HHS Public Access

Author manuscript

Prev Med. Author manuscript; available in PMC 2017 December 01.

Published in final edited form as:

Prev Med. 2016 December ; 93: 166–170. doi:10.1016/j.ypmed.2016.09.035.

Repletion of Vitamin D associated with deterioration of sleep quality among postmenopausal women

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Abstract

Reduced health-related quality of life (HRQOL), depressive symptoms and poor sleep quality are important health issues among postmenopausal women and may be associated with low vitamin D status. Overweight postmenopausal women, with serum 25-hydroxyvitamin D [25(OH)D] 10–32 ng/m, were recruited in Seattle, WA (2010–2012) and randomly assigned to 12 months of weight loss + 2000 IU oral vitamin D_3/day or weight loss + daily placebo. The weight-loss program included a reduced-calorie diet and 225 min/week of moderate-to-vigorous aerobic activity. Eight subscales of HRQOL were assessed by the MOS 36-Item Short-Form Health Survey. Depressive symptoms were assessed using the Brief Symptom Inventory-18, and sleep quality was assessed using the Pittsburg Sleep Quality Index (PSQI). Mean 12-month changes in HRQOL, depressive symptoms and sleep quality were compared between groups (intent-to-treat) using generalized estimating equations. Compared to placebo, women receiving vitamin D did not experience any significant change in depressive symptoms ($p=0.78$), HRQOL subscales (all $p>0.05$), or overall sleep quality ($p=0.21$). However, a greater magnitude of change in serum 25(OH)D was associated with an increased need to take medications to sleep ($p_{trend}=0.01$) and overall worse sleep quality ($p_{trend}<0.01$). Women who became vitamin D replete (≥32 ng/mL) also showed a deterioration in total PSQI sleep quality score compared to women who remained <32 ng/mL despite supplementation, even after adjusting for relevant covariates (Non-Replete: −5.7% vs. Replete: +6.2%, $p<0.01$). Vitamin D supplementation of 2000 IU/d may result in overall worse sleep quality for postmenopausal women with low circulating vitamin D undergoing weight loss.

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Disclosures: The authors have no conflicts of interest to report.

Trial Registration: www.clinicaltrials.gov Identifier **NCT01240213**

Keywords

25-hydroxyvitamin D; caloric restriction; exercise; quality of life; sleep; depression

INTRODUCTION

Low vitamin D status is a prevalent condition (Chowdhury et al., 2014) that has been associated with a wide range of adverse health outcomes including insomnia, pain, and depressive symptoms (Andersen and Tufik, 2012; Anglin et al., 2013).

A recent meta-analysis of 14 observational studies (10 cross-sectional, 1 case-control; 3 longitudinal) showed that low serum vitamin D is associated with increased risk of depression (Anglin et al., 2013). However, randomized controlled trials have produced conflicting results, likely due to large differences in dose and duration of supplementation. For example, the Women's Health Initiative Calcium and Vitamin D Trial reported an odds ratio for presenting depressive symptoms of 1.16 (95% CI=0.86–1.56) in 36,282 postmenopausal women randomized to receive vitamin D (400 IU/day) plus calcium (1000 mg/day) supplementation vs. placebo (Bertone-Johnson et al., 2012). In contrast, a smaller trial using higher doses of vitamin D (20,000 or 40,000 IU/week) for 12 months showed a significant reduction in depression scores compared to placebo in 441 overweight and obese adults (Jorde et al., 2008).

Other studies suggest that vitamin D may alleviate pain symptoms and improve sleep quality and health-related quality of life (HRQOL). For example, low serum vitamin D has been associated with higher odds of short (<5 h) sleep duration and lower sleep efficiency in a large sample of community-dwelling older men (Massa et al., 2015), as well as with shorter sleep duration in a multiethnic sample of adults (Bertisch et al., 2015), and with longer time to fall asleep in a population-based US sample (Shiue, 2013). Low circulating vitamin D levels are also associated with poor physical performance and lower muscle strength (Bischoff-Ferrari et al., 2004; Houston et al., 2012). Among U.S. veterans with chronic pain and low serum 25(OH)D (<30 ng/ml), vitamin D supplementation alleviated pain symptoms and improved sleep as well as vitality, general health, and social functioning scores of HRQOL (Huang et al., 2013). In a randomized study of high dose vitamin D (150,000 IU) in 84 adults with musculoskeletal pain, those receiving vitamin D had a lower pain score compared to placebo after 6 weeks (Schreuder et al., 2012). Another trial showed that vitamin D (300,000 IU orally or intramuscularly) improved both physical and mental aspects of HRQOL in 120 older adults (≥65 y)(Sakalli et al., 2012).

Although several trials have reported the effects of vitamin D supplementation on depressive symptoms, few studies have examined the associations between vitamin D, sleep, and HRQOL. Further, few data come from randomized controlled trials, and those that have been published show conflicting results. Therefore, the purpose of this study was to investigate the effects of 12 months of oral vitamin D_3 supplementation (2000 IU/day) versus placebo on changes in 8 HRQOL subscales (physical functioning, role-physical, bodily pain, vitality, general health, social functioning, role-emotional, and mental health), depressive symptoms, and sleep quality, among overweight or obese postmenopausal women with insufficient

levels of circulating vitamin D (serum 25(OH)D ≥10 − <32 ng/mL) participating in a structured behavioral weight loss program.

METHODS & PROCEDURES

The Vitamin D, Diet and Activity (ViDA) study (Trial Registration: www.clinicaltrials.gov Identifier NCT01240213) was a 12-month double-blind, placebo-controlled randomized clinical trial conducted 2010–2012 in Seattle, WA that tested oral vitamin D_3 supplementation (cholecalciferol, 2000 IU/day) vs. placebo on weight and related biomarkers in overweight and obese postmenopausal women with low serum 25(OH)D concentrations who were participating in a lifestyle-based weight-loss program. Study details have been previously published (Mason et al., 2014). Study procedures were reviewed and approved by the Fred Hutchinson Cancer Research Center Institutional Review Board. All participants provided signed Informed Consent.

Briefly, 218 overweight (BMI ≥25 kg/m^2) postmenopausal (50–75 years) women with serum 25(OH)D concentrations ≥10 ng/mL and <32 ng/mL ('insufficient') were randomly assigned to 12 months of either: i) 2000 IU/day vitamin D_3 + a lifestyle-based weight-loss program (n=109; 'Vitamin D'), or ii) daily placebo + a lifestyle-based weight-loss program (n=109; 'Placebo'). All study staff except statisticians were blinded to randomization status.

The vitamin D preparation (2000 IU cholecalciferol) and matching placebo (sunflower oil) gel capsules were created and bottled by J.R. Carlson Laboratories, Inc. (Arlington, IL) as previously described (Mason et al., 2014). The weight loss program included both a diet and exercise component, adapted from a successful intervention based on the Diabetes Prevention Program and Look Ahead lifestyle change weight loss programs (Mason et al., 2014). The goals of the diet intervention were: total daily energy intake of 1200–2000 kcal/day based on baseline weight, <30% daily energy intake from fat, and a 10% reduction in body weight by 6 months with maintenance thereafter to 12 months. The goal of the exercise program was: ≥45 minutes of moderate-to-vigorous intensity exercise (e.g., treadmill walking or jogging, stationary bicycling), 5 days per week (225 min/week) for 12 months completed during supervised sessions at our exercise facility and at home.

All measures were taken at baseline (pre-randomization) and 12 months. HRQOL was assessed by the MOS 36-Item Short-Form Health Survey (SF-36)(Ware, 1993). Eight subscales (physical functioning, role-physical, bodily pain, vitality, general health, social functioning, role-emotional, and mental health) were calculated, per standard scoring protocol. Scores range from 0 to 100 with higher scores indicating better HRQOL. Depressive symptoms were assessed using the Brief Symptom Inventory-18 (BSI) and T scores were assigned according to the scoring manual (Derogatis, 2001) with higher scores indicating more symptoms of depression and anxiety. Sleep quality and disturbances were assessed and scored using the Pittsburg Sleep Quality Index (PQSI) (Buysse et al., 1989) with higher scores associated with worse sleep quality and greater sleep restlessness, and total scores ≥5 indicating poor sleep quality.

Participants also completed a series of questionnaires to assess demographic information, medical history, health habits, reproductive and body weight history, dietary intake and supplement use, physical activity patterns, and habitual sun exposure (Mason et al., 2014). Anthropometric measures were taken using standard methods. Body composition was measured using a dual x-ray absorptiometry (DXA) whole-body scanner (GE Lunar, Madison, WI).

Serum vitamin D was measured as previously described (Mason et al., 2014) from blood collected at baseline and at 12 months. Assays were performed using DiaSorin LIAISON 25-OH Vitamin D Total assay. The inter- and intra-assay coefficients of variability (CVs) were 11.2 % and 8.1%, respectively.

No serious adverse events were reported.

Statistical Analysis

Mean 12-month changes in 25(OH)D, HRQOL, sleep, and depression symptoms, stratified by study arm, were computed. The intervention effects were examined based on the assigned treatment at randomization, regardless of adherence or study retention (i.e. intent-to-treat). Mean 12-month changes in the vitamin D group were compared to placebo using the generalized estimating equations (GEE) modification of linear regression to account for intra-individual correlation over time. Among women randomized to receive vitamin D, changes in the outcome measures were compared according to 12-month changes in serum 25(OH)D (tertiles), as well as in women who did vs. did not become replete (≥32 ng/mL) according to our pre-study definition. Additional analyses examined changes in outcomes across categories of weight loss (gain/no loss, <5% loss, 5–10% loss, ≥10% loss). Models were initially unadjusted, and subsequently adjusted for age, race/ethnicity (white, other), baseline serum 25(OH)D, vitamin D intake (diet + non-study supplements), average sun exposure, caffeine intake and/or alcohol intake, and antidepressant and/or sleep medication use. The GEE approach for mixed-model regression using the available data was applied to address missing data.

All analyses were performed using SAS software version 9.2 (SAS Institute Inc., Cary, NC).

RESULTS

Complete demographic information for randomized women is published elsewhere (Mason et al., 2014). The majority (86%) were non-Hispanic white; the mean age and BMI were 59.6 ± 5.1 years and 32.4 ± 5.8 kg/m^2, respectively. The mean baseline serum 25(OH)D concentration was 21.4 ± 5.1 ng/mL, and the mean 12-month changes in serum 25(OH)D were +13.6 ng/mL in the vitamin D arm versus − 1.3 ng/mL in the placebo arm ($p<0.0001$). There was no significant difference in mean weight change between groups (Vit D: −8.2% vs. P: −8.4%, p=0.41)(Mason et al., 2014). Unused study pills were returned by only 55% of participants; however pill compliance was high in this subset (Vit D: 98%, Placebo: 96%).

The 12-month changes in depressive symptoms, HRQOL, and sleep quality are shown in Table 1. Compared to placebo, women receiving vitamin D supplementation did not

experience any significant change in depressive symptoms (p=0.78) or any of the 8 HRQOL subscales (all p>0.05). Changes in measures of sleep quality also did not significantly differ between study arms at 12-months (all p>0.05).

Among 109 women receiving vitamin D, no significant trends in 12-month changes in average sun exposure, depressive symptoms or HRQOL were detected across tertiles of change in serum 25(OH)D (all p_{trend} >0.05) (results not shown). However, a greater magnitude of change in serum 25(OH)D was associated with an increased need to take medications to sleep (p_{trend}=0.01) and a higher PSQI sleep score (p_{trend}<0.01) indicating overall worse sleep quality (Table 2). When compared to women who remained vitamin D insufficient (N= 40) despite supplementation (i.e., <32 ng/mL), women who became replete (≥32 ng/mL; N= 53) also showed a deterioration in total PSQI sleep quality score after adjusting for age, race/ethnicity (non-Hispanic white, others), baseline serum 25(OH)D, vitamin D intake (diet + non-study supplement), average sun exposure, and caffeine intake (Non-Replete: −5.7% vs. Replete: +6.2%, p<0.01)(results not shown). Additional analyses found no significant changes in any outcome according to percent weight loss (see Supplemental Table).

DISCUSSION

Although insomnia, pain, and depressive symptoms are caused by multiple biological mechanisms, some evidence suggests that low levels of vitamin D could be an underlying contributing factor (Andersen and Tufik, 2012; Anglin et al., 2013). However, we observed no effect of 2000 IU vitamin D supplementation daily for 12 months on depressive symptoms, HRQOL, or sleep quality measured by the PSQI in overweight or obese postmenopausal women.

Based on findings from a 2-year uncontrolled trial of 1500 patients with neurological complaints, it has been hypothesized that vitamin D supplementation may ameliorate multiple sleep disorders (Gominak and Stumpf, 2012). Yet, in our trial, women who experienced the greatest change in circulating 25(OH)D over 12 months were more likely to report needing medications to sleep and experienced a deterioration in total sleep quality. Similar findings were reported among women who reached our pre-study definition of repletion (25(OH)D >32ng/mL) compared to those who remained ≤32ng/mL despite supplementation. Our findings are also consistent with cross-sectional findings from the US National Health and Nutrition Examination Survey (NHANES) that reported more sleep complaints among people with higher levels of vitamin D (Shiue, 2013). The reason for these finding are uncertain. Underlying genetic factors that affect vitamin D metabolism may be involved.

There remains no consensus definition of vitamin D sufficiency and it is unknown whether vitamin D-related outcomes are more strongly related to a specific magnitude of change in 25(OH)D (e.g. 10 ng/mL) or to a change in status defined by reaching a specific threshold level (e.g. >32 ng/mL). This remains an important area for future investigation, as does the effect of individualizing vitamin D therapy to repletion at specific levels. In the aforementioned uncontrolled study that observed improvements in sleep disturbances over a

2 year period, participants maintained a consistent circulating vitamin D level of 60–80 ng/mL over many months (Gominak and Stumpf, 2012). We may have observed stronger effects using a more stringent definition of vitamin D insufficiency, a higher dose of supplementation, or in a study sample reporting more depressive symptoms, poorer HRQOL, and more sleep disturbances at baseline.

Strengths of our study include its double-blind randomized controlled design and its relatively long duration. However, all sleep measures were self-reported, and detailed information on the timing of sleep medication use was not collected; thus, the timing and degree to which the initiation of sleep medications may have affected other aspects of sleep quality and quality of life are unknown. Further, because our study population was relatively homogeneous our results may not be generalizable beyond predominantly Caucasian postmenopausal women. In addition, we did not test the independent effects of vitamin D without a weight loss intervention. Diet and exercise programs have been shown to affect HRQOL, depressive symptoms and sleep, albeit generally improving these outcomes (Imayama et al., 2011; Reid et al., 2010).

CONCLUSION

Given the vast and varied physiological functions of vitamin D, further investigation into its relationship with sleep in diverse populations is needed to better elucidate its potential as a therapeutic agent.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

Susan G. Komen for the Cure Scientific Advisory Council Award 2010–12, the National Cancer Institute (NCI) R03 CA162482-01, and a grant from the Breast Cancer Research Foundation (“Effect of Vitamin D and Weight Loss on Biomarkers of Breast Cancer Risk”).

References

Andersen ML, Tufik S. Vitamin D as an underlying factor in sleep-related issues. J Clin Sleep Med. 2012; 8:699. [PubMed: 23243404]

Anglin RE, Samaan Z, Walter SD, McDonald SD. Vitamin D deficiency and depression in adults: systematic review and meta-analysis. Br J Psychiatry. 2013; 202:100–7. [PubMed: 23377209]

Bertisch SM, Sillau S, de Boer IH, Szklo M, Redline S. 25-Hydroxyvitamin D Concentration and Sleep Duration and Continuity: Multi-Ethnic Study of Atherosclerosis. Sleep. 2015; 38:1305–11. [PubMed: 25669179]

Bertone-Johnson ER, Powers SI, Spangler L, Larson J, Michael YL, Millen AE, Bueche MN, Salmoirago-Blotcher E, Wassertheil-Smoller S, et al. Vitamin D supplementation and depression in the women’s health initiative calcium and vitamin D trial. Am J Epidemiol. 2012; 176:1–13. [PubMed: 22573431]

Bischoff-Ferrari HA, Dietrich T, Orav EJ, Hu FB, Zhang Y, Karlson EW, Dawson-Hughes B. Higher 25-hydroxyvitamin D concentrations are associated with better lower-extremity function in both active and inactive persons aged > or =60 y. Am J Clin Nutr. 2004; 80:752–8. [PubMed: 15321818]

Buysse DJ, Reynolds CF 3rd, Monk TH, Berman SR, Kupfer DJ. The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research. Psychiatry Res. 1989; 28:193–213. [PubMed: 2748771]

Chowdhury R, Kunutsor S, Vitezova A, Oliver-Williams C, Chowdhury S, Kiefte-de-Jong JC, Khan H, Baena CP, Prabhakaran D, et al. Vitamin D and risk of cause specific death: systematic review and meta-analysis of observational cohort and randomised intervention studies. BMJ. 2014; 348:g1903. [PubMed: 24690623]

Derogatis, LR. Brief Symptom Inventory 18: Administration, s., and, procedures manual. Minneapolis: NCS Pearson, I.; 2001.

Gominak SC, Stumpf WE. The world epidemic of sleep disorders is linked to vitamin D deficiency. Med Hypotheses. 2012; 79:132–5. [PubMed: 22583560]

Houston DK, Tooze JA, Neiberg RH, Hausman DB, Johnson MA, Cauley JA, Bauer DC, Cawthon PM, Shea MK, et al. 25-hydroxyvitamin D status and change in physical performance and strength in older adults: the Health, Aging, and Body Composition Study. Am J Epidemiol. 2012; 176:1025–34. [PubMed: 23118104]

Huang W, Shah S, Long Q, Crankshaw AK, Tangpricha V. Improvement of pain, sleep, and quality of life in chronic pain patients with vitamin D supplementation. Clin J Pain. 2013; 29:341–7. [PubMed: 22699141]

Imayama I, Alfano CM, Kong A, Foster-Schubert KE, Bain CE, Xiao L, Duggan C, Wang CY, Campbell KL, et al. Dietary weight loss and exercise interventions effects on quality of life in overweight/obese postmenopausal women: a randomized controlled trial. Int J Behav Nutr Phys Act. 2011; 8:118. [PubMed: 22026966]

Jorde R, Sneve M, Figenschau Y, Svartberg J, Waterloo K. Effects of vitamin D supplementation on symptoms of depression in overweight and obese subjects: randomized double blind trial. J Intern Med. 2008; 264:599–609. [PubMed: 18793245]

Mason C, Xiao L, Imayama I, Duggan C, Wang CY, Korde L, McTiernan A. Vitamin D3 supplementation during weight loss: a double-blind randomized controlled trial. Am J Clin Nutr. 2014; 99:1015–25. [PubMed: 24622804]

Massa J, Stone KL, Wei EK, Harrison SL, Barrett-Connor E, Lane NE, Paudel M, Redline S, Ancoli-Israel S, et al. Vitamin D and actigraphic sleep outcomes in older community-dwelling men: the MrOS sleep study. Sleep. 2015; 38:251–7. [PubMed: 25581929]

Reid KJ, Baron KG, Lu B, Naylor E, Wolfe L, Zee PC. Aerobic exercise improves self-reported sleep and quality of life in older adults with insomnia. Sleep Med. 2010; 11:934–40. [PubMed: 20813580]

Sakalli H, Arslan D, Yucel AE. The effect of oral and parenteral vitamin D supplementation in the elderly: a prospective, double-blinded, randomized, placebo-controlled study. Rheumatol Int. 2012; 32:2279–83. [PubMed: 21556746]

Schreuder F, Bernsen RM, van der Wouden JC. Vitamin D supplementation for nonspecific musculoskeletal pain in non-Western immigrants: a randomized controlled trial. Ann Fam Med. 2012; 10:547–55. [PubMed: 23149532]

Shiue I. Low vitamin D levels in adults with longer time to fall asleep: US NHANES, 2005–2006. Int J Cardiol. 2013; 168:5074–5. [PubMed: 23938219]

Ware, JE. SF 36 health survey: manual and interpretation guide. Boston, MA: The Health Institute New England Medical Center; 1993.

Highlights

- Low vitamin D may be associated with poor sleep and reduced quality of life (QOL)
- We compared 2000 IU vitD/day vs placebo in women completing a weight loss program
- Vit D did not significantly improve sleep, depressive symptoms or QOL over 12 months
- Vitamin D repletion >32 ng/mL was associated with worse sleep quality

Table 1

12-month changes in depressive symptoms, health-related quality of life (HRQOL), and sleep quality in women randomized to 2000IU/d vitamin D versus placebo

	Placebo								Vitamin D									
	Baseline			12 month			Change		Baseline			12 month			Change		P-value	
Variable	**N**	**Mean**	**STD**	**N**	**Mean**	**STD**	**Abs**	**%**	**N**	**Mean**	**STD**	**N**	**Mean**	**STD**	**Abs**	**%**	**P***	**P†**
Depression symptoms[1]	109	44.2	7.13	91	44.3	6.05	0.07	0.16	109	44.8	7.01	89	44.9	6.92	0.06	0.12	0.85	0.78
Health-related Quality of Life[2]																		
Physical functioning	109	84.5	17.5	91	91.2	13.7	6.69	7.9	109	85.4	18.0	89	88.1	17.5	2.72	3.2	0.21	0.61
Role-physical	109	86.0	25.8	91	89.0	25.6	3.00	3.5	109	86.7	28.0	89	86.2	28.7	−0.46	−0.5	0.45	0.34
Bodily pain	109	77.3	19.5	91	73.4	19.4	−3.91	−5.1	109	76.7	18.4	89	77.0	19.3	0.33	0.4	0.07	0.08
General health	108	57.4	11.1	90	59.3	13.1	1.92	3.4	109	57.6	12.3	89	61.9	11.0	4.22	7.3	0.18	0.21
Vitality	109	67.2	14.9	91	73.0	14.9	5.80	8.6	109	65.1	18.4	89	71.7	15.5	6.59	10.1	0.67	0.56
Social functioning	109	91.7	14.6	91	92.0	15.5	0.29	0.3	109	90.5	15.3	89	94.5	11.6	4.04	4.5	0.13	0.10
Role-emotional	109	83.8	31.6	91	91.9	21.3	8.15	9.7	109	86.2	28.4	89	91.8	22.6	5.52	6.4	0.47	0.52
Mental health	109	79.9	13.4	91	81.8	13.4	1.91	2.4	109	79.0	13.6	89	81.8	13.0	2.76	3.5	0.65	0.71
Sleep Quality[3]																		
Sleep duration	109	0.6	0.8	91	0.7	0.8	0.05	8.7	109	0.6	0.8	89	0.6	0.8	0.02	3.0	0.70	0.96
Sleep disturbances	105	1.3	0.5	87	1.3	0.5	0.01	0.4	104	1.3	0.5	84	1.3	0.5	−0.04	−3.0	0.74	0.99
Sleep latency	108	1.0	0.9	89	0.9	0.9	−0.06	−6.1	108	0.9	1.0	89	1.0	1.0	0.02	2.3	0.44	0.53
Daytime function due to sleepiness	109	0.6	0.6	91	0.6	0.6	−0.05	−7.9	109	0.6	0.7	89	0.5	0.6	−0.16	−25.8	0.31	0.65
Sleep efficiency	107	2.7	0.9	89	2.6	1.0	−0.10	−3.7	109	2.7	0.9	88	2.7	0.9	0.06	2.4	0.39	0.36
Overall sleep quality	108	1.0	0.7	90	1.0	0.7	−0.01	−0.6	109	0.9	0.8	89	1.0	0.8	0.03	3.1	0.79	0.63
Needs medication to sleep	109	0.6	1.0	91	0.5	1.0	−0.04	−7.7	109	0.4	0.9	89	0.6	1.0	0.12	27.6	0.18	0.06
Total PSQI sleep quality score	102	7.7	3.2	84	7.4	2.8	−0.29	−3.7	103	7.5	2.9	83	7.6	2.9	0.14	1.9	0.38	0.21

*p value comparing 12-month changes in vitamin D vs. placebo, unadjusted

†p value comparing 12-month changes in vitamin D vs. placebo, adjusted for relevant covariates.

[1]Measured by the Brief Symptom Inventory-18; T scores were assigned according to the scoring manual (Derogatis, 2001) with higher scores indicating more symptoms of depression and anxiety. Relevant adjusting covariates included age, race/ethnicity, marital status, antidepressant use, baseline serum 25(OH)D, vitamin D intake (diet + non-study supplement), alcohol intake, average sun exposure.

[2]Measured by the MOS 36-Item Short-Form Health Survey (Ware, 1993). Scores range from 0 to 100 with higher scores indicating better HRQOL. Relevant adjusting covariates included age, race/ethnicity, marital status, antidepressant use, baseline serum 25(OH)D, vitamin D intake (diet + non-study supplement), alcohol intake, average sun exposure.

[3]Assessed and scored using the Pittsburg Sleep Quality Index (Buysse et al., 1989) with higher scores associated with worse sleep quality and greater sleep restlessness, and total scores ≥5 indicating poor sleep quality. Relevant adjusting covariates included age, race/ethnicity (non-Hispanic white, others), baseline serum 25(OH)D, vitamin D intake (diet + non-study supplement), caffeine intake, average sun exposure.

Table 2

12-month change in sleep quality and disturbances according to tertile* of change in circulating 25(OH)D among women randomized to receive 2000 IU/d vitamin D.

		Baseline			12 month			Change			
Variable		**N**	**Mean**	**STD**	**N**	**Mean**	**STD**	**Abs**	**%**	**P†**	**P‡**
Sleep duration	T1	31	0.7	0.9	28	0.6	0.8	−0.1	−18.2	*ref*	
	T2	31	0.4	0.7	30	0.4	0.7	0.1	22.1	*0.39*	*0.19*
	T3	31	0.6	0.9	31	0.7	0.8	0.1	21.1	*0.29*	*0.18*
	P-trend									*0.29*	*0.19*
Sleep disturbances	T1	30	1.1	0.5	26	1.1	0.4	−0.1	−5.0	*ref*	
	T2	27	1.5	0.5	27	1.4	0.5	−0.1	−9.8	*0.46*	*0.79*
	T3	31	1.2	0.4	31	1.3	0.5	0.1	11.1	*0.19*	*0.06*
	P-trend									*0.20*	*0.07*
Sleep latency	T1	31	1.0	1.1	28	0.9	0.9	−0.1	−11.4	*ref*	
	T2	31	0.9	0.8	30	0.8	0.8	0.0	−4.3	*0.70*	*0.61*
	T3	31	1.00	0.9	31	1.2	1.1	0.2	19.4	*0.10*	*0.10*
	P-trend									*0.09*	*0.10*
Daytime function due to sleepiness	T1	31	0.6	0.8	28	0.4	0.5	−0.3	−44.6	*ref*	
	T2	31	0.6	0.7	30	0.4	0.6	−0.1	−25.4	*0.47*	*0.18*
	T3	31	0.6	0.6	31	0.5	0.7	−0.1	−10.5	*0.27*	*0.06*
	P-trend									*0.27*	*0.07*
Sleep efficiency	T1	31	2.7	0.8	27	2.7	0.9	0	−0.2	*ref*	
	T2	31	2.8	0.6	30	2.7	0.8	−0.1	−3.7	*0.31*	*0.47*
	T3	31	2.6	1.0	31	2.7	0.9	0.1	3.7	*0.66*	*0.30*
	P-trend									*0.62*	*0.27*
Overall sleep quality	T1	31	1.1	0.9	28	1.1	0.8	0	0.6	*ref*	
	T2	31	1.00	0.7	30	0.8	0.7	−0.2	−20	*0.25*	*0.54*
	T3	31	0.7	0.8	31	1.00	0.9	0.3	40.9	*0.21*	*0.24*
	P-trend									*0.19*	*0.21*
Needs medication to sleep	T1	31	0.8	1.2	28	0.5	1.0	−0.2	−30.8	*ref*	
	T2	31	0.5	0.9	30	0.7	1.1	0.2	47.6	*0.05*	*0.06*

Variable		Baseline			12 month			Change			
		N	Mean	STD	N	Mean	STD	Abs	%	P†	P‡
	T3	31	0.1	0.4	31	0.5	1.0	0.4	275	*0.01*	*0.01*
	P-trend									*0.01*	*0.01*
Total PSQI sleep quality score	T1	30	8.2	3.5	25	7.4	2.4	−0.8	−10.1	*ref*	
	T2	27	7.7	2.5	27	7.5	2.9	−0.3	−3.3	*0.50*	*0.18*
	T3	31	6.8	2.1	31	8.0	3.2	1.1	16.5	*0.01*	*<0.01*
	P-trend									*0.01*	*<0.01*