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The Association between Vitamin D and Depression among College-Aged Women

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THE ASSOCATION BETWEEN VITAMIN D AND DEPRESSION AMONG COLLEGE-AGED WOMEN

A Thesis Presented

By

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ABSTRACT

THE ASSOCIATION BETWEEN VITAMIN D AND DEPRESSION AMONG COLLEGE-AGED WOMEN

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Approximately 15 million Americans are diagnosed with a major depressive disorder each year, with higher rates among women and college-aged adults. Recent research suggests a vitamin D insufficiency may be associated with an increased risk of depression among the elderly. However, studies have not been conducted among young women. A recent study of young adults in Massachusetts suggests that two-thirds of this population is vitamin D deficient. We evaluated the association between dietary vitamin D intake and serum levels of 25-hydroxyvitamin D ($25(OH)D_3$) and history of depression using data from the UMass Vitamin D Status Study, a cross-sectional study of 237 college-aged women. Information on depression and health-related factors was collected by questionnaire at a single clinic visit. Dietary vitamin D intake was assessed by a Food Frequency Questionnaire, and serum $25(OH)D_3$ levels were assessed in fasting blood samples by radioimmunoassay. In multivariable analyses, we observed the suggestion of an association between vitamin D from food sources and history of depression. For each 100 IU/day increase of dietary vitamin D there is a 13% decreased risk of depression (95% CI: 0.6, 1.2). However, total vitamin D intake (foods and supplements combined)

was not associated with history of depression. Compared to women in the lowest tertile (median=51 nmol/L) of serum 25(OH)D_3, women in the second tertile (median=72 nmol/L) had an 82% decreased risk of depression (95% CI: 0.04, 0.90; p_{trend}=0.008). The results of this study are consistent with vitamin D as a modifiable risk factor for depression and may inform intervention studies among college-aged women.

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CHAPTER I

INTRODUCTION

Depression is the most common disability around the world and in the United States among men and women ages 15-44 years old.[1,2] Approximately 20.9 million American adults (9.5% of the population) suffer from at least one type of mood disorder and almost 14.8 million Americans adults (6.7%) are diagnosed with a major depressive disorder each year.[2] Overall, there is a high prevalence of depression found in women (6.7%, vs. 4.0% in males) and young adults 4.7% vs. 7.3% in older adults).[2,3] Recent trends show Americans are now being diagnosed with depression earlier in life compared to previous decades.[2] The average age of onset of depressive symptoms among Americans is during the mid 20s.[4]

Doctors often prescribe antidepressants for the treatment of depression. Monoamine oxidase inhibitors (MAOIs), tricyclic antidepressants (TCAs), tetracyclic antidepressants (TeCAs), selective serotonin reuptake inhibitors (SSRIs), and serotonin-norepinephrine reuptake inhibitors (SNRIs) are all commonly prescribed forms of antidepressants. These antidepressants alter brain chemistry in an attempt to relieve depressive symptoms, generally by increasing or decreasing the levels of specific neurotransmitters. In recent years, antidepressant use among adults and adolescents has increased in the United States. The National Health and Nutrition Examination Survey estimated that antidepressant use increased from 2.5% between 1994 and 1998 to 8.1% between 1999 and 2001. It was estimated that between 2001 and 2003, 10.1% of adults between the years of 15 and 54 used antidepressants.[5]

Depression is a highly treatable illness in most cases; however, depression is often left untreated. Depression is associated with low mood, a decline in cognitive functions, and decreased energy levels.[3] People of low socio-economic status (SES) have a higher rate of depression likely because of their inability to afford necessary care.[6] Many people are unlikely to seek treatment because of the social stigma tied to depression.[7] If left untreated, depression may result in a decreased quality of life, poor physical health, and an inability to maintain daily activities.[3] Friendships and family connections may suffer, work ethics may be disrupted, and productivity may be decreased. In college-aged women, a woman's ability to excel and complete her education may be hindered. Previously, studies have found that approximately 80% of people diagnosed with depression report some level of functional impairment due to their illness.[3] Depression is linked with higher rates of alcoholism, drug use, and suicide rates.[3]

Researchers have identified a multitude of risk factors that increase the risk of developing or triggering the onset of depression. Individuals are at greater risk if they are female, have a family history of depression and/or alcoholism, had a traumatic experience as a child, or are experiencing stressful life events.[2] Low self-esteem, self-critical and pessimistic personalities, and being of low socio-economic status are also related to the development of depression.[2] Serious chronic diseases, such as cancer, heart disease, Alzheimer's, and AIDS/HIV, are all associated with an increased risk of depression.[2]

Although the prevalence of depression is high, the exact cause is still unknown; however, depression is believed to be a result of numerous different factors. Biological evidence suggests that differences in brain structure, changes in hormone production, and malfunctions of the biological feedback mechanisms that regulate neurotransmitter

activity are involved in the development of depression.[3] A new hypothesis suggests that a vitamin D deficiency may be associated with a disruption of these biological mechanisms and with the occurrence of depression.[8]

Adults over the age of 60 years old have a prevalence of insufficient vitamin D levels between 25% and 54%. Although the prevalence may vary by geographic region and ethnicity, vitamin D deficiencies are common throughout the United States.[9] In a recent study conducted at Boston Medical Center, Boston Massachusetts, 36% of young adults aged 18–29 years old had insufficient levels of vitamin D. These young adults also showed the greatest seasonal variation of vitamin D levels compared to older participants (50+) suggesting that young adults may have an equal risk of a vitamin D deficiency compared with older adults.[10]

Vitamin D deficiency (<25 nmol/L) may be a risk factor for depression and other psychological disorders. This association may be a result of malfunctions of biological mechanisms involved in either the neuroendocrine or central nervous systems, but relatively little is known about these relationships.[11,12] Recent research suggests that vitamin D supplementation may have antidepressant properties and help regulate the neuroendocrine system.[13]

To our knowledge, no epidemiological studies have evaluated the association between dietary vitamin D and serum 25-hydroxyvitamin D ($25(OH)D_3$) and the risk of depression in college-aged women. However, three recent cohort[12,14,15] and three cross-sectional[16-18] studies among middle-aged and older men and women found a positive association between vitamin D deficiency and depressive symptoms, while two cross-sectional studies found no association.[8,11] Other studies have found an association

between a deficiency of serum vitamin D levels and elevated parathyroid hormone (PTH) levels which have been associated with an increased risk of depressive symptoms in adults.[12,15] PTH regulates the conversion of vitamin D into its active form; therefore, further suggesting that increased levels of PTH is proportionate to insufficient levels of vitamin D increasing ones risk of depression.[12,15]

Evaluating this relationship in young women is particularly important given that rates of depression are higher in young adults and women as compared to older adults and males. Therefore, we evaluated both total and dietary intake and serum $25(OH)D_3$ levels and the risk of depression among the University of Massachusetts Vitamin D Status Study, a sample of 237 young, college-aged women. We also evaluated the association between total and dietary vitamin D intake and serum $25(OH)D_3$ levels and antidepressant use.

CHAPTER II

PHYSIOLOGY OF VITAMIN D AND DEPRESSION

Several biological mechanisms may explain the relationship with vitamin D deficiency and the risk of depression. Specifically, research scientists have proposed that vitamin D deficiency may contribute to disruptions in the neuroendocrine and central nervous systems.[18,19]

To better understand the physiology of vitamin D and depression, it is critically important to understand the general process of vitamin D absorption and metabolism in the human body. Vitamin D is a secosteroid hormone with target receptors all over the body and plays an important role in many physiological processes.[18,19] Vitamin D may be produced after exposure to sunlight. First, the skin absorbs ultraviolet B radiation which immediately converts 7-dehydrocholesterol to pre-vitamin D_3, which is then converted to vitamin D_3 (cholecalciferol).[19] Vitamin D_3 is transported to the liver by vitamin D binding proteins.

Vitamin D may also be absorbed from dietary intake. Foods, like milk, eggs, cereal, and some fish for example, naturally contain or are fortified with vitamin D_3. Vitamin D_3 absorbed from the diet is transported to the liver by chylomicrons.[4] Vitamin D_3 is metabolized into $25(OH)D_3$. $25(OH)D_3$ is the metabolite used to assess an individual's vitamin D status. $25(OH)D_3$ is then converted into its active form, 1, 25-dihydroxy vitamin D (1, $25(OH)_2D$ [calcitriol]) by 1-α-hydroxylase enzymes in the kidneys and other target tissues. This process is tightly regulated by parathyroid hormone (PTH), serum calcium, and phosphorous levels to other factors. Vitamin D receptors for

1, 25$(OH)_2$D are found on glial cells, neurons, glucocorticoids, and other cells involved in the regulation of cellular function, glucocorticoid signaling, and gene transcription.[4,19,20] Receptors are also found in many areas of the human brain (ie. prefrontal cortex, hippocampus, cingulated gyrus, thalamus, hypothalamus, and substantia nigra), all of which have been previously linked to the physiology of depression.[4]

In terms of the neuroendocrinological system one mechanism potentially linking vitamin D and depression is based on a study of humans suffering from mental illness. Glucocorticoid levels have been found to be higher in patients suffering from major depressive disorder and other severe mental disorders. A malfunction in glucocorticoid signaling and the release of cortisol may be a result of low vitamin D levels.[19,21] However, the exact mechanism linking glucocorticoids, vitamin D, and depression is still unknown.[19]

In terms of the central nervous system mechanism, vitamin D receptors have been found on neuron and glial cells in the hippocampus,[419] which demonstrates 1-α-hydroxylase activity, suggesting that these cells are capable of converting 25(OH)D into 1,25$(OH)_2$D.[4] Active receptors in the limbic system, cortex, and cerebellum regulate behavior by potentially stimulating the release of neurotrophins, which regulate neural development. Areas of the cerebellum that are important for cognition have been found to produce the enzyme 1-α-hydoxylase.[13] Vitamin D possibly helps in the regulation of neurotransmission, neuroprotection, neuroimmumodulation, and nerve growth factor synthesis.[18] Therefore, a vitamin D deficiency might lead to inactivated receptors and a disruption to the pathway that may result in depression.

The regulation of neurotransmitters is also involved in the central nervous system. Neurotransmitters regulate normal brain function. Abnormal levels of neurotransmitters may lead to impairment in neural function and could potentially contribute to depression. Antidepressants medications are designed to regulate abnormal brain function by increasing neurotransmitter levels. Vitamin D may affect neurotransmitter function.[13] $1,25(OH)_2D$ has been shown to increase the production of tyrosine hydroxylase, a precursor to norepinephrine potentially involved in depression. Recent animal studies also suggest that $1,25(OH)_2D$ may influence the upregulation of glial cell line-derived neurotrophic factors (GDNF) that influence levels of dopamine.[4]

In summary, there are two potential mechanisms by which vitamin D deficiency could lead to depression. Simply, a lot is still unknown on the biological cause of depression due to the influence of independent factors, including: hormonal, lifestyle, and genetic factors; however, biologic research continues to suggest vitamin D may play a role with the onset of depression.

CHAPTER III

EPIDEMIOLOGY OF VITAMIN D AND DEPRESSION

Within the last five years, a total of nine epidemiologic studies have assessed the relationship between vitamin D status and the risk of depression. Studies have prospectively,[14,20] or cross-sectionally [8,9,14,22] evaluated the association between serum vitamin D levels and depressive symptoms or cognitive function in elderly adults outside the United States. To our knowledge, only one study has evaluated this association in adults within the United States.[11] Overall, the majority of studies found an inverse association between vitamin D levels and depressive symptoms,[9,12,14-16,18,17] though two studies observed no association.[8,11] Of the prior studies, all nine evaluated serum vitamin D and none evaluated dietary vitamin D intake.

In a cross-sectional analysis of a population-based cohort study of 1,282 community residents between the ages of 65 and 95 years old in the Netherlands, Hoogendijk *et al.*[15] (2008) were the first to evaluate the association between decreased serum 25(OH)D levels and depression status and depression severity. Study participants were apart of the ongoing Longitudinal Aging Study in Amsterdam. Non-fasting blood samples were obtained from all participants and a competitive binding protein assay was used to determine serum 25(OH)D concentrations. Serum concentrations less than 20 ng/ml were considered to be vitamin D deficient. At the first follow-up, the Center for Epidemiologic Studies-Depression (CES-D) scale was used to assess depression status and severity. Seventy-one percent of the study population who suffered from minor depression and 80.8% of those who suffered from major depressive disorder were

females. Overall, 25(OH)D levels were 14% lower in the 169 participants suffering from minor depression (mean=19 ng/ml; $p<0.001$) and 14% lower in the 26 participants suffering from major depressive disorder (mean=19 ng/ml; $p<0.001$) compared to the non-depressed population (mean=22 ng/ml; $p<0.001$). After adjustment for confounders, including residential geographical location or the season of blood draw, serum 25(OH)D levels were inversely associated with depressive symptoms (p-value=0.03).

This study had several limitations. First, the study population was limited to elderly adults.[15] Older adults have a higher prevalence of being depressed, and suffer from other chronic conditions that could affect vitamin D levels. The authors did not adjust for race, ethnicity, and socio-economic status, even though they are risk factors for depression. Non-fasting blood samples were obtained from all women. Food consumption prior to the blood drawing may have attenuated the assessment of average serum vitamin D levels.

To our knowledge, Zhao *et al*. (2010)[11] are the only researchers who evaluated the relationship between serum vitamin D status and depression in the United States. The authors conducted a cross-sectional study using data from the 2005-2006 National Health and Nutrition Examination Survey (NHANES) among 3,916 participants older than 20 years of age. Depressive symptoms were assessed using the Patient Health Questionnaire-9 (PHQ-9) diagnostic algorithm. Serum vitamin D concentrations were measured using the DiaSorin RIA procedure. No statistically significant associations were found for people with vitamin D serum levels of 15-20 ng/ml compared to those with < 15 ng/ml serum vitamin D levels in terms of risk for moderate-to severe depression (1.24; 95% CI: 0.74-2.10), major depression (1.23; 95% CI: 0.51-3.01), and

minor depression (1.34; 95% CI: 0.79-2.28) after adjusting for age and other potential confounders. Among the three classifications of depression, the OR decreased linearly with increasing quartiles of 25(OH)D, although this trend was not statistically significantly. Zhao *et al.* (2010)[11] used similar exposure and outcome measurements, along with a similar statistical analysis procedure to Hoogendijk *et al.* but found conflicting results.

Milaneschi *et al*. (2010)[14] studied the relationship between serum 25(OH)D and depressive symptoms over a 6-year follow-up period of among 654 older adults (≥ 65 years) from Tuscany Italy. Participants of this population-based cohort study were a part of the Invecchiare in Chianti, Aging in the Chianti Area (InCHIANTI) study conducted in 1998-1999. Depressive symptoms were assessed at baseline and at the 3- and 6-year follow-up visits using the CES-D scale. Vitamin D status was measured from the fasting blood draw at baseline and measured by the DiaSorin RIA procedure. Compared to women with sufficient 25(OH)D levels, women with levels < 50 nmol/L at baseline had an increase in CES-D scores (ß=2.2; SE=1.0; p=0.03) after 3 years, and further increases after 6 years (ß=2.5; SE=1.3; p=0.05). When vitamin D status was classified as a dichotomous variable, women with low vitamin D levels had 2.1 (SE=0.9; p=0.02) and 2.2 (SE=1.1; p=0.04) points higher CES-D scores at the 3 and 6 year follow up respectively, compared to women with normal vitamin D levels. Women with low vitamin D levels also had a significantly higher risk of developing depressive mood over the follow up (HR=2.0; 95% CI: 1.2-3.2; p=0.005) as compared to women with normal vitamin D status. This study was limited because it did not study the association in young adults.

To our knowledge, there are no epidemiologic studies that assessed the association between vitamin D status and antidepressant use, a proxy for current depression. Jorde *et al.*(2008)[23] designed a randomized double blinded trial in Norway which assigned 441 overweight and obese participants to 20,000 or 40,000 IU of vitamin D or a placebo every week for one year. The Beck Depression Inventory (BDI) was used to measure individual depression status at baseline and follow-up visits. In both intervention groups, there was a modest but significant improvement in BDI scores after one year (p=0.05) compared to the placebo group, suggesting that vitamin D supplements have antidepressant qualities, although a small proportion of the study population were depressed.

In summary, no previous studies have evaluated the association of vitamin D status on the risk of depression in college-aged women. Other studies have found conflicting results in older adults, but overall support the hypothesis that a deficiency of vitamin D levels is associated with a higher risk of depression. Previous research has not analyzed the association between dietary vitamin D intake and risk of depression.

CHAPTER IV

SUMMARY

Depression is one of the most common psychiatric disorders across the world, with approximately 9.5% of American adults currently experiencing depressive symptoms. In recent years Americans are being diagnosed with depression earlier in life. A growing body of research suggests an association between vitamin D status and the risk of depression. The exact mechanisms involved are still unknown, but there are three potential mechanisms by which vitamin D status could lead to depression. Although the highest rates of depression are amongst women and young adults, epidemiologic studies to date have focused on older populations. Most studies suggest a positive association between vitamin D deficiencies and depressive symptoms in elderly populations around the world. However, no epidemiologic studies have evaluated this association in college-aged women living in the United States. Current research has been limited to serum $25(OH)D_3$ levels and has not assessed the association with total and dietary intake estimated by a validated food frequency questionnaire. This is important because public health recommendations related to vitamin D are based on increased dietary intake; as opposed to increase sun exposure because of the skin cancer risk associated with sun exposure. Vitamin D deficiencies and depression affect millions of Americans each year making them both public health concerns. Understanding the potential association between the two could help public health officials prevent both.

Therefore, we evaluated the association between total and dietary vitamin D intake and serum $25(OH)D_3$ levels and the risk of depression among young women.

CHAPTER V

HYPOTHESES AND SPECIFIC AIMS

Using a cross-sectional design, we evaluated the relationship between vitamin D and depression among college-aged women. The following aims were addressed:

Specific Aim 1: To evaluate the association between vitamin D and the history of depression.

Hypothesis 1a: High total vitamin D intake is associated with a decreased risk of depression among college-age women.

Hypothesis 1b: High dietary vitamin D intake is associated with a decreased risk of depression among college-age women.

Hypothesis 1c: High serum 25(OH)D_3 levels are associated with a decreased risk of depression among college-age women.

Specific Aim 2: To evaluate the association between vitamin D and current use of antidepressants as a proxy for current depression.

Hypothesis 2a: High total vitamin D intake is associated with a decreased likelihood of antidepressant use among college-age women

Hypothesis 2b: High dietary vitamin D intake is associated with a decreased likelihood of antidepressant use among college-age women.

Hypothesis 2c: High serum 25(OH)D_3 levels are associated with a decreased likelihood of antidepressant use among college-age women.

Specific Aim 3: To evaluate the association between vitamin D and prevalent depressive symptoms.

Hypothesis 3a: High total vitamin D intake is inversely associated with prevalent depressive symptoms among college-age women.

Hypothesis 3b: High dietary vitamin D intake is inversely associated with prevalent depressive symptoms among college-age women.

CHAPTER VI

METHODS

Study Design and Population

We conducted a cross-sectional analysis among 237 healthy, premenopausal college-aged women, aged 18-30 years old and living in the Amherst, MA area enrolled in the University of Massachusetts Vitamin D Status Study between March 2006 and May 2010 (Phase One: March 2006 – May 2008 and Phase Two: September 2008 – May 2010). The Vitamin D Status Study recruited women by advertising among the University of Massachusetts Amherst community by posting fliers, putting table tents in the dining halls, and making classroom announcements. Women were ineligible to participate in the study if they: (1) were pregnant or not currently menstruating; (2) were experiencing untreated depression (only phase 1); (3) reported a history of high blood pressure or elevated cholesterol, kidney or liver disease, bone disease such as osteomalacia, digestive disorders, rheumatologic disease, multiple sclerosis, thyroid disease, hyperparathyroidism, cancer, type 1 or type 2 diabetes, or polycystic ovaries; or (4) were taking corticosteroids, anabolic steroids, anticonvulsants, cimetidine, or propranolol. Information on demographic, lifestyle, and behavioral factors was collected at a single clinic visit scheduled during each participant's late luteal phase of their menstrual cycle.[24]

Exposure Assessment

Each participant's dietary vitamin D and dietary supplement intake for the prior two months was assessed with a 131 item food frequency questionnaire (FFQ) at the single clinic visit. The FFQ used by the UMass Vitamin D Status Study is modified version of the Harvard Food Frequency Questionnaire.[24] The FFQ changed slightly between phase one and phase two of the study. All FFQs were analyzed at Harvard University, following the University of Minnesota's NCC-Nutrient Database and the USDA Food and Nutrient Database. Vitamin D intake was calculated by multiplying the reported intake of each food by its portion size and its vitamin D content and then summing the contributions for all food items together to obtain the vitamin D intake (IU per day). Total and dietary intake of vitamin D were assessed as continuous, categorical (tertiles determined by the sample population), and dichotomous (sufficient [≥400 IU/day] vs. insufficient [<400 IU/day]) variables (Table 1).

Each participant also provided a fasting blood sample at their clinic visit. Blood samples were processed and stored at -80 ºC at the University of Massachusetts, within two hours of draw. Radioimmunoassay kits from DiaSorin (MN, USA) were used to measure serum 25(OH)D_3 concentrations, a technique that was previous validated.[25] A Beckman Gamma 4000 counter (Beckman Coulter, California, USA) was used to quantify gamma irradiation of I^{125} (in counts per minute; CPM), and GraphPad Prism version 4.00 for windows (GraphPad Software, San Diego, CA) was used to convert CPM into concentration units. Serum 25(OH)D_3 levels were assessed as continuous, categorical (tertiles determined by the sample population), and dichotomous (sufficient [≥50 nmol/L] vs. insufficient [<50 nmol/L]) variables (Table 1).

Validity of Exposure Assessment

The FFQ used by the UMass Vitamin D Status Study is a modified version of the Harvard Food Frequency Questionnaire. The Harvard FFQ has been extensively validated for use among women in the United States. In one study, four one-week diet records and two FFQs completed over the course of a year by 173 participants were compared to assess the FFQs reproducibility and validity. Correlation coefficients comparing nutrient intake assessed by the two FFQs and coefficients comparing the mean of the four diet records with intake assessed by FFQ were high and reproducible. For example, the *r* for vitamin A measured by two FFQs was 0.49. The *r* comparing the diet records to the second FFQ assessment was 0.41. The results indicated that a single FFQ is both valid and reproducible for assessing micronutrient intake.[26] A validation study by Hollis *et al.* was previously conducted for the radioimmunoassay kit used to measure serum 25(OH)D_3 concentrations, and both within- and between-assay CVs were low (2.2–8.6%).[25]

Outcome Assessment

We assessed three outcomes of interest: 1) history of depression; 2) current antidepressant use; and 3) current depressive symptoms score among a subset of the population. Information on the three outcomes was collected by self-report questionnaire at the time of each participant's one clinic visit.

To obtain information on history of depression, the first outcome of interest, women were asked: "Have you ever had any of the following clinician-diagnosed illnesses?" the responses included "Depression (unipolar depression)" and "Bipolar

disorder (manic depressive illness)." A positive response to "Depression (unipolar depression)" was interpreted as a "yes" for a history of depression, which was assessed as a dichotomous variable during the analysis (Table 1).

To assess the second outcome of interest, information on current antidepressant use was collected by asking women: "Are you currently taking any of the following medications?" with the responses included "Selective serotonin reuptake inhibitiors/SSRIs (Prozac, Zoloft, Paxil, Effector, etc.)," "Other antidepressants (Elavil, Wellbutrin, MAOIs such as Parnate and Nardil, etc.)," "Tranquilizers (Valium, Thorazine, Xanax, BuSpar, etc.)," and "Lithium." A positive response to either "SSRIs" or "Other antidepressants" will be interpreted as a "yes" for current antidepressant use, was assessed as a dichotomous variable during the analysis (Table 1).

To assess each participant's current level of depressive symptoms, the third outcome of interest, women in phase two of the study (n=50) were asked additional questions modified from the Inventory of Depression and Anxiety Symptoms scale,[27] which were then used to calculate a continuous depressive symptom score. Participants were asked twenty questions on feelings, sensations, problems and experiences during the last two weeks, with the response options including "not at all," "a little bit," "moderately," "quite a bit," and "extremely." The Inventory of Depression and Anxiety Symptoms (IDAS) was designed to assess symptoms of depression by analyzing three large study groups (college students, psychiatric patients, and community adults).[27] Current depressive score was assessed as a continuous variable in the analysis (Table 1).

Validity of Outcome Assessment

Sanchez-Villegas *et al*. (2008) assessed the validity of a self-reported physician diagnosis of depression among 133 women aged 24 – 84 using a Structured Clinical Interview for DSM-IV (SCID-1) as the Gold Standard and they found adequate validity. Specifically, among the participants whom self-reported a physician's diagnosis of depression, 74.2% was confirmed depressed, and among the participants who reported no prior diagnosis of depression, 81% did not suffer from depression.[28] Cotterchio *et al*. (1997) found that there was a high agreement rate (80%) between subject- and physician-reported antidepressant use ($\kappa = 0.60$; 95% CI: 0.47-0.74) in women aged 20 – 74 years old.[29] The Inventory of Depression and Anxiety Symptoms scale has been shown to be internally consistent, showing excellent validity compared with self-report of depression ($r=0.67$; $p<0.01$) and interview based surveys ($r=0.87$; $p<0.01$).[27]

Covariate Assessment

Lifestyle and demographic factors including smoking status, use of oral contraceptives, racial/ethnicity, and current alcohol use were collected by a self-report in a questionnaire at the time of the clinic visit. Physical activity,[30] BMI,[31] alcohol use,[30] smoking status,[30] and use of oral contraceptives[32] have been associated with depression in previous studies. Omega-3 fatty acids,[33] season,[34] and BMI[34] may be associated with an individual's vitamin D status. Weight and height were directly measured at the clinic visit and body mass index (BMI; weight (kg)/height $(m)^2$) was calculated. Recreational physical activity levels were calculated using a modified version of the NHSII questionnaire, validated within the NHS II study population.[35] Specifically participants

were asked to report the amount of time they spent each week walking, jogging, running, bicycling, aerobics/dancing, tennis/racket sports, swimming, yoga/Pilates, and weight training, and MET-hours per week of activity were calculated.[36] The FFQ was also used to measure omega-3 fatty acid intake.

Data Analysis Plan

Univariate Analysis

The distribution of study participants by dietary vitamin D intake and serum $25(OH)D_3$, and by history of depression, current antidepressant use, and depression score were assessed.

Bivariate Analysis

We examined the distribution of covariates according to exposure status. We then compared the distribution of covariates according to history of depression, and current antidepressant use, using the chi-squared test. The chi-square test was used to determine if the observed distribution fit the expected distirubution when the cell size was sufficient, and with Fisher's Exact test if cell counts were small (<5). We examined the distribution of each exposure across categories of each outcome variable. Statistical significance was defined as $p < 0.05$.

Multivariate Analysis

Specific Aim 1: To evaluate the association between vitamin D and the history of depression among college age women.

We modeled the relationship between total and dietary vitamin D intake and serum 25(OH)D_3 levels and prevalent depression using logistic regression. Multivariable models were then built to determine a subset of variables that best predict the risk of depression according to vitamin D status following a stepwise logistic regression procedure. Covariates were added to the model if their addition changed the odds ratio for the main exposure >10%. Both total and dietary vitamin D intake and serum 25(OH)D_3 levels were dichotomized based on clinical recommendations, with insufficient levels set as the reference group for each and also using tertiles. In addition, we modeled vitamin D continuously in the multivariable regression model.

Specific Aim 2: To evaluate the association between vitamin D and current use of antidepressants as a proxy for depression among college age women.

We modeled the relationship between total and dietary vitamin D intake and serum 25(OH)D_3 levels and current antidepressant use using multivariable logistic regression as described for aim 1. Total and dietary vitamin D intake and serum 25(OH)D_3 levels were included in the models as continuous, dichotomous, and categorical variables as listed above.

Specific Aim 3: To evaluate the association between vitamin D and prevalent depressive symptoms among college age women.

We used linear regression to model the relationship between total and dietary vitamin D intake and prevalent depressive symptoms score adjusted for potential covariates. Total and dietary vitamin D intake was included in the model as continuous, dichotomous, and categorical variables. Statistical significance will be defined as $p < 0.05$. SAS v 9.2 software was used for all analyses (SAS Institute, Inc., Cary, North Carolina).

CHAPTER VII

SIGNIFICANCE

To our knowledge, no epidemiological studies have evaluated the association between dietary vitamin D and serum $25(OH)D_3$ and the risk of depression among young, college-aged women. This research suggests that risk of depression may be reduced with individual changes in dietary intake and environmental exposure to vitamin D among young, college-aged women. Findings could inform a public health campaign to promote a modifiable risk factor through which young, college-aged women may reduce their risk of depression.

CHAPTER VIII

HUMAN SUBJECT PROTECTION

The University of Massachusetts Vitamin D Status Study was approved by the Institutional Review Board of the University of Massachusetts Amherst. To participate in the study all participants were required to sign an informed consent form articulating that there was no obligation to participate, was minimal risk involved, and that they could withdrawal from the study at any time.

In an attempt to ensure subject confidentiality, each participant was assigned a study ID. Name and addresses of each participant are kept separate from their study ID. Information of each study participant is stored on the password protected computer network in the School of Public Health and Health Sciences, and only study personnel have access.

Study participants were faced with minor immediate risks associated with participation of this study. Participants were at risk of slight pain and bruising at the blood draw site. The risk of infection was minimal as a sterile one-time-use needle was used. The benefits of participating in this study greatly outweighed the risk. Study participants gained knowledge of factors influencing their individual vitamin D status, while helping to advance understanding of vitamin D in a population underrepresented in prior literature.

CHAPTER IX

PERMISSION TO ACCESS DATA

I, Constance Barysauskas, have completed and passed the Human Subject's Training through the Collaborative Institution Training Initiative (CITI) registered with the University of Massachusetts Amherst. Upon completion, Elizabeth Bertone-Johnson, co-Principal Investigator of the UMass Vitamin D Status Study, granted permission to use the UMass Vitamin D Status Study data for the purposes of this thesis.

Signed:

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Elizabeth R. Bertone-Johnson

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Constance Barysauskas

CHAPTER X

RESULTS

The study population consists of 237 primarily non-Hispanic white women with a mean age of 21.6 years old (range from 18 years to 30 years) who enrolled primarily in the spring months at UMass**.** The mean BMI of the study population was 23 kg/m^2 (SD=3.2). Information on total vitamin D and intake from foods were presented in Table 2. The mean total vitamin D intake was 378 IU/day (SD=298.6) and mean dietary vitamin D intake was 214 IU/day (SD=146.6). Mean serum $25(OH)D_3$ levels in the 182 women for whom levels were available was 79 nmol/L (SD=31.8) (Table 2). A total of 26 women (11%) were previously diagnosed with depression and 15 women (7%) were currently taking antidepressants at the time of enrollment (Table 3).

Characteristics of the participants by total, dietary and serum vitamin D are described in Tables 4, 5, and 6. Omega-3 fatty acids and calcium intake were significantly and positively related to total and dietary vitamin D intake (Table 4 and 5). Alcohol intake was significantly higher in those women who had insufficient total vitamin D intake and serum $25(OH)D_3$ levels compared to those with sufficient total intake and serum $25(OH)D_3$ levels (Table 4 and 6). Physical activity was positively related to dietary vitamin D intake (Table 5). Past and current oral contraceptive use was associated with serum 25 (OH)D levels (Table 6). Age, race, body mass index (BMI), education level, and current and history of smoking were not associated with total and dietary vitamin D intake, or serum $25(OH)D_3$ levels.

BMI was significantly higher in women who had a previous diagnosis of depression compared to those who were never diagnosed with depression (p=0.04) (Table 7). Alcohol intake was significantly higher in those participants who were not current taking antidepressants compared to those who were (Table 8). Season was marginally associated with history of depression and current antidepressant use (Table 7 and 8). Age, race, education level, history of oral contraceptive use, history of smoking, physical activity, omega-3 fatty acids, and calcium intake was not associated with a previous diagnosis of depression and current antidepressant use.

In bivariate analyses, there was no association between dietary and total vitamin D intake assessed continuously, dichotomously, and in tertiles and a history of depression (Table 9). Serum 25(OH)D_3 levels showed an overall significant association with history of depression (p=0.03). Total and dietary intake and serum vitamin levels were not associated with current antidepressant use (Table 9).

In unadjusted and adjusted analyses, dietary vitamin D intake was associated with history of depression, though results were not statistically significant (Table 10). For each 100 IU/day increase in dietary vitamin D there was a 17% decreased risk of depression (95% CI: 0.61, 1.13). Compared to woman in the lowest tertile of dietary vitamin D intake (median = 68 IU/day), the women in tertile 2 and 3 reported a lower rate of depression (tertile 2: OR=0.86, 95% CI: 0.33, 2.25; tertile 3: OR=0.66, 95%: 0.24, 1.85; p_{trend}=0.89). After adjustment for energy, age, BMI, season, history of oral contraceptive use, calcium, omega-3 fatty acids, and alcohol consumption, for each 100 IU/day increase of dietary vitamin D intake there was a 13% decreased risk of depression (95% CI: 0.63, 1.20). After adjustment, women consuming more that 400 IU/day had a

77% decreased risk of depression compared with women who consumed less than 400 IU/day (95% CI: 0.03, 1.84). After adjustment, woman in the lowest tertile of dietary vitamin D intake (median = 68 IU/day) compared to women in tertile 2 and 3 showed a lower risk of depression (tertile 2: OR=0.96, 95% CI: 0.34, 2.76; tertile 3: OR=0.78, 95%: 0.27, 2.26; p_{trend}=0.89).

In multivariable analyses, women in the lowest tertile of serum 25(OH)D_3 levels (median=51 IU/day), compared to women in tertile 2 (median=72) had an 82% lower risk of depression (95% CI: 0.04, 0.90, p_{trend}=0.03). Risk was higher in women in tertile 3 (median=109) showed an increased risk (OR_{adj}=1.58; (95% CI: 0.51, 4.86)) compared to those in tertile 1 (p_{trend}=0.03). We could not assess the association between the recommended daily vitamin D intake (600 IU/day) and history of depression because our study population had overall low vitamin D intake.

In unadjusted and adjusted analyses, decreased vitamin D was associated with current antidepressant use, though the results were not statistically significant and the confidence intervals were wide (Table 11). Women with higher intake of dietary vitamin D had a 48% lower risk of current antidepressant use compared to women with intake less than 400 IU/day (95% CI: 0.07, 4.08). In multivariable analyses higher total vitamin D intake was associated with a 31% lower risk of current antidepressant use compared to less than 400 IU/day (95% CI: 0.22, 2.22). For every 100 IU/day increase of dietary vitamin D intake there was a 15% lower risk of current antidepressant use (95% CI: 0.55, 1.32). Compared to women with serum 25(OH)D_3 levels less than 50 nmol/L, women with levels greater than 50 nmol/L were 48% less likely to be taking antidepressants (95% CI: 0.12, 2.29).

In unadjusted analyses among a small subset of the population who had completed the IDAS depressive symptoms questionnaire, for every 100 IU/day unit increase of total vitamin D there is a 0.02 decrease in depressive symptom score (p=0.96); however this was not statistically significant (Table 12). Multivariable analyses showed a 0.0003 decrease in depressive symptom score for each 100 IU/day increase of total vitamin D (p=0.99). Every 100 IU/day increase in dietary vitamin D intake was associated with a 0.81 increase in depressive symptom score (p=0.47), again these findings were not statistically significant.

CHAPTER XI

DISCUSSION

Results from this cross-sectional analysis of young college-aged women suggest that high dietary and total vitamin D intake and high levels of serum 25(OH)D_3 may be associated with a lower risk of depression; however our findings were not statistically significant. In some analyses, higher intake of dietary vitamin D and high levels of serum 25(OH)D_3 were inversely but not significantly associated with history of depression in young women. Higher intake of dietary vitamin D and high levels of serum 25(OH)D_3 were also inversely but not significantly associated with current antidepressant use, but results were not consistent across all analyses. However, in a sub-analysis of 50 young women with available data, vitamin D intake was not associated with the IDAS depressive symptoms score.

Our results are consistent with those of several prior cross-sectional and cohort studies that reported lower levels of vitamin D are associated with an increased risk of depression.[9,12,14-18] These studies were mainly conducted in elderly adults outside of the United States. Hoogendijk *et al.*,[15] in their cross-sectional analysis found that depression symptoms measured by the CED-S score was significantly associated with 25(OH)D_3 in the Longitudinal Aging Study Amsterdam. Serum 25(OH)D_3 levels of participants with major depressive disorder and minor depression were 14% lower than those of nondepressed participants. Milaneschi *et al.*[14] in their prospective cohort analysis found women with low serum vitamin D had a significantly higher risk of developing a depressive mood during the six year follow-up period (HR: 2.0; 95% CI: 1.2, 3.2; *p*-

value=0.005). To our knowledge, Zhao *et al.*[11] in their cross-sectional study found a null relationship between vitamin D status and depression in the United States and found a null association after adjusting for confounding factors (15-20 ng/ml of serum vitamin D compared to < 15 ng/ml: moderate-to severe depression (1.24; 95% CI: 0.74-2.10), major depression (1.23; 95% CI: 0.51-3.01), and minor depression (1.34; 95% CI: 0.79-2.28)). Similarly, we found that women with $25(OH)D_3$ levels greater than 50 nmol/L had a 18% decreased risk of depression compared to women with levels less than 50 nmol/L (95% CI: 0.23, 2.96). Differences in findings between our study and that of Hoogendijk and Milaneschi may be due to a small sample size and lack of power.

Previous research has identified several different biological mechanisms that may explain the relationship of vitamin D deficiency and depression. Vitamin D deficiency may contribute to disruptions in the neuroendocrine and central nervous systems, which may lead to further disruptions in the regulation of neurotransmission, neuroprotection, neuroimmumodulation, and the release of cortisol and neurotransmitters.[13,18,24]

Nondifferential Misclassification of the Exposure

Each study participant completed a validated, self-report FFQ administered at the single clinic visit to measure intake of vitamin D from foods and supplements. Each woman was administered the same FFQ, which was systematically analyzed at Harvard University to reduce the potential of nondifferential misclassification of the exposure. However, due to the complexity of reporting dietary intake during the last two months, it was possible that the young women over- or under- reported intake of foods containing vitamin D. This form of nondifferential misclassification of the exposure may have biased our results towards the null. However, we believe this form of nondifferential

misclassification is unavoidable. The FFQ we used was previously validated in a similar population limiting measurement error; however, it was difficult to limit reporting issues.

Each subject provided a blood sample during their luteal phase of their menstrual cycle at the clinic visit. Standard procedure was followed for each sample collection and each sample was then aliquoted into batches. Samples were then stored under the same conditions to minimize sources of nondifferential misclassification of the exposure and then and vitamin D levels were assayed. All samples were tested following the same procedure; however, laboratory error may have occurred resulting in nondifferential misclassification of the exposure, which may have reduced the risk estimate of the relation of vitamin D and depression. However, we expect nondifferential misclassification in this example to be minor as the technique used for analysis has previously been validated and we had sufficient CVs (low $25(OH)D_3$ CV=15.0; high $25(OH)D_3$ CV=11.9).

Nondifferential Misclassification of the Outcome

We assessed three different outcomes to measure depression status. First, information on history of depression was collected by self-report questionnaire at the single clinic visit. Cases of depression were not confirmed with physician medical records; therefore, an under- or over-reporting of depression status may have occurred. Depression status is closely associated with a social stigma; therefore, individuals suffering from depression may be less likely to report their diagnosis or get diagnosed from fear of adverse social consequences. Under-reporting of depression status could have resulted in nondifferential misclassification of the outcome, and therefore a decreased risk estimate of the relationship between vitamin D and depression.

Participants may have been self-diagnosed with depression instead of by a physician, resulting in nondifferential misclassification of the outcome. Over-reporting of depression status may have resulted in a bias towards the null, an underestimation of the relationship of vitamin D and depression. We believe this source of nondifferential misclassification to be unlikely, as validation studies in similar populations have shown that self-report of depression history is adequately valid.

In terms of the second outcome, we assessed the relationship between vitamin D and antidepressant use as a proxy for current or recurrent depression. Current antidepressant use was measured by self-report questionnaire at the single clinic visit and was also not confirmed with physician medical records; therefore, an under- or over-reporting of antidepressant use may have occurred. Antidepressants are not only used to treat depression but other common disorders, resulting in a potential overestimation, which could bias our results towards the null. While 26 women reported a history of depression in our study population, only 15 women reported current use of antidepressants. There are 11 women previously diagnosed with depression and not currently taking antidepressants, these women may have been previously treated and no longer taking medication. Therefore, an underestimation of the outcome may have resulted in a bias towards the null, an underestimation of the risk estimate between vitamin D and depression. We believe nondifferential misclassification in this example to be minor.

Finally in terms of the third outcome, the Inventory of Depression and Anxiety Symptoms (IDAS) questionnaire was administered to women participating in phase 2 of the study. It is possible that young women over- or under-reported their depressive

symptoms, as it is a sensitive issue. This nondifferential misclassification of the outcome would bias our results towards the null. We believe this potential bias to be minimal as IDAS has been previously validated.

We assessed three different measures of outcome because our study questionnaire was not initially designed to assess the association between vitamin D status and current depression. A history of depression, current antidepressant use, and the depressive symptoms score each capture a different aspect of our outcome. Each outcome has its own limitations, but together they provide general insight into the relationship between vitamin D and depression risk.

Selection Bias

Study participants enrolled in the University of Massachusetts Vitamin D Status Study on a volunteer basis after seeing flyers and hearing classroom announcements around the university campus. Those who participated were likely to be healthier, had better diets, were more motivated, and had a greater interest in personal health issues than nonparticipants. Depressed people may have been less likely to participate in the study because they perceive themselves as being unhealthy or were unmotivated to do so. The mean BMI for women previously not diagnosed with depression was less than previously diagnosed participants ($BMI_{depressed}$=24.7 kg/m^2 (SD=4.5) vs. ($BMI_{non\text{-}depressed}$=22.8 kg/m^2 (SD=2.9)). If depressed women are more likely to stay inside their homes where they are exposed to less sun and perceive themselves as being unhealthy, then they would be less likely to participate in the study compared with depressed women with higher vitamin D. This may have resulted in an underrepresentation of depressed people with a high vitamin

D status. Therefore, this type of selection bias may have biased our results towards the null and underestimate the association between low vitamin D status and depression.

Information Bias

Depressed young, college-aged women may have a bad personal outlook and may report a more unhealthy diet than they actually eat or complete the questionnaire less thoroughly. If depressed study participants reported their diets as lower quality (e.g. lower levels of vitamin D) as compared to non-depressed participants, this would have resulted in an information bias. This type of information bias may have biased our results away from the null and overestimated the association between low vitamin D status and depression. However, we believe it is unlikely that this bias occurred in this study because our FFQ was previously validated in a similar population.

Confounding

We collected information on confounding factors through the self-report questionnaire completed at the clinic visit. We evaluated most confounding factors recognized in the literature. Women with hormonal and endocrine related disorders were restricted from the study population. We did not collect information on yearly income. Potentially, study participants of lower income may eat unhealthier and therefore have lower vitamin D levels and tend to be depressed due to their current situation than of women of higher income. This confounder could result in an overestimation of the association between low vitamin D status and depression. However, we do not suspect this to be a concern as a large proportion of our study population is students who obtain most meals at the university dining halls. Residual confounding is possible though we

collected information on most if not all confounding factors to control for influential factors in our analysis between vitamin D status and depression risk.

Temporal Bias

An association between vitamin D status and depression may be difficult to capture in a cross-sectional analyses. We were unable to determine if a vitamin D deficiency came before the diagnosis of depression or vice versa because information on both variables were collected at the same time. Clinically detectable depression may take years to develop; therefore, a study participant may have been vitamin D deficient at time of enrollment but was previously not diagnosed from depressive symptoms, but may have been diagnosed after enrollment. In addition depression also leads to a unhealthy diet and low physical activity levels, thus resulting in low vitamin D intake and $25(OH)D_3$ levels. Therefore, we were unable to determine a causal inference between vitamin D status and depression in this cross-sectional analysis.

Survival Bias

We do not believe survivor bias was a major issue in this cross-sectional design. If severe vitamin D deficiencies led to serious forms of depression, individuals may have an increased risk suicide. This survivor bias would have resulted and underestimated the association between low vitamin D and depression. However, it was unlikely that this bias occurred in this study, because it is unlikely that such low vitamin D levels led to suicide (a rare outcome).

Generalizability

The results of this study could be generalized to young, college-aged women of different racial and ethnic groups as the physiology of vitamin D and risk of depression is likely consistent across different groups around the world. It is unclear whether the results of our study could be generalized to men because the development of depression may be associated with female hormones, like estrogen. The results of this study cannot be generalized to older women because they usually suffer from multiple chronic conditions that may also be related to vitamin D status that may be associated with the development of depression.

Conclusions

Results from our small cross-sectional analysis suggest the possibility of an inverse association between vitamin D status and depression. Long-term longitudinal studies with repeated exposure and outcome assessments should be performed to further assess whether lower total and dietary vitamin D intake and lower serum $25(OH)D_3$ levels are associated with the risk of depression.

TABLES

Table 1. Classification of the study variables: UMass Vitamin D Status Study, 2006-2009

Name	Description	Type
Outcome Variables		
Prev_Diag_Dep	*Previously Diagnosed with Depression* 0 = no 1 = yes	Dichotomous
ANTI	*Current Antidepressant Use* 0 = no 1 = yes	Dichotomous
Depress_score	*Depression Score*	Continuous
Exposure Varaibles		
vitdadj2	*Total Vitamin D Intake* (IU/day) 1 = Tertile 1 (Median = 107) 2 = Tertile 2 (Median = 307) 3 = Tertile 3 (Median = 619)	Categorical
vitdadj1	*Total Vitamin D Intake*(IU/day) 0 = ≥ 400 1 = < 400	Categorical
vitd100adj	*Total Vitamin D Intake* (100 IU/day)	Continuous
vitdadj2c	*Dietary Vitamin D Intake* (IU/day) 1 = Tertile 1 (Median = 68) 2 = Tertile 2 (Median = 180) 3 = Tertile 3 (Median = 350)	Categorical
vitdadj1c	*Dietary Vitamin D Intake*(IU/day) 0 = ≥ 400 1 = < 400	Categorical
vitd100Tadj	*Dietary Vitamin D Intake* (100 IU/day)	Continuous
vitd2b	*Serum 25(OH)D_3* (nmol/L) 1 = Tertile 1 (Median = 51) 2 = Tertile 2 (Median = 72) 3 = Tertile 3 (Median = 109)	Categorical
vitd1b	*Serum 25(OH)D_3* (nmol/L) 0 = ≥ 50 1 = < 50	Categorical

Name	Description	Type
Exposure Variables Continued		
vitd10	*Serum 25(OH)D_3* (nmol/L)	Continuous
Covariates		
age	*Age at enrollment*	Continuous
cage	*Age at enrollment* 1 = < 19.9 years 2 = 19.9 - 22.3 yrs 3 = > 22.3 yrs	Categorical
BMI	*BMI at enrollment*	Continuous
BMI_c	*BMI at enrollment* 1 = <18.5 2 = 18.5-24.9 3 = 25.0-29.9 4 = ≥30.0	Categorical
educ_d	*Education* 1 = No College Degree 2 = College Degree	Dichotomous
race_d	*Race/Ethnicity* 1 = White 2 = Other	Dichotomous
cur_oc	*Current Oral Contraceptive Use* 0 = no 1 = yes	Dichotomous
ev_oc	*Ever Oral Contraceptive Use* 0 = never 1 = ever	Dichotomous
cur_smk	*Currently Smoking* 0 = no 1 = yes	Dichotomous
ever_smk	*Ever Smoke* 0 = never 1 = ever	Dichotomous
alco2	*Current Alcohol Consumption* (g/day) 1 = Tertile 1 (Median = 0) 2 = Tertile 2 (Median = 3) 3 = Tertile 3 (Median = 12)	Categorical

Name	Description	Type
alco1	*Current Alcohol Consumption* (g/day) 1 = Low (Median = 2) 2 = High (Median = 12)	Categorical
alco	*Current Alcohol Consumption* (g/day)	Continuous
calc2	*Calcium Intake* (IU/day) 1 = Tertile 1 (Median = 772) 2 = Tertile 2 (Median = 1285) 3 = Tertile 3 (Median = 1745)	Categorical
calc1	*Calcium Intake* (IU/day) 0 = ≥ 1200 1 = < 1200	Categorical
calc	*Calcium Intake* (IU/day)	Continuous
omega2	*Omega-3 Fatty Acids* (IU/day) 1 = Tertile 1 (Median = 0.03) 2 = Tertile 2 (Median = 0.2) 3 = Tertile 3 (Median = 0.46)	Categorical
omega1	*Omega-3 Fatty Acids* (IU/day) 0 = ≥ 0.3 1 = < 0.3	Categorical
omega	*Omega-3 Fatty Acids* (IU/day)	Continuous
season	*Season at Enrollment* 1 = Winter 2 = Spring 3 = Summer/Fall	Categorical
pa_cat	*Phyisical Activity* (METs/week) 1 = Tertile 1 (Median = 106) 2 = Tertile 2 (Median = 177) 3 = Tertile 3 (Median = 264)	Categorical
pa_tot	*Phyisical Activity* (METs/week)	Continuous

Table 2. Distribution of Vitamin D (n=237): UMass Vitamin D Status Study, 2006-2009

	N	%
Total Vitamin D Intake (IU/day)		
< 400	143	60.3
≥ 400	94	39.7
Total Vitamin D Intake (IU/day)		
Tertile 1 (Median = 107)	79	33.3
Tertile 2 (Median = 307)	80	33.8
Tertile 3 (Median = 619)	78	32.9
Dietary Vitamin D Intake (IU/day)		
< 400	207	87.3
≥ 400	30	12.7
Dietary Vitamin D Intake (IU/day)		
Tertile 1 (Median = 68)	78	32.9
Tertile 2 (Median = 180)	80	33.8
Tertile 3 (Median = 350)	79	33.3
Serum 25(OH)D_3 Level (nmol/L)[a]		
< 50	28	15.4
≥ 50	154	84.6
Serum 25(OH)D_3 Level (nmol/L)[a]		
Tertile 1 (Median = 51)	60	33.0
Tertile 2 (Median = 72)	60	33.0
Tertile 3 (Median = 109)	62	34.0
	Mean	**Std**
Total Vitamin D Intake (IU/day)	378.3	298.6
Dietary Vitamin D Intake (IU/day)	214.2	146.6
Serum 25(OH)D_3 Level (nmol/L)	79.3	31.8

[a] Serum 25(OH)D_3, n=182

Table 3. Distribution of Depression (n=237): UMass Vitamin D Status Study, 2006-2009

	N	%
History of Depression		
Yes	26	10.97
No	211	89.03
Antidepressant Use		
Yes	15	6.97
No	207	93.24
	Mean	**Std**
Depression Score [a]	36	9.93

[a] Depression scale, n=50

Table 4. Distribution of Covariates According to Total Vitamin D Intake (n=237): The UMass Vitamin D Status Study, 2006-2009

	Total Vitamin D Intake						
	Tertile 1 (median = 107) *N (%)*	**Tertile 2** (median = 307) *N (%)*	**Tertile 3** (median = 619) *N (%)*	***p*-value**[a]	**< 400 IU/day** *N (%)*	**≥ 400 IU/day** *N (%)*	***p*-value**[a]
Age							
< 19.9 yrs	23 (29.1)	30 (37.5)	25 (32.1)		47 (32.9)	31 (33.0)	
19.9 - 22.3 yrs	37 (46.8)	31 (38.8)	35 (44.9)	0.82	61 (42.7)	42 (42.7)	0.92
> 22.3 yrs	19 (24.1)	19 (23.8)	18 (23.1)		35 (24.5)	21 (22.3)	
Race							
White	67 (84.8)	70 (87.5)	66 (84.6)	0.85	123 (86.0)	80 (85.1)	0.85
Other	12 (15.2)	10 (12.5)	12 (15.4)		20 (14.0)	14 (14.9)	
Education							
No College Degree	64 (81.0)	64 (80.0)	63 (80.8)	0.99	118 (81.4)	75 (79.8)	0.70
College Degree	15 (19.0)	16 (20.0)	15 (19.2)		27 (18.6)	19 (20.2)	
BMI (Kg/m^2)							
<18.5	2 (3.8)	2 (2.5)	2 (3.9)		4 (2.8)	4 (4.3)	
18.5-24.9	56 (70.9)	63 (78.8)	55 (70.5)	0.88[b]	108 (75.5)	66 (70.2)	0.72[b]
25.0-29.9	17 (21.5)	14 (17.5)	18 (23.1)		27 (18.9)	22 (23.4)	
≥30.0	3 (3.8)	1 (1.3)	2 (2.6)		4 (2.8)	2 (2.1)	
Current Oral Contraceptive Use							
Yes	29 (36.7)	33 (41.3)	36 (46.2)	0.49	57 (39.9)	41 (44.6)	0.57
No	50 (63.3)	47 (58.8)	42 (53.9)		86 (60.1)	53 (56.4)	
Ever Contraceptive Use							
Ever Used	43 (54.4)	45 (57.0)	43 (55.1)	0.95	80 (56.3)	51 (54.3)	0.75
Never Used	35 (45.6)	34 (43.0)	35 (434.9)		62 (43.7)	43 (45.7)	
Currently Smoke							
Yes	4 (5.1)	4 (5.0)	3 (3.9)	>0.99[b]	8 (5.6)	3 (3.2)	0.53[b]
No	75 (94.9)	76 (95.0)	75 (96.2)		135 (94.4)	91 (96.8)	
Ever Smoke							
Yes	11 (13.9)	16 (20.0)	8 (10.3)	0.22	25 (17.5)	10 (10.6)	0.15
No	68 (86.1)	64 (80.0)	70 (89.7)		118 (582.5)	84 (89.4)	
Current Alcohol Consumption (g/day)							
Low (Median = 2)	51 (64.6)	44 (55.0)	60 (76.9)	0.01	84 (58.7)	71 (75.5)	0.01
High (Median = 12)	28 (35.4)	36 (45.0)	18 (23.1)		59 (41.3)	23 (24.5)	
Current Alcohol Consumption (g/day)							
Tertile 1 (Median = 0)	22 (27.9)	26 (32.5)	30 (38.5)		42 (29.4)	36 (38.3)	
Tertile 2 (Median = 3)	29 (36.7)	20 (25.0)	31 (39.7)	0.05	43 (30.1)	37 (39.4)	0.01
Tertile 3 (Median = 12)	28 (35.4)	34 (42.5)	17 (21.8)		58 (40.6)	21 (22.3)	
Physical Activity (METs/week)[c]							
Tertile 1 (Median = 106)	34 (43.0)	25 (31.3)	21 (26.9)		56 (39.2)	24 (25.5)	
Tertile 2 (Median = 177)	31 (39.2)	34 (42.5)	38 (48.7)	0.24	57 (39.9)	46 (48.9)	0.09
Tertile 3 (Median = 264)	14 (17.7)	21 (26.3)	19 (24.4)		30 (21.0)	24 (25.5)	
Season of Enrollment							
Winter	8 (10.1)	12 (15.0)	17 (21.8)		18 (12.6)	19 (20.2)	
Spring	58 (73.4)	57 (71.3)	45 (57.7)	0.18	105 (73.4)	55 (58.5)	0.06
Summer/Fall	13 (16.5)	11 (13.8)	16 (20.5)		20 (14.0)	20 (21.3)	
Omega-3 Fatty Acids (g/day)							
Tertile 1 (Median = 0.03)	37 (46.8)	20 (25.0)	18 (23.1)		53 (37.1)	22 (23.4)	
Tertile 2 (Median = 0.2)	32 (40.5)	31 (38.8)	19 (24.4)	<0.001	55 (38.5)	27 (28.7)	< 0.001
Tertile 3 (Median = 0.5)	10 (12.7)	29 (36.3)	41 (52.6)		35 (24.5)	45 (47.9)	
Omega-3 Fatty Acids (g/day)							
≥ 0.3	13 (16.5)	32 (40.0)	45 (57.7)	<0.001	39 (27.3)	51 (54.3)	< 0.001
< 0.3	66 (83.5)	48 (60.0)	33 (42.3)		104 (72.7)	43 (45.7)	
Calcium (mg/day)							
≥ 1200	18 (22.8)	41 (51.3)	50 (64.1)	<0.001	50 (35.0)	59 (62.8)	< 0.001
< 1200	61 (77.2)	39 (48.8)	28 (35.9)		93 (65.0)	35 (37.2)	
Calcium (mg/day)							
Tertile 1 (Median = 772)	52 (75.8)	33 (41.3)	20 (25.6)		81 (56.6)	24 (25.5)	
Tertile 2 (Median = 1285)	23 (29.1)	26 (32.5)	27 (34.6)	<0.001	43 (30.1)	33 (35.1)	< 0.001
Tertile 3 (Median = 1745)	4 (5.1)	21 (26.3)	31 (39.7)		19 (13.3)	37 (39.4)	
	Mean (Std)	**Mean (Std)**	**Mean (Std)**	***p*-value**[a]	**Mean (Std)**	**Mean (Std)**	***p*-value**[a]
Age (yrs)	21.6 (3.0)	21.5 (3.0)	21.6 (3.2)	0.96	21.5 (2.9)	21.6 (3.2)	0.92
BMI (Kg/m^2)	23.2 (3.2)	22.7 (3.0)	23.2 (3.3)	0.46	23.0 (3.1)	23.1 (3.3)	0.84
Omega-3 Fatty Acids (g/day)	0.1 (0.1)	0.3 (0.2)	0.5 (0.4)	<0.001	0.20 (0.19)	0.41 (0.4)	< 0.001
Physical Activity (METs/week)[c]	163.9 (67.7)	183.2 (67.5)	182.5 (71.9)	0.15	171.2 (66.9)	187.7 (71.3)	0.15
Current Alcohol Consumtion (g/day)	6.3 (7.5)	8.1 (8.2)	5.3 (9.0)	0.09	7.2 (7.9)	5.5 (8.9)	0.13
Calcium Intake (mg/day)	885.5 (378.9)	1186.5 (403.8)	1504.3 (676.8)	<0.001	1033.4 (423.5)	1443.5 (659.6)	< 0.001

[a] *p*-values from chi-square tests for the categorical variables

[b] *p*-values from Fisher's Exact Test if cell count is less than 5

[c] METs, metabolic equivalents

Table 5. Distribution of Covariates According to Dietary Vitamin D Intake (n=237): The UMass Vitamin D Status Study, 2006-2009

	Dietary Vitamin D Intake						
	Tertile 1 (median = 68) *N (%)*	**Tertile 2** (median = 180) *N (%)*	**Tertile 3** (median = 350) *N (%)*	***p*-value[a]**	**< 400 IU/day** *N (%)*	**≥ 400 IU/day** *N (%)*	***p*-value[a]**
Age							
< 19.9 yrs	24 (30.8)	29 (36.3)	25 (31.7)	0.39	68 (32.9)	10 (33.3)	0.13
19.9 - 22.3 yrs	34 (43.6)	29 (36.3)	40 (50.0)		86 (41.6)	17 (56.7)	
> 22.3 yrs	20 (25.6)	22 (27.5)	14 (17.7)		53 (25.6)	3 (10.0)	
Race							
White	68 (87.2)	66 (82.5)	69 (87.3)	0.61	176 (85.0)	27 (90.0)	0.59[b]
Other	10 (12.8)	14 (17.5)	10 (12.7)		31 (15.0)	3 (10.0)	
Education							
No College Degree	60 (76.9)	62 (77.5)	69 (87.3)	0.18	163 (78.7)	28 (93.3)	0.06
College Degree	18 (23.1)	18 (22.5)	10 (12.7)		44 (21.3)	2 (6.7)	
BMI (Kg/m^2)							
<18.5	3 (3.9)	3 (3.8)	2 (2.5)	0.37[b]	7 (3.4)	1 (3.3)	0.97[b]
18.5-24.9	59 (75.6)	55 (68.8)	60 (76.0)		152 (73.4)	22 (73.3)	
25.0-29.9	15 (19.2)	17 (21.3)	17 (21.5)		42 (20.3)	7 (23.3)	
≥30.0	1 (1.3)	5 (6.3)	1 (1.3)		6 (2.9)	0 (0.0)	
Current Oral Contraceptive Use							
Yes	26 (33.3)	36 (45.0)	36 (45.6)	0.21	87 (42.0)	11 (36.7)	0.58
No	52 (66.7)	44 (55.0)	43 (54.4)		120 (58.0)	19 (63.3)	
Ever Contraceptive Use							
Ever Used	39 (50.0)	48 (60.8)	44 (55.7)	0.40	116 (56.3)	15 (50.0)	0.52
Never Used	39 (50.0)	31 (38.2)	35 (44.3)		90 (43.7)	15 (50.0)	
Currently Smoke							
Yes	6 (7.7)	2 (2.5)	3 (3.8)	0.27	1 (3.3)	10 (4.8)	> 0.99[b]
No	72 (92.3)	78 (97.5)	76 (96.2)		29 (96.7)	197 (96.7)	
Ever Smoke							
Yes	12 (15.4)	9 (11.3)	14 (17.7)	0.51	30 (14.5)	5 (16.7)	0.78[b]
No	66 (84.6)	71 (88.8)	65 (82.3)		177 (85.5)	25 (83.3)	
Current Alcohol Consumption							
Low (Median = 2)	52 (66.7)	51 (63.8)	52 (65.8)	0.92	130 (62.8)	25 (83.3)	0.03
High (Median = 12)	26 (33.3)	29 (36.3)	27 (34.2)		77 (37.2)	5 (16.7)	
Current Alcohol Consumption (g/day)							
Tertile 1 (Median = 0)	28 (35.9)	22 (27.5)	28 (35.4)	0.79	64 (30.9)	14 (46.7)	0.09
Tertile 2 (Median = 3)	25 (32.1)	30 (37.5)	25 (31.7)		69 (33.3)	11 (36.7)	
Tertile 3 (Median = 12)	25 (32.1)	28 (35.0)	26 (32.9)		74 (35.8)	5 (16.7)	
Physical Activity (METs/week)[c]							
Tertile 1 (Median = 106)	32 (41.0)	28 (35.0)	20 (25.3)	0.03	73 (35.3)	7 (23.3)	0.25
Tertile 2 (Median = 177)	37 (47.4)	30 (37.5)	36 (45.6)		90 (43.3)	13 (43.3)	
Tertile 3 (Median = 264)	9 (11.5)	22 (27.5)	23 (29.1)		44 (21.3)	10 (33.3)	
Season of Enrollment							
Winter	7 (9.0)	18 (22.5)	12 (15.2)	0.15	31 (15.0)	6 (20.0)	0.39
Spring	54 (69.2)	52 (65.0)	54 (68.4)		143 (69.1)	17 (59.7)	
Summer/Fall	17 (21.8)	10 (12.5)	13 (16.5)		33 (15.9)	7 (23.3)	
Omega-3 Fatty Acids (g/day)							
Tertile 1 (Median = 0.03)	45 (57.7)	17 (21.3)	13 (16.5)	< 0.001	72 (34.8)	3 (10.0)	< 0.001
Tertile 2 (Median = 0.2)	28 (35.9)	34 (42.5)	20 (25.3)		74 (35.8)	8 (26.7)	
Tertile 3 (Median = 0.5)	5 (6.4)	29 (36.3)	46 (58.2)		61 (29.5)	19 (63.3)	
Omega-3 Fatty Acids (g/day)							
≥ 0.3	9 (11.5)	30 (37.5)	51 (64.6)	< 0.001	67 (32.4)	23 (76.7)	< 0.001
< 0.3	69 (88.5)	50 (62.5)	28 (35.4)		140 (67.6)	7 (23.3)	
Calcium (mg/day)							
≥ 1200	23 (29.5)	31 (38.8)	55 (69.6)	< 0.001	88 (42.5)	21 (70.0)	< 0.01
< 1200	55 (70.5)	49 (61.3)	24 (30.4)		119 (57.5)	9 (30.0)	
Calcium (mg/day)							
Tertile 1 (Median = 772)	46 (59.0)	43 (53.8)	16 (20.3)	< 0.001	100 (48.3)	5 (16.7)	< 0.01
Tertile 2 (Median = 1285)	24 (30.8)	20 (25.0)	32 (40.5)		63 (30.4)	13 (43.3)	
Tertile 3 (Median = 1745)	8 (10.3)	17 (21.3)	31 (39.2)		44 (21.3)	12 (40.0)	
	Mean (Std)	**Mean (Std)**	**Mean (Std)**	***p*-value[a]**	**Mean (Std)**	**Mean (Std)**	***p*-value[a]**
Age (yrs)	21.7 (3.1)	21.7 (3.3)	21.3 (2.8)	0.70	21.7 (3.1)	20.8 (2.4)	0.16
BMI (Kg/m^2)	22.9 (2.9)	23.4 (3.5)	22.8 (2.9)	0.36	23.0 (3.2)	23.2 (2.8)	0.79
Omega-3 Fatty Acids (g/day)	0.1 (0.2)	0.3 (0.2)	0.5 (0.4)	< 0.001	0.3 (0.3)	0.5 (0.3)	< 0.001
Physical Activity (METs/week)[c]	162.2 (63.01	175.8 (69.9)	191.8 (72.6)	0.03	173.7 (68.0)	196.3 (76.9)	0.10
Current Alcohol Consumtion (g/day)	5.8 (6.8)	7.0 (7.9)	6.8 (10.0)	0.60	6.9 (8.6)	4.0 (5.3)	0.07
Calcium Intake (mg/day)	983.0 (438.8)	1141.1 (556.2)	1462.0 (586.6)	< 0.001	1155.2 (561.0)	1477.8 (522.4)	< 0.01

[a] *p*-values from chi-square tests for the categorical variables

[b] *p*-values from Fisher's Exact Test if cell count is less than 5

[c] METs, metabolic equivalents

Table 6. Distribution of Covariates According to Serum 25(OH)D_3 (n=182): The UMass Vitamin D Status Study, 2006-2009

	Serum 25(OH)D_3 Level						
	Tertile 1 (median = 51) *N (%)*	**Tertile 2** (median = 72) *N (%)*	**Tertile 3** (median = 109) *N (%)*	***p*-value**[a]	**< 50 nmol/L** *N (%)*	**≥ 50 nmol/L** *N (%)*	***p*-value**[a]
Age							
< 19.9 yrs	23 (38.3)	23 (38.3)	22 (35.5)		9 (32.1)	59 (38.3)	
19.9 - 22.3 yrs	21 (35.0)	23 (38.3)	29 (46.8)	0.68	11 (39.3)	62 (40.3)	0.68
> 22.3 yrs	16 (26.7)	14 (23.3)	11 (17.7)		8 (28.6)	33 (21.4)	
Race							
White	45 (75.0)	53 (88.3)	58 (93.6)	0.01	18 (64.3)	138 (89.6)	0.002[b]
Other	15 (25.0)	7 (11.7)	4 (6.5)		10 (35.7)	16 (10.4)	
Education							
No College Degree	46 (76.7)	48 (80.0)	53 (85.5)	0.46	22 (78.6)	125 (81.2)	0.79[b]
College Degree	14 (23.3)	12 (20.0)	9 (14.5)		6 (21.4)	29 (18.8)	
BMI (Kg/m^2)							
<18.5	3 (5.0)	4 (6.7)	0 (0.0)		2 (7.1)	5 (3.3)	
18.5-24.9	38 (63.3)	39 (65.0)	52 (83.9)	0.03[b]	18 (64.3)	111 (72.1)	0.40[b]
25.0-29.9	16 (26.7)	17 (28.3)	9 (14.5)		7 (25.0)	35 (22.7)	
≥30.0	3 (5.0)	0 (0.0)	1 (1.6)		1 (1.6)	3 (1.9)	
Current Oral Contraceptive Use							
Yes	11 (18.3)	22 (36.7)	39 (62.9)	< 0.001	5 (17.9)	67 (43.5)	0.01
No	49 (81.7)	38 (63.3)	23 (37.1)		23 (82.1)	87 (56.5)	
Ever Contraceptive Use							
Ever Used	20 (33.3)	29 (48.3)	39 (62.9)	0.005	9 (32.1)	79 (51.3)	0.06
Never Used	40 (66.7)	31 (51.7)	23 (37.1)		19 (67.9)	75 (48.7)	
Currently Smoke							
Yes	2 (3.3)	3 (5.0)	4 (6.5)	0.91[b]	1 (3.6)	8 (5.2)	> 0.99[b]
No	58 (96.7)	57 (95.0)	58 (93.6)		27 (96.4)	146 (94.8)	
Ever Smoke							
Yes	6 (10.0)	9 (15.0)	8 (12.9)	0.71	2 (7.1)	21 (13.6)	0.54[b]
No	54 (90.0)	51 (85.0)	54 (87.1)		26 (92.9)	133 (86.4)	
Current Alcohol Consumption							
Low (Median = 2)	48 (80.0)	42 (70.0)	37 (59.7)	0.05	25 (89.3)	102 (66.2)	0.01
High (Median = 12)	12 (20.0)	18 (30.0)	25 (40.3)		3 (10.7)	52 (33.8)	
Current Alcohol Consumption (g/day)							
Tertile 1 (Median = 0)	26 (43.3)	21 (35.0)	17 (27.4)		14 (50.0)	50 (32.5)	
Tertile 2 (Median = 3)	23 (38.3)	21 (35.0)	21 (33.9)	0.15	12 (42.9)	53 (34.4)	0.02
Tertile 3 (Median = 12)	11 (18.3)	18 (30.0)	24 (38.7)		2 (7.1)	51 (33.1)	
Physical Activity (METs/week)[c]							
Tertile 1 (Median = 106)	25 (41.7)	15 (25.0)	15 (24.2)		13 (46.4)	42 (27.3)	
Tertile 2 (Median = 177)	25 (41.7)	29 (48.3)	29 (46.8)	0.17	11 (39.3)	72 (46.8)	0.11
Tertile 3 (Median = 264)	10 (16.7)	16 (26.7)	18 (29.0)		4 (14.3)	40 (25.9)	
Season of Enrollment							
Winter	11 (18.3)	14 (23.3)	6 (9.7)		5 (17.9)	26 (16.9)	
Spring	38 (63.3)	30 (50.0)	43 (69.4)	0.17	22 (78.6)	89 (57.8)	0.03
Summer/Fall	11 (18.3)	16 (26.7)	13 (21.0)		1 (3.6)	39 (25.3)	
Omega-3 Fatty Acids (g/day)							
Tertile 1 (Median = 0.03)	21 (35.0)	14 (23.3)	21 (33.9)		13 (46.4)	43 (27.9)	
Tertile 2 (Median = 0.2)	24 (40.0)	22 (36.7)	20 (32.3)	0.38	9 (32.1)	57 (37.0)	0.13
Tertile 3 (Median = 0.5)	15 (25.0)	24 (40.0)	21 (33.9)		6 (21.4)	54 (35.1)	
Omega-3 Fatty Acids (g/day)							
≥ 0.3	18 (30.0)	27 (45.0)	24 (38.7)	0.24	7 (25.0)	62 (40.3)	0.13
< 0.3	42 (70.0)	3 (55.0)	38 (61.3)		21 (75.0)	92(59.7)	
Calcium (mg/day)							
≥ 1200	24 (40.0)	29 (48.3)	24 (38.7)	0.51	13 (46.4)	64 (41.6)	0.63
< 1200	36 (60.0)	31 (51.7)	38 (61.3)		15 (53.6)	90 (58.4)	
Calcium (mg/day)							
Tertile 1 (Median = 772)	30 (50.0)	24 (40.0)	32 (51.6)		14 (50.0)	72 (46.8)	
Tertile 2 (Median = 1285)	19 (31.7)	24 (40.0)	16 (25.8)	0.53	7 (25.0)	52 (33.8)	0.62
Tertile 3 (Median = 1745)	11 (18.3)	12 (20.0)	14 (22.6)		7 (25.0)	30 (19.5)	
	Mean (Std)	**Mean (Std)**	**Mean (Std)**	***p*-value**[a]	**Mean (Std)**	**Mean (Std)**	***p*-value**[a]
Age (yrs)	21.9 (3.6)	21.4 (3.3)	21.2 (2.7)	0.53	21.9 (3.6)	21.4 (3.1)	0.49
BMI (Kg/m^2)	23.6 (3.6)	23.2 (3.0)	22.4 (2.8)	0.11	23.4 (3.5)	23.0 (3.1)	0.63
Omega-3 Fatty Acids (g/day)	0.27 (0.3)	0.33 (0.3)	0.26 (0.3)	0.33	0.2 (0.3)	0.3 (0.3)	0.07
Physical Activity (METs/week)[c]	164.2 (65.8)	183.5 (67.1)	191.3 (74.3)	0.09	163.3 (74.9)	182.7 (68.7)	0.17
Current Alcohol Consumtion (g/day)	4.4 (6.5)	5.3 (5.8)	8.4 (11.3)	0.02	2.7 (3.1)	6.7 (8.9)	< 0.001
Calcium Intake (mg/day)	1100 (535.4)	1179.3 (527.7)	1137.5 (445.5)	0.57	1169.5 (703.5)	1140.4 (459.9)	0.83

[a] *p*-values from chi-square tests for the categorical variables

[b] *p*-values from Fisher's Exact Test if cell count is less than 5

[c] METs, metabolic equivalents

Table 7. Distribution of covariates according to history of depression (n=237): The UMass Vitamin D Status Study, 2006-2009

	No History of Depression *n* (%)	History of Depression *n* (%)	*p*-value[a]
Age			
< 19.9 yrs	72 (34.1)	6 (23.1)	
19.9 - 22.3 yrs	93 (44.1)	10 (38.5)	0.15
> 22.3 yrs	46 (21.8)	10 (38.5)	
Race - Dicotomized			
White	181 (85.8)	22 (84.6)	0.77[b]
Other	30 (14.2)	4 (15.4)	
Education - Dictomized			
No College Degree	173 (82.0)	18 (69.2)	0.12
College Degree	38 (18.0)	8 (30.8)	
BMI (Kg/m^2)			
<18.5	8 (3.8)	0 (0.0)	
18.5-24.9	160 (75.8)	14 (53.9)	<0.008[b]
25.0-29.9	40 (18.9)	9 (34.6)	
≥30.0	3 (1.4)	3 (11.5)	
Current Oral Contraceptive Use			
Yes	89 (42.2)	9 (34.6)	0.46
No	122 (57.8)	17 (65.4)	
Ever Oral Contraceptive Use			
Ever Use	120 (57.1)	11 (42.3)	0.15
Never Use	90 (42.9)	15 (57.7)	
Currently Smoke			
Yes	11 (5.2)	0 (0.0)	0.62[b]
No	200 (94.8)	26 (100.0)	
Ever Smoke			
Yes	30 (14.2)	5 (19.2)	0.56[b]
No	181 (85.8)	21 (80.8)	
Current Alcohol Consumption			
Low (Median = 2)	135 (64.0)	20 (76.9)	0.19
High (Median = 12)	76 (36.0)	6 (23.1)	
Current Alcohol Consumption (g/day)			
Tertile 1 (Median = 0)	72 (34.1)	6 (23.1)	
Tertile 2 (Median = 3)	66 (31.3)	14 (53.9)	0.07
Tertile 3 (Median = 12)	73 (34.6)	6 (23.1)	
Physical Activity (METs/week)[c]			
Tertile 1 (Median = 106)	71 (33.7)	9 (34.6)	
Tertile 2 (Median = 177)	90 (42.7)	13 (50.0)	0.61
Tertile 3 (Median = 264)	50 (23.7)	4 (15.4)	
Season of Enrollment			
Winter	34 (16.1)	3 (11.5)	
Spring	146 (69.2)	14 (53.9)	0.05[b]
Summer/Fall	31 (14.7)	9 (34.6)	
Omega-3 Fatty Acids (g/day)			
Tertile 1 (Median = 0.03)	65 (30.8)	10 (38.5)	
Tertile 2 (Median = 0.2)	76 (36.0)	6 (23.1)	0.42
Tertile 3 (Median = 0.5)	70 (33.2)	10 (38.5)	
Omega-3 Fatty Acids (g/day)			
≥ 0.3	79 (37.4)	11 (42.3)	0.63
< 0.3	132 (62.6)	15 (57.7)	
Calcium (mg/day)			
≥ 1200	97 (46.0)	12 (46.2)	0.99
< 1200	114 (54.0)	14 (53.9)	
Calcium (mg/day)			
Tertile 1 (Median = 772)	93 (44.1)	12 (46.2)	
Tertile 2 (Median = 1285)	68 (32.2)	8 (30.8)	0.98
Tertile 3 (Median = 1745)	50 (23.7)	6 (23.1)	
	Mean (Std)	**Mean (Std)**	***p*-value**[a]
Age (yrs)	21.4 (2.9)	22.6 (3.4)	0.06
BMI (Kg/m^2)	22.8 (2.9)	24.7 (4.5)	0.04
Omega-3 Fatty Acids (g/day)	0.28 (0.3)	0.29 (0.3)	0.84
Physical Activity (METs/week)[c]	178 (70.5)	165.4 (60.1)	0.38
Current Alcohol Consumtion (g/day)	6.6 (8.5)	5.9 (6.3)	0.69
Calcium Intake (mg/day)	1195.6 (583.4)	1199.7 (399.9)	0.96

[a] *p*-values from chi-square tests for the categorical variables

[b] *p*-values from Fisher's Exact Test if cell count is less than 5

[c] METs, metabolic equivalents

Table 8. Distribution of covariates according to current antidepressant use (n=237): The UMass Vitamin D Status Study, 2006-2009

	No Antidepressant Use *n* (%)	Antidepressant Use *n* (%)	*p* -value[a]
Age			
< 19.9 yrs	71 (31.8)	7 (50.0)	
19.9 - 22.3 yrs	100 (44.8)	3 (21.4)	0.17[b]
> 22.3 yrs	52 (23.3)	4 (28.6)	
Race - Dicotomized			
White	190 (85.2)	13 (92.9)	0.70[b]
Other	33 (14.8)	1 (7.1)	
Education - Dictomized			
No College Degree	180 (80.7)	11 (78.6)	0.74[b]
College Degree	43 (19.3)	3 (21.4)	
BMI (Kg/m^2)			
<18.5	8 (3.6)	0 (0.0)	
18.5-24.9	165 (74.0)	9 (64.3)	0.10[b]
25.0-29.9	46 (20.6)	3 (21.4)	
≥30.0	4 (1.8)	2 (14.3)	
Current Oral Contraceptive Use			
Yes	93 (41.7)	5 (35.7)	0.66
No	130 (58.3)	9 (67.3)	
Ever Oral Contraceptive Use			
Yes	125 (56.3)	6 (42.9)	0.33
No	97 (43.7)	8 (57.1)	
Currently Smoke			
Yes	11 (4.9)	0 (0.0)	>0.99[b]
No	212 (95.1)	14 (100.0)	
Ever Smoke			
Yes	34 (15.3)	1 (7.1)	0.70[b]
No	189 (84.8)	13 (92.9)	
Current Alcohol Consumption			
Low (Median = 2)	143 (64.1)	12 (85.7)	0.15[b]
High (Median = 12)	80 (35.9)	2 (14.3)	
Current Alcohol Consumption (g/day)			
Tertile 1 (Median = 0)	73 (32.7)	5 (35.7)	
Tertile 2 (Median = 3)	73 (32.7)	7 (50.0)	0.24[b]
Tertile 3 (Median = 12)	77 (34.5)	2 (14.3)	
Physical Activity (METs/week)[c]			
Tertile 1 (Median = 106)	75 (33.6)	5 (35.7)	
Tertile 2 (Median = 177)	95 (42.6)	8 (57.1)	0.33[b]
Tertile 3 (Median = 264)	53 (23.8)	1 (7.1)	
Season of Enrollment			
Winter	34 (15.3)	3 (21.4)	
Spring	154 (69.1)	6 (42.9)	0.06[b]
Summer/Fall	35 (15.7)	5 (35.7)	
Omega-3 Fatty Acids (gday)			
≥ 0.3	84 (37.7)	6 (42.9)	0.7
< 0.3	139 (62.3)	8 (57.1)	
Omega-3 Fatty Acids (gday)			
Tertile 1 (Median = 0.03)	69 (30.9)	6 (42.9)	
Tertile 2 (Median = 0.2)	80 (35.9)	2 (14.3)	0.24[b]
Tertile 3 (Median = 0.5)	74 (33.2)	6 (42.9)	
Calcium (mg/day)			
≥ 1200	102 (45.7)	7 (50.0)	0.76
< 1200	121 (54.3)	7 (50.0)	
Calcium (mg/day)			
Tertile 1 (Median = 772)	99 (44.4)	6 (42.9)	
Tertile 2 (Median = 1285)	73 (32.7)	3 (21.4)	0.49[b]
Tertile 3 (Median = 1745)	51 (22.9)	5 (35.7)	
	Mean (Std)	**Mean (Std)**	***p* -value**[a]
Age (yrs)	21.6 (3.1)	21.4 (3.2)	0.87
BMI (Kg/m^2)	22.9 (3.0)	24.8 (4.9)	0.19
Omega-3 Fatty Acids (g/day)	0.3 (0.3)	0.3 (0.4)	0.58
Physical Activity (METs/week)[c]	178 (70.6)	154.9 (43.0)	0.08
Current Alcohol Consumtion (g/	6.7 (8.5)	3.9 (3.3)	0.01
Calcium Intake (mg/day)	1191.1 (572.5)	1274.6 (449.2)	0.59

[a] *p*-values from chi-square tests for the categorical variables

[b] *p*-values from Fisher's Exact Test if cell count is less than 5

[c] METs, metabolic equivalents

Table 9. Distribution of vitamin D according to history of depression and current antidepressant use (n=237 [Total and Dietary Vitamin D]; n=182 [Serum 25(OH)D_3): The UMass Vitamin D Status Study, 2006-2009

	No History of *n* (%)	History of Depression *n* (%)	*p*-value[a]	No Antidepressant use *n (%)*	Antidepressant use *n (%)*	*p*-value[a]
Total Vitamin D Intake (IU/day)						
< 400	127 (60.2)	16 (61.5)	0.89	134 (60.1)	9 (64.3)	0.76
≥ 400	84 (39.8)	10 (38.5)		89 (39.9)	5 (35.7)	
Total Vitamin D Intake (IU/day)						
Tertile 1 (Median = 107)	69 (32.7)	10 (38.5)		75 (33.6)	4 (28.6)	
Tertile 2 (Median = 307)	74 (35.1)	6 (32.1)	0.47	75 (33.6)	5 (35.7)	> 0.94[b]
Tertile 3 (Median = 619)	68 (32.2)	10 (38.5)		73 (32.7)	5 (35.7)	
Dietary Vitamin D Intake (IU/day)						
< 400	182 (86.3)	25 (96.2)	0.22[b]	194 (87.0)	13 (92.9)	>0.99[b]
≥ 400	29 (13.7)	1 (3.9)		29 (13.0)	1 (7.1)	
Dietary Vitamin D (IU/day)						
Tertile 1 (Median = 68)	68 (32.2)	10 (38.5)		73 (32.7)	5 (35.7)	
Tertile 2 (Median = 180)	71 (33.7)	9 (34.6)	0.73	76 (34.1)	4 (28.6)	0.89[b]
Tertile 3 (Median = 350)	72 (34.1)	7 (26.9)		74 (33.2)	5 (35.7)	
Serum 25(OH)D_3 Level (nmol/L)						
< 50	24 (15.1)	4 (17.4)	0.76[b]	25 (14.7)	3 (25.0)	0.40[b]
≥ 50	135 (84.9)	19 (82.6)		145 (85.3)	9 (75.0)	
Serum 25(OH)D_3 Level (nmol/L)						
Tertile 1 (Median = 51)	49 (30.8)	11 (47.8)		54 (31.8)	6 (50.0)	
Tertile 2 (Median = 72)	58 (36.5)	2 (8.7)	0.03	59 (34.7)	1 (8.3)	0.14[b]
Tertile 3 (Median = 109)	52 (32.7)	10 (43.5)		57 (33.5)	5 (41.7)	
	Mean (Std)	**Mean (Std)**	**p-value**[a]	**Mean (Std)**	**Mean (Std)**	***p*-value**[a]
Total Vitamin D Intake (IU/day)	374 (295.6)	409 (326.6)	0.57	376.8 (298.7)	403 (306.7)	0.75
Dietary Vitamin D Intake (IU/day)	232.8 (182.5)	1.72.4 (107.7)	0.15	227.9 (179.4)	198.4 (128.0)	0.65
Serum 25(OH)D_3 Level (nmol/L)	79.4 (31.8)	78.4 (31.7)	0.89	79.5 (31.8)	76.8 (33.4)	0.78

[a] *p*-values from chi-square tests for the categorical variables
[b] *p*-values from Fisher's Exact Test if cell count is less than 5

Table 10. Association of vitamin D intake (n=237) and serum 25(OH)D_3 (n=182) levels with history of depression: The UMass Vitamin D Status Study, 2006-2009

	Unadjusted OR	95 % CI	Age-Adjusted OR[a]	95 % CI	Fully Adjusted OR	95 % CI	p_{trend}
Total Vitamin D Intake (IU/day)							
< 400	1.00	referent	1.00	referent	1.00	referent	0.76
≥ 400	0.95	0.41, 2.2	0.93	0.40, 2.17	0.87[b]	0.36, 2.11	
Total Vitamin D Intake (IU/day)							
Tertile 1 (Median = 107)	1.00	referent	1.00	referent	1.00	referent	
Tertile 2 (Median = 307)	0.56	0.19, 1.62	0.56	0.19, 1.63	0.63[b]	0.21, 1.91	0.64
Tertile 3 (Median = 619)	1.01	0.40, 2.59	1.01	0.39, 2.59	1.04[b]	0.39, 2.82	
Total Vitamin D Intake (per 100 IU/day)	1.04	0.91, 1.18	1.03	0.91, 1.17	1.04[b]	0.90, 1.21	0.56
Dietary Vitamin D Intake (IU/day)							
< 400	1.00	referent	1.00	referent	1.00	referent	0.16
≥ 400	0.25	0.03, 1.92	0.28	0.04, 2.13	0.23[b]	0.03, 1.84	
Dietary Vitamin D Intake(IU/day)							
Tertile 1 (Median = 68)	1.00	referent	1.00	referent	1.00	referent	
Tertile 2 (Median = 180)	0.86	0.33, 2.25	0.85	0.32, 2.24	0.96[b]	0.34, 2.76	0.89
Tertile 3 (Median = 350)	0.66	0.24, 1.84	0.69	0.25, 1.91	0.78[b]	0.27, 2.26	
Dietary Vitamin D (per 100 IU/day)	0.83	0.61, 1.13	0.84	0.61, 1.15	0.87[b]	0.63, 1.20	0.39
Serum 25(OH)D_3 Level (nmol/L)							
< 50	1.00	referent	1.00	referent	1.00	referent	0.76
≥ 50	0.84	0.26, 2.70	1.11	0.28, 2.89	0.82[c]	0.23, 2.96	
Serum 25(OH)D_3 Level (nmol/L)							
Tertile 1 (Median = 51)	1.00	referent	1.00	referent	1.00	referent	
Tertile 2 (Median = 72)	0.15	0.03, 0.73	0.16	0.03, 0.76	0.18[c]	0.04, 0.90	0.03
Tertile 3 (Median = 109)	0.86	0.33, 2.20	0.93	0.36, 2.43	1.58[c]	0.51, 4.86	
Serum 25(OH)D_3 Level (per 10 nmol/L)	0.99	0.86, 1.14	1.00	0.87, 1.15	1.08[c]	0.91, 1.28	0.37

[a] Model adjusted for age (continuously)
[b] Model adjusted for age (continuously), BMI (continuous), season (winter, spring, summer/fall), and ever oral contraceptive use (Y/N)
[c] Model adjusted for age (continuously), BMI (continuous), season (winter, spring, summer/fall), ever oral contraceptive use (Y/N), and ever smoke (Y/N)

Table 11. Association of vitamin D intake (n=237) and serum 25(OH)D_3 (n=182) levels with current antidepressant use: The UMass Vitamin D Status Study, 2006-2009

	Unadjusted OR	95 % CI	Age-Adjusted OR[a]	95 % CI	Fully Adjusted OR	95 % CI	p_{trend}
Total Vitamin D Intake (IU/day)							
< 400	1.00	referent	1.00	referent	1.00	referent	0.54
≥ 400	0.84	0.27, 2.58	0.84	0.27, 2.58	0.69[b]	0.22, 2.22	
Total Vitamin D Intake (IU/day)							
Tertile 1 (Median = 107)	1.00	referent	1.00	referent	1.00	referent	0.80
Tertile 2 (Median = 307)	1.25	0.32, 4.84	1.25	0.32, 4.83	1.59[b]	0.39, 6.37	
Tertile 3 (Median = 619)	1.28	0.33, 4.97	1.29	0.33, 4.98	1.18[b]	0.29, 4.74	
Total Vitamin D Intake (per 100 IU/day)	1.03	0.87, 1.22	1.03	0.87, 1.22	1.01[b]	0.85, 1.21	0.89
Dietary Vitamin D Intake (IU/day)							
< 400	1.00	referent	1.00	referent	1.00	referent	0.42
≥ 400	0.52	0.07, 4.08	0.51	0.06, 4.03	0.42[c]	0.05, 3.51	
Dietary Vitamin D Intake (IU/day)							
Tertile 1 (Median = 68)	1.00	referent	1.00	referent	1.00	referent	0.85
Tertile 2 (Median = 180)	0.77	0.12, 2.98	0.77	0.12, 2.98	0.68[c]	0.16, 2.79	
Tertile 3 (Median = 350)	0.99	0.27, 3.56	0.98	0.27, 3.54	0.94[c]	0.22, 4.03	
Dietary Vitamin D Intake (per 100 IU/day)	0.91	0.61, 1.35	0.91	0.62, 1.35	0.85[c]	0.55, 1.32	0.47
Serum 25(OH)D_3 Level (nmol/L)							
< 50	1.00	referent	1.00	referent	1.00	referent	0.39
≥ 50	0.52	0.13, 2.04	0.50	0.13, 2.0	0.52[d]	0.12, 2.29	
Serum 25(OH)D_3 Level (nmol/L)							
Tertile 1 (Median = 51)	1.00	referent	1.00	referent	1.00	referent	0.20
Tertile 2 (Median = 72)	0.15	0.02, 1.31	0.15	0.12, 1.27	0.14[d]	0.02, 1.24	
Tertile 3 (Median = 109)	0.79	0.23, 2.74	0.76	0.22, 2.65	0.89[d]	0.24, 3.32	
Serum 25(OH)D_3 Level (per 10 nmol/L)	0.97	0.81, 1.18	0.97	0.80, 1.17	1.00[d]	0.82, 1.23	0.99

[a] Model adjusted for age (continuous)
[b] Model adjusted for age (continuous), BMI (continuous), current alcohol consumption (dichotomous)
[c] Model adjusted for age (continuous), BMI (continuous), calcium (continuous), current physical activity (continuous), and current alcohol consumption (dichotomous)
[d] Model adjusted for age (continuous), current alcohol consumption (dichotomous), season (winter, spring, summer/fall), and calcium (dichotomous)

Table 12. Association of vitamin D intake and the depressive symptoms score (n=50): The UMass Vitamin D Status Study, 2006-2009

	Unadjusted β (SE)	*p*-value[a]	Age-Adjusted β (SE)	*p*-value[a]	Fully Adjusted β[b] (SE)	*p*-value[a]
Total Vitamin D Intake (IU/day)						
< 400	1.00	referent	1.00	referent	1.00	referent
≥ 400	2.48 (3.08)	0.42	2.47 (3.11)	0.43	3.72 (3.09)	0.24
Total Vitamin D Intake (IU/day)						
Tertile 1 (Median = 107)	1.00	referent	1.00	referent	1.00	referent
Tertile 2 (Median = 307)	(-) 2.39 (3.28)	0.47	(-) 2.47 (3.33)	0.46	(-) 2.59 (3.30)	0.44
Tertile 3 (Median = 619)	1.99 (3.63)	0.59	1.91 (3.69)	0.61	3.80 (3.70)	0.31
Total Vitamin D Intake (per 100 IU/day)	(-) 0.02 (0.38)	0.96	(-) 0.02 (0.38)	0.96	(-) 0.003 (0.42)	0.99
Dietary Vitamin D Intake (IU/day)						
< 400	1.00	referent	1.00	referent	1.00	referent
≥ 400	7.56 (4.60)	0.11	7.67 (4.66)	0.11	6.18 (4.46)	0.17
Dietary Vitamin D Intake (IU/day)						
Tertile 1 (Median = 68)	1.00	referent	1.00	referent	1.00	referent
Tertile 2 (Median = 180)	(-) 4.81 (4.01)	0.24	(-) 5.02 (4.10)	0.23	(-) 2.64 (4.29)	0.54
Tertile 3 (Median = 350)	(-) 0.60 (3.32)	0.86	(-) 0.80 (3.41)	0.82	0.49 (3.48)	0.89
Dietary Vitamin D Intake (per 100 IU/day)	1.02 (1.11)	0.36	1.01 (1.12)	0.38	0.81 (1.11)	0.47

[a] *p*-values from *t*-tests for continuous variables

[b] Model adjusted for age (continuous), BMI (continuous), current physical activity (continuous), and season (winter, spring, summer/fall)

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