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Associations between Vitamin D Levels and Depressive Symptoms in Healthy Young Adult Women

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Abstract

There have been few studies of whether vitamin D insufficiency is linked with depression in healthy young women despite women's high rates of both problems. Female undergraduates (n = 185) living in the Pacific Northwest during fall, winter, and spring academic terms completed the Center for Epidemiologic Studies Depression (CES-D) scale weekly for four weeks (W1–W5). We measured serum levels of vitamin D_3 and C (ascorbate; as a control variable) in blood samples collected at W1 and W5. Vitamin D insufficiency (<30ng/mL) was common at W1 (42%) and W5 (46%), and rates of clinically significant depressive symptoms (CES-D ≥ 16) were 35–42% at W1–W5. Lower W1 vitamin D_3 predicted clinically significant depressive symptoms across W1–W5 ($\beta = -.20$, $p < .05$), controlling for season, BMI, race/ethnicity, diet, exercise, and time outside. There was some evidence that lower levels of depressive symptoms in Fall participants (vs. Winter and Spring) were explained by their higher levels of vitamin D_3. W1 depressive symptoms did not predict change in vitamin D_3 levels from W1 to W5. Findings are consistent

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Conflict of interest

David T. Zava is CEO of ZRT Laboratory. The authors have no other conflicts to disclose.

Contributors

David Kerr conceptualized the study, served as PI on the grant and study, conducted the data analyses, and had primary responsibility for writing the manuscript. David Zava supervised the vitamin D assays, wrote critical portions of the methods and limitations, and edited and approved the manuscript. Walter Piper played a chief role in recruiting participants, and the collection, processing, and storage of blood samples; contributed to study conceptualization and literature review; and reviewed and approved the manuscript. Sarina Saturn participated in conceptualization of the study and grant proposal; contributed to the literature review and wrote sections of the introduction and discussion; and reviewed and approved the manuscript. Balz Frei contributed to study conceptualization; provided institutional support for the project; supervised the vitamin C assays; contributed to the literature review; and edited and approved the manuscript. Adrian Gombart contributed to conceptualization of the study and grant proposal; supervised procedures related to collection and storage of blood samples; contributed to the literature review; wrote sections of the introduction, method, and discussion; and edited and approved the manuscript.

with a temporal association between low levels of vitamin D and clinically meaningful depressive symptoms. The preventive value of supplementation should be tested further.

Keywords

depressive symptoms; vitamin D; seasonal affective disorder

1. Introduction

Depression is a major public health problem that is linked with premature death by suicide and other causes (Chesney et al., 2014), and disability and economic burden (Greenberg et al., 2003). According to a nationally representative study lifetime prevalence of major depressive disorder was 25% among American women (vs. 16% for men; Kessler et al., 2003). Moreover, a longterm repeated measures study through age 30 years recently indicated the cumulative incidence rate was a staggering 63.4% for women (vs. 34.7% among men; Rohde et al., 2013[1]). Thus, depression places an enormous health burden on young women, in particular.

Some epidemiological studies suggest low levels of vitamin D [25-hydroxyvitamin D or 25(OH)D] may contribute to depression. Proposed biological mechanisms for this association include that vitamin D: 1) has receptors that are distributed in brain areas involved in emotional processing and affective disorders (Eyles et al., 2013, Kesby et al., 2011); 2) regulates serotonin synthesis via transcriptional activation of the tryptophan hydroxylase 2 gene (Patrick & Ames, 2014); and 3) impacts innate immunity and the production of proinflammatory cytokines that in turn influence mood by activating the stress response (Capuron & Miller, 2004; Raison et al., 2006; Silverman et al., 2005; Zhang et al., 2012).

However, evidence for an association between vitamin D sufficiency status and depression is inconclusive. Meta-analyses (Li et al., 2013; Shaffer et al., 2014) indicate vitamin D supplementation trials have not shown significant effects on depression. Likewise, a meta-analysis of 10 cross-sectional studies indicated the odds of depression were not significantly elevated among those with low levels of vitamin D compared to others (Anglin et al., 2013). Importantly, researchers often have not adjusted for important confounders, and have used definitions of vitamin D insufficiency or deficiency that are based on risk for medical conditions. These cut-offs may be arbitrary with respect to risk for depression, and thus their use in research may have contributed to null findings. Indeed, levels (vs. cut-offs) of vitamin D in 18–65 year olds were found to be lower among participants with current or remitted depression relative to controls, and associated with symptom severity and a worsened two-year course (Milaneschi et al., 2014). Thus, alternative measurement and design approaches are needed.

Another problem with the current evidence base on relations between vitamin D and depression is that findings may not generalize to healthy young women. Indeed, most

[1]Rates by gender given by P. Rohde & J. M. Gau, personal communication, May 1, 2014.

experimental and observational research concerns older or medically compromised populations (e.g., Jorde et al., 2008; Parker and Brotchie, 2011; Sanders et al., 2011). In an important exception, Ganji and colleagues (2010) found that rates of current depression were associated with vitamin D deficiency in a nationally representative U.S. sample of young adults. Of note, however, they did not control for season of the year or some other important confounds.

Studying young healthy women minimizes the possibility that observed associations between vitamin D and depression are explained by significant health conditions, age variation, or gender. However, a number of potential confounders remain, including race/ethnicity, health behaviors, and season (Ganji et al., 2010; Hollis, 2005; Norman, 1998). Regarding seasonal effects, humans can generate sufficient vitamin D subcutaneously when exposed to sunlight (Norman, 1998). During non-summer months, however, meteorological and behavioral factors can limit skin exposure to sunlight and lead to decreased production of vitamin D_3 and rapid depletion of body reserves. For this reason, individuals from a range of climates often become vitamin D insufficient in the winter and do not regain sufficiency for months (Holick, 2007).

Given that vitamin D levels vary with season of the year and may have an inverse relationship with depressive symptoms, some have suggested vitamin D may play a role in explaining seasonal affective disorder (SAD) and seasonality (the milder spectrum of sensitivity of mood and behavior to seasonal changes). Leading models of SAD emphasize the disruption of vulnerable individuals' circadian rhythms following seasonal changes in day length (Rohan et al., 2009). However, day length is confounded with other factors (intensity of solar radiation, cloud cover, clothing) that explain seasonal variation in vitamin D. Thus, it is possible that seasonal changes in vitamin D levels account for some of the seasonal variation in depressive symptoms. Despite the intuitive appeal of this theory, it has not been studied extensively. In a case control study Kjaergaard and colleagues (2012) found that participants from Northern Norway showed a range of seasonality scores, but scores did not differ for those with insufficient versus sufficient vitamin D levels. Furthermore, they found that seasonality scores did not decrease more following high-dose vitamin D supplementation than following placebo. Reviews of the topic yield little conclusive support for a role of vitamin D in the etiology and treatment of SAD or seasonality (see Bertone-Johnson, 2009; Parker & Brotchie, 2011). However, further research is needed using larger samples and stronger study designs.

The present study builds on the extant literature in several ways. First, we test whether vitamin D levels are associated with depressive symptoms in healthy young women; such women rarely have been considered in this literature despite their high risk for depression and the straightforward implications such research may have for prevention. Second, we use a latent variable to estimate clinically significant depressive symptoms over a four week period, a measurement approach that is more reliable than using a cut-off score based on a single assessment. Third, in addition to controlling for participant characteristics and health behaviors, we control for vitamin C levels to evaluate the specificity of the vitamin D path of interest. Finally, we integrate prior findings on seasonal and racial/ethnic group differences in the separate literatures on vitamin D sufficiency and depressive symptoms

(Eisenberg et al., 2013; Ganji et al., 2010; Hollis, 2005; Norman, 1998). That is, we hypothesize that any differences in depressive symptoms by season or race/ethnicity will be explained in part by group differences in vitamin D levels (i.e., indirect effects).

2. Methods

2.1. Participants

Participants were 185 undergraduate women ages 18–25 years [mean (SD) = 19.66 (1.56)] who were enrolled at a large university in the northwestern United States. Inclusion criteria for participation were: female gender; not currently pregnant; self-reported weight of 110 pounds or greater[2]; and willingness to complete web-based surveys and contribute two 10-mL blood samples. From the initial sample of 190 enrolled participants, 5 were excluded from the present analyses because they were over the age of 25 years (n = 3) or did not have data on vitamin D level at baseline (n = 2). Participants identified as White (n = 153, 82.7%), African American (n = 4, 2.2%), Asian (n = 20, 10.8%), Pacific Islander (n = 3, 1.6%), Native American (n = 3, 1.6%), Hispanic (n = 21, 11.4%), and “other” (n = 3, 1.6%) race/ethnicity.

2.2. Procedures

Participants were recruited from a psychology department subject pool in the fall, winter, or spring terms (n = 86, 36, and 63, respectively). Participants were recruited each week for the first half of each 10-week term (baseline recruitment dates of 9/26/2011–10/26/2011; 1/16/2012–2/1/2012; 4/3/2012–5/2/2012) and surveyed weekly for 4 weeks. Participants were not recruited after the fifth week of the term to avoid conflicts with final exams and university breaks. In an in-person baseline appointment individuals answered whether they were eligible based on inclusion criteria described above. Eligible women completed informed consent. Participants who enrolled completed the W1 web-based survey on a lab computer. They scheduled non-fasting blood draw appointments for 2–3 days later (W1) and 4 weeks later (W5). Following the first blood draw, participants began receiving a survey web link by email once per week for 4 weeks (W2–W5). Participants were allowed 48 hours to complete each survey before the link became inactive. After the final survey (W5), participants were reminded of their second blood draw appointment.

Time of day of blood draws was variable (9am–4pm). Phlebotomists recorded participants' heights and weights and then collected 10 mL of venous blood. Samples were settled for 20–30 minutes and then centrifuged for 10 minutes at 1500 g at room temperature. Serum was aliquoted and stored at −80°C. Vitamins D and C were assayed in separate labs.

Participants were compensated for completing the five surveys and W1 blood draw with course extra-credit; participants were paid $25 for the W5 blood draw. All procedures were approved by the university IRB. Participation rates on online surveys at W2–W5 were high (98%, 98%, 95%, 98%), and 95% of participants completed all surveys. Participation rate at the W5 blood draw also was high (98%).

[2]The IRB used this cut-off for defining a study as minimal risk.

2.3 Measures

2.3.1. Depressive symptoms—On the five W1 through W5 surveys, participants completed the 20-item Center for Epidemiologic Studies Depression (CES-D) scale (Radloff, 1977). Participants used a 4-point scale (rarely or none of the time [0–1 day] coded '0' to most or all of the time [5–7 days] coded '3') to report how often they felt symptoms in the past week. Internal consistency was adequate at all waves (α = .89 to .92). Scores also were coded as clinically significant (yes '1' or no '0') if they reached the cut-off score of 16.

2.3.2. Vitamin D and C blood concentrations—Total 25(OH)D concentrations were determined by measuring 25(OH)D_2 and 25(OH)D_3 in solvent-extracted serum samples by LC-MS/MS at ZRT Laboratory (Beaverton, OR; Newman et al., 2009). This assay was calibrated using National Institute of Standards Technology (NIST) standard reference materials. Continued method accuracy was ensured by participation in College of American Pathologists (CAP) and Vitamin D External Quality Assessment Scheme (DEQAS) proficiency testing schemes that require laboratories to meet performance targets assigned by the CDC Reference Laboratory and NIST Reference Measurement Procedure respectively. Vitamin D_2 levels were below detectable levels (<4 ng/mL) in 98% of samples and thus did not contribute to total blood concentration estimates. Therefore, statistical models used vitamin D_3 levels only; descriptive statistics on deficiency and insufficiency rates were based on total vitamin D as is the convention. Vitamin C (ascorbate) blood level was analyzed by ion-paired, reverse phase HPLC with electrochemical detection (Suh et al., 2003) at Linus Pauling Institute (Corvallis, OR).

2.3.3. Season—For regression models two variables (Winter vs. Fall, and Spring vs. Fall) were created to represent the academic term of participation. Fall term was the referent (coded 0, 0); winter and spring term participation were coded 1, 0 and 0, 1 respectively.

2.3.4. Body Mass Index (BMI)—Participant height and weight (no shoes) were measured at the time of the W1 blood sample and converted to BMI.

The remaining covariates were collected on the W1 self-report survey.

2.3.5. White, non-Hispanic race/ethnicity—This variable was coded "1" for participants (73.5%, n=136) who did not endorse any race/ethnicity other than White, non-Hispanic, and "0" for all others (also referred to as *women of color*).

2.3.6. Exercise time—Duration in minutes was calculated from responses to the question, "How many hours and minutes of exercise did you get in total this week?" Reported exercise from one outlying participant who reported 26 hours of exercise was excluded.

2.3.7. Time outside in daylight hours—Duration in minutes was calculated from the question, "Including exercise, how many hours and minutes of time this week did you spend outside during daylight hours?" and then was natural log transformed to reduce skewness.

2.3.8. Dietary intake of vitamin D—Past month dietary intake of vitamin D was estimated using a screening instrument developed by Blalock and colleagues (2003). For

each of 22 vitamin D rich or fortified foods (e.g., 2% milk, shrimp, eggs) participants answered how often they consumed the food in the past month and what sized serving they usually consumed (small, medium or large; defined for each food). Intake was then calculated in micrograms per month using tables provided by the National Cancer Institute (2009). A square root transformation reduced skewness.

2.3.9. Antidepressant and multivitamin use—Participants answered the questions (no '0', yes '1'), "Do you currently take an antidepressant medication (such as Prozac, Paxil, Zoloft, Lexapro, Celexa, Effexor, Cymbalta, Strattera, or Wellbutrin) for depression, anxiety, inattention, or another reason?" and "Do you take a vitamin D supplement or a multivitamin that includes vitamin D?"

2.4. Data analysis

We first examined descriptive statistics for continuous and binary measures of depressive symptoms and vitamin D_3 levels to characterize the sample. We also evaluated univariate associations between these variables, and relations depressive symptoms and vitamin D_3 levels had with study covariates. Next we fit a latent variable[3] model with binary indicators for clinically significant symptoms at W1–W5 using Mplus version 6.12. We used the default robust weighted least squares estimator, which uses probit regressions to regress the binary indicators on a latent factor (Muthen & Muthen, 2011). The model fit the data when a covariance between W4 and W5 depression scores was specified [Model χ^2 (df = 4) = .706, p = .95].

We tested our primary hypothesis using this latent variable representing clinically significant depressive symptoms. To do so we regressed the latent variable on W1 vitamin D_3 blood concentration while simultaneously regressing both variables on multiple potentially confounding covariates (including season and race/ethnicity).

Finally, using this model we explored whether any prediction of depressive symptoms from season of participation would be explained by an indirect effect through vitamin D_3 levels. Similarly, we explored whether any effects of race/ethnicity on depressive symptoms would be partially explained by racial/ethnic group differences in vitamin D_3 levels. These possibilities were evaluated by examining total, direct, and indirect effects of these predictors on depressive symptoms. An indirect effect would be supported if a significant total effect of a predictor on depressive symptoms could be decomposed into a significant indirect effect via vitamin D_3 levels and a significant or non-significant remaining direct effect.

[3]We initially explored whether a growth model for level and change in clinically significant depressive symptoms from W1 to W5 could be identified. However, a number of different growth models (e.g., linear, linear spline, quadratic) failed to specify patterns of change over the 4 week study period.

3. Results

3.1. Descriptive statistics

Descriptive statistics are reported in Table 1. At each of five observations, 34% to 41% of participants reported clinically significant depressive symptoms. Rates of vitamin D insufficiency [*n* = 58 (31%) at 20–29.99 ng/mL] and deficiency [*n* = 19 (10%) at <20ng/mL] at baseline and at four week follow-up [*n* = 57 (31%) insufficient and *n* = 27 (15%) deficient, out of 182 participants] were common. Antidepressant medication and multivitamin use were reported by 10% and 42% of participants, respectively. Statistics on other covariates are listed in Table 1.

3.2. Unadjusted associations between vitamin D_3 and depressive symptoms

Consistent with our hypothesis, vitamin D_3 levels and depressive symptoms generally were negatively correlated (see Table 2). Tests of these associations using cut-off scores for both variables further illustrate these results. That is, chi-square analyses indicated women who were vitamin D sufficient at W1 less often had clinically significant depressive symptoms across W1–W5 [χ^2 (1) = 5.40 to 8.48, all $p < .05$]. For example, 26% (28 of 108) of participants with sufficient vitamin D at W1 reported depressive symptoms that exceeded the clinical cut-off at W1 compared to 45% (35 of 77) of participants with deficient or insufficient W1 levels. Sufficiency at W5 also was consistently related to W1–W5 depressive symptom cut-off scores in the predicted direction, but was only significantly associated at W3 and W4 [χ^2 (1) = 7.33 and 5.21, respectively, $p < .05$].

3.3. Associations of covariates with depressive symptoms and vitamin D_3

Correlations that study covariates had with depressive symptoms and vitamin D_3 levels (see Table 3) supported the need to control for them in the final model. Lower depressive symptoms generally were associated with White/non-Hispanic race/ethnicity, having lower BMI, and not using antidepressants. Regarding seasonal differences in depressive symptoms, mean symptom scores across W1–W5 were lowest among participants recruited in fall term [ANOVA F (2, 179) = 3.73, $p < .05$]; CES-D means (SD) for fall, winter, and spring term participants were 12.3 (8.2), 16.4 (7.3), and 14.9 (8.6), respectively.

Correlations that covariates had with vitamin D_3 levels also are reported in Table 3; higher levels were associated with being White/non-Hispanic, having lower BMI, exercising more, taking a multivitamin, and having higher levels of vitamin C. Differences in vitamin D_3 by season were examined using repeated measures ANOVA. As expected, vitamin D_3 level [F (2, 178) = 4.49, $p < .05$] and change [F (2, 178) = 27.67, $p < .001$] varied by whether women participated in fall, winter, or spring term. Vitamin D tended to be lower in winter than in fall and spring terms, and from W1 to W5 levels tended to decrease among fall participants, remain stable among winter participants, and increase among spring participants[4]. Chi-square analyses also showed that W1 vitamin D sufficiency rates differed by race/ethnicity

[4]Specifically, mean (SD) vitamin D_3 levels for fall, winter, and spring participants at W1 were = 37.37 (12.55), 28.05 (10.98), and 31.05 (11.38) ng/mL, respectively; and at W5 were 32.58 (12.07), 27.91 (12.11), and 34.64 (11.84) ng/mL, respectively. Considered differently, rates of sufficiency at W1 in fall, winter, and spring terms were 73%, 33%, and 52%, respectively [χ^2 (2) = 18.06, p< .001] and at W5 were 55%, 31%, and 65% [χ^2 (2) = 11.14, p < .01].

[χ^2 (1) = 10.54, p< .01] and vitamin supplement use [χ^2 (1) = 11.13, p< .001]; specifically, sufficiency rates were 39% for women of color, compared to 65% for other women; and 73% for those taking supplements versus 48% for others.

3.4. Multivariate prediction model of clinically significant depressive symptoms

Next we built on the unconditional model described in the data analysis section by regressing the latent variable (representing clinically significant depressive symptoms) on W1 vitamin D_3 levels, and simultaneously regressing both of these variables on: race/ethnicity, BMI, dietary D intake, exercise, time outside, vitamin C levels, antidepressant use, and the two variables representing season of recruitment. As shown in Table 4, vitamin D_3 was negatively associated with the probability of clinically significant depressive symptoms after covariates were controlled[5]. Antidepressant use was the only other independent predictor of symptoms.

We then explored whether the previously identified associations of season and race/ethnicity with depressive symptoms were explained by effects on vitamin D_3 levels (see Table 4 notes). Indirect paths were significant for season[6] of participation and race/ethnicity suggesting effects of these variables on depressive symptoms were partially explained by their effects on vitamin D_3.

4. Discussion

Vitamin D_3 levels were negatively related to clinically significant depressive symptoms across five weekly assessments in healthy young adult women. These findings are important given that previous studies often have concerned older adults and special medical populations, or have not controlled for important confounds (Ganji et al., 2010; Jorde et al., 2008; Sanders et al., 2011). Without an experimental design we cannot conclude that low vitamin D levels caused depressive symptoms (or that high levels were protective). However, we found no evidence for the reverse causal sequence; depressive symptoms did not predict change in vitamin D_3 across the four week study, whereas other factors did.

Mean depressive symptoms were lower in women who participated in Fall than in other terms, and this pattern was partially explained by their higher levels of vitamin D_3 relative to those of Winter and Spring participants. Thus, seasonal changes in vitamin D_3 may be an underappreciated mechanism in models of seasonality and SAD. Although we controlled for time spent outside, it remains possible that low vitamin D_3 levels are simply a proxy for low sunlight exposure or reduced day length that influence depression through other (e.g.,

[5]Our modeling approach did not provide information about temporal ordering of associations between W1 vitamin D_3 and W1–W5 depressive symptoms. Thus, we tested an alternative model that depressive symptoms led to decreases in vitamin D. We regressed W5 vitamin D_3 levels on W1 depressive symptoms and covariates (term of participation, BMI, race/ethnicity, dietary vitamin D, exercise, time outside, antidepressant use, and multivitamin use). The strong predictive path from vitamin D_3 levels at W1 to levels at W5 was controlled [Est (SE) = .83 (.05), β = .84, p < .001]; thus the W5 vitamin D_3 outcome is interpreted as *change* in vitamin D_3 levels from W1 to W5. Relatively positive changes in vitamin D_3 from W1 to W5 (more pronounced increases or less pronounced decreases) were predicted by winter and spring participation [vs. fall; Est (SE) = 2.72 (1.35), β = .09, p < .05 and Est (SE) = 6.92 (1.07), β = .27, p < .001, respectively], and White, non-Hispanic race/ethnicity [Est (SE) = 2.61 (1.11), β = .09, p < .05], but not by W1 depressive symptom scores [Est (SE) = .07 (.05), β = .05, p = n.s.] or other predictors. Results did not differ appreciably when the binary depression variable (clinically significant depressive symptoms) was used, or when the same model was run using W2 depressive symptoms as the predictor. Thus, the alternative hypothesis was not supported.

[6]The effects of winter vs. fall (significant) and spring vs. fall (marginally significant) must be interpreted jointly.

circadian) mechanisms. Studies that disentangle multiple etiological mechanisms by which depressive symptoms are responsive to time of the year are needed, as few high quality studies exist (Bertone-Johnson, 2009). In the present sample, seasonal differences in depressive symptoms were very modest overall, suggesting season is not a prominent influence on depressive symptoms in young adult women. Thus, larger samples of individuals at high risk for SAD will be needed for etiological studies.

Consistent with prior research, our findings indicated that young women of color were more often vitamin D insufficient and depressed than other women (Eisenberg et al., 2013; Ganji et al., 2010; Hollis, 2005; Norman, 1998). Notably, the association between race/ethnicity and depressive symptoms was partially explained by levels of vitamin D_3. To our knowledge this is the first study to report such a pattern. Although the reasons for these effects are unknown (e.g., effects of melanin on endogenous vitamin D_3 production; Norman, 1998) it is possible that vitamin D insufficiency contributes to mental health problems in young minority women, and that supplementation may help reduce this burden. To date, no supplementation trials have focused on preventing or reducing depression among people of color, despite their separately documented risks for vitamin D insufficiency and depression.

Finally, a few observed patterns in vitamin D_3 levels deserve further comment. Vitamin D_3 levels showed the expected seasonal patterns in terms of absolute level and change over the four week follow-up; these patterns likely reflected seasonal changes in intensity and duration of skin exposure to sunlight. Still, insufficiency was observed in all three seasons (assessments spanned eight months of the year, end of September to end of May). Additionally, null findings regarding dietary intake of vitamin D were consistent with the notion that even foods that are fortified or naturally rich in vitamin D make negligible contributions to blood levels relative to season (sunlight exposure) or vitamin supplement use (Holick et al., 2011). Thus, supplementation may be relevant to some populations year-round.

4.1. Limitations

Our sample was recruited from a university and a single geographic location; how representative participants were of healthy young adult women is unknown. Another limitation was the reliance on self-report measures of health behaviors and depressive symptoms rather than, for example, a clinical interview to establish a diagnosis of depression. Additionally, although our repeated measures design was an advance over prior studies, the follow-up period was so short and the constructs of interest were so stable during this period that statistical power may have been too low to detect and predict change over time. Finally, we did not screen for health factors that may affect vitamin D levels such as anticonvulsant or antiretroviral medication use, inflammatory bowel disease, or tanning bed use, which is widespread (36% of U.S. women ages 18–24 years; Choi et al., 2010) and associated with vitamin D production (Tangpricha et al., 2004).

4.2. Conclusions

Vitamin D deficiency and insufficiency occur at high rates in healthy young women, and lower vitamin D_3 levels are related to clinically significant depressive symptoms. Supplementation is a simple, low cost, and low risk intervention. Given the lifespan health risks associated with insufficiency (e.g., Giovannucci, 2009), supplementation is warranted whether or not the modest role of vitamin D in depression observed here generalizes more broadly. Future research on multi-dimensional etiological models of seasonal depression should include measures of vitamin D levels. Controlled trials are needed to examine the extent to which vitamin D supplementation can prevent seasonal and non-seasonal forms of depression, and whether women of color are especially likely to benefit.

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Highlights

- Depressive symptoms and vitamin D were measured in 185 healthy women across four weeks.
- Significant symptoms and vitamin D insufficiency were common, and differed by season.
- Initially low vitamin D levels were associated with clinically significant depressive symptoms across follow-up.
- Between-subjects differences in depression by season were partially explained by seasonal changes in vitamin D.
- Racial-ethnic differences in depression were partially explained by group differences in vitamin D levels.

Table 1

Descriptive statistics on study measures.

Study measure	Continuous Scale	Categorical Scale
Depressive symptoms	Mean (SD)	Clinically significant
W1	14.04 (9.11)	34%
W2	15.23 (9.68)	42%
W3	14.13 (10.15)	39%
W4	13.21 (9.55)	35%
W5	13.43 (10.22)	36%
Vitamin D_3 (ng/mL), blood concentration	Mean (SD)	Sufficiency[1]
W1	33.40 (12.42)	31% insufficient
		10% deficient
W5	32.36 (12.17)	31% insufficient
		15% deficient
Body mass index (kg/m^2)	Mean (SD)	CDC cut-points
W1	24.79 (4.79)	1% underweight
		62% normal
		27% overweight
		10% obese
Dietary vitamin D intake (μg/month)	Mean (SD)	
W1 unadjusted[2]	182.45 (178.37)	
W1 ln-transformed	4.79 (0.97)	
Exercise (minutes/week)	Mean (SD)	
W1	282.31 (193.68)	
Time outside (minutes/week)	Mean (SD)	
W1 unadjusted	522.97 (520.29)	
W1 square root-transformed	20.32 (10.52)	
Ascorbate (μM), blood concentration	Mean (SD)	
W1	59.31 (21.79)	

Note.

[1] rates based on total vitamin D (D_2 + D_3).

[2] for reference, current U.S. recommended dietary allowance is 15 μg per day (~450 μg/month; Holick et al., 2011)

Table 2

Correlations among CES-D depressive symptoms (W1–W5) and vitamin D_3 (ng/mL, W1 and W5).

	CES-D, W1	**CES-D, W2**	**CES-D, W3**	**CES-D, W4**	**CES-D, W5**	**Vit D_3, W1**	**Vit D_3, W5**
CES-D, W1		.72***	.68***	.62***	.56***	−.13†	−.07
CES-D, W2			.74***	.65***	.59***	−.23**	−.15*
CES-D, W3				.77***	.61***	−.18*	−.17*
CES-D, W4					.68***	−.24**	−.13†
CES-D, W5						−.21**	−.13†
Vitamin D_3, W1							.82***
Vitamin D_3, W5							

Note. CES-D: Center for Epidemiologic Studies Depression scale; W1–W5: Wave 1 – Wave 5.

† $p < .10$.

* $p < .05$.

** $p < .01$

*** $p < .001$.

Table 3

Correlations of study covariates with outcomes.

	Depressive symptoms (CES-D)					Vitamin D_3	
	W1	**W2**	**W3**	**W4**	**W5**	**W1**	**W5**
White/non-Hispanic	−.10	−.22**	−.22**	−.13†	−.12	.33***	.38***
BMI	.12	.17*	.19*	.17*	.18*	−.17*	−.17*
Dietary D intake (ln)	−.08	−.08	−.10	−.13†	−.08	.09	.01
Exercise	.00	.05	−.02	−.01	−.07	.18*	.13†
Time outside (square root)	−.06	−.12	−.17*	−.15†	−.08	.02	.04
Vitamin C	.01	−.08	−.10	−.14†	−.12	.20**	.11
Multivitamin use	−.02	−.01	−.02	−.02	−.00	.19*	.21**
Antidepressant use	.17*	.12	.14†	.20**	.29***	.10	.13†

Note. CES-D: Center for Epidemiologic Studies Depression scale; BMI: body mass index.

† $p < .10$.

* $p < .05$.

** $p < .01$

*** $p < .001$.

Table 4

Results of untrimmed path model predicting depressive symptoms from vitamin D and covariates.

	Vitamin D_3 (observed)		Depressive symptoms (latent factor)	
Predictor	**Est (SE)**	**β**	**Est (SE)**	**β**
Vitamin D_3			−.02 (.01)	$-.20^{*}$
Winter vs. Fall	−9.06 (2.21)	$-.29^{***}$	.18 (.22)	.07
Spring vs. Fall	−5.80 (1.89)	$-.22^{**}$	.16 (.19)	.08
White/non-Hispanic	8.41 (2.22)	$.30^{***}$	−.25 (.19)	−.11
BMI	−.29 (.25)	−.11	.03 (.02)	.15
Dietary D intake (ln)	.72 (.72)	.06	.04 (.09)	.04
Exercise	.01 (.00)	$.16^{*}$	.00 (.00)	.02
Time outside (square root)	−.08 (.08)	−.07	−.01 (.02)	$-.14^{\dagger}$
Vitamin C	.07 (.04)	$.13^{*}$	−.00 (.00)	−.03
Antidepressant use	4.44 (2.06)	$.11^{*}$	.71 (.29)	$.22^{*}$

Note. Covariance of W4 and W5 depressive symptoms Est (SE) = .17 (.09), β = .17*. Vitamin D3 intercept Est (SE) = 23.64 (7.79), $p < .01$. Model χ^2 ($df = 44$) = 40.19, $p = .64$. Total and indirect effects on depressive symptoms were as follows: Winter term participation: total [Est (SE) = .33 (.21), β = .13, p = n.s.] and indirect [Est (SE) = .15 (.07), β = .06, $p < .05$] effects; Spring term participation: total [Est (SE) = .25 (.19), β = .12, p = n.s.] and indirect [Est (SE) = .09 (.05), β = .05, $p = .06$]; White/non-Hispanic race/ethnicity: total [Est (SE) = −.39 (.18), β = −.18, $p < .05$] and indirect [Est (SE) = −.15 (.07), β = −.06, $p < .05$] effects.

$^{\dagger}p < .10$.

$^{*}p < .05$.

$^{**}p < .01$

$^{***}p < .001$.