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Duration of Physical Activity and Serum 25-hydroxyvitamin D Status of Postmenopausal Women

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Abstract

Purpose—To investigate whether the association between physical activity and serum 25 hydroxyvitamin D (25(OH)D) concentrations is independent of sun exposure, body size, and other potential explanatory variables.

Methods—Using data from a sample of 1,343 postmenopausal women, from the Women's Health Initiative, linear regression was used to examine the associations of duration (minutes/ week) of recreational activity and of yard work with 25(OH)D concentrations (nmol/L).

Results—In age-adjusted analyses, positive associations were observed between 25(OH)D concentrations and both duration of recreational physical activity (β=0.71, SE(0.09), *P*<0.001) and yard work (β=0.36, SE(0.10), *P*=0.004). After further adjustment for vitamin D intake, self-

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reported sunlight exposure, waist circumference, and season of blood draw, 25(OH)D was significantly associated with recreational activity (β =0.21, SE(0.09), P=0.014) but not with yard work ($β=0.18$, SE(0.09), $P=0.061$). Interactions were observed between season and both recreational activity (*Pinteraction*=0.082) and yard work (*Pinteraction*=0.038) such that these activity-25(OH)D associations were greater during summer/fall compared to winter/spring. Selfreported sunlight exposure and measures of body size did not modify the associations.

Conclusion—The observed age-adjusted activity-25(OH)D associations were attenuated after adjusting for explanatory variables and were modified by season of blood draw. Adopting a lifestyle that incorporates outdoor physical activity during summer/fall, consuming recommended amounts of vitamin D, and maintaining a healthy weight may improve or maintain vitamin D status in postmenopausal women.

Keywords

25-hydroxyvitamin D; vitamin D; serum; sunlight exposure; physical activity; epidemiology; women

INTRODUCTION

The role of vitamin D in the etiology and prevention of chronic disease, such as cancer, osteoporosis, and autoimmune diseases, is of growing interest among healthcare providers and in public health settings (1). Identifying modifiable determinants of vitamin D status, therefore, may have broad population health benefits. Some of the most commonly reported predictors of sufficient 25-hydroxyvitamin D (25(OH)D) status include age, race, dietary and supplemental vitamin D intake, sunlight exposure, body size, and physical activity (2– 9).

The observed positive association between physical activity and 25(OH)D status is most likely explained by increased sunlight exposure (1) and decreased body size (10) in more physically active individuals, though few studies have reported data comparing outdoor and indoor activities (11–13). Alternately, it has been hypothesized that the mechanics of physical activity may affect calciotropic hormone levels (reviewed in 14) through increasing post-activity calcium absorption and circulating vitamin D levels (15–16), most likely to help maintain or increase bone mineral density. Additionally, in postmenopausal women, physical activity may increase 25(OH)D concentrations through an IGF-1 mediated process $(17–19)$.

Using data from the Carotenoids in Age-Related Eye Disease Study (CAREDS), an ancillary study of the Women's Health Initiative Observational Cohort Study (WHI-OS), we investigated whether physical activity among postmenopausal women is associated with serum 25(OH)D concentration, independent of sunlight exposure, body size, or other known factors (e.g., age) associated with both physical activity and vitamin D status . This knowledge can help elucidate the role that promoting physical activity could have in maintaining a healthy vitamin D status (1).

The purpose of this cross-sectional study was to determine if duration (minutes/week) of recreational physical activity and of yard work were associated with serum 25(OH)D concentrations (nmol/L). Additionally, we examined if the association between duration of physical activity and 25(OH)D concentrations was 1) modified by measures of sunlight exposure and body size and 2) explained by other extraneous factors.

MATERIALS AND METHODS

Study sample

The WHI-OS, a prospective cohort study, assessed morbidity and mortality in 93,676 postmenopausal women (50–79 years) recruited from 40 sites throughout the United States (1993–1998) (20–22). CAREDS is an ancillary study of the WHI-OS that examined the association between dietary intake of carotenoids, lutein and zeaxanthin, and the prevalence of age-related eye disease including macular degeneration (23). Participants with baseline carotenoid intake $>78^{th}$ or $<28^{th}$ percentiles were eligible for CAREDS and were recruited (2001–2004) from three WHI-OS centers in Madison, WI, Iowa City, IA, and Portland, OR (*n*=3,143). Demographic and other health-related data did not differ between the overall sample of women enrolled in WHI-OS and the subsample enrolled in CAREDS (23). The study was approved by the Institutional Review Board at each research center and women provided written informed consent to participate in study activities.

Among women eligible for enrollment in CAREDS, 96 (3.05%) died or were lost to followup, leaving 3,047 women who were invited to participate, of whom 1,042 (34.2%) declined. Out of the 2,005 women who agreed to enroll, 1,894 (94.5%) completed the CAREDS study visits and 1,475 had serum 25(OH)D concentrations available. Of these, women with missing data for physical activity (*n*=20), sunlight exposure (*n*=37), body mass index (BMI) (*n*=7), or other covariate data (*n*=7); and women who self-reported or were missing data on malabsorbtive conditions (e.g., Crohn's disease) at WHI-OS baseline (*n*=75), which could affect absorption of vitamin D, were excluded. The final sample for analyses included 1,343 women.

Women who were included in this study (*n*=1,343) were significantly younger (mean: 62.87 vs. 64.38 years, *P*<0.05) and expended less energy from yard work (mean: 5.77 vs. 6.97 MET-hours/week, *P*<0.05) compared to women who were excluded (*n*=662). No statistically significant differences were found with respect to recreational physical activity, sunlight exposure, body size, education level, clinic center, or hormone use.

Serum vitamin D

A fasting venous blood sample was obtained at WHI-OS baseline and serum was stored at −80°C. The Diasorin LIAISON® chemiluminescence method (Heartland Assays, Inc. (Ames, IA)) was used to assay serum 25(OH)D concentrations. Two percent of the assayed samples had insufficient serum volume for the LIAISON® method and were run using a standard radioimmunoassay (Diasorin, Stillwater, MN). Distributions of 25(OH)D were similar between methods. Assays included blind duplicates for 328 paired participants, which were used to calculate a coefficient of variation of 8.9%. Based on previous studies (9,24–25), 25(OH)D concentrations of $\langle 50, 50-\langle 75, 100\rangle$ and $\langle 275 \rangle$ nmol/L were used to define categories of deficiency, insufficiency, and sufficiency, respectively.

Data collection

Physical activity—Usual physical activity, without reference to a specific timeframe, was assessed with a self-administered questionnaire previously shown to be valid and reliable (26–27). Participants reported usual duration ($\langle 20, 20, 20, 39, 40, 59, 60 \rangle$ minutes/day) and frequency (days/week) for recreational physical activities, including walking, mild (e.g., golf), moderate (e.g., biking), and strenuous (e.g., jogging) physical activity. Weekly duration (minutes/week) of each activity was estimated by multiplying median duration (minutes/day) by frequency (days/week). These values were then summed to compute total weekly recreational activity duration for all activities combined. Location (indoor/outdoor) of recreational activities was not queried.

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Duration of yard work (minutes/week) was examined separately from recreational activity since this physical activity was done outdoors and could facilitate sunlight exposure. Yard work was defined as activities that were done in the yard including raking, mowing, shoveling snow, and gardening. Frequency (months/year) and duration (hours/week during the months the participant was engaged in yard work) of yard work were assessed with a self-administered questionnaire. To estimate overall duration (minutes/week) of yard work, the following equation was used: duration (hours/week) \times frequency (months/year) \times ((60) minutes/hour)/(12 months/year)).

Sunlight exposure—A questionnaire, administered at CAREDS baseline (2001–2004), was used to collect information about the time $(\langle 1, 1-3, 0r \rangle)$ hours per day) spent in direct sunlight during peak daily sun times (10 AM–4 PM) on weekdays and weekends from April to September for *each* location in which the participant lived since the age of 18. From this information, a retrospective estimate of sunlight exposure at the time of baseline enrollment in WHI-OS (1993–1998), concurrent to serum 25(OH)D assessment, was obtained. Additionally, season of blood draw (summer/fall: June–November, winter/spring: December-May; hereafter referred to as *season*) at WHI-OS baseline was examined in this study as a proxy measure of the availability of solar radiation (28).

Body size measures—Height (m) was measured with a stadiometer and weight (kg) with a calibrated balance beam or digital scale and from these measures BMI $\frac{\text{(kg/m)}{\text{}}\text{was}}$ calculated (20) and categorized as underweight/normal (<24.99 kg/m²), overweight (25.00– 29.99 kg/m²), and obese ($\geq 30.00 \text{ kg/m}^2$) (29). Waist circumference was measured with a tape measure, halfway between the iliac crest and the bottom of the rib cage, to the nearest 0.1 cm (30) and was dichotomized using a standard clinical cutoff (≤ 88 and > 88 cm) (20,31).

Other potential confounders—Total vitamin D intake (mcg) included vitamin D intake from diet and supplements, estimated from the validated WHI food frequency questionnaire and supplement use questionnaire, respectively (32–34). Self-reported age, race/ethnicity, education, smoking, alcohol use, and use of hormone therapy also were obtained at WHI-OS baseline (20).

Statistical analysis

Descriptive statistics were computed for 25(OH)D concentrations and duration of physical activity, and Spearman correlations were computed to examine the crude activity-25(OH)D associations. Differences in mean 25(OH)D concentrations and duration of recreational physical activity by demographic and lifestyle characteristics were examined using analysis of variance.

Multiple linear regression was used to examine the activity-25(OH)D associations with recreational physical activity and yard work, separately, while controlling for the effect of potential confounding factors. Since the physical activity variables were not normally distributed, a square root transformation was applied prior to analysis. Regression coefficients were considered significant at *P*<0.05. Measures of sunlight exposure (selfreported sunlight exposure and season) and body size (BMI and waist circumference) were examined as potential effect modifiers of the activity-25(OH)D association and interaction product terms were considered significant if *P*<0.10.

All models were adjusted minimally for age and further adjusted for potential confounding factors that were significantly related in univariate analyses to both 25(OH)D and duration of physical activity, and that changed the regression coefficient for physical activity by 10%

or more when added to the linear regression model. Vitamin D intake, sunlight exposure, season, waist circumference, and BMI met these criteria.

Waist circumference and BMI were strongly correlated ($r=0.82$), thus we chose not to include them both simultaneously in regression analyses. When examined as potential confounding factors, the percent change in the regression coefficient for physical activity was slightly greater for waist circumference than BMI and thus we chose to only adjust for waist circumference. When primary analyses were repeated with BMI instead, the findings were materially the same as those seen for waist circumference.

All statistical analyses were performed with SAS® version 9.2 (35).

RESULTS

The average 25(OH)D concentration among all participants was 57.7 nmol/L (*SE*=0.65), with 39.24% of the sample vitamin D deficient (<50 nmol/L), 39.99% insufficient (50–75 nmol/L) and 20.77% sufficient (\geq 75 nmol/L). The average weekly duration of recreational physical activity was 207.77 minutes/week (*SE*=5.26) and yard work was 86.48 minutes/ week (*SE*=3.47). Recreational physical activity (*r*=0.21, *P*<0.001) and yard work (*r*=0.10, *P*=0.004) were each correlated with 25(OH)D and were correlated with each other (*r*=0.14, *P*<0.001). The prevalences of inactivity (0 minutes/week) were 11.43% for recreational physical activity and 35.82% for yard work. Figure 1 illustrates the significant trend for higher 25(OH)D across incremental recreational physical activity quintile medians (*P*<0.001). A similar trend was observed for 25(OH)D and yard work (not shown).

Average 25(OH)D concentrations were higher among women who resided in Wisconsin, were of Caucasian race/ethnicity, had more years of education, drank alcohol more frequently, consumed more vitamin D from foods and supplements, were leaner, spent more time in the sun, and had their blood draw in the summer/fall (Table 1). Average duration of recreational physical activity was also greater among women with the same characteristics; although no differences were observed in duration of activity and racial/ethnic group, and duration of activity was lowest among current smokers.

In age-adjusted linear regression analyses, both recreational physical activity and yard work were positively associated (*Ps*<0.01) with 25(OH)D concentrations (Table 2). These associations were attenuated with the addition of each covariate (vitamin D intake, selfreported sunlight exposure and waist circumference), with waist circumference having the largest effect on the regression coefficient. The activity-25(OH)D association remained significant for recreational physical activity $(P=0.002)$ but was no longer significant for yard work ($P=0.298$). Additional adjustment for season further attenuated the relationship with recreational activity and slightly strengthened the association with yard work.

Table 3 shows the activity-25(OH)D associations stratified by measures of sunlight exposure and body size. Season significantly modified the age-adjusted associations of serum 25(OH)D with both recreational physical activity (*P* for interaction=0.082) and yard work (*P* for interaction=0.038). The age-adjusted associations of recreational physical activity with serum 25(OH)D were significant in each season, but were greatest during the summer/fall months when ultraviolet B (UVB) exposure is greatest in Northern latitudes. The ageadjusted associations between yard work and serum 25(OH)D were significant during summer/fall but not during winter/spring. After adjusting the season-stratified models for additional covariates, the regression coefficients for recreational physical activity and yard work remained significant during the summer/fall, but not during the winter/spring. The associations between 25(OH)D and physical activity were not significantly modified by selfreported sunlight exposure or waist circumference (*P*s>0.10).

DISCUSSION

Similar to previous studies (5–6,8–9,11–12,16,36–49), we found positive activity-25(OH)D associations with recreational physical activity and yard work. Differences in vitamin D intake, self-reported sunlight exposure, waist circumference, and season accounted for much of the observed activity-25(OH)D associations. Further adjustment of age-adjusted activity-25(OH)D associations for these covariates reduced the magnitude of associations by at least 50%.

A stronger activity-25(OH)D relationship was observed with recreational physical activity than yard work. One would hypothesize that the association between 25(OH)D and physical activity would be strongest in an activity (yard work) conducted exclusively outside. It is possible that unmeasured behaviors might have confounded the association with yard work. Women may have worn more clothing when they participated in yard work (subsequently minimizing their dermal vitamin D production) than when they participated in recreational physical activity. However, we could not examine this further because data regarding the amount of clothing worn during physical activity was not collected in this study. Alternatively, the weaker association with yard work may have been explained by a narrower distribution of time spent in activity among women conducting yard work (~7 minutes/day to a little over $1 \frac{1}{2}$ hours per day) than among those engaged in recreational physical activity $(\sim 10 \text{ minutes/day to} \sim 4 \text{ hours per day}).$

Similar to previous studies (11,38,47), season modified the activity-25(OH)D associations such that the associations were only significant for summer/fall. All participants of this study resided above 40° N, a latitude at which the amount of UVB photons reaching the earth from November through February (50) is limited. If physical activity was associated with 25(OH)D concentrations independent of sunlight exposure one would expect to also observe an association during winter/spring, the time of year when dermal production of 25(OH)D is limited by reduced exposure to UVB (50). Thus, the observed activity-25(OH)D associations largely reflect the effect of sunlight exposure during outdoor physical activity. We found no evidence to suggest that physical activity, independent of the other factors accounted for in this study, contributes to variation in 25(OH)D concentrations.

This is one of the first studies to specifically investigate the activity-25(OH)D association in postmenopausal women, while also considering the impact of potential explanatory factors of this association. The majority of previous studies has only presented physical activity as a determinant of 25(OH) D status (5–6,8–9,12,37–44,46–49) and did not examine their association in more depth. However, using data from the Third National Health and Nutrition Examination Survey (NHANES III), Scragg et al. (11) found a positive association between the self-reported frequency of outdoor, but not indoor, leisure activities during the past month and 25(OH)D, even after adjustment for age, sex, race/ethnicity, BMI, month of year, and vitamin D intake from food and supplements. When stratified by month of examination, stronger associations were seen between outdoor activity and serum 25(OH)D during the summer/fall compared to winter/spring. The results of the present study in older women are consistent with those reported by Scragg et al., suggesting that seasonal variation in sunlight exposure likely explains a large amount of the activity-25(OH)D association.

Several aspects of our study expand on the findings reported by Scragg et al. (11). First, Scragg et al.'s activity questionnaire did not allow for quantifying the dose of activity because only frequency, and not duration, of activities done in the past month was measured. Our activity exposure is based both on frequency and on duration, which likely results in a better assessment of activity dose. Second, NHANES III's activity questionnaire did not assess the location of activities. Instead, the investigators classified self-reported activities as

indoor or outdoor based on their judgment of the likely location of the activity, leading to potential misclassification of activity location. Although our study also did not assess specific location for recreational physical activity, we additionally queried about yard work which allowed us to examine the effect of a known outdoor activity on 25(OH)D. Third, individual level information on sunlight exposure was not available in the study by Scragg et al. Instead, the investigators used month of clinical examination as a proxy measure for sunlight exposure, which was further complicated by NHANES collecting data (e.g., blood draws) at northern latitudes in the summer/fall and at southern latitudes in the winter/spring. In our study, self-reported sunlight exposure was assessed and all women resided at a similar latitude (>40°N). These data, together with season of blood draw, provides a more complete assessment of overall sunlight UVB exposure than seasonality alone. However, we found that self-reported sunlight exposure did not modify any of the activity-25(OH)D associations, and only partially explained the observed associations after adjustment in the multivariate models.

Body size appears to be a relevant confounder of the observed association because body size tends to be inversely related to physical activity levels (10) and inversely related to 25(OH)D levels (1); the latter most likely due to the sequestration of vitamin D in fat tissue (51). This association was attenuated by 48–57% when waist circumference was added to multivariate models. It appears that regardless of body size, higher physical activity levels are associated with higher serum 25(OH)D concentrations.

There are several limitations to this study. Our measures of physical activity and sunlight exposure were subjective and retrospective, and thus might have resulted in measurement error. Participants were asked to provide an estimate of their usual recreational physical activity and yard work habits; however a specific recall timeframe or season was not delineated. Other than yard work, we could not distinguish between indoor and outdoor activity because location was not assessed. The physical activity questionnaire did not provide sufficient detail to differentiate between activities according to weight-bearing characteristics and this information could be relevant for examining how activity, related specifically to increasing bone health, affects 25(OH)D concentrations.

Self-reported sunlight exposure might not have been observed as an effect modifier or a stronger confounder, because of measurement error in sunlight exposure assessment. On CAREDS' baseline (2001–2004) questionnaires, women retrospectively estimated their average sunlight exposure during WHI-OS baseline (1993–1998). Changes in sunlight exposure behaviors from WHI-OS baseline to CAREDS baseline may have affected the accuracy of women's recall. Furthermore, the questionnaire required women to report a single estimate of their activities and behaviors which contributed to sunlight exposure for each location in which they lived since they were 18 and this estimate would not have captured any variation in sunlight exposure for the duration of time at each location.

The women in our study have similar demographics, medical characteristics, physical activity levels and serum 25(OH)D as other women in the WHI-OS. Notably, women who participated in WHI-OS were highly educated volunteers and were likely healthier than the general population. Additionally, compared to national estimates, our participants were more active than women of similar age (52). Greater than 30% of women 50 years and above reported being inactive from 1993–1998 according to the Behavioral Risk Factor Surveillance System survey data (52), whereas only about 12% of our sample was inactive. The relatively low prevalence of inactivity in our study sample of older women may reflect greater measurement error using questionnaire-based activity assessment in our study than in national surveillance programs, or it may further indicate that our study sample tended to be more health conscious than women of similar age in the overall population.

In conclusion, a better understanding of the activity-25(OH)D association could have important public health implications. Research shows that physical activity, vitamin D intake, sunlight exposure, and decreased body size are modifiable predictors of a healthy 25(OH)D status (1,9). Therefore, incorporating these factors into one's lifestyle could help to maintain a healthy 25(OH)D status which has been associated with reduced risk for disease (e.g., cancer, osteoporosis) (1). Our findings emphasize the relevance of these issues among a subgroup of postmenopausal women in whom levels of physical activity and serum vitamin D tend to be lower than recommended.

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WHI Investigators

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Amy E. Millen had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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Figure 1. Mean (SE) Serum 25(OH)D (nmol/L) by Quintiles of Duration of Recreational Physical Activity (minutes/week)

Mean serum 25-hydroxyvitamin D (25(OH)D) concentrations and standard errors are plotted for postmenopausal women in each quintile of duration of recreational physical activity: the Carotenoids in Age-Related Eye Disease Study (CAREDS), N=1,343. Test of linear trend across quintile medians, P<0.001.

Table 1

Mean values of serum 25 (OH)D concentrations (nmol/L) and recreational physical activity duration (minutes/week) for postmenopausal women in the Carotenoids in Age-Related Eye Disease Study (CAREDS) by WHI-OS baseline (1993–1998) characteristics, Mean values of serum 25 (OH)D concentrations (nmol/L) and recreational physical activity duration (minutes/week) for postmenopausal women in the Carotenoids in Age-Related Eye Disease Study (CAREDS) by WHI-OS baseline (199

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^{*} Analysis of variance (ANOVA) was used to compute P-values for which statistical significance was set at an alpha level of 0.20. Analysis of variance (ANOVA) was used to compute *P*-values for which statistical significance was set at an alpha level of 0.20.

 7 Sunlight exposure at WHI-OS baseline (1993–1998) was retrospectively estimated at CAREDS baseline (2001–2004). *†*Sunlight exposure at WHI-OS baseline (1993–1998) was retrospectively estimated at CAREDS baseline (2001–2004).

 $^{\neq}$ Summer/Fall: June–November; Winter/Spring: December-May *‡*Summer/Fall: June–November; Winter/Spring: December-May

Table 2

Regression coefficient (β), standard error (SE) and p-value for physical activity from linear regression analysis of physical activity (minutes/week) on serum 25(OH)D (nmol/L) adjusted*** for various covariates: the Carotenoids in Age-Related Eye Disease Study (CAREDS), *N*=1,343.

*** The following variables were added to the linear regression models: age (years), vitamin D intake from food and supplements combined (mcg/ day), self-reported sunlight exposure ((<1, 1-3, or >3 hours per day), waist circumference (cm), and season (summer/fall [June–November] and winter/spring [December-May]).

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Table 3

Regression coefficient (β), standard error (SE) and p-value for physical activity from linear regression of physical activity minutes/week) on serum
25(OH)D (nmol/L) stratified by measures of sunlight exposure and body 25(OH)D (nmol/L) stratified by measures of sunlight exposure and body size: the Carotenoids in Age-Related Eye Disease Study (CAREDS), N=1,343. Regression coefficient (β), standard error (SE) and p-value for physical activity from linear regression of physical activity minutes/week) on serum
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Adjusted age (years), vitamin D intake from food and supplements combined (mcg/day), self-reported sumlight exposure (<1, 1-3, or >3 hours per day), waist circumference (cm), and season (summer/fall *†*Adjusted age (years), vitamin D intake from food and supplements combined (mcg/day), self-reported sunlight exposure (<1, 1–3, or >3 hours per day), waist circumference (cm), and season (summer/fall June-November] and winter/spring [December-May]). Analyses stratified by self-reported sunlight exposure were not adjusted for self-reported sunlight exposure. [June–November] and winter/spring [December-May]). Analyses stratified by self-reported sunlight exposure were not adjusted for self-reported sunlight exposure.

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