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## Sociodemographic and Clinical Characteristics associated with Vitamin D Status in Newly Diagnosed Pediatric Cancer Patients

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### Abstract

**Background:** Vitamin D deficiency and insufficiency are associated with serious sequelae in childhood cancer survivors. However, data on vitamin D deficiency in children with newly diagnosed cancer are scarce and the role of sociodemographic factors and vitamin D supplementation is largely unknown.

**Methods:** We assessed vitamin D status and its socio-demographic and clinical correlates in 163 children with newly diagnosed cancer, using 25-hydroxy vitamin D (25(OH)D) concentrations and assessed longitudinal changes following vitamin D supplementation.

**Results:** Sixty-five percent of the patients with newly diagnosed cancer had low 25(OH)D concentrations. Fifty-two patients (32%) were vitamin D deficient ( < 20 ng/mL 25(OH)D

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#### Disclaimers

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concentration), and 53(33%) were insufficient (21–29 ng/mL 25(OH)D concentration). Age over 10 ( $P=0.019$ ), Hispanic ethnicity ( $P=0.002$ ), and female sex ( $P=0.008$ ) were significantly associated with lower 25(OH)D concentration at diagnosis. Vitamin D supplementation resulted in significant increase in 25(OH)D concentrations ( $P<0.001$ ). However, this increase was less pronounced in Hispanic patients vs. non-Hispanic ( $P=0.007$ ), and in children with solid vs. hematological malignancies ( $P=0.003$ ) following supplementation in the longitudinal analysis.

**Conclusion:** Vitamin D deficiency and insufficiency are common in children with newly diagnosed cancer. Hispanic patients, females and older children were at higher risk for vitamin D deficiency and insufficiency. Although supplementation appeared to increase 25(OH)D concentrations over time, this increase was not as pronounced in certain subsets of patients. Prospective trials of the effects of vitamin D supplementation on bone health in children with newly diagnosed cancer are warranted, particularly in Hispanics and patients with solid tumors.

### Keywords

Vitamin D; nutrition; pediatric cancer; cancer disparities; supplementation

### Introduction

Vitamin D has long been known to be important for childhood and adulthood bone health.<sup>1</sup> Recent research has revealed that vitamin D receptor is expressed in a wide variety of body tissues, and vitamin D may play a much broader role than previously thought, with contributions to immune function, metabolism<sup>1–3</sup> and cancer pathophysiology.<sup>4</sup>

Children with cancer have high rates of skeletal complications, particularly in patients with newly diagnosed acute lymphoblastic leukemia<sup>5–6</sup> and low bone mineral density in survivors, even years after the completion of cancer treatment.<sup>7</sup> Moreover, suboptimal 25-hydroxy vitamin D (25(OH)D) concentrations have been associated with lower one-year overall survival rates following stem-cell transplant.<sup>8</sup>

While vitamin D deficiency has been reported in survivors with rates ranging from 14 to 61%,<sup>2, 11–13</sup> data on newly diagnosed patients is scarce, particularly in patients with solid tumors or those not exposed to high doses of steroids.<sup>2, 9–10</sup> In a meta-analysis, published in 2014, only 3 of 19 studies included children with newly diagnosed cancer.<sup>2</sup> In this meta-analysis, results on prevalence of vitamin D deficiency and insufficiency are difficult to interpret, given that only 2 of the 19 studies were found to be of high-quality. As a result, the authors stressed the need for future high-quality studies. Furthermore, there is a lack of research on improving vitamin D status in children with cancer. A study based on 16 children with newly diagnosed acute lymphoblastic leukemia, revealed that vitamin D supplementation did not affect mean bone mineral density;<sup>14</sup> however, no data was provided on changes in serum 25(OH)D concentration over time.

To address this knowledge gap on the prevalence of vitamin D deficiency and insufficiency in children with newly diagnosed cancer, we assessed vitamin D status and associated socio-demographic and clinical characteristics in a population of newly-diagnosed cancer patients

and longitudinal changes in 25(OH)D concentrations following vitamin D supplementation in these patients.

## Materials and Methods

### Study Population and Data Sources

Our retrospective cross-sectional and longitudinal study included 163 children with newly diagnosed cancer, receiving treatment at Rady Children's Hospital San Diego in California (Latitude: 32.7157° N, 117.1611° W). The Institutional Review Board for the University of California San Diego/Rady Children's Hospital San Diego approved this study.

Participants were identified from our cancer registry database, and were included if they were between the ages of 0–21 years and diagnosed with cancer at our institution between September 1<sup>st</sup>, 2012 and April 30<sup>th</sup>, 2015, with either a new solid tumor or a hematological malignancy. We excluded patients who had a benign or a non-malignant diagnosis, had a relapsed cancer or a second malignancy, were diagnosed at another institution, had 25(OH)D concentration ordered but not drawn, did not have 25(OH)D concentration obtained during the study period, were taking vitamin D supplements or multivitamins with vitamin D prior to the diagnosis of cancer, or were receiving enteral nutrition containing Vitamin D.

We collected data from each patient's medical record retrospectively, including age at diagnosis, sex, race/ethnicity, cancer type, insurance type, patient zip code (to ascertain neighborhood-level income), height and weight (to ascertain body mass index [BMI z-score]). Serum 25(OH)D concentrations were measured at baseline and four different time points during supplementation (months 2, 6, 12 and 18). Additionally the season when measurements were obtained and the duration and dosage of any vitamin D supplementation were documented.

Cancer type was categorized as either solid tumor or non-solid hematological malignancy. Hematological malignancies included all acute and chronic leukemias and lymphomas. Patients were also classified according to insurance type; Medicaid insurance was categorized as public and all other insurance providers were categorized as private. We ascertained mean income levels at neighborhood-level by linking each patient's zip code to the U.S. Census Bureau's data.<sup>15</sup> Height and weight were used to calculate patients' BMI z-scores based on Centers for Disease Control and Prevention (CDC) growth charts.<sup>16</sup> We categorized BMI z-scores as underweight ( $z < -1.65$ ), healthy weight ( $-1.65 < z < 1.05$ ), overweight ( $1.05 < z < 1.65$ ), and obese ( $z > 1.65$ ).

### Vitamin D Status and Supplementation

Although the active form of vitamin D is 1,25-dihydroxy vitamin D, 25(OH)D concentration was used as the biomarker for vitamin D status being it is a more reliable indicator of vitamin D status, and as is routinely used as the clinical standard assessment of vitamin D status.<sup>17</sup> 25(OH)D concentration was measured at diagnosis (baseline), and during cancer treatment at our institution's clinical laboratory using the ARCHITECT chemiluminescent microparticle immunoassay (CV%:7%; Abbott-Laboratories, Abbott Park, IL). Concentrations outside the laboratory reference range ( $<13$  ng/mL or  $>96$  ng/mL), were

considered outside of the detection range of the test and were excluded, resulting in 8 exclusions. To categorize vitamin D status, we used the definitions endorsed by the Endocrine Society Clinical Practice Guideline,<sup>18</sup> which are widely used in pediatrics and utilize clear cutoffs. Namely, vitamin D deficiency was defined as 25(OH)D concentration <20ng/mL, insufficiency as 21–29 ng/mL, and ≥30ng/mL as sufficient. 25(OH)D concentration measurements were classified as taken during summer or winter. Using data from the National Oceanic and Atmospheric Administration,<sup>19</sup> summer was defined as April 1<sup>st</sup> – September 30<sup>th</sup> and other months as winter.

Supplementation with vitamin D is routinely used at Rady Children’s Hospital San Diego as a part of clinical care. A standardized protocol for supplementation was not fully implemented at the time of this study. Supplementation was generally started when 25(OH)D concentration was <30 ng/mL, and based on the clinical judgement of the patient’s physician. Patients were considered to be supplemented if they had been prescribed vitamin D supplements of any dose, or had non-prescribed supplementation recorded in the medical record. Patients were considered to be on supplementation until the end date of the prescription indicated in the medical record, and for non-prescribed supplementation until the self-reported end date. We excluded patients who relapsed during treatment, died or were lost to follow-up.

### Statistical Analyses

Descriptive statistics were performed. The chi-square test and Fisher exact test (for variables with cell counts less than 5) were used to examine differences among the vitamin D deficient, insufficient and sufficient groups according to age, sex, race/ethnicity, cancer type, insurance type, mean income, BMI z-score, and season of measurement. These same predictors were then used in a univariable linear model to assess their association with baseline 25(OH)D concentration and vitamin D status (deficient, insufficient and sufficient). Significant predictors ( $P < 0.1$ ) were then included in a multivariable model (Table 1).

To assess changes following supplementation over time, linear mixed effects models were used to analyze 25(OH)D concentrations longitudinally, based on repeated 25(OH)D concentrations during the study period. We further assessed changes in 25(OH)D concentrations following supplementation using multivariable linear regression including: age (<10 years vs. ≥10 years), ethnicity (non-Hispanics vs. Hispanics), cancer type (solid vs. hematological malignancies), and BMI z-score (underweight [ $z < -1.65$ ], healthy weight [ $-1.65 < z < 1.05$ ], overweight [ $1.05 < z < 1.65$ ], and obese [ $z > 1.65$ ]). This model included covariates for supplementation (yes/no) and time. All tests used a significance level of  $\alpha = 0.05$ . All analyses were conducted using R software.<sup>20</sup>

## Results

### Baseline Vitamin D Status in Patients Undergoing Treatment

A total of 377 patients were screened for eligibility, and 214 of these were excluded. Reasons for exclusion included: 1) benign or non-malignant diagnosis (n=34); 2) relapsed cancer or second malignancy (N=33); 3) no 25(OH)D concentration obtained during the

study period (N=114); 4) diagnosed at another institution (N=26); 5) taking vitamin D supplements prior to cancer diagnosis (N=4); and 6) 25(OH)D concentration ordered but not drawn (N=3). Sociodemographic characteristics of excluded patients were not different from the final study population ( $P=0.243$ , data not shown). These exclusions resulted in a final study population of 163.

Mean 25(OH)D concentration at diagnosis was 27.5 ng/mL ( $\pm 12.1$  ng/mL), with a median level of 25 ng/mL. Table 1 summarizes patient characteristics according to vitamin D status at baseline. Overall, 52 patients (32%) were deficient with a mean 25(OH)D concentration of 16.1 ( $\pm 3.1$  ng/mL), 53 (33%) were insufficient with a mean 25(OH)D concentration of 24.7 ( $\pm 2.5$  ng/mL), and 58 (36%) were sufficient with a mean 25(OH)D concentration of 40.1 ( $\pm 12.8$  ng/mL). The proportion of older children ( $\geq 10$  years) in the deficient group was significantly higher than in the insufficient or sufficient groups ( $P=0.020$ ). The distribution of vitamin D status was also significantly different between Hispanic and non-Hispanic patients, with a higher proportion of deficient patients being Hispanic (69%) than non-Hispanic (31%), ( $P<0.001$ ). Seventy-five percent of Hispanic patients had public insurance, compared to 35.0% of non-Hispanic patients ( $P=0.038$ ). BMI z-scores were not significantly different among the groups ( $P=0.247$ ).

We fit univariable linear models for baseline 25(OH)D concentration, with covariates for age, sex, race/ethnicity, cancer type, insurance type, income, BMI z-score, and season (Table 1). We found a significant effect for sex (females having 25(OH)D concentrations 5.7 ng/mL lower than males,  $P=0.005$ ), ethnicity (Hispanics having 25(OH)D concentrations 7.5 ng/mL lower than non-Hispanics,  $P<0.001$ ) and insurance type (patients with public insurance having 25(OH)D concentrations 4.1 ng/mL lower than those with private insurance,  $P=0.042$ ). In the multivariable model, 25(OH)D concentrations in children older than 10 years of age were 4.6 ng/mL lower than in children younger than 10 years of age ( $P=0.019$ ), and 25(OH)D concentrations in females were 5.1 ng/mL lower than in males ( $P=0.008$ ). Finally, Hispanic children had 25(OH)D concentration 6.5 ng/mL lower, compared to non-Hispanics ( $P=0.002$ ).

### Changes in Vitamin D Concentration Following Supplementation

Of the 163 patients included in the study, 115 received vitamin D supplementation and 48 did not (Table 2). Prescribed doses of vitamin D ranged from 3,000–50,000 IU per week. Patients that were prescribed supplementation, were more likely to be Hispanic than non-Hispanic (61% vs. 39%), and to have a hematological malignancy vs. a solid tumor (74% vs. 26%). Vitamin D supplementation resulted in a significant increase in 25(OH)D concentration by an average of 11.76 ng/mL, when compared to children who were not supplemented ( $P<0.001$ ). A total of 86 patients were found to have a higher 25(OH)D concentration at the last measurement in the study period, compared to their baseline measurement. Of these, 78 (90.7%) were prescribed supplementation at some point during the study, while 8 (9.3%) were not prescribed supplementation.

Table 3 shows the longitudinal changes in 25(OH)D concentration, adjusted for supplementation and a linear effect for time for patients stratified by age, ethnicity, cancer type, and BMI z-scores. Although, vitamin D supplementation resulted in significant

increase in 25(OH)D concentrations ( $P<0.001$ ), this increase was not as pronounced in certain subsets of patients. Hispanic patients averaged 25(OH)D concentrations 5.3 ng/mL lower than non-Hispanic patients ( $P=0.007$ ), and patients with solid tumors averaged 25(OH)D concentrations 7.0 ng/mL lower ( $P=0.003$ ) than patients with hematologic malignancies. Increased age and higher BMI z-scores were not significantly associated with lower 25(OH)D concentrations.

## Discussion

Our study builds on previous research by showing that vitamin D deficiency and insufficiency are significant problems in the pediatric cancer population, both at the time of diagnosis and during therapy. Sixty-five percent of our patients were deficient or insufficient at baseline, and the mean 25(OH)D concentration of 27.5 ng/mL was below the level considered sufficient (30 ng/mL). The prevalence of deficiency (33%) and insufficiency (32%) in our population, which resides in a relatively low latitude, are higher than that reported in a recent meta-analysis, noting deficiency and insufficiency to be 14% and 23%, respectively.<sup>2</sup> Of note, most of the 19 studies included in the meta-analysis, were smaller than ours and had inconsistent definitions of vitamin D deficiency. Our results are consistent with a more recent study, which found that 64% of children with cancer, were either vitamin D deficient or insufficient,<sup>21</sup> as well as an earlier study which concluded that 72% of the study population had 25(OH)D concentration below 30 ng/mL.<sup>9</sup>

According to the latest population-based National Health and Nutrition Examination Survey (NHANES) data, the mean 25(OH)D concentration in U.S. children is 27.24 ng/mL,<sup>22</sup> which is nearly identical to the mean value in our study. The rate of deficiencies in their study population was 69%, similar to the 65% in ours. Thus, our findings are consistent with previous studies which report that high rates of vitamin D deficiency are not unique to children with cancer.<sup>11, 12, 20</sup> Nevertheless, as reported by Choudary *et al*, these deficiencies are particularly consequential in children with cancer given their increased risk of skeletal complications, including osteopenia, fractures, and osteonecrosis.<sup>11</sup> Of particular concern are vertebral compression fractures without any preceding trauma. In addition, recent research shows that even one month of treatment with chemotherapy, has significant adverse effects on bone density in patients with acute lymphoblastic leukemia.<sup>23</sup> Moreover, another study reported that the average vitamin D intake in pediatric cancer survivors, was less than a third of the intake recommended by nutritional guidelines.<sup>24</sup>

There are a number of biologically plausible reasons why patients with cancer may be particularly vulnerable to vitamin D deficiency during treatment.<sup>2, 8</sup> Sunlight is required for the biosynthesis of vitamin D,<sup>1</sup> and some patients with cancer are advised to limit time outdoors due to phototoxic treatments and immunosuppression. Hepatic and renal toxicity are also common side effects of chemotherapy, which could result in impairment of vitamin D biosynthesis.<sup>25, 26</sup> These factors may contribute to lower 25(OH)D concentrations in children with cancer while undergoing treatment; however, they are not related to low 25(OH)D concentrations at diagnosis.

Given the lack of local or national guidelines on vitamin D supplementation, and data on interventions to improve vitamin D status in children with cancer,<sup>2, 10, 13</sup> we explored the changes following prescription of vitamin D supplements in 25(OH)D concentration over time. Our results suggest that supplementation increases 25(OH)D concentrations during cancer treatment. This has not been well studied in children undergoing cancer treatment, and our results suggest that although vitamin D status is poor in these patients at diagnosis, oral absorption and metabolism appear to be sufficient for vitamin D supplementation to increase 25(OH)D concentration. These results are consistent with a study conducted in Scotland.<sup>21</sup> Vitamin D supplementation based on vitamin D status in newly diagnosed cancer patients, is now routinely considered at our institution as a part of clinical care. A standardized protocol for supplementation has been developed and is being implemented.

Racial/ethnic differences in vitamin D status and changes following supplementation may be associated to biological or socioeconomic factors, and a contribution of our study relates to the high proportion of Hispanic patients, which offered a unique opportunity to examine these differences. Compared to non-Hispanic Whites, Hispanic patients were found to have a significantly lower 25(OH)D concentrations at baseline ( $-7.6$  ng/mL) and a smaller increase during the course of treatment ( $-5.3$  ng/mL) following supplementation. Lower 25(OH)D concentrations in Hispanics were previously reported in pediatric and adult cancer survivors,<sup>13, 27</sup> as well as in the general population;<sup>26, 29</sup> however, data are lacking on children with cancer at diagnosis and in those undergoing treatment.<sup>30</sup> Our findings suggest that Hispanic patients with lower 25(OH)D concentrations, might be a high-risk group for poor bone health outcomes, and might particularly benefit from vitamin D supplementation to prevent sequelae. African Americans also tend to have lower 25(OH)D concentrations in population studies,<sup>24, 28</sup> and there is debate as to whether African Americans may have a lower “normal” physiologic range of 25(OH)D concentration.<sup>31, 32</sup> Our population included a very small proportion of African-Americans (3%), which hindered comparisons to this racial group. Further investigation is warranted in racial/ethnic minorities, such as Hispanics, to further elucidate factors that affect vitamin D status in these populations. Alternatively, disparities in vitamin D status in Hispanic patients and in those with public insurance may be related to barriers to access to healthcare, including language, cultural and insurance barriers, and lack of adherence to treatments, as it has been described in Hispanic children with acute lymphoblastic leukemia receiving oral chemotherapy.<sup>33</sup>

We also found that patients with solid tumors had smaller improvement in 25(OH)D concentrations following supplementation, compared to children with hematological malignancies in the longitudinal analysis. Helou *et al* also observed higher vitamin D deficiency in children with solid tumors in comparison to children with leukemias and lymphomas.<sup>9</sup> Vitamin D studies in pediatric cancer, have usually focused on patients with leukemia who have received steroids. Future studies including patients with solid tumors are warranted to elucidate the effects of chemotherapy agents used to treat these tumors on vitamin D metabolism. Older patients had lower 25(OH)D concentrations at diagnosis, but not following supplementation which is consistent with previous studies.<sup>9, 11, 13</sup> This may be due to lower dairy intake in adolescents. In contrast to previous studies of both children with cancer and healthy children,<sup>2, 10, 29</sup> season was not a significant factor in any of our analyses, possibly due to relatively low seasonal variability in sun exposure in Southern

California, with more than 300 days of sun per year<sup>19</sup> facilitating consistent synthesis of vitamin D throughout the year.

Limitations in our study include the retrospective design, and the assessment of supplementation, which relied entirely on existing documentation in the medical record. Thus, it was impossible to take into account over the counter supplementation and adherence to supplementation, which were not consistently recorded in the medical record. Patients on enteral nutrition or multivitamins containing vitamin D, were not included in the cohort. We did not include in the analysis treatment intensity categories, prevalence of osteonecrosis or fractures, steroid use or measurements of PTH, calcium, magnesium or phosphate, as these were not consistently documented at the same time of vitamin D measurements. We were not able to differentiate between supplementation regimens and duration, and thus we could not assess different dosing strategies. We did not measure the active metabolite (1,25OH<sub>2</sub>D) of vitamin D, as this is not routinely measured clinically. It is possible that we have missed a small number of vitamin D deficient patients after starting therapy, despite adequate 25(OH)D concentrations. This is likely a result of the known inhibitory effect of steroids on the renal conversion of 25(OH)D to 1,25OH<sub>2</sub>D. Since the patients in our cohort were newly diagnosed patients, we were not able to assess long-term bone health outcomes. Finally, a significant number of patients (N=118) had to be excluded due to lack of 25(OH)D concentration measurements. Nonetheless, our study provides one of the largest analyses of vitamin D status and supplementation in children with newly diagnosed cancer published to date that includes a large Hispanic population.

In conclusion, our findings show that vitamin D deficiency and insufficiency affect approximately two-thirds of pediatric patients with newly diagnosed cancer receiving treatment at our institution, with significant lower baseline 25(OH)D concentrations identified in Hispanics, females, and older children. While mean 25(OH)D concentration and rates of deficiencies are similar to those in the general population, they are particularly concerning given the disease and treatment sequelae of pediatric cancer patients. Our results also suggest that supplementation may benefit these patients by increasing 25(OH)D concentrations over time. Hispanic patients and those with solid tumors seemed to have a smaller increase in 25(OH)D concentrations following vitamin D supplementation, compared to non-Hispanic Whites and patients with hematological malignancies, respectively. Local and national guidelines on vitamin D supplementation for pediatric patients with chronic diseases would greatly facilitate uniform supplementation in this particular population. Future research is warranted, including a more thorough examination of vitamin D status in the diverse pediatric cancer populations, including the effects of cancer treatment on vitamin D deficiency and insufficiency, and prospective trials of vitamin D supplementation, and adherence in newly diagnosed patients to assess improvement in short-term and long-term bone health outcomes (e.g. osteonecrosis and fractures), particularly in high-risk populations. Preventive interventions with vitamin D supplementation in children with newly diagnosed cancer may mitigate the effects on bone health associated with chemotherapy. With the evolving changes in racial and ethnic distribution of children in the U.S., action must be taken to assess the health needs to equitably serve racial/ethnic minority patients, with the ultimate goal of reducing disparities in clinical outcomes in underserved children.



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**TABLE 1.**

Baseline Vitamin D Status According to Patient Sociodemographic Characteristics, Body Mass Index, Season, and Cancer Type<sup>a</sup> and Univariable and Multivariable Models for Associations Between Baseline 25(OH)D Concentrations and Sociodemographic Characteristics, Body Mass Index, Season, and Cancer type.

	Baseline Vitamin D Category			Overall N=163	Univariable P-value <sup>1</sup>	Multivariable <sup>*****</sup> P-value <sup>2</sup>
	Deficient N=52	Insufficient N=53	Sufficient N=58			
<b>Age at Diagnosis (years)</b>						
Mean (SD) <sup>*</sup>	10.3 (5.2)	7.3 (4.6)	8.5 (5.0)	8.3 (5.1)		
<10	25 (48.1%)	39 (73.6%)	39 (67.2%)	103 (63.2%)	0.020	0.019
10	27 (51.9%)	14 (26.4%)	19 (32.8%)	60 (36.8%)		
<b>Sex</b>						
Female	26 (50.0%)	26 (49.1%)	22 (37.9%)	74 (45.4%)	0.369	0.008
Male	26 (50.0%)	27 (50.9%)	36 (62.1%)	89 (54.6%)		
<b>Race</b>						
African American	4 (7.7%)	0 (0.0%)	1 (1.7%)	5 (3.1%)	0.143	*****
Asian / Pacific Islander	4 (7.7%)	6 (11.3%)	4 (6.9%)	14 (8.6%)		
Multiracial	14 (26.9%)	11 (20.8%)	8 (13.8%)	33 (20.2%)		
White	30 (57.7%)	36 (67.9%)	45 (77.6%)	111 (68.1%)		
<b>Ethnicity</b>						
Hispanic	36 (69.2%)	29 (54.7%)	18 (31.0%)	83 (50.9%)	< 0.001	0.002
Non-Hispanic	16 (30.8%)	24 (45.3%)	40 (69.0%)	80 (49.1%)		
<b>Cancer type</b>						
Hematological	39 (75.0%)	41 (77.4%)	49 (84.5%)	129 (79.1%)	0.443	0.054
Solid	13 (25.0%)	12 (22.6%)	9 (15.5%)	34 (20.9%)		
<b>Health Insurance Type</b>						
Private	18 (34.6%)	25 (47.2%)	30 (51.7%)	73 (44.8%)	0.184	0.407
Public / None	34 (65.4%)	28 (52.8%)	28 (48.3%)	90 (55.2%)		

	Baseline Vitamin D Category			Overall N=163	Univariable P-value <sup>1</sup>	Multivariable P-value <sup>2</sup>
	Deficient N=52	Insufficient N=53	Sufficient N=58			
<b>Median Income</b> <sup>**</sup> (\$)						
\$25–50,000	10 (25.6%)	11 (26.2%)	7 (13.7%)	28 (21.1%)	0.234	****
\$50–75,000	21 (53.8%)	21 (50.0%)	24 (47.1%)	66 (50.0%)		
>\$75,000	8 (20.5%)	10 (23.8%)	20 (39.2%)	38 (28.6%)		
<b>BMI</b> <sup>***</sup> z-Score						
Underweight	7 (13.5%)	9 (17.0%)	8 (13.8%)	24 (14.7%)	0.247	****
Healthy Weight	28 (53.8%)	35 (66.0%)	39 (67.2%)	102 (62.6%)		
Overweight	8 (15.4%)	7 (13.2%)	4 (6.9%)	19 (11.7%)		
Obese	9 (17.3%)	2 (3.8%)	7 (12.1%)	18 (11.0%)		
<b>Season of measure</b>						
Summer (Apr-Sep)	23 (44.2%)	27 (50.9%)	31 (53.4%)	81 (49.7%)	0.617	****
Winter (Oct-Mar)	29 (55.8%)	26 (49.1%)	27 (46.6%)	82 (50.3%)		

<sup>a</sup>Data represent count (percentage)

\* SD: Standard Deviation

\*\* Based on the median income level of patient's home zip code. Data unavailable for n=31 patients

\*\*\* Body mass index

\*\*\*\* NHW: Non-Hispanic Whites

\*\*\*\*\* Covariates with a p-value > 0.10 were not included.

<sup>1</sup>: From Univariable model

<sup>2</sup>: From Multivariable model

**TABLE 2.**

Patient Characteristics According to Vitamin D Supplementation

	Vitamin D Supplementation	
	Yes <sup>a</sup> N=115	No <sup>b</sup> N=48
<b>Mean (SD<sup>*</sup>)</b>		
<b>Age at Diagnosis (years)</b>		
<10	71 (62%)	31 (65%)
10	44 (38%)	17 (35%)
Mean, (SD <sup>*</sup> )	8.3 (+/-5.2)	8.5 (+/-4.9)
<b>Sex</b>		
Male	60 (52%)	29(60%)
Female	55 (48%)	19 (40%)
<b>Race</b>		
African American	4 (3%)	0 (0%)
Asian/Pacific Islander	12 (10%)	2 (4%)
Mixed Multiracial	27 (23%)	7 (15%)
White	72 (63%)	39(81%)
<b>Ethnicity</b>		
Hispanic	70 (61%)	14 (29%)
Non-Hispanic	45 (39%)	34(71%)
<b>Cancer Type</b>		
Hematological	85(74%)	44 (92%)
Solid	30 (26%)	4 (8%)
<b>Health Insurance Type</b>		
Private	69 (60%)	27 (56%)
Public / None	46 (40%)	21 (44%)
<b>Median Income<sup>**</sup></b>		
\$25–50,000	23 (26%)	5 (12%)
\$50–75,000	45 (50%)	21 (51%)
>\$75,000	22 (24%)	15 (37%)
<b>BMI<sup>***</sup> z-Score</b>		
Underweight	17 (14.8%)	7 (14.6%)
Healthy Weight	66 (57.4%)	36 (75.0%)
Overweight	18 (15.7%)	1 (2.1%)
Obese	14 (12.2%)	4 (8.3%)

Data represent count (percentage). Some percentages do not add to 100% due to rounding

<sup>a</sup>Deficient N=52, Insufficient N=53 and Sufficient N=10

<sup>b</sup>Deficient N=0, Insufficient N=0 and Sufficient N=48

\* SD: Standard Deviation

\*\*  
Based on median income level of patient's home zip code, when available

\*\*\*  
Body Mass Index

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**TABLE 3.**

Multivariable Mixed Model for Longitudinal Changes in 25(OH)D Concentrations According to Age, Hispanic Ethnicity, Cancer Type, and Body Mass Index z-score <sup>a</sup>

	Estimate	Standard Error	95% Confidence interval	P-value
Age at diagnosis (years), >10 vs. 10)	-2.620	2.294	(-7.102, -1.862)	0.255
Non-Hispanic vs. Hispanic	5.320	1.943	(1.524, 9.117)	0.007
Solid vs. hematological malignancy	-6.949	2.322	(-11.485, -2.413)	0.003
Body mass index z-score	-0.289	0.242	(-0.762, 0.183)	0.234

<sup>a</sup>Model included time and supplementation

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