Title

A Cross-Sectional Examination of Vitamin D, Obesity, and Measures of Pain and Function in Middle-Aged and Older Adults with Knee Osteoarthritis

Authors

Toni L. Glover, PhD, GNP-BC, Burel R. Goodin, PhD, Christopher D. King, PhD, Kimberly T. Sibille, PhD, Matthew S. Herbert, PhD, Adriana S. Sotolongo, MPH, Yenisel Cruz-Almeida, PhD, Emily J. Bartley, PhD, Hailey W. Bulls, BS, Ann L. Horgas RN, David T. Redden, PhD, Joseph L. Riley III, PhD, Roland Staud, MD, Barri J. Fessler, MD, Laurence A. Bradley, PhD & Roger B. Fillingim, PhD

Affiliations

1University of Florida, College of Nursing, Adult and Elderly Nursing, Gainesville FL; 2University of Alabama at Birmingham, Departments of Psychology and Anesthesiology, Birmingham, AL; 3University of Florida, College of Dentistry, Department of Community Dentistry and Behavioral Science, Gainesville, FL; 4University of Alabama at Birmingham, Department of Psychology, Birmingham, AL; 5University of Alabama at Birmingham, Department of Medicine, Division of Clinical Immunology and Rheumatology, Birmingham, AL; 6University of Florida, Institute on Aging, Department of Aging and Geriatric Research,
Gainesville, FL; 7University of Alabama at Birmingham, Department of Biostatistics, Birmingham, AL; 8University of Florida, Department of Medicine, Gainesville, FL; 9University of Alabama at Birmingham School of Medicine, Department of Clinical Immunology and Rheumatology, Birmingham, AL

**Corresponding Author**

Toni L. Glover, PhD, GNP-BC
University of Florida
College of Nursing, Adult and Elderly Nursing
Pain Research and Intervention Center of Excellence (PRICE)
1225 Center Drive, HPNP 3229
PO Box 100197
Gainesville, Florida 32610-0197
Office: 352-273-6334
Cell: 352-494-7215
Fax: 352-273-6536
Email: tglover@ufl.edu

**Co-Author Contact Information**

Burel R. Goodin, PhD bgoodin1@uab.edu
Christopher D. King, PhD CKING@dental.ufl.edu
Kimberly T. Sibille, PhD ksibille@ufl.edu
Matthew S. Herbert, PhD mherbert@uab.edu
Adriana S. Sotolongo, MPH adriana@uab.edu
Yenisel Cruz-Almeida, PhD cryeni@ufl.edu
Emily J. Bartley, PhD EBartley@dental.ufl.edu
Hailey W, Bulls, BS hwbulls@uab.edu
Ann L. Horgas RN, PhD ahorgas@UFL.EDU
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Conflicts of Interest

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Abstract

Objectives: The prevalence of knee osteoarthritis is increasing with the aging population and is exacerbated by the growing numbers of obese older adults. Low levels of vitamin D, measured by serum 25-hydroxyvitamin D (25(OH)D), in older adults and obese individuals are correlated with several negative health conditions, including chronic pain. This cross-sectional study sought to examine the interactive influence of 25(OH)D levels and obesity on knee osteoarthritis pain and functional performance measures.

Methods: The sample consisted of 256 (63% female) racially-diverse (55% Black/African Americans) middle-aged and older adults (mean age 56.8 years). Blood was collected for analysis of 25(OH)D by high performance liquid chromatography. Participants provided self-report regarding knee osteoarthritis pain and underwent a lower extremity functional performance test.

Results: Results demonstrated that obesity was associated with lower levels of 25(OH)D. Participants with adequate 25(OH)D levels reported significantly less knee osteoarthritis pain compared to participants with deficient or insufficient levels, regardless of obesity status. Furthermore, there was a significant interaction between obesity and 25(OH)D levels for lower extremity functional performance, such that obese individuals with adequate 25(OH)D levels demonstrated better performance than those obese participants with deficient or insufficient 25(OH)D levels.

Discussion: The mechanisms by which adequate 25(OH)D levels are associated with pain severity and improved function have not been completely elucidated. It may be that the pleiotropic role of biologically active 25(OH)D influences pain and pain processing via peripheral and central mechanisms. Alternatively, higher levels of pain may lead to reduced
outdoor activity, which may contribute to both obesity and decreased vitamin D. Thus, investigating vitamin D status in obese and non-obese individuals with knee osteoarthritis warrants further study.

*Keywords:* vitamin D; osteoarthritis pain; obesity; lower extremity function; older adults
Introduction

The phenotype of symptomatic osteoarthritis is characterized by pain, stiffness, and limitations in physical function. With the aging of the population, the prevalence of osteoarthritis is on the rise.\textsuperscript{1,2} It is estimated that over half of all adults aged 65+ have been diagnosed with osteoarthritis.\textsuperscript{3} In fact, osteoarthritis contributes significantly to fall-related injuries\textsuperscript{4} and is the leading cause of disability in older adults.\textsuperscript{5,6} Obesity also contributes to the osteoarthritis phenotype\textsuperscript{7,8} and increases the likelihood of osteoarthritis-related disability.\textsuperscript{9,10} In the National Health and Nutrition Examination Survey (NHANES) for 2005-2006, approximately 69% of adults aged 60+ were overweight or obese.\textsuperscript{11} Obesity among older adults is projected to contribute to an increased prevalence of advanced osteoarthritis over the next 10 years.\textsuperscript{9}

Vitamin D status, measured by serum 25-hydroxyvitamin D level (25(OH)D) represents a potentially important contributor to both obesity and osteoarthritis-related symptoms.\textsuperscript{12,13} In obese individuals, 25(OH)D is sequestered in fat cells, decreasing its bioavailability for hormonal actions.\textsuperscript{14-16} Furthermore, obese individuals may expose less body surface area to sun exposure, contributing to lower vitamin D status.\textsuperscript{17,18} In a study of post-menopausal women, sufficient 25(OH)D level was associated with lower weight gains over a 4-5 year period.\textsuperscript{19} Thus, adequate levels of 25(OH)D may help prevent weight gain associated with the physiologic changes of aging, including decreased caloric need and reduced energy expenditure.

Humans primarily meet their vitamin D needs through exposure to ultraviolet-B (UVB) radiation.\textsuperscript{20} The ability to effectively synthesize vitamin D during UVB exposure decreases with age, placing older adults at risk for 25(OH)D deficiency, chronic disease, and disability.\textsuperscript{21-23} In 2013, the American Geriatrics Society released a consensus statement recommending older adults maintain serum 25(OH)D levels at a minimum of 30 ng/mL with the goal of reducing falls
and fall-related injuries.\textsuperscript{24} For all other adults, the optimal serum concentration of 25(OH)D is believed to be between 30-60 ng/mL.\textsuperscript{25-27} Clinical practice guidelines further cite 25(OH)D levels <30 ng/mL as \textit{inadequate}, levels between 21-29 ng/mL as \textit{insufficient}, levels <20 ng/mL as \textit{deficient}, and levels less than 10 ng/mL as \textit{severe deficiency}.\textsuperscript{28}

The aim of this cross-sectional study was to examine the interactive associations of 25(OH)D levels and obesity with self-reported knee pain and functional performance measures in a sample of middle-aged and older adults with symptomatic knee osteoarthritis. We hypothesized: 1) obesity will be associated with diminished 25(OH)D levels; and, 2) there will be a significant interaction between 25(OH)D levels and obesity, such that obese individuals with low 25(OH)D levels will report higher levels of osteoarthritis pain and dysfunction.

\textbf{Materials and Methods}

\textit{Participants and Procedures}

The current study is part of a larger ongoing project at the University of Florida and the University of Alabama at Birmingham that aims to enhance the understanding of racial/ethnic differences in pain and limitations among individuals with osteoarthritic disease (Understanding Pain and Limitations in OsteoArthritic Disease; UPLOAD). Participants were recruited via posted fliers, radio and print media advertisements, orthopedic clinic recruitment, and word-of-mouth referral. All study procedures were reviewed and approved by the University of Florida and University of Alabama at Birmingham Institutional Review Boards. Participants provided written informed consent and were compensated for their participation. The individuals described in the current study were recruited at both study sites between January, 2010 and February, 2014. The measures and procedures described below are limited to those involved in the current analyses.
Participants were provided a description of the protocol and screened for eligibility by recruitment staff via telephone. Criteria for inclusion into the study were as follows: 1) between 45 and 85 years of age; 2) unilateral or bilateral symptomatic knee osteoarthritis based upon American College of Rheumatology clinical criteria; 29 and, 3) availability to complete the two-session protocol. Individuals were excluded from participation if they met any of the following criteria: 1) prosthetic knee replacement or other clinically significant surgery to the affected knee; 2) uncontrolled hypertension, heart failure, or history of acute myocardial infarction; 3) peripheral neuropathy; 4) systemic rheumatic disorders, including rheumatoid arthritis, systemic lupus erythematosus, and fibromyalgia; 5) daily opioid use; 6) cognitive impairment (Mini Mental Status Exam (MMSE) score ≤ 22); 30 7) excessive anxiety regarding protocol procedures (e.g., blood draws or quantitative sensory testing procedures); and, 8) hospitalization within the preceding year for psychiatric illness. Eligible participants were scheduled for an appointment at the Clinical Research Units at the Center for Clinical and Translational Science at both university sites.

Health Assessment Session. Prior to the health assessment session, participants completed study questionnaires in which they rated the severity of their knee osteoarthritis symptoms. The following demographic and health data were obtained: sex (female, male), age, self-reported race (Black/African American, non-Hispanic White), health history, and study site (University of Florida, University of Alabama at Birmingham). Anthropometric data and vital signs were measured at the beginning of the health assessment session. Cognitive capacity to provide informed consent was assessed using the MMSE. The study rheumatologist or nurse practitioner: 1) reviewed all current prescribed and over-the-counter medications, as well as complementary and alternative strategies used to promote health and reduce pain; and, 2)
performed a bilateral knee joint evaluation and identified the participants’ most symptomatic/painful knee (classified as the index knee). Following these assessments, eligible participants completed an assessment of lower extremity function.

**Measures**

**Ethnicity/Race.** Individuals provided self-report regarding ethnicity and racial background using response options consistent with the 2000 United States census survey. In view of the study aims, the primary groups enrolled self-identified as Black/African American or non-Hispanic White.

**Height, Weight, and Body Mass Index.** Using the same scale for all participants, weight was measured without shoes to the nearest 0.1 kilogram (kg). Height was measured to the nearest 0.1 centimeter (cm) using a wall-mounted stadiometer which was calibrated daily with a standardized measuring rod. Body mass index (BMI) was calculated using the following algorithm: weight in kg/height in m\(^2\). A BMI greater than 30 kg/m\(^2\) indicated obesity.

**25-Hydroxyvitamin D assay.** A blood sample was collected from a forearm or hand vein at the onset of the quantitative sensory testing session. Following collection and processing, plasma was stored in a -80 degree freezer. Serum 25(OH)D analysis was performed by high performance liquid chromatography (total 25-hydroxyvitamin D = 25(OH)D2 plus 25(OH)D3) within six months of the date of collection. Clinical laboratory assessment of serum 25(OH)D best characterizes vitamin D status because it reflects vitamin D synthesized cutaneously as well as through dietary intake. Results of 25(OH)D testing were shared with participants and, if their level was ≤ 30 ng/mL, they were encouraged to discuss the result with their primary care provider.
Western Ontario and McMaster Universities Index of Osteoarthritis (WOMAC).

The WOMAC is frequently used in clinical and research settings to assess individuals’ retrospective self-report of knee osteoarthritis symptoms over the preceding 48 hours.\textsuperscript{33} The WOMAC includes 24 items and can be divided into subscales of pain, stiffness, and physical function. The WOMAC pain subscale score was used in this analysis (range 0-20), with higher scores indicating increased osteoarthritis phenotypic symptoms. High construct validity and test-retest reliability has been found in paper and computerized versions of the WOMAC for the overall measure and its respective subscales.\textsuperscript{33,34}

Short Physical Performance Battery (SPPB). The SPPB assesses lower extremity function with balance, chair, and walking tests.\textsuperscript{35} Specifically, participants were asked to: 1) stand with their feet together in the side-by-side, semi-tandem, and tandem positions for up to one minute; 2) rise from a seated position in a chair and return to a seated position five times; and, 3) walk a 4-meter course twice. If the participant did not feel it was safe to perform the activity, they received a score reflecting non-participation. For each category, based on their performance, they received a score of 0-4 (total score 0-12). A lower score indicates worse function and greater likelihood of disability.\textsuperscript{36}

Center for Epidemiological Studies Depression Scale (CES-D). The CES-D is a 20-item self-report tool that measures symptoms of depression, including depressed mood, guilt/worthlessness, helplessness/hopelessness, psychomotor retardation, loss of appetite, and sleep disturbance over the past week.\textsuperscript{37} The total score of the CES-D (range 0-60) was used in the current study as an estimate of the degree of participants’ depressive symptomatology. The validity and internal consistency of the CES-D in the general population has been reported to be acceptable, with scores ≥ 16 indicating clinically relevant depressive symptoms.\textsuperscript{38}
Data Analysis

All statistical analyses were performed using SPSS version 21.0 (SPSS Inc. Chicago, IL). Pearson correlations were used to assess zero-order relations among continuous study variables. Analysis of variance (ANOVA) and Chi-square were used to assess mean differences and relations among categorical study variables, respectively. In the case of unequal sample sizes across categorical variables, the parametric assumptions of data normality and homogeneity of variance were visually inspected and tested using Shapiro-Wilk statistics and Levene’s tests, respectively. Analysis of covariance (ANCOVA) was used to examine relations among obesity status, 25(OH)D levels, and measures of knee osteoarthritis pain and physical function. Significant and main effects and interactions were further analyzed via post-hoc tests using Tukey’s Honestly Significant Difference (HSD). Analyses include the squared partial eta ($\eta_p^2$) as a measure of effect size where appropriate. Following the conventions of Cohen,$^{39}$ $\eta_p^2 = 0.01$ is considered a small effect, $\eta_p^2 = 0.06$ a medium-sized effect and $\eta_p^2 = 0.14$ a large effect. Significance was set at the 0.05 level unless multiple comparisons necessitated a control for type I error inflation.

Results

Participant Characteristics

A total of 302 participants with symptomatic knee osteoarthritis were recruited and eligible for study inclusion. Serum 25(OH)D data were available for 265 participants. One individual, who was undergoing prescription vitamin D correction, had a 25(OH)D level more than five standard deviations above the mean, and as a result was excluded from analyses. In addition, eight participants were deemed multivariate outliers based on elevated Mahalanobis distances with a conservative probability level of $p < 0.001$. Thus, they were not considered
representative of the target population and were excluded from analyses. The final sample included 256 participants. The mean age of the final sample was 56.8 years (SD = 7.49) and ranged from 45 to 85 years. The sample was comprised of 161 women (63%) and 95 men (37%), while the racial composition was 141 Black/African Americans (55%) and 115 non-Hispanic Whites (45%). The majority of the participants were recruited from a single study site, such that 178 (70%) participated at the University of Florida and the remaining 78 (30%) participated at the University of Alabama at Birmingham. Of the total sample, 113 participants (44%) reported they were taking vitamin D supplementation. The mean 25(OH)D level was 23.11 ng/mL (SD = 9.12) and ranged from 2.90 ng/mL to 48.01 ng/mL. The mean pain rating on the WOMAC pain subscale was 7.12 (SD = 4.25) and ranged from 0 to 19, while the mean physical function performance on the SPPB was 9.90 (SD = 1.61) and ranged from 5 to 12.

**Correlations and Group Differences**

The Pearson correlations for all continuously-measured study variables are shown in Table 1. Results showed that BMI was significantly correlated with ratings of knee osteoarthritis pain and with physical function. Serum 25(OH)D levels were significantly correlated with knee osteoarthritis pain ratings but not physical function. Greater ratings of knee osteoarthritis pain were significantly correlated with poorer physical function. Severity of depressive symptoms was significantly associated with greater ratings of knee osteoarthritis pain and poorer physical function. Age was not significantly correlated with either knee osteoarthritis pain or physical function.

Table 2 displays mean differences in knee osteoarthritis pain ratings and physical function according to participants’ sex, race, vitamin D supplementation, and the study site where they participated. Results of ANOVA demonstrated that Blacks/African Americans
reported significantly greater knee osteoarthritis pain and displayed poorer physical function compared to non-Hispanic Whites. There were no significant differences in knee osteoarthritis pain or physical function between men and women. Likewise, there were no significant differences in knee osteoarthritis pain ratings or physical function between those who did and did not take vitamin D supplements. Lastly, participants at the University of Florida study site reported greater knee osteoarthritis pain and had poorer physical function compared to participants at the University of Alabama at Birmingham study site.

**Obesity and 25(OH)D Levels**

Table 1 shows that BMI was significantly and negatively correlated with 25(OH)D levels, such that greater BMI was associated with lower levels of 25(OH)D ($r = -0.42, p < .001$). The obesity status of all participants was classified according to their BMI as either obese ($\geq 30$ kg/m$^2$) or non-obese ($<30$ kg/m$^2$). Of the 256 participants included in this study, 126 (49%) were obese while the remaining 130 (51%) were non-obese. Serum 25(OH)D levels of all participants were also categorized according to clinical practice guidelines as deficient ($\leq 20$ ng/mL), insufficient (21-29 ng/mL), or adequate ($\geq 30$ ng/mL). Consistent with the study hypothesis, results indicated that the proportions of vitamin D deficiency, insufficiency, and adequacy significantly differed as a function of obesity status ($\chi^2 = 35.10, p < .001$). Among the 126 obese participants, 68 (54%) were vitamin D deficient and 45 (36%) were insufficient, while only 13 (10%) were adequate. Of the 130 participants who were non-obese, only 29 (22%) showed deficient vitamin D levels, 55 (42%) were insufficient, and 46 (36%) were adequate. Figure 1 shows the data support our first hypothesis suggesting that obesity is significantly associated with clinically-relevant vitamin D deficiency.
Associations with Physical Function and Knee Osteoarthritis Pain

**Covariates.** Several variables were included as statistical controls in all subsequent analyses examining the interactive relation between obesity and 25(OH)D levels with knee osteoarthritis pain and physical function. These controls were participants’ age, sex, and race, depressive symptoms (CES-D), vitamin D supplementation, as well as study site location. There are four reasons for including the statistical controls. First, significant age, sex, and race differences have previously been reported for physical function and knee osteoarthritis pain.\textsuperscript{3,9,41} Second, given the psychomotor effects of depression as well as the overlap between measures of negative mood and pain reports, it is advisable that any analysis of physical function and pain adjust for depressive symptoms.\textsuperscript{42,43} Third, recent longitudinal studies have tentatively shown that vitamin D status may impact knee pain and physical performance,\textsuperscript{44,45} warranting controlling for vitamin D supplementation. Finally, it is necessary to control for the significant differences in knee osteoarthritis pain and dysfunction between the two study site locations.

**Knee Osteoarthritis Pain.** Ratings of knee osteoarthritis pain on the WOMAC pain subscale were found to be approximately normally distributed with homogenous variances across 25(OH)D levels and obesity status as indicated by Shapiro-Wilk statistics ($p$’s > 0.05) and Levene’s test ($F(5, 250) = 1.82, p = .109$), respectively. Results of a 3 x 2 factorial ANCOVA revealed a significant main effect of 25(OH)D level on ratings of knee osteoarthritis pain ($F(2, 244) = 4.02, p = .019, \eta_p^2 = .032$). However, the main effect of obesity status ($F(1, 244) = 0.66, p = .42, \eta_p^2 = .003$) and the Obesity Status X 25(OH)D Level interaction ($F(2, 244) = 0.69, p = .50, \eta_p^2 = .006$) were non-significant. Follow up post-hoc tests using Tukey’s HSD were completed for the main effect of 25(OH)D level. Participants with adequate 25(OH)D levels reported significantly lower levels of knee osteoarthritis pain reported on the WOMAC pain
subscale than participants with deficient \((p < 0.001)\) and insufficient \((p = .016)\) levels regardless of obesity status. However, as shown in Figure 2, there was no significant difference in knee osteoarthritis pain ratings between obese and non-obese participants with deficient and insufficient levels of 25(OH)D \((p = .143)\).

**Lower Extremity Function.** An additional 3 x 2 factorial ANCOVA was carried out to evaluate the effects of obesity and 25(OH)D levels on lower extremity function measured by the SPPB. The obesity and vitamin D clinical categorizations described above were used for this analysis. Despite unequal samples sizes across categorizations, homogeneity of variance was not violated according to Levene’s test \((F(5, 250) = 2.06, p = .072)\). The distributions of SPPB scores were approximately normal across obesity groups and 25(OH)D levels as indicated by Shapiro-Wilk statistics \((p’s > 0.05)\). After adjustment for covariates, results indicated a non-significant main effect for obesity status \((F(1, 244) = 0.06, p = .809, \eta^2_p = .001)\) and a non-significant main effect for 25(OH)D levels \((F(2, 244) = 2.24, p = .109, \eta^2_p = 0.018)\). However, a significant Obesity Status X 25(OH)D Level interaction emerged for lower extremity function on the SPPB \((F(2, 244) = 3.05, p = .049, \eta^2_p = .024)\). Because the interaction between obesity and 25(OH)D levels was significant, differences in physical function according to 25(OH)D levels were examined separately for obese and non-obese participants. Figure 3 shows that among non-obese participants, there were no significant differences in lower extremity function across 25(OH)D levels \((F(2, 127) = 0.77, p = .463, \eta^2_p = .012)\). Conversely, there were significant differences in lower extremity performance as a function of 25(OH)D levels among the obese participants \((F(2, 123) = 4.49, p = .013, \eta^2_p = .068)\). Follow-up post-hoc tests with Tukey’s HSD were conducted to evaluate the three pair-wise differences in SPPB means across 25(OH)D levels for obese participants. Obese participants with deficient \((p = .009)\) and insufficient \((p =
.045) levels of 25(OH)D performed significantly worse on the SPPB (i.e., poorer physical function) than individuals with adequate 25(OH)D levels. There was no significant SPPB difference between those obese participants with deficient and insufficient 25(OH)D levels (p = .720).

**Discussion**

In accordance with results of previous studies, we found that obesity was significantly correlated with knee osteoarthritis pain and poorer functional performance.\(^7,10,44-49\) Consistent with the first hypothesis, obesity was associated with vitamin D deficiency and insufficiency. Participants with adequate 25(OH)D levels reported significantly lower levels of knee osteoarthritis pain than participants with insufficient and deficient levels, regardless of obesity status. Additionally, 25(OH)D levels and obesity interacted to predict functional performance, with the findings indicating that deficient and insufficient 25(OH)D levels were related to significantly poorer function in comparison to adequate 25(OH)D levels only among obese individuals. This finding should be interpreted with caution, however, given that the obese group with adequate 25(OH)D was comprised of only 13 participants (10% of obese participants). Accumulating a larger sample of obese participants with adequate 25(OH)D from which to draw comparisons was unlikely given the support we found for our first hypothesis. On balance, our second hypothesis was partially supported in that obese individuals with deficient and insufficient 25(OH)D levels displayed the poorest physical function.

There are multiple potential explanations for the observed association between obesity, low 25(OH)D levels, and knee osteoarthritis pain. One possibility is that the pleiotropic role of biologically active 25(OH)D could influence pain and pain processing via multiple mechanisms.\(^50\) For example, vitamin D deficiency increases bone turnover, thereby affecting
bone quality, which results in greater sensitivity to mechanical forces associated with osteoarthritis.\textsuperscript{51} Also, both reductions in 25(OH)D and obesity are associated with a pro-inflammatory state conducive, which could contribute to increased pain sensitivity among individuals with osteoarthritis.\textsuperscript{6,52,53,54} In contrast, sufficient levels of cellular 25(OH)D may have a protective effect on cell function and serve to reduce inflammation.\textsuperscript{20,55-57} Another possibility is that higher levels of osteoarthritis pain could lead to reduced physical activity, including outdoor activity, which would lead to both decreased vitamin D levels and increased obesity. Further, recent findings indicate that older individuals with higher levels of vitamin D show greater declines in body fat with physical activity compared to those with low vitamin.\textsuperscript{58} Thus, deficient vitamin D may inhibit activity-induced weight loss, leading to increased obesity and thus higher levels of osteoarthritis-related pain.

Because of the strong association between 25(OH)D levels and knee osteoarthritis pain, it is reasonable to postulate that vitamin D supplementation may help reduce pain affiliated with the condition. However, in a recent randomized-controlled clinical trial, McAlindon and colleagues found vitamin D supplementation to levels of 36 ng/mL did not improve WOMAC pain severity scores or slow knee cartilage volume loss over a two-year period (it is important to note that only 61\% of the treatment group reached the target 25(OH)D level).\textsuperscript{59} Nevertheless, there was a tendency ($p = .07$) for vitamin D supplementation to improve physical function assessed by a timed 20-meter walk and chair-rise test. There also are some positive findings in the literature. In a non-randomized trial by Huang and colleagues; vitamin D supplementation in veterans was demonstrated to significantly decrease pain level, number of pain sites, use of pain medication, as well as improve sleep and health-related quality of life.\textsuperscript{60} Finally, in a recent pilot randomized trial of knee osteoarthritis pain and dysfunction, Sanghi and colleagues demonstrated
a small, but significant, improvement in the group treated for chronic pain with vitamin D supplementation. Thus, the effects of vitamin D supplementation on pain in individuals with knee osteoarthritis are equivocal and warrant further investigation.

An expert panel of the American College of Rheumatology now advises all patients with osteoarthritis to achieve a healthy weight, enroll in aerobic and/or resistance-based exercise, and participate in osteoarthritis self-management programs, including psychosocial interventions, physical therapy, and instruction in the use of thermal agents, bracing, and walking aids. The use of nutraceuticals (i.e., dietary supplements) for chronic pain comprises a new area of research. Given the risk of side effects from medications typically employed for osteoarthritis pain and heightened consumer interest in nutritional supplement use, maintaining adequate 25(OH)D levels may provide a new strategy in the clinical armamentarium to reduce osteoarthritis pain and dysfunction, with reduced risk of adverse side effects. Although rare, vitamin D toxicity may cause kidney stones, hypercalcemia, and death. Well-designed intervention studies are needed to causally determine if higher serum levels of 25(OH)D can safely and reliably reduce pain and decrease functional limitation in older adults with knee osteoarthritis.

Some important limitations of this study need to be considered when interpreting the results and will need to be addressed in future research. The cross-sectional study design does not allow us to determine causality between 25(OH)D level, obesity, and osteoarthritis-related outcomes. It is possible that decreased 25(OH)D precedes declines in physical activity which contributes to weight gain that exacerbates chronic pain. It is also possible that individuals with chronic knee osteoarthritis pain and limitations in physical function do not spend as much time outdoors and have less sun exposure, thereby reducing vitamin D production. This cross-sectional examination was a secondary analysis of data from a larger study; measures of physical
activity, amount of sun exposure, and dietary nutrient intake were not collected. Despite the limitations, the current cross-sectional study highlights a relationship between obesity, low levels of 25(OH)D, and knee osteoarthritis-related pain and dysfunction that deserves further study. Screening for vitamin D deficiency among obese Americans may be warranted – especially for those with chronic knee osteoarthritis pain.
References


Figure 1. The association between obesity and vitamin D status.

Note: Clinical practice guidelines cite 25(OH)D levels >30 ng/mL as *adequate*, values between 21-29 ng/mL are defined as *insufficient*, values <20 ng/mL as *deficient*. Each bar represents the sample size for that particular group.

Figure 2. Average knee osteoarthritis pain severity as a function of weight and vitamin D status.

Note: The following covariates are significant: race (p = .05), depressive symptoms (p < .001), and study site location (p = .05). There was no significant difference in knee osteoarthritis pain ratings between obese and non-obese participants with deficient and insufficient levels of 25(OH)D (p = .143).

Abbreviations: WOMAC, Western Ontario and McMaster Osteoarthritis Index; BMI, Body Mass Index.

Figure 3. Average lower extremity function as a function of weight and vitamin D status.

Note: *p < .05, **p < .01. The following covariates were significant: age (p < .01), race (p < .001), depressive symptoms (p < .01), and study site location (p < .001).

Abbreviations: SPPB, Short Physical Performance Battery; BMI, Body Mass Index.
Table 1. Pearson correlations among study variables.

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Note: *p < .05, **p < .01.

Abbreviations: CES-D, Center for Epidemiologic Studies Depression Scale; BMI, Body Mass Index; SPPB, Short Physical Performance Battery; WOMAC, Western Ontario and McMaster Osteoarthritis Index.
Table 2. Group differences in ratings of knee osteoarthritis pain on the WOMAC pain subscale and lower extremity function on the SPPB.

<table>
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Abbreviations: UF, University of Florida; UAB, University of Alabama at Birmingham; WOMAC, Western Ontario and McMaster Osteoarthritis Index; SPPB, Short Physical Performance Battery.