U-shaped association. However, there were more associations present when analyzing the data in 25(OH)D categories compared to as a continuous variable, which suggests either a threshold effect or a U-shaped relationship.

Our results show that children with vitamin D deficiency are more likely to have allergic sensitization to various allergens, both food and environmental. Recent reviews have discussed the possible mechanisms by which Vitamin D is implicated in the regulation of allergic responses [23], mostly by inhibition of the inflammatory response of innate immune cells. Two smaller, observational studies show results similar to those we present. A large cross-sectional study of asthmatic children in Costa Rica showed that 25(OH)D levels were inversely associated with total serum IgE levels and with dust mite sensitization. [30] A smaller study of approximately 100 asthmatic children also showed an unadjusted inverse

relationship between 25(OH)D levels and total serum IgE and aeroallergen skin tests.[31] It should be noted that many of the associations found in the unadjusted linear regression were attenuated or disappeared after adjusting for confounders.

It is unclear why associations between 25(OH)D deficiency and allergic sensitization was seen in children and adolescents but not in adults. We found that children and adolescents were more likely to have IgE sensitization to allergens. Previous studies have found that food allergies in children have increased 18% between 1997 and 2007 [13]. If most food allergies start in childhood, 25(OH)D levels closer to the initiation of the allergy (still in childhood and adolescence), may be more reflective of the vitamin D status at the time of allergic sensitization. In adults, if the allergies started in childhood, levels of 25(OH)D in adulthood may not be reflective of 25(OH)D status at the time of allergic sensitization. It may also be that different mechanisms are responsible for allergic sensitization in adults versus children and adolescents [33] .

Vitamin D deficiency and insufficiency, although common in children in the US, has been shown to have racial/ethnic predispositions in some groups. Two recent studies have explored prevalence data within the NHANES surveys [7,34], and demonstrated that Hispanic and Non-Hispanic black children are at higher risk for deficiency. Hispanic ethnicity was found to be associated with higher cord blood IgE levels in a screening birth cohort of 874 infants in Boston, MA [35]. Total and allergen-specific IgE has been shown to be consistently higher among those of non-Hispanic black race [36,37]. Yang et al. noted that although this might be due to environmental factors such as urban/rural residence, self-reported race continues to be a strong predictor of allergic sensitization [38]. The prevalence of both vitamin D deficiency and increased atopy in these groups should be explored with future epidemiologic studies.

This study has several limitations, including its cross-sectional design, limiting the determination of causality for the observed atopic differences with vitamin D deficiency. As in any observational study, there are probably measured and unmeasured confounders for which we did not adjust. Notably, IgE levels and allergic symptoms vary by season and geographic location,[39,40] both important potential confounder which we did not have available. NHANES samples northern states in the summer and southern states in the winter in order to ensure comparable conditions. Therefore, vitamin D levels may be underestimated and because of the geographic differences in allergies, there may be residual confounding. Another limitation is that we did not adjust for multiple comparisons because of the exploratory hypothesis generating nature of this analysis. However, our study maintains many strengths including information on several thousand participants who are representative of the general US population. The consistent associations between low 25(OH)D levels and most allergens tested in children and adolescents suggests that further research is warranted in this area.

In this nationally representative population, we found consistent associations between 25(OH)D deficiency and a higher prevalence for 11 out of 17 allergens tested in children and adolescents. These associations were not seen in adults. The prevalence of both allergic symptoms and vitamin D deficiency are increasing in the United States, and this study suggests these two phenomena may be linked.

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Abbreviations

NHANES	National Health and Nutrition Examination Survey
SES	socio-economic status
NCHS	National Center for Health Statistics, 25-hydroxyvitamin D (25(OH)D)
OR	odds ratio

References

- Mathieu C, Adorini L. The coming of age of 1,25-dihydroxyvitamin D(3) analogs as immunomodulatory agents. *Trends Mol Med*. 2002; 8(4):174–179. [PubMed: 11927275]
- Lemire JM, et al. Prolongation of the survival of murine cardiac allografts by the vitamin D3 analogue 1,25-dihydroxy-delta 16-cholecalciferol. *Transplantation*. 1992; 54(4):762–763. [PubMed: 1412777]
- Andjelkovic Z, et al. Disease modifying and immunomodulatory effects of high dose 1 alpha (OH) D3 in rheumatoid arthritis patients. *Clin Exp Rheumatol*. 1999; 17(4):453–456. [PubMed: 10464556]
- Hernan MA, Olek MJ, Ascherio A. Geographic variation of MS incidence in two prospective studies of US women. *Neurology*. 1999; 53(8):1711–1718. [PubMed: 10563617]
- Correale J, Ysraelit MC, Gaitan MI. Immunomodulatory effects of Vitamin D in multiple sclerosis. *Brain*. 2009; 132(Pt 5):1146–1160. [PubMed: 19321461]
- Holick MF. Resurrection of vitamin D deficiency and rickets. *J Clin Invest*. 2006; 116(8):2062–2072. [PubMed: 16886050]
- Kumar J, et al. Prevalence and Associations of 25-Hydroxyvitamin D Deficiency in US Children: NHANES 2001–2004. *Pediatrics*. 2009
- Ginde AA, Liu MC, Camargo CA Jr. Demographic differences and trends of vitamin D insufficiency in the US population, 1988–2004. *Arch Intern Med*. 2009; 169(6):626–632. [PubMed: 19307527]
- Looker AC, et al. Serum 25-hydroxyvitamin D status of the US population: 1988–1994 compared with 2000–2004. *Am J Clin Nutr*. 2008; 88(6):1519–1527. [PubMed: 19064511]
- Weisberg P, et al. Nutritional rickets among children in the United States: review of cases reported between 1986 and 2003. *Am J Clin Nutr*. 2004; 80(6 Suppl):1697S–1705S. [PubMed: 15585790]
- Gordon CM, et al. Prevalence of vitamin D deficiency among healthy adolescents. *Arch Pediatr Adolesc Med*. 2004; 158(6):531–537. [PubMed: 15184215]
- Law M, et al. Changes in atopy over a quarter of a century, based on cross sectional data at three time periods. *Bmj*. 2005; 330(7501):1187–1188. [PubMed: 15833748]
- Branum AM, Lukacs SL. Food allergy among children in the United States. *Pediatrics*. 2009; 124(6):1549–1555. [PubMed: 19917585]
- Milner JD, et al. Early infant multivitamin supplementation is associated with increased risk for food allergy and asthma. *Pediatrics*. 2004; 114(1):27–32. [PubMed: 15231904]
- Long KZ, Santos JI. Vitamins and the regulation of the immune response. *Pediatr Infect Dis J*. 1999; 18(3):283–290. [PubMed: 10093956]
- Camargo CA Jr, et al. Regional differences in EpiPen prescriptions in the United States: the potential role of vitamin D. *J Allergy Clin Immunol*. 2007; 120(1):131–136. [PubMed: 17559916]
- Ezzati TM, et al. Sample design: Third National Health and Nutrition Examination Survey. *Vital Health Stat 2*. 1992; (113):1–35. [PubMed: 1413563]
- Cole TJ, et al. Establishing a standard definition for child overweight and obesity worldwide: international survey. *BMJ*. 2000; 320(7244):1240–1243. [PubMed: 10797032]
- McKeever TM, et al. Serum nutrient markers and skin prick testing using data from the Third National Health and Nutrition Examination Survey. *J Allergy Clin Immunol*. 2004; 114(6):1398–1402. [PubMed: 15577844]

20. Lemire JM, et al. Immunosuppressive actions of 1,25-dihydroxyvitamin D3: preferential inhibition of Th1 functions. *J Nutr.* 1995; 125(6 Suppl):1704S–1708S. [PubMed: 7782931]
21. Griffin MD, Xing N, Kumar R. Vitamin D and its analogs as regulators of immune activation and antigen presentation. *Annu Rev Nutr.* 2003; 23:117–145. [PubMed: 12651965]
22. Lin R, White JH. The pleiotropic actions of vitamin D. *Bioessays.* 2004; 26(1):21–28. [PubMed: 14696037]
23. Dimeloe S, et al. Regulatory T cells, inflammation and the allergic response- The role of glucocorticoids and Vitamin D. *J Steroid Biochem Mol Biol.* 2010
24. Vassallo MF, et al. Season of birth and food allergy in children. *Ann Allergy Asthma Immunol.* 104(4):307–313. [PubMed: 20408340]
25. Sidbury R, et al. Randomized controlled trial of vitamin D supplementation for winter-related atopic dermatitis in Boston: a pilot study. *Br J Dermatol.* 2008; 159(1):245–247. [PubMed: 18489598]
26. Oren E, Banerji A, Camargo CA Jr. Vitamin D and atopic disorders in an obese population screened for vitamin D deficiency. *J Allergy Clin Immunol.* 2008; 121(2):533–534. [PubMed: 18177693]
27. Schaubert J, Gallo RL. Antimicrobial peptides and the skin immune defense system. *J Allergy Clin Immunol.* 2008; 122(2):261–266. [PubMed: 18439663]
28. Ghoreishi M, et al. Expansion of antigen-specific regulatory T cells with the topical vitamin D analog calcipotriol. *J Immunol.* 2009; 182(10):6071–6078. [PubMed: 19414758]
29. Litonjua AA. Childhood asthma may be a consequence of vitamin D deficiency. *Curr Opin Allergy Clin Immunol.* 2009; 9(3):202–207. [PubMed: 19365260]
30. Brehm JM, et al. Serum vitamin D levels and markers of severity of childhood asthma in Costa Rica. *Am J Respir Crit Care Med.* 2009; 179(9):765–771. [PubMed: 19179486]
31. Searing DA, et al. Decreased serum vitamin D levels in children with asthma are associated with increased corticosteroid use. *J Allergy Clin Immunol.* 125(5):995–1000. [PubMed: 20381849]
32. Hypponen E, et al. Serum 25-hydroxyvitamin D and IgE - a significant but nonlinear relationship. *Allergy.* 2009; 64(4):613–620. [PubMed: 19154546]
33. Storaas T, et al. Occupational rhinitis: diagnostic criteria, relation to lower airway symptoms and IgE sensitization in bakery workers. *Acta Otolaryngol.* 2005; 125(11):1211–1217. [PubMed: 16353405]
34. Mansbach JM, Ginde AA, Camargo CA Jr. Serum 25-hydroxyvitamin D levels among US children aged 1 to 11 years: do children need more vitamin D? *Pediatrics.* 2009; 124(5):1404–1410. [PubMed: 19951983]
35. Scirica CV, et al. Predictors of cord blood IgE levels in children at risk for asthma and atopy. *J Allergy Clin Immunol.* 2007; 119(1):81–88. [PubMed: 17208588]
36. Grundbacher FJ, Massie FS. Levels of immunoglobulin G, M, A, and E at various ages in allergic and nonallergic black and white individuals. *J Allergy Clin Immunol.* 1985; 75(6):651–658. [PubMed: 4008794]
37. Litonjua AA, et al. Variation in total and specific IgE: effects of ethnicity and socioeconomic status. *J Allergy Clin Immunol.* 2005; 115(4):751–757. [PubMed: 15805994]
38. Yang JJ, et al. Differences in allergic sensitization by self-reported race and genetic ancestry. *J Allergy Clin Immunol.* 2008; 122(4):820–827. e9. [PubMed: 19014772]
39. Di Gioacchino M, et al. Influence of total IgE and seasonal increase of eosinophil cationic protein on bronchial hyperreactivity in asthmatic grass-sensitized farmers. *Allergy.* 2000; 55(11):1030–1034. [PubMed: 11097312]
40. Chang JW, et al. Higher incidence of Dermatophagoides pteronyssinus allergy in children of Taipei city than in children of rural areas. *J Microbiol Immunol Infect.* 2006; 39(4):316–320. [PubMed: 16926978]

Prevalence of IgE Sensitization, % of Population

Allergens

Figure 1.

A and 1B Prevalence (%) of allergens (A = perennial/food and B = seasonal allergens) by serum 25-hydroxyvitamin D levels (ng/mL) in United States children and adolescents aged 1–21.

Prevalence of IgE sensitization, % of

Allergens

Figure 2.

A and 2B Prevalence (%) of allergens (A = perennial/food and B = seasonal allergens) by serum 25-hydroxyvitamin D levels (ng/mL) in United States adults older than 21 years.

Table 1

Participant characteristics by 25-hydroxyvitamin D levels, for participants aged 1–21 years of the National Health and Nutrition Examination Survey 2005–2006

Characteristic	All participants (N=3136)	25(OH)D $\geq$ 30 ng/mL (N = 397)	25(OH)D 15–29 ng/mL (N = 1985)	25(OH)D <15 ng/mL (N = 754)	P-trend
Age, mean (SE)	12.5 (0.2)	11.6 (0.5)	12.3 (0.3)	15.1 (0.4)	<0.001
Male sex, % (SE)	52.4 (1.2)	56.2 (3.1)	52.5 (1.3)	45.4 (2.4)	0.004
Race/ethnicity, % (SE)					
Non-Hispanic white	61.9 (3.4)	86.3 (2.6)	62.9 (3.6)	15.5 (3.5)	<0.001
Non-Hispanic black	14.1 (2.5)	2.2 (0.5)	10.9 (1.8)	50.4 (7.5)	<0.001
Mexican-American	16.9 (2.1)	5.6 (1.4)	19.2 (2.3)	24.5 (4.9)	<0.001
Other	7.1 (1.6)	5.9 (1.9)	7.0 (1.8)	9.6 (2.2)	0.22
Low SES*, % (SE)	20.3 (1.8)	15.8 (2.3)	19.7 (2.1)	31.2 (2.8)	0.009
Vitamin D supplement use, % (SE)	25.6 (1.2)	31.8 (3.7)	26.9 (1.5)	8.2 (1.4)	<0.001
TV/computer use in hours/day, % (SE)					
<2 hours	37.6 (1.2)	46.1 (1.8)	37.1 (1.4)	25.5 (2.9)	<0.001
2–4 hours	37.7 (1.3)	37.6 (2.2)	38.8 (1.6)	32.3 (1.9)	0.14
>4 hours	23.1 (1.0)	14.3 (2.1)	22.8 (1.7)	39.5 (3.3)	<0.001
None	1.7 (0.3)	2.0 (0.7)	1.3 (0.4)	2.8 (0.6)	0.66
Frequency of milk intake past 30 days, % (SE)					
Daily	73.8 (1.5)	80.6 (3.4)	76.0 (1.7)	51.3 (4.4)	0.003
Once per week	19.2 (1.2)	13.9 (2.2)	18.9 (1.6)	29.7 (2.7)	0.001
Rarely	6.9 (0.5)	5.4 (1.6)	5.1 (0.6)	19.0 (3.0)	0.001
Obesity, % (SE)	17.1 (1.5)	8.6 (2.4)	16.4 (1.7)	34.6 (3.0)	<0.001
Serum cotinine, % (SE)					
<2.9 ng/mL	85.6 (1.4)	81.6 (3.2)	87.9 (1.3)	80.6 (3.0)	0.78
2.9–20 ng/mL	4.0 (0.6)	5.4 (1.3)	3.2 (0.5)	5.7 (1.0)	0.77
>20 ng/mL	10.4 (1.0)	13.1 (2.8)	8.9 (0.9)	13.7 (3.0)	0.84

Abbreviations: SES: socioeconomic status, SE: standard error

* SES – percentage of those with Poverty to Income Ratio <1.00

Table 2

Participant characteristics by 25-hydroxyvitamin D levels, for participants aged >21 years of the National Health and Nutrition Examination Survey 2005–2006 for

Characteristic	All participants (N=3454)	25(OH)D ≥ 30 ng/ml (N = 481)	25(OH)D 15- 29 ng/mL (N = 2073)	25(OH)D <15 ng/mL (N= 900)	P-trend
Age, mean (SE)	47.4 (0.8)	45.0 (1.0)	48.0 (0.9)	47.5 (1.0)	0.13
Male sex, % (SE)	47.7 (0.6)	41.9 (2.4)	51.1 (1.0)	41.7 (2.0)	0.76
Race/ethnicity, % (SE)					
Non-Hispanic white	73.6 (2.8)	92.1 (1.9)	77.7 (2.4)	43.7 (5.3)	<0.001
Non-Hispanic black	10.4 (1.7)	1.2 (3.6)	6.4 (1.1)	31.4 (4.4)	<0.001
Mexican-American	11.1 (1.3)	3.7 (0.6)	10.9 (1.4)	18.3 (3.1)	<0.001
Other	4.9 (0.7)	3.0 (1.3)	4.9 (0.6)	6.6 (1.5)	0.13
Low SES*, % (SE)	10.6 (0.8)	8.2 (1.8)	9.3 (0.9)	16.9 (1.7)	0.005
Vitamin D supplement use, % (SE)	41.1 (1.4)	56.0 (2.0)	43.7 (1.8)	19.6 (1.5)	<0.001
TV/computer use in hours/day, % (SE)					
<2h	40.1 (1.3)	48.7 (2.6)	40.3 (1.4)	32.0 (2.3)	<0.001
3–4h	38.7 (1.3)	35.9 (2.3)	39.7 (1.6)	38.0 (3.3)	0.66
>4h	20.2 (1.1)	14.2 (1.6)	19.2 (1.2)	29.0 (2.2)	<0.001
None	0.9 (0.2)	1.2 (0.2)	0.8 (0.2)	1.0 (0.4)	0.32
Frequency of milk intake past 30 days, % (SED)					
Daily	50.6 (1.8)	60.3 (2.6)	52.6 (2.6)	36.2 (2.1)	<0.001
Once per week	32.0 (1.7)	27.3 (1.9)	31.4 (2.2)	37.7 (2.4)	0.004
Rarely	17.5 (1.0)	12.4 (1.7)	16.2 (1.4)	26.1 (1.7)	<0.001
Obesity**, % (SE)	76.6 (1.2)	64.1 (3.0)	78.2 (1.2)	82.2 (1.1)	<0.001
Serum cotinine, % (SE)					
<2.9 ng/mL	72.2 (1.2)	67.1 (2.1)	75.2 (1.5)	66.9 (2.5)	0.82
2.9–20 ng/mL	2.0 (0.4)	2.8 (1.2)	1.7 (0.3)	2.3 (0.4)	0.73
>20 ng/mL	25.8 (1.4)	30.1 (2.6)	2.3 (1.5)	30.7 (2.6)	0.73

Abbreviations: SES: socioeconomic status, SE: standard error

* SES – percentage of those with Poverty to Income Ratio < 1.00

Associations between total and antigen-specific IgE levels and 25(OH)D levels < 15 ng/ml and 15–29 ng/ml compared to reference group (≥ 30 ng/mL) for all children and adolescents aged 1–21 years of age

Table 3

Allergen (number with allergic sensitization/ total number tested)	Unadjusted β coefficient (95% CI) for log transformed IgE levels and continuous 25(OH)D levels	Multivariable adjusted β coefficient (95% CI) for log transformed IgE levels and continuous 25(OH)D levels	Multivariate adjusted** OR (95% CI) D 15–29 ng/ml	Multivariate adjusted** OR (95% CI) D <15	p-trend
Mite (n=712/3121)	-0.13 (-0.19 to -0.07) ^a	-0.04 (-0.1 to 0.1)	1.46 (0.86, 2.48)	1.76 (0.89, 3.50)	0.09
Mite 2 (n=723/3136)	-0.14 (-0.20 to -0.08) ^a	-0.04 (-0.1 to 0.1)	1.33 (0.77, 2.27)	1.54 (0.79, 3.01)	0.18
Cat (n=397/3136)	-0.01 (-0.08 to 0.05)	-0.01 (-0.1 to 0.1)	1.44 (1.04, 2.00) [†]	1.40 (0.76, 2.60)	0.11
Dog (n=484/3136)	-0.03 (-0.09 to 0.02)	-0.01 (-0.1 to 0.1)	1.58 (0.98, 2.56)	2.32 (1.19, 4.54) [†]	0.01
Cockroach (n=443/3133)	-0.12 (-0.15 to -0.10) ^a	-0.04 (-0.1 to -0.02) [†]	1.94 (0.87, 4.31)	2.80 (1.16, 6.78) [†]	0.01
Alternaria (n=418/3132)	-0.05 (-0.11 to 0.01)	-0.002 (-0.1 to 0.1)	1.47 (0.79, 2.71)	2.20 (1.05, 4.62) [†]	0.04
Aspergillus (n=317/2766)	-0.05 (-0.09 to -0.002) [†]	-0.003 (-0.06 to 0.06)	1.96 (0.94, 4.10)	2.31 (0.96, 5.61)	0.06
Peanut (n=356/3132)	-0.07 (-0.11 to -0.03) [†]	-0.05 (-0.1 to -0.003) [†]	1.82 (1.07, 3.10) [†]	2.39 (1.29, 4.45) [†]	0.005
Egg (n=147/3064)	0.001 (-0.001 to 0.026)	0.01 (-0.007 to 0.03)	0.94 (0.44, 2.03)	0.78 (0.28, 2.16)	0.71
Milk (n=325/3098)	-0.001 (-0.027 to 0.025)	-0.005 (-0.02 to 0.02)	1.40 (0.95, 2.07)	1.16 (0.60, 2.24)	0.31
Shrimp (n=241/2767)	-0.06 (-0.07 to -0.04) ^a	-0.01 (-0.04 to 0.02)	2.31 (0.97, 5.49)	3.08 (1.16, 8.19) [†]	0.02
Ragweed (n=542/2769)	-0.06 (-0.13 to -0.003) [†]	-0.03 (-0.09 to 0.04)	1.57 (1.07, 2.30) [†]	1.83 (1.20, 2.80) [†]	0.005
Ryegrass (n=738/2769)	-0.16 (-0.28 to -0.04) [†]	-0.07 (-0.2 to 0.03)	1.48 (1.11, 1.98) [†]	1.77 (1.07, 2.95) [†]	0.02
Bermuda grass (n=586/2769)	-0.13 (-0.23 to -0.03) [†]	-0.09 (-0.2 to -0.02) [†]	1.48 (1.02, 2.17) [†]	1.96 (1.08, 3.57) [†]	0.03
Oak (n=459/2768)	-0.10 (-0.17 to -0.03) [†]	-0.06 (-0.1 to -0.01) [†]	2.29 (1.51, 3.48) [†]	4.75 (1.53, 4.94) [†]	0.001
Birch (n=392/2768)	-0.07 (-0.13 to -0.01) [†]	-0.05 (-0.09 to -0.01) [†]	1.44 (0.98, 2.13)	2.04 (1.07, 3.87) [†]	0.03
Thistle (n=438/2764)	-0.07 (-0.14 to 0.004)	-0.04 (-0.1 to 0.03)	1.67 (1.02, 2.73) [†]	2.10 (1.12, 3.92) [†]	0.02
Total high IgE (n=747/3136)	-0.2 (-0.3 to -0.1) [†]	-0.06 (-0.2 to 0.01)	1.42 (0.96, 2.08)	1.43 (0.90, 2.27)	0.08
Allergy (n=1635/2771)	N/A	N/A	1.17 (0.85, 1.61)	1.21 (0.77, 1.90)	0.33
Perennial (n=1266/2748)	N/A	N/A	1.40 (0.90, 2.18)	1.80 (1.08, 3.00) [†]	0.03
Pollen (n=923/2765)	N/A	N/A	1.39 (1.09, 1.78) [†]	1.59 (0.96, 2.63)	0.04

* Individual allergen Ns differ due to lack of testing of <6 year olds and due to some allergens not being tested in all participants due to inadequate serum

Adjusted for age, sex, race/ethnicity, obesity, low socioeconomic status, milk intake, TV, videogame and computer use, serum cotinine levels and Vitamin D supplement use

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[†] p-value <0.05,

[‡] p-value <0.01

^a p-value <0.001

β coefficients represent increase in log IgE level per 10 ng/mL increase in 25(OH)D

Associations between total and antigen-specific IgE levels and 25(OH)D levels < 15 ng/mL and 15–29 ng/mL compared to reference group (≥ 30 ng/mL) and continuous vitamin D for all adults aged >21 years

Table 4

Allergen (number with allergic sensitization/ total number tested)	Unadjusted β coefficient (95% CI) for log transformed IgE levels and continuous 25(OH)D levels	Multivariable adjusted β coefficient (95% CI) for log transformed IgE levels and continuous 25(OH)D levels	Multivariate adjusted** OR 25(OH)D 15–29 ng/mL	Multivariate adjusted** OR 25(OH)D <15 ng/mL	p-trend
Mite (n=645/3453)	–0.006 (–0.05 to 0.04)	0.02 (–0.02 to 0.08)	0.83 (0.63, 1.10)	0.72 (0.46, 1.13)	0.13
Mite 2 (n=650/3453)	–0.005 (–0.05 to 0.04)	0.03 (–0.02 to 0.07)	0.94 (0.72, 1.21)	0.92 (0.60, 1.41)	0.67
Cat (n=369/3453)	0.02 (–0.03 to 0.07)	0.009 (–0.05 to 0.07)	0.89 (0.67, 1.19)	0.96 (0.66, 1.40)	0.32
Dog (n=350/3453)	0.002 (–0.03 to 0.04)	0.004 (–0.04 to 0.05)	0.71 (0.53, 0.96) [†]	0.71 (0.43, 1.18)	0.16
Cockroach (n=428/3449)	–0.04 (–0.07 to –0.008) [†]	0.007 (–0.03 to 0.04)	0.64 (0.43, 0.94) [†]	0.69 (0.38, 1.25)	0.30
Alternaria (n=246/3443)	0.02 (–0.02 to 0.06)	0.02 (–0.04 to 0.07)	0.73 (0.47, 1.12)	0.67 (0.36, 1.26)	0.19
Aspergillus (n=221/3442)	–0.02 (–0.03 to 0.001)	–0.001 (–0.02 to 0.02)	0.80 (0.41, 1.53)	0.74 (0.36, 1.52)	0.40
Peanut (n=267/3443)	0.01 (–0.013 to 0.04)	0.04 (–0.001 to 0.07)	0.68 (0.40, 1.17)	0.55 (0.24, 1.27)	0.15
Egg (n=95/3364)	–0.002 (–0.02 to 0.01)	–0.005 (–0.03 to 0.02)	1.32 (0.63, 2.77)	1.02 (0.28, 3.84)	0.95
Milk (n=133/3404)	–0.01 (–0.03 to 0.003)	–0.02 (–0.04 to 0.002)	1.20 (0.71, 2.03)	1.97 (0.81, 4.79)	0.13
Shrimp (n=226/3441)	–0.03 (–0.05 to –0.008) [‡]	–0.006 (–0.02 to 0.01)	0.75 (0.51, 1.09)	0.74 (0.44, 1.23)	0.28
Ragweed (n=546/3444)	0.05 (–0.02 to 0.11)	0.07 (–0.01 to 0.1)	0.68 (0.46, 1.00) [†]	0.60 (0.40, 0.89) [†]	0.02
Ryegrass (n=690/3443)	–0.004 (–0.07 to 0.06)	0.02 (–0.06 to 0.1)	0.82 (0.64, 1.04)	0.78 (0.54, 1.12)	0.16
Bermuda grass (n=530/3443)	–0.02 (–0.08 to 0.04)	0.01 (–0.06 to 0.09)	0.85 (0.62, 1.16)	0.95 (0.66, 1.36)	0.78
Oak (n=377/3443)	0.03 (–0.02 to 0.08)	0.04 (–0.02 to 0.1)	0.77 (0.53, 1.12)	0.65 (0.38, 1.12)	0.12
Birch (n=308/3443)	0.05 (–0.002 to 0.1)	0.05 (–0.01 to 0.1)	0.79 (0.53, 1.17)	0.68 (0.41, 1.13)	0.11
Thistle (n=387/3440)	0.007 (–0.04 to 0.05)	0.02 (–0.03 to 0.08)	0.93 (0.67, 1.29)	0.85 (0.44, 1.65)	0.62
Total high IgE (n=597/3454)	–0.19 (–0.28 to –0.11) ^a	–0.06 (–0.1 to 0.03)	1.13 (0.92, 1.39)	1.18 (0.82, 1.71)	0.38
Allergy (n=1541/3454)	N/A	N/A	1.05 (0.83, 1.32)	0.97 (0.69, 1.35)	0.85
Perennial (n=1157/3432)	N/A	N/A	0.94 (0.76, 1.16)	0.87 (0.59, 1.29)	0.47
Pollen (n=913/3440)	N/A	N/A	0.81 (0.60, 1.09)	0.76 (0.54, 1.08)	0.11

* Individual allergen Ns differ due to lack of testing of <6 year olds and due to some allergens not being tested in all participants due to inadequate serum

** Adjusted for age, sex, race/ethnicity, obesity, low socioeconomic status, milk intake, TV, videogame and computer use, serum cotinine levels and Vitamin D supplement use

[†] p-value <0.05,

[†] p-value <0.01
^a p-value <0.001

β coefficients represent increase in log IgE level per 10 ng/mL increase in 25(OH)D

Table 5

Prevalence of allergic symptoms by 25-hydroxyvitamin D levels and multivariable adjusted* associations between allergic symptoms and vitamin D levels for all children and adolescents ages 1–21 years of age (n= 3121) (top panel) and adults >21 years of age (n=3517) (bottom panel)

Allergy assessed	25(OH)D ≥ 30 ng/ml	25(OH)D 15–29 ng/ml	25(OH)D <15 ng/ml	Multivariate adjusted* OR 25(OH)D 15–29 ng/ml	p-value	Multivariate adjusted* OR 25(OH)D <15	p-value	p-trend
Prevalence of symptoms in children and adolescents, % (SE)								
Any allergy	22.2 (2.4)	28.0 (1.9)	30.7 (3.2)	1.50 (1.04, 2.17)	0.03	1.79 (1.10, 2.93)	0.02	0.02
Hayfever	2.9 (1.1)	4.4 (0.9)	4.4 (1.3)	1.73 (0.83, 3.58)	0.13	1.82 (0.60, 5.53)	0.27	0.17
Eczema	13.1 (2.2)	11.5 (1.0)	11.3 (1.4)	0.93 (0.62, 1.40)	0.71	1.08 (0.65, 1.78)	0.75	1.00
Pet avoidance due to sx.	4.7 (1.6)	6.0 (0.8)	2.9 (1.2)	1.27 (0.53, 3.04)	0.51	0.40 (0.10, 1.64)	0.97	0.51
Prevalence of symptoms in adults % (SE)								
Any allergy	34.2 (2.4)	34.7 (1.2)	33.8 (2.4)	1.14 (0.88, 1.49)	0.29	1.27 (0.82, 1.98)	0.26	0.26
Hayfever	17.4 (2.2)	13.5 (1.3)	8.7 (1.1)	0.79 (0.51, 1.22)	0.26	0.59 (0.31, 1.14)	0.11	0.11
Eczema	7.2 (1.5)	8.2 (1.1)	5.5 (1.0)	1.29 (0.78, 2.13)	0.30	0.88 (0.48, 1.64)	0.67	0.79
Pet avoidance due to sx.	7.9 (1.3)	7.0 (1.0)	4.6 (0.9)	0.95 (0.57, 1.60)	0.85	0.59 (0.31, 1.10)	0.09	0.12

* Adjusted for age, sex, race/ethnicity, obesity, low socioeconomic status, milk intake, TV, videogame and computer use, serum cotinine levels and Vitamin D supplement use
SE: standard error