

# **Association of Vitamin D and Dental Caries in Children using NHANES 2005–2006 Data**

**Karin Herzog**

A thesis  
submitted in partial fulfillment of the  
requirements for the degree of

Masters of Science in Dentistry

University of Washington

2015

Committee:

Ana Lucia Seminario

JoAnna Scott

Philippe Hujoel

Program Authorized to Offer Degree:  
Pediatric Dentistry

©Copyright 2015

Karin Herzog

University of Washington

**Abstract**

Association of Vitamin D and Dental Caries in Children using NHANES 2005–2006 Data

Karin Herzog

Chair of the Supervisory Committee:  
Ana Lucia Seminario DDS, PhD  
Pediatric Dentistry

**Purpose:** This study seeks to determine associations between serum vitamin D levels and dental caries in non-institutionalized U.S. children ages 5-12.

**Methods:** National Health and Nutrition Examination Survey 2005-2006 was utilized. Vitamin D deficiency and inadequacy were defined according to the Institute of Medicine 2011 guidelines. Associations between vitamin D and caries were examined after adjustment for relevant confounders using multivariate logistic regression at a critical value of 5%. Sample weights were used to generate nationally representative estimates.

**Results:** The overall prevalence of vitamin D deficiency and vitamin D inadequacy among 5–12 year olds was 3% and 16%, respectively. Prevalence of vitamin D deficiency was greater among Blacks (13%), females (3%), severe asthmatics (10%), those of lower ratio of family income to poverty threshold (4%), who had public health insurance (4%), were not physically active (7%), consumed less than 1 milk product per week (6%) and spent 5 or more hours watching television, playing videos games or on the computer (5%). Prevalence of dental caries among 5–12 year olds with sufficient vitamin D levels was 19%. Prevalence of vitamin D deficiency and inadequacy among children with dental caries was 3% and 18%, respectively. No significant association was found between vitamin D deficiency ( $P=.839$ ) or inadequacy ( $P=.984$ ) and dental caries.

**Conclusions:** Our findings do not provide convincing evidence of a relationship between vitamin D exposure and dental caries, but nor does it provide convincing evidence to the contrary. Interventional studies are needed to further examine this topic.

## Introduction

Vitamin D is a hormone precursor that controls calcium absorption into the small intestine, mediates skeletal mineralization and maintains calcium hemostasis in the blood stream (Kulie et al., 2009). Vitamin D is naturally produced in certain plants and fish (Holick, 2007) and can be found in supplements or fortified foods, such as milk products, juices, and breakfast cereals (Bailey et al., 2010). It is also synthesized in the skin after exposure to ultraviolet B rays of sunlight. Although Vitamin D is known mainly for its role in calcium hemostasis, it has been found to be associated with various conditions and diseases. Theodoratou et al. (Theodoratou et al., 2014)'s umbrella review of vitamin D and health outcomes found suggestive evidence (evidence from randomized controlled trials with an effect at  $0.001 \leq p \leq 0.05$  or evidence from meta-analyses of observational studies showing an association of  $p \leq 0.001$ ) of relation between high vitamin D concentrations or vitamin D supplementation and decreased risk of colorectal cancer, non-vertebral fractures, cardiovascular disease, hypertension, stroke, depression, body mass index, and type II diabetes.

Vitamin D exposures in early life may also play a role in dental caries prevention. Dental caries has remained the most prevalent chronic disease of childhood, five times more frequent than asthma and seven times more common than hay fever (U.S. Department of Health and Human Services [DHHS], 2000). Scroth et al. (Scroth et al., 2013) found that caries-free children were twice as likely to have serum 25-hydroxyvitamin D (25(OH)D) concentrations  $\geq 30$  ng/ml and those with severe early childhood caries were at nearly three times the odds of having levels below 14 ng/ml. Furthermore, Hujoel found that supplemental Vitamin D was associated with a 47% reduced risk of caries (Hujoel, 2013). Theodoratou et al. (Theodoratou et al., 2014)'s categorized Hujoel's findings as probable evidence (significant evidence from both observational studies and randomized controlled trials at  $p \leq 0.001$ ) of relation between high vitamin D

concentrations or vitamin D supplementation and decreased risk of dental caries in children. However, vitamin D supplementation was ineffective after the age of 13 years, particularly for girls, suggesting that growth and variations in body fat may influence the way vitamin D is stored and metabolized and alter the effectiveness of the fat-soluble vitamin D in caries prevention (Hujoel, 2013).

Possible mechanisms by which vitamin D decreases dental caries includes improved tooth development (Scroth et al., 2013; Hujoel, 2013) and better dentinal mineralization responses to caries. Ameloblasts and odontoblasts are target cells for 1,25-dihydroxyvitamin D, the active form of vitamin D. Thus, vitamin D plays a role in enamel and dentin formation (Berdal, 2005). Deficiency in vitamin D during periods of tooth development may result in developmental defects (Berdal, 2005; Scroth et al., 2013), such as enamel hypoplasia (Purvis, 1973; Cockburn, 1980), a significant risk factor for dental caries (Hong, 2009; Pascoe, 1994) and for early childhood caries (Scroth et al., 2013). Vitamin D also has an immunological role as it can induce the production of antimicrobial peptides such as cathelicidin and certain defensins, which protect from oral pathogens (Grant, 2011; Hewison, 2010; Griffin et al., 2003; Scroth et al., 2013).

Multiple studies have analyzed the relationship of dental caries and vitamin D levels (Schroth et al., 2012; Schroth et al., 2014; Mellanby, 1928; Mellanby, 1934; Dietrich, 2004; Grant, 2008; Grant, 2011; Hildebolt, 2005; Hujoel, 2013). However, to our knowledge, none have looked at the relationship of dental caries and vitamin D on a national scale in the pediatric population. Thus, this study sets out to determine the association between serum vitamin D levels and dental caries in non-institutionalized children in the United States, between the ages of 5 and 12.

## **Methods**

### **Study Population**

This study examined civilian non-institutionalized U.S. children, between the ages of 5 to 12, who participated in the 2005–2006 National Health and Nutrition Examination Survey (NHANES). NHANES is a stratified, multistage, probability sample survey conducted annually by the National Center for Health Statistics. NHANES excludes all people in supervised care or custody in institutional settings, all active-duty military personnel, active-duty family members living overseas, and any other U.S. citizens residing outside the 50 states and the District of Columbia (Johnson et al., 2013). The 2005–2006 data set was chosen because the most recently released Vitamin D NHANES data is from 2005–2006. The age range of 5 to 12 was chosen because children under age 5 were not eligible for NHANES oral health examinations. Because NHANES data are de-identified, the institutional review board of the University of Washington, Seattle, waived review of this study.

### **Variables**

Demographic variables:

Demographic data for children under 12 years old was collected by parental/guardian report during in-person NHANES interviews. Demographic variables in the current analysis include age, gender, race/ethnicity, health insurance and ratio of family income to poverty threshold. Age was measured in years. Race was categorized as non-Hispanic White, non-Hispanic Black, Hispanic and other. Health insurance was categorized into no health insurance,

private health insurance or public insurances. The ratio of family income to poverty threshold was categorized as <1.00, 1.00 – <2.00, 2.00 – <5.00 and >5.00.

Dental variables (Center for Disease Control, 2009):

The dental examinations in NHANES were conducted by registered dental hygienists, who were trained by licensed dentists with expertise in conducting dental surveys. During the basic screening exam (BSE) the dental examiner assessed study participants with a disposable dental mirror (no tactile assessment with an explorer) and determined whether untreated decay and restorations were present, not present or could not be assessed.

Three dental variables were used in this study: untreated dental decay, dental restorations and overall caries experience. All three were classified in NHANES as binary variables. The presence of dental decay was defined in NHANES as at least one tooth with untreated decay. The tooth or teeth could be primary or permanent. Untreated decay was a cavity in a tooth that appeared as a darkened fracture with irregular breakdown of the enamel surface of the tooth. The area may have appeared soft-spongy in texture. The following were not considered decay: teeth with stains or pigmentations, stained occlusal pit or fissures with no apparent breakdown of the enamel structure, white spot lesions, dark, shiny and pitted areas of enamel and tooth wear or erosion. The presence of a dental restoration was defined as the presence of at least one tooth with a restoration. A dental restoration was a filling in a tooth that could be silver amalgam, yellow or white gold, metal crown, a temporary filling, restorative materials using tooth-colored porcelain, ceramic or composite resins. Fractured or missing fillings were scored as if the restoration was intact. The following were not considered restorations: sealants, denture teeth and crowns that were placed because of malformations, esthetics or traumatic injuries.

Caries experience combines untreated dental decay and restorations present into one variable.

#### Body Measures:

During the physical examination, each participant's height and weight were measured using standardized protocols and calibrated instruments. Weight was measured in kilogram (kg) and standing height in cm. Body mass index (BMI) was calculated as weight in kilograms divided by height in meters squared ( $\text{kg}/\text{m}^2$ ). In this analysis, obesity and overweight variables were calculated using the Center for Disease Control (CDC) BMI cutoffs by age and gender. Obesity was defined as BMI greater than or equal to the 95th percentile by age and gender and overweight was defined as a BMI between the 85th and 95th percentiles by age and gender. Healthy-weight was defined as BMI between the 5th and 85th percentile and underweight was defined as BMI less than the 5th percentile.

#### Asthma:

During household interviews participants were asked the following asthma related questions: "do you still have asthma," "had asthma attack in past year," and "had emergency care visit for asthma in the past year?" These are self reported characteristics.

#### Physical activity:

Duration of physical activity per week was determined from the mean number of times per day that respondents reported "playing or exercising enough to sweat or breathe hard". In this

analysis, physical activity was categorized as none, less than one time per day, one time per day or greater than once per day.

#### Milk consumption:

Milk intake was assessed from the diet, behavior and nutrition section of the NHANES sample person questionnaire. Past 30 day milk product consumption was determined by the following question: "In the past 30 days, how often did {you/SP} have milk to drink or on {your/his/her} cereal? Please include chocolate and other flavored milks as well as hot cocoa made with milk. Do not count small amounts of milk added to coffee or tea." In this analysis, milk consumption was categorized as less than one time per week, between once a week to less than once per day and once per day.

#### Time spent watching television, playing videos games or on the computer:

During household interviews, participants were asked about hours spent watching television, playing video games and using the computer. Combined television, video and computers hours were categorized as 0 to 2 hours, 3 to 4 hours and greater than 4 hours.

#### Vitamin D

In NHANES, serum 25-hydroxyvitamin D (25(OH)D) measurements were performed on venous blood samples collected in mobile examination centers by using standardized protocols. Measurements were performed by using the DiaSorin radioimmunoassay kit (Stillwater, MN) at the National Center for Environmental Health, Centers for Disease Control and Prevention (CDC; Atlanta, GA).

In this analysis, vitamin D deficiency was defined by using the Institute of Medicine 2010 report. Vitamin D Deficiency was defined as serum 25(OH)D less than 12 ng/mL. Vitamin D inadequacy was defined as serum 25(OH)D between 12 and 19 ng/mL. Sufficient vitamin D was defined as serum 25(OH)D between 20 and 50 ng/mL. Possibly harmful vitamin D levels was defined as serum 25(OH)D greater than 50 ng/mL (IOM 2011).

### **Data Analysis**

Prevalence rates were used to examine the distribution of vitamin D deficiency, inadequacy, sufficiency and possibly harmful vitamin D. Unadjusted and adjusted slopes were estimated from linear regression to examine the association between vitamin D and body measures. The linear regression analysis was adjusted by age, gender, race/ethnicity and ratio of family income to poverty threshold. Adjusted and unadjusted odds ratios (OR) from logistic regression examined the association between vitamin D and asthma, as well as vitamin D and dental caries. The multivariate logistic regression analyzing the association between vitamin D and dental caries was adjusted by age, race/ethnicity and ratio of family income to poverty threshold. The regression analyzing the association between vitamin D and asthma was adjusted by age, race/ethnicity, ratio of family income to poverty threshold and physical activity.

Data analysis was performed using statistical software (STATA Version 12.1, Stata-Corp, College Station, Texas). Survey sampling methods adjusted for appropriate sampling weights were utilized for all analysis. Weighting schemes allow estimates to reflect the relative proportions in the population as a whole. For this analysis, an  $\alpha < 0.05$  was considered statistically significant.

## Results

The overall prevalence of vitamin D deficiency and vitamin D inadequacy among 5–12 year olds was 2.54% (95% CI: 1.62–3.98) and 16.2% (95% CI: 12.91–20.13) respectively. The prevalence of dental caries among 5–12 year olds with sufficient vitamin D levels was 19.13% (95% CI: 12.93–25.33). The prevalence of vitamin D deficiency among 5–12 year olds was greater among Non-Hispanic Blacks (12.58% [95% CI: 8.03–19.17]), females (3.42% [95% CI: 2.28–5.09]), those of lower ratio of family income to poverty threshold (4.56% [95% CI: 2.26–8.99]), and children who had public health insurance (3.51% [95% CI: 2.02–6.02]). The prevalence of vitamin D inadequacy was greater among Non-Hispanic Blacks (36.94% [95% CI: 32.36–41.76]), females (19.03% [95% CI: 14.67–24.31]), children with lower ratio of family income to poverty threshold (22.24% [95% CI: 17.31–28.10]), and those who had no insurance (22.73% [95% CI: 14.62–33.57]). Non-Hispanic Whites (91.80% [95% CI: 87.05–94.91]), males (83.57% [95% CI: 79.71–86.81]), those with higher ratio of family income to poverty threshold (90.62% [95% CI: 83.05–95.01]), and children with private health insurance (83.13% [95% CI: 77.72–87.44]) had a higher prevalence of sufficient vitamin D (Table 1).

The prevalence of vitamin D deficiency among underweight, healthy-weight, overweight and obese was 5.41% (95% CI: 1.35–19.34), 1.55% (95% CI: 0.85–2.79), 4.41% (95% CI: 2.51–7.62) and 3.91% (95% CI: 2.10–7.16), respectively (Table 2). The prevalence of inadequate vitamin D among underweight, healthy-weight, overweight and obese was 12.87% (95% CI: 3.42–38.14), 13.39% (95% CI: 9.71–18.18), 20.42% (95% CI: 13.28–30.07) and 22.17% (95% CI: 15.47–30.72), respectively. The prevalence of vitamin D deficiency and inadequacy among children with dental caries was 2.75% (95% CI: 1.45–5.16) and 18% (95% CI: 10.96–28.14), respectively. The prevalence of vitamin D deficiency and inadequacy among children with

dental restorations was 2.16% (95% CI: 1.22–3.79) and 15.11% (95% CI: 10.77–20.78), respectively. The prevalence of vitamin D deficiency and inadequacy among children with caries or restoration was 2.37% (95% CI: 1.37–4.05) and 15.79% (95% CI: 11.67–21.02), respectively. The prevalence of vitamin D deficiency and inadequacy among children without active caries was 2.48% (95% CI: 1.31–3.65) and 15.93% (95% CI: 12.12–19.74), respectively (Table 2).

The prevalence of vitamin D deficiency was greater among severe asthmatics, who had an emergency visit for asthma within the last year (10.33% [95% CI: 4.05–23.93]) (Table 2). In addition, the prevalence of vitamin D deficiency was greater among children who were not physically active (6.86% [95% CI: 1.39–27.73]), who consumed less than 1 milk product per week (5.84% [95% CI: 1.75–17.72]) and who spent 5 or more hours of watching television, playing videos games or on the computer (5.38% [95% CI: 2.36– 11.77]) (Table 3).

Multivariate logistic regression analysis indicated no significant association between vitamin D deficiency and dental caries or vitamin D inadequacy and dental caries. Dental caries is a binary variable, classified as either having at least one tooth with untreated dental decay or not having any active caries. This association was still not significant after stratifying by either having no history of sealants or at least one tooth with a sealant. Furthermore, this association was not significant after adjusting the multivariable logistic regression model for age, race/ethnicity, and ratio of family income to poverty threshold (Table 4).

There was a significant association between vitamin D deficiency and asthma ( $p = 0.019$ ) after adjusting for age, race/ethnicity, gender, ratio of family income to poverty threshold, and physical activity. The odds of having asthma in a child who was vitamin D deficient was 0.137 (95% CI: 0.027–0.691) times the odds of having asthma in a child with sufficient vitamin D levels (Table 5).

The multivariate linear regression model, which was adjusted for age, gender, race/ethnicity, and ratio family income to poverty threshold, indicated a significant association between vitamin D inadequacy and BMI ( $p = 0.023$ ), vitamin D inadequacy and weight ( $p = 0.008$ ), and vitamin D inadequacy and standing height ( $p = 0.001$ ). Having inadequate vitamin D levels increased BMI, weight and standing height by  $0.808 \text{ kg/m}^2$  (95% CI: 0.128–1.487) ,  $2.712 \text{ kg}$  (95% CI: 0.818–4.605) and  $2.12 \text{ cm}$  (95% CI: 1.067–3.177), respectively, compared to having sufficient vitamin D levels. In addition, overall vitamin D level was significantly associated with weight ( $p = 0.03$ ) and standing height ( $p = 0.0005$ ). Potentially harmful vitamin D levels was significantly associated with standing height ( $p = 0.001$ ). A child with harmful levels of vitamin D was on average  $4.6 \text{ cm}$  (95% CI: 2.220–6.925) taller than a child with sufficient vitamin D (Table 6).

## **Discussion**

This is the first study, to our knowledge, in which researchers have examined the association between vitamin D and dental caries in a nationally representative sample of U.S. children. Since dental caries remains the most common chronic disease in childhood (U.S. Department of Health and Human Services [DHHS], 2000), efforts to prevent caries beyond the oral cavity should be investigated. Vitamin D may aid in preventing dental caries through its role in enamel and dentin formation (Berdal, 2005) and production of antimicrobial peptides, which protect from oral pathogens (Grant, 2011; Hewison, 2010; Griffin et al., 2003; Scroth et al., 2013). Furthermore, interventions that provide adequate levels of vitamin D could decrease the prevalence of dental caries in children, while impacting other health outcomes.

Admittedly, the 25(OH)D levels recommended as cutoffs to define vitamin D deficiency and inadequacy are controversial and differ between the US IOM report and the US Endocrine Society guideline. The US Endocrine Society guideline defines vitamin D deficiency as serum 25(OH)D level below 20 ng/ml and vitamin D insufficiency as 25(OH)D between 21 and 29 ng/ml (Hollick et al., 2011). On the other hand, the US IOM report defines vitamin D deficiency as serum 25(OH)D less than 12 ng/mL and vitamin D inadequacy as serum 25(OH)D between 12 and 19 ng/mL (IOM 2011). The differences in the specification of cut-points for serum 25(OH)D levels reflect different views on current evidence, and have serious ramifications for the prevalence of vitamin D, public policy and clinical practice (IOM 2011). This study uses the US IOM guideline definitions. Utilizing the US Endocrine Society guideline cutoffs would have inflated the prevalence results and altered our conclusions.

Multiple studies have suggested that vitamin D can prevent caries onset and progression. Much of the early research assessing the relationship between vitamin D and caries was conducted by May Mellanby, who identified an association between vitamin D supplementation and reduced caries risk (Mellanby & Pattison 1928, Mellanby 1937). More recent analyses have found that children with caries were significantly more likely to have low vitamin D concentrations (Schroth et al. 2013). Kuhnisch et al. found that a 4 ng/ml increase in serum 25(OH)D concentrations was significantly associated with a lower odds ratio of having hypomineralized teeth (Kuhnisch et al., 2014). Furthermore, higher 25(OH)D values were associated with a reduced incidence of caries (Hujoel, 2013; Kuhnisch et al., 2014).

Our findings on vitamin D deficiency and dental caries were in the direction hypothesized; however, we did not observe statistically significant associations between vitamin D deficiency and dental caries. This is likely due to several important study limitations. We were

limited by a lack of information on several potential important confounders, including the season of measurement of 25(OH)D levels, lack of information on sun exposure, fluoride exposure, detailed geographic data and location of participants' home. In addition, like most population-based sample surveys, NHANES experiences both participant and component non-response biases (Johnson et al., 2013).

Another limitation of the study includes the way caries and restorations were diagnosed and classified in NHANES. In NHANES 2005-2006 the presence of caries or restorations was diagnosed by visual examination, without radiographs or tactile exploration of teeth. Thus, the results underestimate the true prevalence of caries. Furthermore, the caries and restoration variables were binary variables, coded as either having the presence of at least one tooth with caries or restoration or no teeth with dental caries or restorations, respectively. Therefore, it was not possible to model caries as a continuous variable or know which tooth, type of tooth (primary or permanent) or tooth surface had caries. With more detailed caries information, we could have further explored the relationship between vitamin D and caries.

Our findings of a significant association between vitamin D deficiency and asthma are consistent with a large existing body of literature. Numerous studies have found vitamin D deficiency associated with wheezing, lower lung function and reduced asthma control in childhood (Brehm et al., 2009; Brehm et al., 2010; Camargo et al., 2011; Chinellato et al., 2010; Chinellato et al., 2011; Freishtat et al., 2010; Hughes et al., 2010; Hyponnen et al., 2004; Searing et al., 2010). Vitamin D deficiency is also associated with an increased risk of severe asthma exacerbations and asthma related hospitalizations (Brehm et al., 2010). Several studies have reported that lower maternal vitamin D status during pregnancy or early childhood increases the risk of asthma in the offspring (Camargo et al., 2007; Miyake et al., 2010; Devereux et al., 2007; erkkola et al., 2009; Sutherland et al., 2010). Analysis of the Third NHANES from 1988 to 1994, indicates that high vitamin D concentration is associated with better lung function as

measured by forced expiratory volume in 1 second and forced vital capacity (Black & Scrag, 2005). Vitamin D's ability to regulate inflammation (Searing & Leung, 2010; Mahon et al, 2003; Xystrakis et al., 2006) or induce antimicrobial peptides (De Smet & Contreras, 2005) may explain the mechanism by which it can improve asthma and lung function.

Similarly, our findings of a significant association between vitamin D inadequacy and body measures are supported by existing research. Vitamin D is vital to skeletal growth and development. Specifically, vitamin D deficiency has been found to be significantly associated with shorter stature (Kremer, 2009; Pettifor, 2005; Hatun et al., 2005), muscle weakness (Simpson et al., 1985; Foo et al., 2009; Ward et al., 2009; Visser et al., 2003), decreased rate of bone mass accumulation (Outila et al., 2001; Cheng et al., 2003) and growth retardation, which is often manifested by bone abnormalities such as seen in rickets and osteomalacia (Holick, 2006; Foo et al., 2009). Theodoratou et al. found suggestive evidence (i.e. evidence from randomized controlled trials with an effect at  $0.001 \leq p \leq 0.05$  or evidence from meta-analyses of observational studies showing an association of  $p \leq 0.001$ ) of relation between high vitamin D concentrations or vitamin D supplementation and increased levels of head circumference at birth, bone mineral density in the femoral neck, muscle strength, body mass index and non-vertebral fractures.

Vitamin D deficiency impacts multiple health outcomes, especially in children. Thus, interventions that provide adequate levels of vitamin D, as well as current and ongoing investigations on the role of vitamin D, can help improve the overall wellbeing of children. Further studies are needed to explore these areas.

## **Conclusion**

Our findings add to a growing body of knowledge of childhood vitamin D levels and dental caries. The findings of this study do not provide convincing evidence of a relationship between vitamin D exposure and dental caries, but nor does it provide convincing evidence to the contrary. More interventional studies are needed to further examine this topic.

## References

Bailey RL, Dodd KW, Goldman JA, Gahche JJ, Dwyer JT, Moshfegh AJ, Sempos CT, Picciano MF. Estimation of total usual calcium and vitamin D intakes in the United States. *J Nutr.* 2010 Apr;140(4):817-22. doi: 10.3945/jn.109.118539. Epub 2010 Feb 24.

Berdal A, Bailleul-Forestier I, Davideau J, et al: Dento-alveolar bone complex and vitamin D. In *Vitamin D*. Edited by Feldman D, Pike J, Glorieux F. Burlington: Elsevier Academic Press; 2005:599–607.

Black PN, Scragg R. Relationship between serum 25-hydroxyvitamin d and pulmonary function in the third national health and nutrition examination survey. *Chest.* 2005;128:3792–8.

Brehm JM, Celedon JC, Soto-Quiros ME, Avila L, Hunninghake GM, Forno E, Laskey D, Sylvia JS, Hollis BW, et al. Serum vitamin D levels and markers of severity of childhood asthma in Costa Rica. *Am J Respir Crit Care Med.* 2009;179:765–71.

Brehm JM, Schuemann B, Fuhlbrigge AL, Hollis BW, Strunk RC, Zeiger RS, Weiss ST, Litonjua AA. Serum vitamin D levels and severe asthma exacerbations in the Childhood Asthma Management Program study. *J Allergy Clin Immunol.* 2010;126:52–58 e55.

Camargo CA Jr, Ingham T, Wickens K, Thadhani R, Silvers KM, Epton MJ, Town GI, Pattermore PK, Espinola JA, et al. Cord-blood 25-hydroxyvitamin D levels and risk of respiratory infection, wheezing, and asthma. *Pediatrics.* 2011;127:e180–7.

Camargo CA Jr, Rifas-Shiman SL, Litonjua AA, Rich-Edwards JW, Weiss ST, Gold DR, Kleinman K, Gillman MW. Maternal intake of vitamin D during pregnancy and risk of recurrent wheeze in children at 3 y of age. *Am J Clin Nutr.* 2007;85:788–95.

Center for Disease Control (2009). National Health and Nutrition Examination Survey (NHANES) Oral Health Examiners Manual. Retrieved December 14, 2013 from [http://www.cdc.gov/nchs/data/nhanes/nhanes\\_09\\_10/OralHealth\\_Examiners.pdf](http://www.cdc.gov/nchs/data/nhanes/nhanes_09_10/OralHealth_Examiners.pdf)

Cheng S, Tylavsky F, Kroger H, Karkkainen M, Lyytikainen A, Koistinen A, Mahonen A, Alen M, Halleen J, Vaananen K, Lamberg-Allardt C. Association of low 25-hydroxyvitamin D concentrations with elevated parathyroid hormone concentrations and low cortical bone density in early pubertal and prepubertal Finnish girls. *Am J Clin Nutr.* 2003; 78:485–492.

Chinellato I, Piazza M, Sandri M, Peroni DG, Cardinale F, Piacentini GL, Boner AL. Vitamin D serum levels and exercise-induced bronchoconstriction in children with asthma. *Eur Respir J.* Epub 2010 Nov 11.

Chinellato I, Piazza M, Sandri M, Peroni D, Piacentini G, Boner AL. Vitamin D serum levels and markers of asthma control in Italian children. *J Pediatr.* 2011;158:437–41.

Cockburn F, Belton NR, Purvis RJ, et al. Maternal vitamin D intake and mineral metabolism in mothers and their newborn infants. *Br Med J.* 1980;281:11–14.

De Smet K, Contreras R. Human antimicrobial peptides: defensins, cathelicidins and histatins.

*Biotechnol Lett.* 2005;27:1337–47.

Devereux G, Litonjua AA, Turner SW, Craig LC, McNeill G, Martindale S, Helms PJ, Seaton A,

Weiss ST. Maternal vitamin D intake during pregnancy and early childhood wheezing. *Am J Clin*

*Nutr.* 2007;85:853–9.

Dietrich T, Joshipura KJ, Dawson-Hughes B, et al: Association between serum concentrations of

25-hydroxyvitamin D3 and periodontal disease in the US population. *Am J Clin Nutr.* 2004,

80:108–113.

Erkkola M, Kaila M, Nwaru BI, Kronberg-Kippila C, Ahonen S, Nevalainen J, Veijola R,

Pekkanen J, Ilonen J, et al. Maternal vitamin D intake during pregnancy is inversely associated

with asthma and allergic rhinitis in 5-year-old children. *Clin Exp Allergy.* 2009;39:875–82.

Foo LH, Zhang Q, Zhu K, Ma G, Trube A, Greenfield H, Fraser DR. Relationship between

vitamin D status, body composition and physical exercise of adolescent girls in Beijing.

*Osteoporos Int.* 2009 Mar;20(3):417-25. doi: 10.1007/s00198-008-0667-2. Epub 2008 Jul 16.

Freishtat RJ, Iqbal SF, Pillai DK, Klein CJ, Ryan LM, Benton AS, Teach SJ. High prevalence of

vitamin D deficiency among inner-city African American youth with asthma in Washington, DC.

*J Pediatr.* 2010;156: 948–52.

Grant WB: Vitamin D, periodontal disease, tooth loss, and cancer risk. *Lancet Oncol.* 2008, 9:612–613.

Grant WB: A review of the role of solar ultraviolet-B irradiance and vitamin D in reducing risk of dental caries. *Dermatoendocrinol.* 2011,3:193–198.

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.

Hatun S, Islam O, Cizmecioglu F, Kara B, Babaoglu K, Berk F, Gokalp AS 2005 Subclinical vitaminD deficiency is increased in adolescent girls who wear concealing clothing. *J Nutr.* 135:218–222.

Hewison M: Vitamin D and the immune system: new perspectives on an old theme. *Endocrinol Metab Clin North Am.* 2010, 39:365–379. table.

Hildebolt CF: Effect of vitamin D and calcium on periodontitis. *J Periodontol.* 2005, 76:1576–1587.

Holick MF. High prevalence of vitamin D inadequacy and implications for health. *Mayo Clin Proc.* 2006; 81(3):353–373.

Holick MF: Vitamin D deficiency. *N Engl J Med.* 2007, 357:266–281.

Holick M, Binkley N, Bischoff-Ferrari H, Gordon C, Hanley D, Heaney R, Murad H and Weaver C. Evaluation, Treatment, and Prevention of Vitamin D Deficiency: An Endocrine Society Clinical Practice Guideline. *Journal of Clinical Endocrinology & Metabolism.* July 2011, 96(7): 1911-1930.

Hong L, Levy SM, Warren JJ, et al. Association between enamel hypoplasia and dental caries in primary second molars: a cohort study. *Caries Res.* 2009;43: 345–353.

Hughes AM, Lucas RM, Ponsonby AL, Chapman C, Coulthard A, Dear K, Dwyer T, Kilpatrick TJ, McMichael AJ, et al. The role of latitude, ultraviolet radiation exposure and vitamin D in childhood asthma and hay fever: an Australian multicenter study. *Pediatr Allergy Immunol.* Epub 2010 Sep 30.

Hujoel PP: Vitamin D, and dental caries in controlled clinical trials: systematic review and meta-analysis. *Nutr Rev* 2013, 71:88–97.

Hypponen E, Sovio U, Wjst M, Patel S, Pekkanen J, Hartikainen AL, Jarvelinb MR. Infant vitamin D supplementation and allergic conditions in adulthood: northern Finland birth cohort 1966. *Ann N Y Acad Sci.* 2004;1037:84–95.

Institute of Medicine. Dietary reference intakes for calcium and vitamin D. Washington, DC: *National Academies Press*. 2011.

Johnson CL, Paulose-Ram R, Ogden CL, et al. National Health and Nutrition Examination Survey: Analytic guidelines, 1999-2010. National Center for Health Statistics. *Vital Health Statistics*. 2013; 2(161).

Kühnisch J, Thiering E, Kratzsch J, Heinrich-Weltzien R, Hickel R, Heinrich J. Elevated Serum 25(OH)-Vitamin D Levels Are Negatively Correlated with Molar-Incisor Hypomineralization. *Journal of Dental Research*.. 2014.

Kremer et al. Vitamin D Status and its Relationship to Body Fat, Final Height, and Peak Bone Mass in Young Women. *Journal of Clinical Endocrinology & Metabolism*, 2008; DOI: 10.1210/jc.2008-1575.

Kulie T, Groff A, Redmer J, Hounshell J, Schrager S. Vitamin D: an evidence-based review. *J Am Board Fam Med*. 2009 Nov-Dec;22(6):698-706. doi: 10.3122/jabfm.2009.06.090037.

Mahon BD, Wittke A, Weaver V, Cantorna MT. The targets of vitamin D depend on the differentiation and activation status of CD4 positive T cells. *J Cell Biochem*. 2003;89:922–32.

Mellanby M: Diet and the teeth. An experimental study. In *The effect of diet on dental structure and disease in man*. IIIth edition. Edited by Medical Research Council. London: His Majesty's Stationery Office; 1934:1–180.

Mellanby M: The role of nutrition as a factor in resistance to dental caries. *Br Dent J*. 1937, 62(5):241–252.

Mellanby M, Pattison C: The action of vitamin D in preventing the spread and promoting the arrest of caries in children. *Br Med J*. 1928, 2:1079–1082.

Miyake Y, Sasaki S, Tanaka K, Hirota Y. Dairy food, calcium and vitamin D intake in pregnancy, and wheeze and eczema in infants. *Eur Respir J*. 2010;35:1228–34.

Moore C, Murphy MM, Keast DR, Holick MF. Vitamin D intake in the United States. *J Am Diet Assoc*. 2004;104(6):980–983.

Outila TA, Karkkainen MU, Lamberg-Allardt CJ . Vitamin D status affects serum parathyroid hormone concentrations during winter in female adolescents: associations with forearm bone mineral density. *Am J Clin Nutr*. 2001; 74:206–210.

Pascoe L, Seow WK. Enamel hypoplasia and dental caries in Australian aboriginal children: prevalence and correlation between the two diseases. *Pediatr Dent*. 1994;16:193–199.

Pettifor JM. Vitamin D deficiency and nutritional rickets in children. In: Feldman DPW, Glorieux FH, eds. *Vitamin D*. 2nd ed. Boston: Elsevier Academic Press; 2005. 1065–1084

Purvis RJ, Barrie WJ, MacKay GS, et al. Enamel hypoplasia of the teeth associated with neonatal tetany: a manifestation of maternal vitamin-D deficiency. *Lancet*. 1973;2:811–814.

Schroth R, Jeal N, Kliewer E, et al: The relationship between vitamin D and severe early childhood caries: a pilot study. *Int J Vitam Nutr Res*. 2012, 82:53–62.

Schroth RJ, Levi J, Kliewer E, et al: Association between iron status, iron deficiency anaemia, and severe early childhood caries: a case–control study. *BMC Pediatr*. 2013, 13:22.

Searing DA, Leung DY. Vitamin D in atopic dermatitis, asthma and allergic diseases. *Immunol Allergy Clin North Am*. 2010;30:397–409.

Searing DA, Zhang Y, Murphy JR, Hauk PJ, Goleva E, Leung DY. Decreased serum vitamin D levels in children with asthma are associated with increased corticosteroid use. *J Allergy Clin Immunol*. 2010;125: 995–1000.

Simpson RU, Thomas GA, Arnold AJ. Identification of 1,25-dihydroxyvitamin D<sub>3</sub> receptors and activities in muscle. *J Biol Chem*. 1985;260:8882–91

Sutherland ER, Goleva E, Jackson LP, Stevens AD, Leung DY. Vitamin D levels, lung function, and steroid response in adult asthma. *Am J Respir Crit Care Med.* 2010;181:699–704.

Theodoratou E, Tzoulaki I, Zgaga L, Ioannidis JP. Vitamin D and multiple health outcomes: umbrella review of systematic reviews and meta-analyses of observational studies and randomised trials. *BMJ.* 2014 Apr 1;348:g2035. doi: 10.1136/bmj.g2035.

U.S. Department of Health and Human Services. Oral Health in America: A Report of the Surgeon General. National Institute of Dental Craniofacial Research, National Institutes of Health. Rockville, MD; 2000.

Visser M, Deeg DJH, Lips P. Low vitamin D and high parathyroid hormone levels as determinants of loss of muscle strength and muscle mass (sarcopenia): the longitudinal aging study Amsterdam. *J Clin Endocrinol Metab.* 2003;88:5766–72.

Ward KA, Das G, Berry JL, Roberts SA, Rawer R, Adams JE, Mughal Z. Vitamin D status and muscle function in post-menarchal adolescent girls. *J Clin Endocrinol Metab.* 2009 Feb;94(2):559-63. doi: 10.1210/jc.2008-1284. Epub 2008 Nov 25.

Xystrakis E, Kusumakar S, Boswell S, Peek E, Urry Z, Richards DF, Adikibi T, Pridgeon C, Dallman M, et al. Reversing the defective induction of IL-10-secreting regulatory T cells in glucocorticoid-resistant asthma patients. *J Clin Invest.* 2006;116:146–55.

**Table 1. Prevalence of vitamin D Deficiency among US children age 5–12 year by demographic characteristics**

	<b>Deficient Vit D Prevalence (95% CI)</b>	<b>Inadequate Vit D Prevalence (95% CI)</b>	<b>Sufficient Vit D Prevalence (95% CI)</b>	<b>Harmful Vit D Prevalence (95% CI)</b>
<b>Age (years)</b>				
5 yrs	0.73% (0.15, 3.49)	10.05% (6.55, 15.13)	89.22% (83.60, 93.07)	0.00%
6 yrs	0.85% (0.36, 2.00)	14.25% (9.59, 20.65)	84.90% (78.09, 89.86)	0.00%
7 yrs	0.85% (0.10, 6.82)	11.35% (5.49, 22.02)	87.80% (78.07, 93.56)	0.00%
8 yrs	1.54% (0.76, 3.09)	9.22% (4.82, 16.93)	89.24% (81.22, 94.08)	0.00%
9 yrs	2.49% (0.87, 6.91)	22.60% (15.64, 31.49)	73.30% (62.81, 81.70)	1.61% (0.19, 12.19)
10 yrs	2.23% (0.77, 6.27)	13.68% (8.84, 20.57)	84.09% (77.28, 89.15)	0.00%
11 yrs	5.39% (2.98, 9.55)	19.80% (13.82, 27.53)	72.93% (64.41, 80.05)	1.88% (0.22, 14.02)
12 yrs	5.88% (3.27, 10.35)	27.89% (20.27, 37.06)	65.13% (54.38, 74.53)	1.10% (0.13, 8.42)
5–12 yrs	2.54% (1.62, 3.98)	16.20% (12.91, 20.13)	80.71% (76.28, 84.48)	0.55% (0.16, 1.85)
<b>Gender</b>				
Male	1.75% (0.66, 4.58)	13.64% (10.41, 17.67)	83.57% (79.71, 86.81)	1.04% (0.31, 3.44)
Female	3.42% (2.28, 5.09)	19.03% (14.67, 24.31)	77.56% (71.23, 82.83)	0.00%
<b>Race/Ethnicity</b>				
White	0.00%	7.26% (4.07, 12.63)	91.80% (87.05, 94.91)	0.94% (0.29, 3.01)
Black	12.58% (8.03, 19.17)	36.94% (32.36, 41.76)	50.48% (43.05, 57.90)	0.00%
Hispanic	3.26% (1.85, 5.71)	26.83% (20.24, 34.62)	69.91% (61.37, 77.26)	0.00%
Other	1.89% (0.49, 7.00)	19.61% (7.90, 40.95)	78.51% (59.86, 89.94)	0.00%
<b>Poverty Ratio Level</b>				
<1	3.72% (2.20, 6.23)	22.24% (17.31, 28.10)	74.04% (66.81, 80.17)	0.00%
1 – <2	4.56% (2.26, 8.99)	16.68% (11.07, 24.36)	78.75% (69.40, 85.83)	0.00%
2 – <5	1.22% (0.70, 2.14)	16.10% (11.62, 21.87)	81.37% (75.94, 85.80)	1.31% (0.38, 4.41)
>5	1.31% (0.26, 6.23)	8.07% (4.06, 15.43)	90.62% (83.05, 95.01)	0.00%
<b>Health Insurance</b>				
None	1.76% (0.70, 4.34)	22.73% (14.62, 33.57)	75.52% (64.04, 84.23)	0.00%
Public	3.51% (2.02, 6.02)	18.58% (13.43, 25.14)	77.91% (69.94, 84.24)	0.00%
Private	2.22% (1.13, 4.31)	13.74% (10.03, 18.53)	83.13% (77.72, 87.44)	0.91% (0.27, 3.01)

**Table 2. Prevalence of vitamin D deficiency among US children age 5–12 year by BMI, oral health measures and asthma characteristics**

	<b>Deficient Vit D Prevalence (95% CI)</b>	<b>Inadequate Vit D Prevalence (95% CI)</b>	<b>Sufficient Vit D Prevalence (95% CI)</b>	<b>Harmful Vit D Prevalence (95% CI)</b>
<b>Body Mass Index (kg/m<sup>2</sup>)</b>				
Obese	3.91% (2.10, 7.16)	22.17% (15.47, 30.72)	72.85% (64.57, 79.80)	1.07% (0.15, 7.38)
Overweight	4.41% (2.51, 7.62)	20.42% (13.28, 30.07)	75.17% (65.13, 83.07)	0.00%
Healthy	1.55% (0.85, 2.79)	13.39% (9.71, 18.18)	85.06% (79.85, 89.11)	0.00%
Underweight	5.41% (1.35, 19.34)	12.87% (3.42, 38.14)	67.26% (41.10, 85.82)	14.45% (3.24, 46.04)
<b>Oral Health Measures</b>				
Decay	2.75% (1.45, 5.16)	18.00% (10.96, 28.14)	79.25% (68.83, 86.85)	0.00%
Restoration	2.16% (1.22, 3.79)	15.11% (10.77, 20.78)	82.25% (75.91, 87.21)	0.48% (0.06, 3.76)
Caries Experience	2.37% (1.37, 4.05)	15.79% (11.67, 21.02)	81.46% (75.73, 86.09)	0.38% (0.05, 3.00)
No decay	2.48% (1.31, 3.65)	15.93% (12.12, 19.74)	80.89% (76.49, 85.29)	0.69% (-0.15, 1.54)
<b>Asthma Characteristics</b>				
Have asthma	3.62% (1.63, 7.85)	15.92% (9.03, 26.54)	80.46% (69.85, 87.98)	0.00%
Asthma attack	3.43% (1.52, 7.55)	16.37% (8.10, 30.31)	80.20% (66.91, 89.02)	0.00%
Emergency visit for asthma	10.33% (4.05, 23.93)	2.89% (0.54, 14.09)	86.78% (73.30, 94.01)	0.00%

**Table 3. Prevalence of vitamin D deficiency among US children age 5–12 year by physical activity, milk consumption and time spent watching television, playing video games or on the computer**

	<b>Deficient Vit D Prevalence (95% CI)</b>	<b>Inadequate Vit D Prevalence (95% CI)</b>	<b>Sufficient Vit D Prevalence (95% CI)</b>	<b>Harmful Vit D Prevalence (95% CI)</b>
<b>Physical activity</b>				
none	6.86% (1.39, 27.73)	22.83% (7.13, 53.28)	70.31% (40.95, 88.99)	0.00%
<1/day	2.73% (1.46, 5.03)	18.78% (13.34, 25.78)	78.49% (71.01, 84.46)	0.00%
1/day	1.59% (1.03, 2.44)	12.14% (8.44, 17.15)	85.85% (80.44, 89.95)	0.43% (0.05, 3.53)
>1/day	0.43% (0.05, 3.74)	7.15% (2.65, 17.91)	89.66% (78.07, 95.48)	2.77% (0.38, 17.68)
<b>Milk consumption</b>				
<1/week	5.84% (1.75, 17.72)	20.94% (8.15, 44.16)	73.22% (49.93, 88.23)	0.00%
1/wk – <1/day	4.14% (1.50, 10.94)	25.32% (15.97, 37.68)	70.54% (58.04, 80.56)	0.00%
1/day	2.14% (1.31, 3.47)	14.47% (11.43, 18.16)	82.73% (78.63, 86.18)	0.66% (0.19, 2.20)
<b>Time spent watching TV, playing video games or on the computer</b>				
0–2 hours	1.97% (1.23, 3.15)	12.79% (9.59, 16.87)	84.48% (80.03, 88.09)	0.75% (0.22, 2.52)
3–4 hours	3.43% (2.00, 5.83)	22.75% (15.88, 31.49)	73.82% (64.21, 81.58)	0.00%
5+ hours	5.38% (2.36, 11.77)	30.95% (18.82, 46.43)	63.67% (48.89, 76.25)	0.00%

**Table 4. Multivariate logistic regression testing the association between vitamin D and dental caries<sup>2</sup>**

	Adjusted <sup>1</sup>			Unadjusted		
	OR	95% CI	p-value	OR	95% CI	p-value
<b>Vitamin D</b>			0.9741			0.8695
<b>Deficient</b>	0.946	(0.533, 1.679)	0.839	1.130	(0.610, 2.097)	0.677
<b>Inadequate</b>	1.006	(0.561, 1.803)	0.984	1.150	(0.640, 2.082)	0.614
<b>Sufficient</b>	reference			reference		
<b>Harmful</b>	1.000			1.000		
	No history of sealants <sup>1</sup>			≥ 1 tooth with sealant <sup>1</sup>		
	OR	95% CI	p-value	OR	95% CI	p-value
<b>Vitamin D</b>			0.545			0.316
<b>Deficient</b>	0.735	(0.419, 1.290)	0.262	3.509	(0.652, 18.90)	0.133
<b>Inadequate</b>	0.968	(0.517, 1.813)	0.913	1.171	(0.271, 5.05)	0.821
<b>Sufficient</b>	reference			reference		
<b>Harmful</b>	1.000			1.000		

<sup>1</sup> The multivariate logistic regression model adjusted for age, race/ethnicity, and ratio of family income to poverty threshold.

<sup>2</sup> Dental caries is a binary variable, classified as either having at least one tooth with untreated dental decay or not having any active caries.

**Table 5. Multivariate logistic regression testing the association between vitamin D and asthma**

	Adjusted <sup>1</sup>			Unadjusted		
	OR	95% CI	p-value	OR	95% CI	p-value
<b>Vitamin D</b>			0.0511			0.3106
<b>Deficient</b>	0.137	(0.027, 0.691)	0.019	0.438	(0.151, 1.273)	0.120
<b>Inadequate</b>	0.401	(0.123, 1.303)	0.119	0.641	(0.263, 1.559)	0.303
<b>Sufficient</b>	reference			reference		
<b>Harmful</b>	1.000			1.000		

<sup>1</sup> The multivariate logistic regression model adjusted for age, race/ethnicity, gender, ratio of family income to poverty threshold, and physical activity

**Table 6. Multivariate linear regression testing the association between vitamin D and body measures**

	Adjusted <sup>1</sup>			Unadjusted		
	Slope	95% CI	p-value	Slope	95% CI	p-value
<b>Body Mass Index (kg/m<sup>2</sup>)</b>						
Vitamin D			0.0641			<0.001
Deficient	1.268	(-0.257, 2.794)	0.097	3.839	(2.541, 5.136)	<0.001
Inadequate	0.808	(0.128, 1.487)	0.023	2.051	(1.250, 2.851)	<0.001
Sufficient	reference			reference		
Harmful	1.868	(-7.008, 10.743)	0.660	0.770	(-6.891, 8.432)	0.833
<b>Weight (kg)</b>						
Vitamin D			0.0309			<0.001
Deficient	3.521	(-0.762, 7.804)	0.100	14.400	(9.613, 19.187)	<0.001
Inadequate	2.712	(0.818, 4.605)	0.008	7.887	(5.339, 10.435)	<0.001
Sufficient	reference			reference		
Harmful	7.559	(-12.637, 27.756)	0.437	11.811	(-7.622, 31.244)	0.215
<b>Standing Height (cm)</b>						
Vitamin D			0.0005			<0.001
Deficient	1.226	(-1.834, 4.286)	0.406	11.041	(6.723, 15.359)	<0.001
Inadequate	2.122	(1.067, 3.177)	0.001	6.773	(4.737, 8.809)	<0.001
Sufficient	reference			reference		
Harmful	4.572	(2.220, 6.925)	0.001	20.820	(8.453, 33.187)	0.003

<sup>1</sup> The multivariate linear regression model adjusted for age, gender, race/ethnicity, and ratio family income to poverty threshold.