Serum Vitamin D and Risk of Back Pain in Older Men

By

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A Thesis

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TABLE OF CONTENTS

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LIST OF ABBREVIATIONS:

AIC - Akaike Information Criteria

ANOVA – Analysis of Variance

BMI – Body Mass Index

CI – Confidence Interval

CNS – Central Nervous System

IOM - The Institute of Medicine

IRB - Institutional Review Board

LCMS - Liquid Chromatography Mass Spectroscopy

MrOS – Osteoporotic Fractures in Men Study

NHANES - National Health and Nutrition Examination Survey

NSAIDs - Non-steroidal Anti-inflammatory Drugs

PASE - Physical Activity Scale for the Elderly

RR – Risk Ratio

SF-12 - Medical Outcomes Study 12-Item Short Form

- MCS – Mental Component Score
- PCS – Physical Component Score

SOF – Study of Osteoporotic Fractures

US – United States

LIST OF TABLES AND FIGURES:

Footnote key

[a]Latitudes and seasons as previously described
[b]Fisher's exact method used
[+] Adjusted for age, season, latitude, mental and physical SF12 scores, prevalent radiographic vertebral fracture, use of centrally acting medications, and a history of problem drinking

Primary Figures and Tables

Appendix Figures and Tables

ABSTRACT

Back pain is a prevalent and costly ailment for older Americans, with significant personal and population level impact. Low serum 25-hydroxyvitamin D [25(OH) vitamin D] levels are common and are hypothesized to contribute to musculoskeletal pain. Cross-sectional studies have indicated an association between vitamin D deficiency and increased back pain but there is a paucity of robust prospective cohort studies representing this topic in the literature, particularly in men.

This prospective cohort study was performed in a random sample of 1608 U.S. men from the Osteoporotic Fractures in Men Study (MrOS) all of whom were at least 65 years of age and community-dwelling. In this sample, baseline 25(OH) vitamin D levels were measured in serum by liquid chromatography mass spectroscopy and back pain was ascertained by questionnaire. Subsequently, new back pain was obtained for three, four month, intervals for a total of 12 months of follow-up. Multivariable log-binomial regression models were used to estimate the risk ratios (RR) and 95% confidence intervals (CI) of back pain in follow up according to baseline 25(OH) vitamin D quartile. Models were adjusted for age, season of blood draw, and latitude as well as mental and physical functioning scores, prevalent radiographic vertebral fracture, use of central nervous system (CNS) active medications, and history of problem drinking. Tests of linear trend were performed across increasing serum 25(OH) vitamin D quartiles. RRs were also estimated in analyses stratified by baseline back pain status.

During follow-up, 785 (49%) men reported at least one episode of back pain. Using serum 25(OH) vitamin D quartile 4 as the referent, RRs (95% CI) for new back pain were 1.1 (0.9, 1.2) in quartile 1, 1.1 (0.9, 1.2) in quartile 2, and 1.1 (0.9, 1.2) in quartile 3. In stratified analyses, the association of 25(OH) vitamin D and new back pain remained null in those with and without back pain in the 12 months before baseline. We conclude that in a population of older men, low serum 25(OH) vitamin D was not associated with the risk of new back pain during follow up.

INTRODUCTION

Over 80% of adults have low back pain at some point during their lifetime and more than a quarter reported back pain in the preceding 3 months [1-3]. Back pain is the second most common reason for clinician visits in the United States and the most prevalent type of pain reported in adults over the age of 65 [1,2,4]. The prevalence of chronic low back pain has increased between 10 and 20 percent over the last decade [5]. On average, older adults report more severe pain and pain that is more limiting to physical activity than do younger persons [6,7]. Back pain can be physically limiting, interfere with employment or activities of daily living, and is associated with lower quality of life scores and depression [8,9]. The total cost associated with back pain is over 100 billion dollars annually in the United States, and more than 75 percent of the cost is attributable to less than 5 percent of patients, of which the majority are older adults [10].

The Institute of Medicine (IOM) recommends a goal of at least 20ng/ml for the general population, and the National Health and Nutrition Examination Survey (NHANES) data (2005-2006) report 41.6% of adults are vitamin D deficient (levels below 20ng/mL) [11,12]. Furthermore, the incidence of vitamin D deficiency is accelerating, and is not fully explained by increases in assay sensitivity [13].

The association of vitamin D deficiency and low bone mass is known; however effects on other health parameters such as pain are less well established [2,4,14,15]. Vitamin D deficiency is hypothesized to cause diffuse musculoskeletal pain by reducing the absorption of calcium, causing bone-related pain and increasing the risk of osteoporotic fractures [16-19]. Vitamin D also promotes protein synthesis in muscle and deficiency is associated with decreased appendicular skeletal muscle mass in women, potentially resulting in direct or indirect pain from muscle instability [17,20-22]. Lastly, vitamin D deficiency is hypothesized to contribute to a central sensitivity to mechanical pain in patients with chronic pain at baseline [23].

Previous cross-sectional studies have shown an association between vitamin D deficiency and musculoskeletal pain in multiple locations, as well as low back pain in particular [18,24-28]. However, the measurement of vitamin D differed in these studies (from serum measures to self-reported diagnosis of

deficiency) and two international studies on the cross-sectional association between vitamin D deficiency and back pain found that this association was significant in women, but not in men [20,22].

The high prevalence of both back pain and vitamin D deficiency, particularly in the population of older U.S. adults, and the large personal and population level impact of back pain makes this association important to investigate. The previously described cross-sectional studies have shown a higher prevalence of vitamin D deficiency in populations with back pain and multiple biologically plausible mechanisms have been hypothesized. However, 'reverse causation' is plausible, because back pain could contribute to vitamin D deficiency through reduced activity. Thus, prospective studies evaluating this association in a representative population are needed.

In this study, we evaluated baseline serum 25(OH) vitamin D levels and new reports of back pain in the ensuing year using data already collected in the Osteoporotic Fractures in Men (MrOS) study, a multi-center prospective study of older U.S. men [19,29]. We hypothesized that lower serum 25(OH) vitamin D levels would be associated with an increased risk of back pain during follow up, independent of confounding factors.

METHODS

Study population

The MrOS study is a multi-center prospective cohort study designed to identify risk factors for fractures and other conditions of aging among community-dwelling men aged 65 years or older. The overall study includes data from 5994 men, enrolled from March 2000 through April 2002. Details of the MrOS enrollment procedures and baseline cohort characteristics have been previously described [29,30]. In brief, men were eligible to participate if they were at least age 65 years, were able to walk without assistance and had not had bilateral hip replacement. Participants were enrolled at 6 US academic centers [Birmingham, AL; Minneapolis, MN; Palo Alto, CA; Pittsburgh, PA; Portland, OR; and San Diego, CA]. Institutional review board (IRB) approval and written informed consent was required at the site of enrollment.

The vitamin D sub-cohort (the analytic cohort) was generated in 2007, when funding became available, by random selection of 1608 serum samples for mass spectrometry liquid chromatography assay, of which 1606 men had available serum 25(OH) vitamin D levels reported.

Baseline Variable Measurements

The comprehensive baseline visit included self-administered and interviewer-administered questionnaires regarding demographic descriptors, health history and personal habits, rating of health and functional status, inventory of medications, physical performance testing, and measures of body habitus including weight, height, and calculated body mass index (BMI). In-person measures, including height and weight, were taken at baseline by an examiner using standard equipment. Physical activity was measured with the Physical Activity Scale for the Elderly (PASE) [31] and participants reported walking for exercise. Instruments used to measure functional status and quality of life included a quality of life questionnaire used in the Study of Osteoporotic Fractures (SOF) and the Medical Outcomes Study 12-Item Short Form (SF-12) [32]. Participants reported any falls in the 12 months, known fracture history, and back pain in the preceding 12 months (as described below). Lateral lumbar and thoracic radiographs were obtained at

baseline to identify prevalent vertebral fractures. Blood draws were also performed and the serum samples stored for later analysis, described below.

Serum vitamin D measurements

As previously described, serum 25(OH) vitamin D liquid chromatography mass spectroscopy assays were performed at the Mayo Clinic in Rochester, MN on serum samples prepared immediately after phlebotomy, foil wrapped, and stored at -70ºC until the time of assay [33]. Assays were precise, with an inter-assay coefficient of variation of 4.4% and intra- assay coefficient of variation of 4.9% [33]. Serum 25(OH) vitamin D was measured as a concentration of ng/ml and ranged from a minimum of 3.1 ng/ml to a maximum of 58.3 ng/ml with a mean of 25.1 ng/ml.

Back Pain Measurements - baseline

Baseline back pain was self-reported occurrence of back pain in the 12 months prior to the baseline visit, utilizing questions modified from the North American Spine Society back and neck pain questionnaires [34]. Participants indicated the location of the back pain on a drawing; upper back, mid back, lower back, or buttocks, which were not mutually exclusive locations. Those who reported back pain were also asked about severity of the pain (mild, moderate, or severe), the frequency with which the back pain occurred (rarely, sometimes, often, or always), and whether their activities were limited secondary to pain.

Back Pain Measurements – follow up

Study participants received a one-page Tri-Annual Questionnaire, every four months after their baseline visit. This questionnaire was used to ascertain new falls, fractures, and back pain during the preceding four month period. Participants self-reported back pain (yes/no), whether the back pain was severe, and whether or not the pain limited daily activities. Each participant was followed for the first three questionnaires for a total of 12 months. The primary outcome measure was 1 year risk (cumulative incidence) of any new back pain, defined as back pain reported at any one or more follow up time period. This was then stratified by the presence of back pain at baseline to denote incident back pain (no back pain at baseline, followed by back pain during follow up) versus recurrent back pain (back pain at

baseline and during follow up). Lastly, back pain during follow up was categorized by whether or not it was severe and whether or not it was reported as limiting.

Statistical Analysis

All analyses were conducted using STATA software version 13.1 (StataCorp. 2013. *Stata Statistical Software: Release 13*. College Station, TX: StataCorp LP). Baseline descriptions of serum vitamin D variables and back pain prevalence were conducted. Serum 25(OH) vitamin D quartiles were defined with quartile one (with range 3.1 ng/ml, <19.9 ng/ml) approximately equal to vitamin D deficiency (<20 ng/ml). A binary variable was also defined to denote vitamin D deficiency ($\leq$ 19.9 ng/ml). The validity of using the same definition of vitamin D quartiles in those with and without back pain at baseline was assessed with a t-test of means in each quartile, which were not significantly different, as well as a comparison of the cut points generated in each stratum and in the analytic cohort as a whole.

Back pain at baseline was categorized as yes/no back pain and, if yes, mild/moderate/severe severity, frequency of pain (rarely, sometimes, often, always), and whether or not the pain was limiting (yes if ever limiting).

For this analysis, a binary variable was created for site latitude (above versus below 40 degrees), and season at which phlebotomy was performed; winter (January- March), spring (April-June), summer (July-September), and fall (October-December), summer was used as the referent season for all analyses. Categorical variables were created for age (below 75 years and 75 years or older), race (white and non-white race), level of highest education (less than high school education, high school education with or without some college, bachelor's degree, or graduate degree), and smoking history (never smoker versus current or former smoker). Drinking habits were assessed with both a standardized CAGE Questionnaire for current problem drinking (score of 2 or greater was considered indicative of current problem drinking) and a self-reported history of problem drinking[35]. Body mass index was categorized as normal (BMI<25), overweight (BMI 25-29.9), and obese (BMI $\geq$ 30)[36]. To measure functional status and quality of life, several instruments were adapted including a quality of life questionnaire used in the Study of

Osteoporotic Fractures (SOF) and the Medical Outcomes Study 12-Item Short Form (SF-12) and binary variables created for poor functioning (component score less than 50) [28] .

Binary variables were created for osteoporosis (self-reported history of osteoporosis or currently taking osteoporosis medication), use of CNS active medications (any use of opioid pain medications, benzodiazepines, anti-depressants, mood stabilizing medications, or anti-seizure medication), use of non-opioid analgesic medication (use of non-steroidal anti-inflammatory drugs (NSAIDs) or acetaminophen), participants' ability to complete a tandem-walking course without losing balance, and for participants' ability to rise from a chair and complete five chair stands .

The baseline characteristics for those in the vitamin D sub-cohort were similar to the parent population, as previously reported, where the prevalence of vitamin D insufficiency (<30ng/mL) was 72% and deficiency (<20ng/mL) 26%. [19]. Retention of subjects was high with 99.2% (n=1593) completing 12 months of follow up.

Characteristics of the analytic cohort at baseline were compared according to vitamin D quartile, utilizing one-way analysis of variance (ANOVA) for continuous variables and Chi-square or Fishers Exact tests for categorical variables. The association between vitamin D quartile and back pain symptoms at baseline was conducted utilizing a chi-square test. For those with back pain at baseline, this analysis was repeated with stratification for described severity and limitation of the pain. This analysis was also conducted for the binary independent variable indicating vitamin D deficiency, defined as less than 20ng/ml.

Due to the high prevalence of back pain in follow up (>10% in all strata), log binomial regression with robust variance estimator was used to build a model for back pain during follow up and risk ratios reported, as suggested by Zou et al [37].

Variables were tested for independent association with back pain during follow up and retained for the full model if found to be significant at an alpha of 0.2, utilizing 2-sided p-values. All variables were then tested concurrently in a full binomial regression model and manual deletion selection was utilized to

remove subsequent variables non-significant at an alpha of 0.05, and not found to be a confounder of the primary independent variables (vitamin D, age, season, and latitude) as indicated by a change in the RR of the primary variables of less than 10% [38]. Lastly, variables were checked for their contribution to the model fit by way of Akaike Information Criteria (AIC) comparison and added back to the model only if there was a decrease in AIC, suggesting improved stabilization of the model [39]. Variables were determined to be independent risk factors if statistically significant ($p < 0.05$).

This analysis was then stratified by reported back pain at baseline; subsequently investigating the association between 25(OH) vitamin D and incident back pain as well as the association between 25(OH) vitamin D and recurrent back pain. No further variable selection was performed prior to this secondary analysis; all variables from the final multivariable model were used in the analysis of each stratum.

The variables found to be independently associated with back pain during follow up include: mental and physical component scores of the SF12, prevalent radiographic vertebral fracture, and use of centrally acting medications. A history of problem drinking was not independently associated with back pain in follow up, nor confounded the relationship between primary variables and back pain, but improved the overall model quality so was retained in the multivariable model.

To determine the associations of low 25(OH) vitamin D on risk of back pain during follow up, we estimated risk ratios (RRs) and 95% confidence intervals for three models: a crude model; an age, season, and latitude adjusted model; and a multivariable-adjusted model including age, season, latitude, mental and physical functioning SF12 component scores, prevalent radiographic vertebral fracture, use of central nervous system (CNS) active medications, and history of problem drinking. The highest vitamin D quartile was used as referent in all models.

RESULTS

Lower serum vitamin D quartile was associated with a baseline visit conducted in winter or spring, study site located in a northern latitude (>40^{o}), older age, non-white race, higher BMI, lower average physical activity (PASE) score, lower physical functioning component (PCS) score, and lower reported health status for age. Those in lower vitamin D quartiles were also less likely to walk daily for exercise, be able to complete a narrow walk; and were more likely to take non-opioid pain medications (Table 1).

The prevalence of back pain at baseline was 67.87% (n=1090) and 48.9% (n=785) of men experienced back pain at least once during this follow-up time period. When stratified by whether or not men had experienced back pain at baseline, 64.2% (n=695) of men with back pain at baseline reported back pain in follow up while 17.6% (n=90) of men without back pain at baseline reported back pain in follow up (Figure 1).

The majority of back pain at baseline was characterized as low back pain (90.3%) that occurred rarely or some of the time (79.0%), was not considered limiting (70.8%), and only a minority (9.2%) reported severe pain. Vitamin D quartile was not associated with back pain at baseline or any of the subsequent descriptors of baseline location or severity. Lastly, back pain at baseline was not associated with hypovitaminosis D, or vitamin D deficiency (as defined by serum 25(OH) vitamin D <20ng/ml).

The majority of men without back pain at baseline did not report any back pain during follow up, but those that did report back pain most commonly reported back pain during only one follow up interval.

The majority of men with back pain at baseline experienced either persistent back pain during all follow up intervals (26.8%) or do not experience any back pain in follow up (36.2%), despite having back pain at baseline (Appendix Table A).

Men with back pain during one year of follow-up were significantly more likely than men without back pain to have lower physical functioning scores, higher BMI, were more likely to be current or former smokers, were less likely to walk daily for exercise, less likely to be able to complete chair stands, had poorer reported health, and poorer physical and mental functioning composite scores. These men were

also more likely to have a history of arthritis, osteoporosis, and recent falls as well as radiographic evidence of a vertebral fracture, were more likely to take CNS active medications and non-opioid analgesic medications (data not shown).

Table 2 presents the RR and 95% confidence intervals for back pain in follow up by quartiles of serum 25(OH) vitamin D. The results of the crude model (includes only the effect of vitamin D quartile) and the multivariable model are reported. Results did not vary substantially between models; the RR for back pain during follow up for individuals in the lowest quartile of serum vitamin D compared to those in the highest quartile of serum vitamin D was not significant (RR 1.1, 95% CI 1.0-1.3). Multivariable adjustment did not substantially modify this risk (RR 1.1, 95% CI 0.9-1.2). Lastly, trends across quartiles of serum vitamin D were not significant ($p>0.3$).

All models were also conducted within strata of those with and without back pain at baseline, (Table 2). Consistent with the results reported for the overall cohort, the risk ratio for incident back pain for the lowest quartile of serum vitamin D compared to those in the highest quartile of serum vitamin D was not significant (RR 1.4, 95% CI 0.8-2.3) and this was not substantially altered by multivariate adjustment (RR 1.3, 95% CI 0.8-2.1). Similarly, recurrent back pain (back pain at baseline and in follow up) did not show any significant association for the lowest vitamin D quartile (RR 1.1, 95% CI 0.9-1.2), or with multivariate adjustment (RR 1.1, 95% CI 0.9-1.2). The trend for vitamin D quartiles also remained insignificant ($p>0.4$). Lastly in further descriptive analyses, no association between lower vitamin D quartile and increased occurrence of severe back pain in follow-up was observed ($p=0.65$). Similarly, there was no observed association between lower vitamin D quartile and severe back pain in follow-up for those with ($p=0.73$) or without ($p=0.75$) back pain at baseline (Appendix Table B).

DISCUSSION

Contrary to our working hypothesis, our findings indicate that within this cohort of generally healthy older U.S. men, serum 25(OH) vitamin D was not associated with increased risk of back pain. This association did not differ for those with and without back pain at baseline. The lack of association between serum 25(OH) vitamin D and new onset back pain was further supported by descriptive analyses in which we observed no association with frequency of severe or limiting back pain.

There is a paucity of prospective studies on the relationship between serum vitamin D and back pain, particularly in men, with subsequently little research available for comparison. However, the present finding contradicts those findings demonstrated for musculoskeletal pain in a cohort of women and findings from cross-sectional studies of populations with low vitamin D and chronic or severe back pain [17,20,21,25]. However, these findings are in concordance with previous cross sectional findings by Parks et al and Hicks et al that demonstrated an association in women, but not in men [20,22]. This could not be addressed with the present study, as this study population was comprised exclusively of older men.

The lack of association demonstrated in the present study must be evaluated for possible alternative explanations such as bias, confounding, or inadequate power. The measure of vitamin D status used in this study (total 25-hydroxyvitamin D), is the most stable form of vitamin D detectable, and therefore reflects an individual's vitamin D stores and is used for indication of vitamin D status in most clinical settings [40]. Furthermore, the liquid chromatography mass spectroscopy assay used to detect 25(OH) vitamin D levels is the gold standard for clinical detection and showed excellent inter and intra-assay reliability [33].

The measurement of back pain was a self-reported binary question; therefore, it is possible that back pain was inaccurately reported [41]. However, because the duration participants were asked to recall (4 months) was relatively short and the 25(OH) vitamin D results were not provided to cohort members, it is unlikely that any inaccuracies in report of back pain would have occurred more frequently in those with lower vitamin D, which would be necessary to counteract any true positive association and result in the lack of

association observed in this study. Variables most likely to be associated with lower vitamin D level, as well as with incident back pain regardless of vitamin D status, were considered as potential confounders and robust variable collection was conducted in this study. Any unknown confounder would require an exceptionally strong negative association with vitamin D and back pain to create an aberrant null result. Furthermore, inadequate power is an unlikely explanation for our results. Using the prevalence of back pain in the referent quartile (4^{th} quartile) as the expected prevalence, this study had greater than 80% power to detect a relative risk of back pain during follow up of 1.2 in the total cohort, and a risk ratio of back pain during follow up of 2.0 in those without back pain at baseline. This is further supported by the narrow confidence intervals of the relative risk of back pain for men with serum 25(OH) vitamin D levels in the lowest quartile, observed across all strata, therefore the likelihood that a true association was present but undetected is low.

Strengths and Limitations

Our study strengths include a prospective evaluation utilizing a large representative cohort of U.S. men with precise independent variable measurement, robust follow up, and comprehensive baseline variable collection. This prospective evaluation allows for the investigation of a temporal relationship between vitamin D deficiency and back pain. Furthermore, multiple follow up time points allowed for interrogation of the assumption that our cumulative incidence of back pain measure met the assumption of homogenous distribution of onset.

The collection of baseline back pain allowed for stratification of the analysis to control for confounding by prevalent back pain. However, this study also has limitations including the observational nature of the study which does not allow inference of causality despite our ability to determine the temporal relationship between baseline vitamin D measures and subsequent back pain during follow up. The small sample sizes in subsequent strata precluded modeling of severe or limiting incident back pain. Lastly, this study was conducted in an ambulatory cohort of generally healthy older U.S. men who were predominantly white. This limits the generalizability, however this is a large prospective cohort study

with high quality measurements, which allows for precise measures of association and sufficient power to detect a clinically meaningful difference for risk of back pain.

In conclusion, no association between serum 25(OH) vitamin D concentrations and back pain was demonstrated in this study. The significant personal and population level impact of back pain remains an important area of research interest as does the manifestations of vitamin D deficiency. The association may exist in other populations, but does not appear significant in older U.S. men. Our study suggests that, while Vitamin D supplementation may be indicated for other reasons, supplementation with the goal of preventing new onset back pain in older men is not supported.

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FIGURES AND TABLES

Figure 1. Sample distribution of back pain prevalence at baseline and in 12 months of follow up

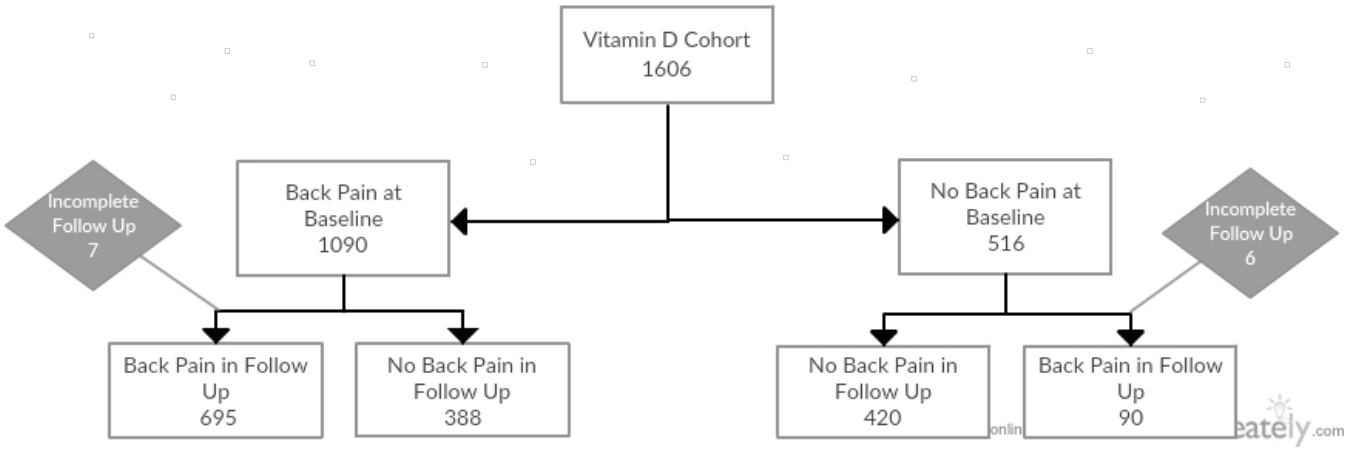

Table 1. Distributions of baseline characteristics among 1606 Men Aged 65 Years and Older according to serum 25(OH)D Quartile

	Serum 25(OH)D Level (ng/ml)				
	Quartile 1 (3.13, ≤19.9) n=406	Quartile 2 (>19.9, ≤25.07) n=397	Quartile 3 (>25.07, ≤29.8) n=402	Quartile 4 (>29.8, 58.3) n=401	*P* Value
Physical Activity (PASE score) (mean, sd)	136.19 (72.5)	147.91 (67.7)	147.08 (64.5)	155.63 (68.7)	0.0009
Age (n, %)					
<75 yrs	212 (23.3)	226 (24.84)	211 (23.19)	261 (28.68)	0.001
≥75 yrs	194 (27.87)	171 (24.57)	191 (27.44)	140 (20.11)	
Race (n, %)					
White	342 (23.30)	369 (25.14)	377 (25.68)	380 (25.89)	<0.0001
Non-white	64 (46.38)	28 (20.29)	25 (18.12)	21 (15.22)	
Education (n,%)					
Less than high school education	40 (36.36)	25 (24.55)	24 (21.82)	21 (19.09)	0.05
High school +/- some college	168 (25.85)	155 (23.85)	179 (27.54)	148 (22.77)	
Bachelors degree	116 (25.11)	117 (25.32)	103 (22.29)	126 (27.27)	
Graduate degree	82 (21.35)	100 (26.04)	96 (25.00)	106 (27.60)	
BMI (n,%)					
Normal (<25)	89 (20.99)	104 (25.53)	111 (26.18)	120 (28.30)	0.003
Overweight (25-29.9)	208 (24.24)	213 (24.83)	217 (25.29)	220 (25.64)	
Obese (≥30)	109 (33.64)	80 (24.69)	74 (22.84)	61 (18.83)	
Current CAGE score ≥2 (n,%)					
Yes	111 (29.21)	94 (24.74)	92 (24.21)	83 (21.84)	0.16
No	295 (24.06)	303 (24.71)	310 (25.29)	318 (25.94)	
History problem drinking (n,%)					
Yes	73 (27.55)	67 (25.28)	62 (23.40)	63 (23.77)	0.75
No	331 (24.78)	330 (24.70)	339 (25.37)	336 (25.15)	
Walks daily for exercise (n,%)					
Yes	179 (22.29)	197 (24.53)	200 (24.91)	227 (28.27)	0.01
No	227 (28.27)	200 (24.91)	202 (25.16)	174 (21.67)	
Able to complete chair stands (n,%)					
Able	388 (24.94)	384 (24.68)	391 (25.13)	393 (25.26)	0.10[b]
Unable	12 (40.00)	9 (30.00)	6 (20.00)	3 (10.00)	
Able to complete narrow walk (n,%)					
Able	336 (23.53)	358 (25.07)	356 (24.93)	378 (26.47)	<0.0001
Unable	55 (39.01)	32 (22.70)	35 (24.82)	19 (13.48)	
Reported Health Status for Age (n,%)					
Good/Excellent	328 (23.96)	333 (24.32)	345 (25.20)	363 (26.52)	0.001
Very Poor/Poor/Fair	77 (32.63)	64 (27.12)	57 (24.15)	38 (16.10)	
SF12 MCS Score					
Poor Mental Functioning (<50,n,%)	78 (31.84)	57 (23.27)	54 (22.04)	56 (22.86)	0.08
Good Functioning (≥50,n,%)	328 (24.10)	340 (24.98)	348 (25.57)	345 (25.35)	
SF12 PCS Score					
Poor Physical Functioning (<50,n,%)	189 (30.24)	143 (22.88)	160 (25.60)	133 (21.28)	0.001
Good Functioning (≥50,n,%)	217 (22.12)	254 (25.89)	242 (24.67)	268 (27.32)	
Radiographic Vertebral Fracture (n,%)					
Yes	65 (26.32)	49 (19.84)	62 (25.10)	71 (28.74)	0.20
No	337 (24.93)	347 (25.67)	338 (25.00)	330 (24.41)	
Fall in the Past Year (n,%)					
Yes	83 (25.15)	83 (25.15)	79 (23.94)	85 (25.76)	0.95
No	323 (25.31)	314 (24.61)	323 (25.31)	316 (24.76)	
Evidence of Osteoporosis (n,%)					
Yes	16 (20.25)	15 (18.99)	24 (30.38)	24 (30.38)	0.26
No	377 (26.13)	356 (24.67)	357 (24.74)	353 (24.46)	
History of Arthritis (n,%)					
Yes	195 (25.66)	191 (25.13)	182 (23.95)	192 (25.26)	0.82
No	211 (24.94)	206 (24.35)	220 (26.00)	209 (24.70)	
Baseline Visit Season[a] (n, %)					
Winter (Jan–Mar)	126 (39.38)	76 (23.75)	73 (22.81)	45 (14.06)	<0.0001
Spring (Apr–June)	115 (27.51)	120 (28.71)	94 (22.49)	89 (21.29)	
Summer (Jul–Sept)	74 (16.05)	97 (21.04)	122 (26.46)	168 (36.44)	
Fall (Oct–Dec)	91 (22.36)	104 (25.55)	113 (27.76)	99 (24.32)	
Latitude of Clinic Site[a] (n,%)					
Southern Latitude (≤40°)	175 (21.58)	198 (24.41)	203 (25.03)	235 (28.98)	<0.0001
Northern Latitude (>40°)	231 (29.06)	199 (25.03)	199 (25.03)	166 (20.88)	
CNS Active medication use (n,%)					
Yes	54 (24.77)	58 (26.61)	54 (24.77)	52 (23.85)	0.91
No	352 (25.36)	339 (24.42)	348 (25.07)	349 (25.14)	
Non-opioid Analgesic Use (n,%)					
Yes	181 (27.85)	174 (26.77)	150 (23.08)	145 (22.31)	0.02
No	225 (23.54)	223 (23.33)	252 (26.36)	256 (26.78)	

[a]Latitudes and seasons as previously described
[b]Fisher's exact method used

Table 2. Association of baseline serum 25(OH)D level with a new report of back pain in the following one year among older men: entire analytic cohort and stratified by history of back pain at baseline.

	Baseline Serum Vitamin D Level				
	Quartile 1	Quartile 2	Quartile 3	Quartile 4	
25(OH)D range	3.1,19.9 ng/ml	>19.9,25.1 ng/ml	>25.1,29.8 ng/ml	>29.8,58.3 ng/ml	
Entire Cohort	N=404	N=394	N=398	N=397	*P* Value
Back pain in next year, n (%)	211 (52)	197 (50)	195 (49)	182 (46)	
Unadjusted RR (95% CI)	1.1 (1.0, 1.3)	1.1 (0.9, 1.3)	1.1 (0.9, 1.2)	1.0 (ref)	0.34
Multivariate Adjusted RR+ (95%CI)	1.1 (0.9,1.2)	1.1 (0.9,1.2)	1.1 (0.9,1.2)	1.0 (ref)	0.74
No Back Pain at Baseline	N=131	N=123	N=121	N=135	
Back pain in next year, n (%)	28 (21)	19 (15)	22 (18)	21 (15)	
Unadjusted RR (95% CI)	1.4 (0.8,2.3)	1.0 (0.6,1.8)	1.2 (0.7,2.0)	1.0 (ref)	0.55
Multivariate Adjusted RR+ (95%CI)	1.3 (0.8,2.1)	1.0 (0.5,1.7)	1.1 (0.7,1.9)	1.0 (ref)	0.72
Back Pain at Baseline	N=273	N=271	N=277	N=262	
Back pain in next year, n (%)	183 (67)	178 (66)	173 (62)	161 (61)	
Unadjusted RR (95% CI)	1.1 (1.0,1.2)	1.1 (0.9,1.2)	1.0 (0.9,1.2)	1.0 (ref)	0.49
Multivariate Adjusted RR+ (95%CI)	1.0 (0.9,1.2)	1.1 (0.9,1.2)	1.0 (0.9,1.1)	1.0 (ref)	0.70

+ Adjusted for age, season, latitude, mental and physical SF12 scores, prevalent radiographic vertebral fracture, use of centrally acting medications, and a history of problem drinking

APPENDIX

Table A. Back Pain Symptom Pattern in 12 Months of Follow Up, Stratified by Baseline Back Pain Status

No back pain in past 12 months at baseline				
Number of intervals in which back pain was reported during follow-up	Interval 1	Interval 2	Interval 3	N (% of stratum)
0 intervals	—	—	—	417 (82.3)
1 interval only	X	—	—	19 (3.8)
	—	X	—	21 (4.1)
	—	—	X	25 (4.9)
2 intervals	X	—	X	2 (0.4)
	—	X	X	10 (2.0)
	X	X	—	7 (1.4)
3 intervals	X	X	X	6 (1.2)
Back pain in past 12 months at baseline				
Number of intervals in which back pain was reported during follow-up	Interval 1	Interval 2	Interval 3	N (% of stratum)
0 intervals	—	—	—	386 (36.2)
1 interval only	X	—	—	84 (7.9)
	—	X	—	71 (6.7)
	—	—	X	62 (5.8)
2 intervals	X	—	X	49 (4.6)
	—	X	X	55 (5.2)
	X	X	—	74 (6.9)
3 intervals	X	X	X	286 (26.8)

Symbols Key: —, back pain not reported; X, back pain reported.

Table B. Association of baseline serum vitamin D level with a new report of severe back pain in following one year in the entire sample of older men and stratified by history of back pain at baseline.

	Baseline Serum Vitamin D Level				
	Quartile 1 3.1,19.9 ng/ml	Quartile 2 >19.9,25.1 ng/ml	Quartile 3 >25.1,29.8 ng/ml	Quartile 4 >29.8,58.3 ng/ml	
Total Sample, 1yr Follow Up	N=404	N=394	N=398	N=397	*P* Value
No Back pain, n (%)	193 (24)	197 (24)	203 (25)	215 (27)	
Back Pain - not severe, n (%)	56 (26)	52 (25)	50 (24)	54 (25)	
Severe Back Pain, n (%)	155 (27)	145 (25)	145 (25)	128 (22)	0.65
No Back Pain at Baseline	N=131	N=123	N=121	N=135	
No Back pain, n (%)	103 (25)	104 (25)	99 (24)	114 (27)	
Back Pain - not severe, n (%)	14 (30)	8 (17)	13 (28)	12 (26)	
Severe Back Pain, n (%)	14 (33)	11 (26)	9 (21)	9 (21)	0.75
Back Pain at Baseline	N=273	N=271	N=277	N=262	
No Back pain, n (%)	90 (23)	93 (24)	104 (27)	101 (26)	
Back Pain - not severe, n (%)	42 (25)	44 (27)	37 (22)	42 (26)	
Severe Back Pain, n (%)	141 (27)	134 (25)	136 (26)	119 (22)	0.73