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The Effect of Physical Activity on Vitamin D Status in Pregnant Women Participating in a Randomized Controlled Trial

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Abstract

Objective: Determine the effect of physical activity on vitamin D (vitD) status in pregnant women.

Design/Methods: Women who presented at 10-14 weeks' gestation participated in vitD supplementation RCT, conducted between November 2012 and June 2016, were randomized into one of two treatment groups: 400 or 4400 IU/day of vitD3. VitD status, as defined by total circulating 25(OH)D concentration, was measured monthly. Physical activity was measured monthly using the Paffenbarger Questionnaire, and responses were categorized as vigorously exercising for $</\geq$ 2.5 h/week during each trimester. Sunlight exposure was measured using skin spectrophotometry (SmartProbe 400). Linear regression and mixed models explored the association of maternal 25(OH)D concentration, sunlight exposure, physical activity, race, treatment group, body mass index, perceived stress score, and visit using SAS software (version 9.4).

Results: 211 pregnant women had physical activity information available. At baseline, vigorously exercising ≥ 2.5 h/week was associated with being older ($p=0.0004$), white/Caucasian ($p=0.011$), privately insured ($p=0.018$), and purposefully pregnant ($p<0.031$). Baseline 25(OH)D did not vary by treatment or exercise groups. In bivariate analysis, at second trimester, vigorously exercising ≥ 2.5 h/week was associated with being white/Caucasian, privately insured, purposefully pregnant, married and with higher 25(OH)D concentration. By third trimester, vigorous exercise was associated with being privately insured, married, gravidity, sunlight exposure and Hispanic. The effect of increased exercise on 25(OH)D concentration was seen only in the 400 IU group at third trimester. In a mixed model controlling for multiple potential confounders, maternal vitD status and exercise were positively associated ($p=0.018$).

Conclusion: Independent of sunlight exposure, pregnant women who vigorously exercised ≥ 2.5 h/week had higher 25(OH)D concentrations than those who did not. Supplementation may have overshadowed the exercise effect; the positive correlation was amplified when looking at the 400 IU group alone, and may suggest that exercise was more critical for those lacking the higher supplementation dose.

Keywords: Vitamin D; 25-hydroxyvitamin D; 25(OH)D; Exercise, Physical activity; Pregnant women; Pregnancy

Introduction

Vitamin D is a fat-soluble vitamin and steroid hormone known to play a vital role in numerous physiologic processes classically involving calcium and bone metabolism, but also involving muscle, lipid and glucose metabolism [1], immune functioning [1], and the cardiovascular system [2,3]. Vitamin D is acquired in two ways: from conversion of 7-dehydrocholesterol into pre-vitamin D_3 in the skin by sunlight (ultraviolet B irradiation) or from diet or supplementation in the form of cholecalciferol (vitamin D_3) or ergocalciferol (vitamin D_2) [1,4]. These forms of vitamin D are converted to 25-hydroxyvitamin D (25(OH)D or calcidiol), the indicator of vitamin D status and the primary circulating form that is ultimately converted to the biologically active form 1,25-dihydroxycholecalciferol (1,25(OH)2D or calcitriol) [1,4]. Vitamin D concentration is affected by many factors, including diet, sunlight exposure, geographic relation to the equator, skin pigmentation, race/ethnicity, age of skin, ability to absorb fat-soluble vitamins, body mass index (BMI), and exercise [2,4].

Previous research has shown a positive association between physical activity and vitamin D levels [5-7]. This association has been noted whether the activity occurs indoors or outdoors [8], in both the young [9] and the old [6,7], and even in patients with active diseases such as cancer [10]. Recent evidence shows a link between physical activity and vitamin D status in postpartum women early after delivery, but little data is available regarding this association during pregnancy [11].

Vitamin D is known to benefit both mothers and their babies during pregnancy. Vitamin D plays an important immunologic role at the maternal-fetal interface as it appears to be involved in immunologic tolerance of the developing fetus while simultaneously protecting against infection [12]. Maternal vitamin D deficiency is not only associated with a higher risk of neonatal vitamin D deficiency and nutritional rickets [13] and craniotabes [14], it is also associated with preterm labor and preterm birth [15,16], and the delivery of babies that are small for gestational age when there is profound deficiency [17]. Additionally, mothers with vitamin D deficiency were more likely to have insulin resistance [18], which has inherent complications of its own. Much research has been performed regarding safety and necessity of vitamin D supplementation during pregnancy [15,19].

Maternal serum 25(OH)D concentrations ≥ 100 nmol/L (≥ 40 ng/mL) compared to <50 nmol/L (<20 ng/mL) significantly decreased the risk of preterm birth and achieved maximal production of 1,25(OH)2D [20]; this was reiterated in a follow-up study involving a large, diverse population of women [21].

While data exist linking exercise and its association with vitamin D status in other groups, little data are available on the specific effects that physical activity duration and intensity have on vitamin D status in pregnant women. The purpose of this study was to explore that relationship. Our hypothesis was that higher intensity and duration of physical activity independent of sunlight exposure would lead to higher concentrations of total circulating 25(OH)D as the indicator of vitamin D status in pregnant women.

Materials and Methods

Study design and sample collection

A prospective randomized controlled trial (RCT) involving pregnant women beginning at 10-14 weeks' gestation was conducted. Women were randomized to one of two treatment groups: 400 or 4400 IU/day of vitamin D_3 (the Kellogg Foundation Vitamin D Pregnancy Study; See 'Study Setting' section below). The women participated in this RCT between November 2012 and June 2016. Any mother age 18-45 years who presented to one of the Medical University of South Carolina (MUSC) facilities within the first 14 weeks after her last menstrual period with confirmation of a singleton pregnancy was eligible for participation in the RCT. Mothers of diverse ethnic backgrounds were actively recruited. Participants were excluded for pre-existing calcium disorders, uncontrolled thyroid disease, parathyroid disorders, requirement of chronic diuretic or cardiac medication including calcium channel blockers, pre-existing sickle cell disease (does not refer to only having sickle cell trait), sarcoidosis, Crohn's disease, ulcerative colitis, or multiple gestations. A sub-group of approximately 100 subjects with known diabetes, hypertension, HIV, or morbid obesity (BMI > 49) were included in a sub-arm of the RCT, but were excluded from this analysis given their preexisting history of chronic disease.

Study setting

The study occurred at latitude 32°78' N at MUSC and its affiliated health care centers, which is an urban academic center that primarily serves the Charleston, South Carolina (USA) Tri-County area, but which also receives patients from the surrounding regions. Approval was granted by MUSC's Institutional Review Board for Human Subjects (HR#20570) and Clinical and Translational Research Center (CTRC; protocol 5620) and registered via ClinicalTrials.gov (NCT#01932788).

Study protocol

Study visits and completion of questionnaires: At the first visit, following their written, informed consent, mothers completed validated questionnaires used in the NICHD vitamin D pregnancy trial (19), which included information regarding sociodemographic information, baseline health status and medical history. At the second visit (V2, 16 weeks of gestation, 1st trimester), 5th visit (V5, 28 weeks of gestation, 2nd trimester) and 7th visit (V7, 36 weeks of gestation, 3rd trimester) visit, exercise degree and intensity as well as perceived stress and sunlight exposure were assessed as described below.

Maternal sociodemographic and health status questionnaires were completed at baseline and then at monthly study visits until delivery. Physical activity assessments as measured by questionnaire (see Physical Activity section below) were performed at V2, V5 and V7. Degree of skin pigmentation at 2 body sites was measured and assessed at each visit (see Degree of Skin Pigmentation section below). Baseline blood samples were obtained at the initial visit; however, the earliest time of randomization following measurement of baseline total circulating 25(OH)D was 10 weeks' gestation with the target upper limit of gestation of 14 weeks' gestation. Irrespective of enrollment gestational age, vitamin D supplementation did not begin before the tenth week of gestation (10 and 0/7th weeks).

Multi-Vitamin and Vitamin D Supplementation: Pregnant women who presented for prenatal care between 10-14 completed weeks of gestation were randomized into one of two treatment regimens of vitamin D_3. The control group received a placebo in gummy form (Church & Dwight Co., Inc., Princeton, NJ) plus a generic prenatal vitamin containing 400 IU vitamin D_3 (totaling 400 IU vitamin D3). The comparative group received 4,000 IU vitamin D_3 in gummy form (Church & Dwight Co., Inc., Princeton, NJ) plus a generic prenatal vitamin containing 400 IU vitamin D_3 (totaling 4,400 IU vitamin D_3). Those women who had a total circulating 25(OH)D <37.5 nmol/L at visit 4 received open label treatment with 4400 IU vitamin D_3/day.

Study measurements

The major measurements collected and utilized in this study were as follows:

Maternal sociodemographics: Measures included maternal age at time of enrollment, her self-defined race/ethnicity, insurance status, educational status, and occupation and employment outside of the home.

Gestational age at enrollment: Participants could be consented and enrolled into the study before the initiation of vitamin D supplementation at 10-14 completed weeks of gestation. Gestational age was based on last menstrual period. If a woman was unsure of her gestational age, the obstetrical estimate at the time of the visit was used. If, at the 20-week fetal ultrasound it was determined by the obstetrician that the gestational age was incorrect, the revised gestational age was used and the discrepancy noted.

Vitamin D status: Maternal blood samples were collected at baseline and during visits 2, 5 and 7, as described above. Circulating 25(OH)D was measured using a commercially available radioimmunoassay (DiaSorin, Stillwater, MN), and serving as the indicator for maternal vitamin D status.

Physical activity: Physical activity was subjectively measured using the validated Paffenbarger Physical Activity Questionnaire [22]. Light activity included office work, driving a car, strolling, standing with little motion, etc. Moderate activity included housework, light sports, regular walking, golf, yard work, lawn mowing, painting, repairing, ballroom dancing, bicycling on ground level, etc. Vigorous activity included digging in the garden, strenuous sports, jogging, aerobic dancing, sustained swimming, brisk walking, heavy carpentry, bicycling on hills, etc.

The intensity of physical activity was initially converted using the Compendium of Physical Activity [23] to metabolic equivalents (METS) and then METS/minute. Because almost every participant in the study reported at least 2.5 h of "moderate" physical activity per week (which is consistent with the U.S. Department of Health and Human Service's recommendation for 150 minutes or 2.5 h of moderate exercise per week) [24], women were categorized according to whether they engaged in greater than or equal to 2.5 h, or less than 2.5 h of "vigorous" physical activity per week. This was measured at the three time points: V2, V5, and V7.

Maternal perceived stress: Maternal stress was measured using the Perceived Stress Scale (PSS), a validated instrument first published in 1983 and since revised, which is the most widely used psychological instrument for measuring the perception of stress [25]. Items were designed to tap how unpredictable, uncontrollable, and overloaded respondents find their lives. Individual scores on the PSS can range from 0 to 40, with higher scores indicating higher perceived stress. Scores ranging from 0-13 would be considered low stress; those ranging from 14-26 would be considered moderate stress; and those ranging from 27-40 would be considered high perceived stress [25].

Maternal BMI measurement: Pre-pregnancy height and weight of each mother were recorded at the first outpatient visit to determine BMI (weight (kg)/height^2 (m^2)) [26]. During subsequent visits, only the mother's weight was recorded, and the initial height and updated weight were used to calculate BMI at each outpatient visit.

Seasonality: Seasonality was defined as spring/summer months from April through September and fall/winter months from October through March.

Degree of Skin Pigmentation (DSP) Differences in Exposed vs. Unexposed Body Sites and Change over Time Using Spectrophotometer Measurements: At the initial visit, the degree of skin pigmentation (DSP) was measured at 2 sites: the left forearm (exposed site) and left lower hip/buttock (unexposed site) using the SmartProbe-400 spectrophotometer (IMS, Portland, ME). The SmartProbe-400 returned a value for DSP on a scale of 0-100, with lower numbers signifying darker skin pigmentation [27,28]. In previous studies conducted by our group [15], the greatest difference was found between the forearm (exposed area) and the lower hip (unexposed area), with lower DSP values for those areas of the body with more sun exposure and darker skin coloration or "tanning" (data not shown). The difference in DSP values between each of the two sites was calculated and the difference in DSP (ΔDSP) between the sites served as a surrogate for sunlight exposure at each visit and between visits.

Statistics

For this aspect of the study, the primary outcome of interest was the effect of physical activity on maternal total circulating 25(OH)D concentration over time, and, secondarily, if, after controlling for sunlight exposure (as measured by greatest change in DSP between exposed and unexposed sites), did these effects on vitamin D status persist. Analyses employed chi-square for categorical variables; ANOVA or Student's t test, as appropriate, for normally distributed variables (with the Bonferroni option for pairwise analysis in ANOVA); and paired Student's t test for within-group changes from baseline to delivery. Variables that were not normally distributed were analyzed with Wilcoxon-Mann-Whitney test. A mixed-model regression analysis was created to assess the relationship of maternal total circulating 25(OH)D concentration with other factors that included time (visit) and which were found to be significant in bivariate analyses or known to be associated with vitamin D status. Specifically, the mixed model explored the association of total circulating 25(OH)D concentration at various time points (visits) with sunlight exposure (as measured by ΔDSP), vigorous exercise dichotomized as ≥ or <2.5 hr/week, race/ethnicity, perceived stress score (PSS), BMI, treatment, and treatment by visit interactions. Significance was set at $p<0.05$. Data were analyzed using SAS 9.4 software (SAS Institute, Cary, NC, USA).

Results

Study participants

As illustrated in Figure 1, of the 407 who were consented, 71 were excluded due to chronic illnesses, prior enrollment in the study during an earlier pregnancy, or open label vitamin D treatment due to a circulating 25(OH)D concentration <15 ng/mL (37.5 nmol/L) at a subsequent study visit. Of the remaining 336 who were randomized, 125 were excluded due to not having physical activity information recorded at V2, V5, or V7. The participants on whom physical activity was not recorded differed somewhat from those for whom physical activity was recorded. Specifically, Caucasian women were more likely to record physical activity than African American or Hispanic pregnant women in the cohort ($p<0.0001$). Non-high school graduates ($p=0.0009$) and non-employed women ($p<0.0001$) were less likely to record physical activity. Older women were more likely to record physical activity ($p=0.03$). Women with lower Perceived Stress Score (PSS) at baseline were more likely to have recorded exercise ($p=0.001$). Women with higher 25(OH)D concentrations at baseline were likely to have recorded exercise ($p=0.01$). There were no differences among participants who recorded physical activity compared to those who did not in terms of marital and insurance status, planned vs. unplanned pregnancy, season of enrollment, gestational age at enrollment, BMI, or treatment group.

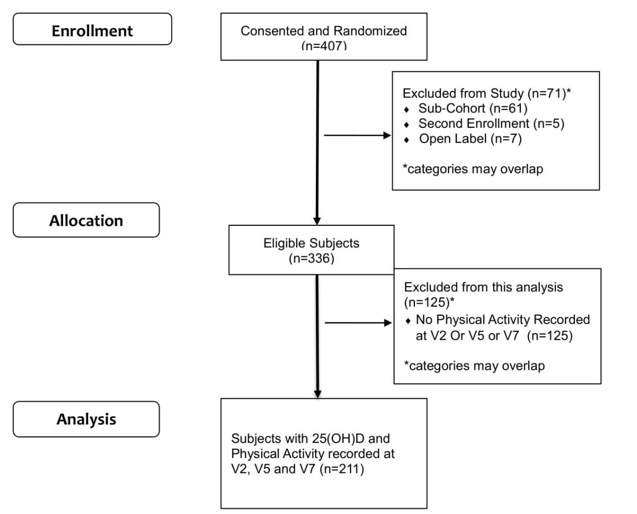

Figure 1: Consort Flow Diagram of Study Enrollment, Allocation and Analysis.

A total of 211 were included in the final analysis presented here. There were 98 women in the 400 IU (Control) group and 113 in the 4400 IU (treatment) group for whom physical activity and exercise information was available (p NS).

Physical activity synopsis of the cohort

Table 1 displays the baseline characteristics of the cohort. At Visit 2 (V2), the mean (± standard deviation, SD) age of those who vigorously exercised less than 2.5 h/week and of those who vigorously exercised ≥ 2.5 h/week was 28 years (4.8) and 30 years (4.6), respectively. This was statistically significant; older women were more likely to vigorously exercise ≥ 2.5 h/week ($p<0.0004$). Comparing participants by race/ethnicity, more Caucasians vigorously exercised ≥ 2.5 h/week ($p<0.011$) compared to Hispanic and African-American subjects. Participants with private insurance compared to those with Medicaid ($p<0.018$); and those with a planned pregnancy vs. those with an unplanned pregnancy ($p=0.031$) were more likely to vigorously exercise ≥ 2.5 h/week. Gestational age at enrollment, gravidity, parity, education, employment, marital status, BMI, season of enrollment, perceived stress score (PSS), baseline 25(OH)D concentration, change in degree of skin pigmentation (ΔDSP) between exposed and unexposed body areas (Table 2), and health rating were not associated with exercise or exercise intensity. At V2, however, PSS was associated with 25(OH)D concentration, with a lower PSS associated with a higher 25(OH)D (Parameter Estimate -0.30, $p=0.026$).

In binomial analyses, at V5 (trimester 2), vigorously exercising ≥ 2.5 h/week was associated with being Caucasian ($p=0.0033$), private insurance ($p=0.006$), planned pregnancy ($p=0.014$), and being married ($p=0.012$). Additionally, an association existed between vigorously exercising ≥ 2.5 h/week and higher 25(OH)D concentrations ($p<0.0001$). Treatment was associated with 25(OH) concentration, with higher 25(OH)D concentrations in the 4400 IU group ($p<0.0001$). The ΔDSP between the exposed and unexposed body areas was not associated with 25(OH)D concentration ($p=0.62$; Table 2) or with exercise as a continuous variable (minutes/week exercise, $p=0.20$) or as a dichotomous variable (± 2.5 hr/week; $p=0.31$). As with V2, perceived stress (PSS) was not associated with minutes of exercise ($p=0.64$) or intensity ($p=0.37$), but was associated with 25(OH)D concentration (Parameter Estimate -0.44, $p=0.026$).

Similarly, in binomial analyses, at V7 (trimester 3), vigorously exercising ≥ 2.5 h/week was associated with being Hispanic ($p<0.0001$), gravidity ($p=0.047$), private insurance ($p=0.0017$), and being married ($p=0.042$), but no longer with higher 25(OH)D concentrations ($p=0.25$). When analyzed separately for each treatment group, vigorous exercise was associated with 25(OH)D concentration in the 400 IU group ($p=0.02$) but not in the 4400 IU group (0.25). Because treatment remained an independent predictor of vitamin D status, it was included in the mixed model analyses described below. Perceived stress again was not associated with exercise ($p=0.95$), but was associated with 25(OH)D concentration (Parameter Estimate -0.81, $p<0.0001$), such that a lower PSS was associated with a higher 25(OH)D concentration. Change in skin pigmentation between the exposed site vs. unexposed site as an indicator of sunlight exposure was not associated with vitamin D status ($p=0.41$) or with time of exercise as a continuous variable ($p=0.22$), but became significant when dichotomized as ± 2.5 h/week ($p=0.048$; see Table 2). Because of the disparate nature of the findings by visit surrounding Δ DSP of exposed vs. unexposed areas, this was included in the mixed model analyses, which are presented below.

Prediction of maternal circulation 25(OH)D using a Mixed-model

As shown in Table 3, in a mixed model exploring the association of maternal 25(OH)D concentration with physical activity (as a dichotomous variable using the US Dept of Health definition of adequate exercise of at least 2.5 h/week), sunlight exposure (as measured by Δ DSP), race/ethnicity, treatment group, BMI, perceived stress score, visit as a factor of time, and treatment by visit, there was a positive association between vigorously exercising and maternal 25(OH)D concentration ($p=0.0013$). ΔDSP, as an indicator of sunlight exposure, was not significantly associated with maternal 25(OH)D ($p=0.59$). In this model, several other factors were independently associated with maternal 25(OH)D concentration: 1) race/ethnicity: when compared to Caucasian women, African American and Hispanic women had lower 25(OH)D concentrations ($p=0.0006$); 2) treatment: 4400 compared to 400 IU/day, $p<0.0001$; 3) BMI <30 ($p=0.015$); 4) PSS ($p=0.019$), and 5) visit as an indicator of progression of pregnancy trimester: with increasing 25(OH)D concentration at V5 and V7 compared to V2, ($p=0.0018$; $p<0.0001$, respectively). A treatment by visit interaction also was seen with higher maternal 25(OH)D concentration at both V5 and V7 in the 4400 IU group compared to V2 and compared to the 400 IU group ($p=0.0022$; $p=0.0029$, respectively).

Discussion

In this study of pregnant women participating in a randomized controlled trial of vitamin D supplementation, exercise when dichotomized as vigorous exercise (defined by ≥ 2.5 h of vigorous aerobic exercise/week) in bivariate and mixed model analyses), was positively associated with vitamin D status. This is the first report of an association between maternal vitamin D status and vigorous exercise during pregnancy in healthy women of a diverse racial/ethnic background.

The findings are consistent with earlier studies, which showed that physical activity was positively associated with 25(OH)D concentration in various non-pregnant populations, including children and adolescents [9], adults [5] and elderly adults [6,7], as well as cancer patients [10] and in lactating postpartum women [11], regardless of indoor vs outdoor physical activity [8]. Extending this association to pregnant women, we hypothesized that independent of sunlight exposure, higher intensity and duration of physical activity would lead to higher concentrations of circulating 25(OH)D as the indicator of vitamin D status in pregnant women. Based on our findings, a small positive association does exist: independent of race/ethnicity, sunlight exposure, BMI, perceived stress, and treatment, women who vigorously exercised ≥ 2.5 h/week had higher 25(OH)D concentrations than those who did not.

Exercise alone was not the only independent predictor of maternal vitamin D status. In fact, race/ethnicity with darker skin pigmentation were negative predictors that were overcome with treatment: women in the 4400 IU group, irrespective of race/ethnicity, had consistently higher 25(OH)D concentrations compared to the 400 IU group at each of the study visits. When change in degree of skin pigmentation between exposed and unexposed areas was included in bivariate analyses, only in the third trimester was this associated with exercise. Further exploring this relationship, in the mixed model that included Δ DSP, Δ DSP was no longer associated with 25(OH)D concentration; however, vigorous exercise ≥ 2.5 h/week remained highly significant.

Maternal Characteristic	< 2.5 hours of exercise per week	≥ 2.5 hours of exercise per week	p-value
Age, Mean Years (SD)	28.0 (4.8)	30.3 (4.6)	0.0004
Gestational Age at Enrollment Mean Weeks (SD)	12.4 (1.7)	12.6 (1.5)	0.3139
Race/Ethnicity N (%)			
African American	41 (66.1)	21 (33.8)	
Hispanic	32 (58.2)	23 (41.8)	0.0112
White/Caucasian	40 (42.6)	54 (57.5)	
Gravidity, Median (25%, 75%)	2.0 (1.0, 3.0)	2.0 (1.0, 4.0)	0.6392
Parity, Median (25%, 75%)	1.0 (0.0, 2.0)	1.0 (0.0, 2.0)	0.9876
High School Graduate, N (%)	104 (54.7)	86 (45.3)	0.3003
Employed during Pregnancy, N (%)	74 (52.5)	67 (47.5)	0.6576
Insured with Medicaid, N (%)	41 (66.1)	21 (33.9)	0.0182
Pregnancy Planned, N (%)	61 (47.7)	67 (52.3)	0.0306
Married, N (%)	77 (50.0)	77 (50.0)	0.0888
BMI >30, N (%)	33 (60.0)	22 (40.0)	0.2650
Season of Enrollment, N (%)			0.8548
April – September	62 (53.0)	55 (47.0)	
October – March	51 (54.3)	43 (45.7)	
Difference in Degree of Skin Pigmentation (DSP) between exposed and unexposed sites	5.4 (4.1)	5.8 (4.0)	0.5969
Perceived Stress Score, Mean (SD)	9.7 (5.5)	10.3 (4.9)	0.4439
Health Likert Scale Rating 1-10, Median (25%, 75%) 1 = worse health; 10 = best health	9.0 (8.0, 10.0)	9.0 (8.0, 10.0)	0.5878
25(OH)D, Mean (SD), ng/mL	34.3 (12.6)	36.8 (11.9)	0.1447
Treatment Group, N (%)			
400 IU Vitamin D_3	53 (54.1, 46.9)	45 (45.9, 45.9)	0.8863
4400 IU Vitamin D_3	60 (53.1, 53.1)	53 (46.9, 54.1)	

Table 1: Maternal Characteristics at Baseline (Visit 2, Trimester 1).

As pregnancy progressed, the women who vigorously exercised ≥ 2.5 h/week tended to be older, married, privately insured, and purposefully pregnant. Exercise time and intensity were not associated with perceived stress as measured by the PSS, but with vitamin D status, with lower stress scores in women with higher 25(OH)D, independent of race/ethnicity. It is interesting that PSS was not associated with exercise duration or intensity, which suggests that other factors including vitamin D status appear to influence perceived stress. Encouraging all women to exercise, but especially those who tend to exercise less, could have a positive impact on their vitamin D status and in general would lead to improved conditioning with a positive impact on the health of those women and their babies [21,29]. A strength of this study is that it included a diverse group of women in a randomized controlled trial. Limitations of this study are that there were participants excluded from the study due to not having physical activity recorded for them. While for those women for whom exercise was recorded, it was not specified whether the exercise took place indoors or outdoors, the change between exposed and unexposed skin pigmentation at each visit and across visits served as a surrogate for sunlight exposure, and this was not associated with exercise in a mixed model.

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Visit	<2.5 hrs/wk	≥ 2.5 hrs/wk	p-value
	Mean (SD)	Mean (SD)	
2 (1st trimester	5.4 (4.1)	5.8 (4.)	0.5969
5 (2nd trimester)	4.9 (3.4)	5.5 (3.4)	0.3093
7 (3rd trimester)	4.0 (3.5)	5.1 (3.6)	0.048
[a]Δ DSP was calculated as the difference in the skin spectrophotometer readings using the SmartProbe 400 between the forearm (exposed skin area) and the lower hip/buttock (unexposed skin area). The SmartProbe-400 reading at the two sites provided a value for DSP on a scale of 0-100, with lower numbers signifying darker skin pigmentation.			

Table 2: Change in Skin Pigmentation (Δ DSP)[a] between Exposed (Forearm) and Unexposed (Lower Hip/Buttock) Sites at Visits 2, 5 and 7.

Characteristic	Parameter Estimate (PE) in ng/mL	p-value
Race/Ethnicity		
African-American	-7.1	0.0006
Hispanic	-5.5	0.0076
Caucasian	----	----
Treatment		<0.0001
4400 IU / day	10.2	----
400 IU / day	----	----
BMI	----	0.015
≤ 30	0.01	----
>30	----	----
Perceived Stress Score	-0.2	0.019
Visit		
5	7.7	0.0018
7	6.7	<0.0001
baseline	----	----
Treatment by Visit		
4400 IU * V5	6.2	0.0022
4400 IU * V7	6.2	<0.0029
4400 IU * V2	---	---
400 IU * V2	---	---
400 IU * V5	---	---
400 IU * V7	---	---
Change in Degree of Skin Pigmentation (DSP) between Exposed and Unexposed Areas	0.086	0.59
Exercise		0.0013
≥ 2.5 h	3.6	----
< 2.5 h	----	----

Table 3: Mixed Model Predicting Maternal Total Circulating 25(OH)D Concentration (ng/mL) with Exercise as a Dichotomous Variable.

Among the excluded participants when compared to those with exercise information available, we found some differences in race/ethnicity, age, education, employment, baseline stress, and baseline 25(OH)D status. This could be related to another limitation: we used a subjective measure of physical activity (the Paffenbarger Physical Activity Questionnaire) as opposed to an objective measure such as a pedometer, accelerometer, or heart rate monitor, and consequently, there was potential for reporting errors if participants over or underestimated their physical activity duration or intensity.

In summary, pregnant women who exercised, and specifically those who vigorously exercised ≥ 2.5 h/week had higher total circulating 25(OH)D concentrations than those who did not, an effect that persisted even after accounting for sunlight exposure and other potentially confounding factors. While women who were most likely to vigorously exercise ≥ 2.5 h/week tended to be older, privately insured, and purposefully pregnant, encouraging pregnant women in general to develop and maintain an appropriate exercise program ultimately may improve their vitamin D status and that of their developing fetus as well as improve their overall health status. Additional studies are needed that examine this relationship more closely with more specific exercise and physical activity tools applied.

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Financial Disclosures and Potential Conflicts of Interest

Drs. Bruce Hollis and Carol Wagner serve as scientific consultants to Church & Dwight Co., Inc., Princeton, NJ regarding vitamin preparations.

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