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A Prospective Cohort Study of Vitamin D Supplementation in AD Soldiers: Preliminary Findings

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ABSTRACT Purpose: To explore response to vitamin D supplementation in active duty (AD) warfighters and translate findings into evidence-based health policy. Background: Soldiers are at risk for musculoskeletal injuries and metabolic dysfunction that impact physical performance and military readiness; the link with low vitamin D status is unclear. Methods: This prospective trial enrolled 152 soldiers; baseline 25 hydroxyvitamin (OH) D level determined assignment to a no-treatment control (CG) or treatment group (TG) receiving a vitamin D_3 supplement for 90 days. Symptoms, diet, sun exposure, and blood biomarkers obtained at baseline (T1) and 3 months (T2). Results: Cohort was predominantly white (58%) with a significant difference in racial distribution for vitamin D status. Mean (SD) 25 (OH)D levels were 37.8 (5.6) ng/mL, 22.2 (5.0) ng/mL, and 22.9 (4.7) ng/mL for the CG, low dose TG, and high-dose TG at T1, respectively. Following three months of treatment, one-way ANOVA indicated a statistically significant difference between groups ($F_{5,246} = 44.37$; $p < 0.0001$). Vitamin D intake was 44% of Recommended Dietary Allowance throughout the first phase of the trial. Patient-Reported Outcomes Measurement Information System scores improved in TG for fatigue and sleep, $p < 0.01$. Conclusions: Vitamin D deficiency is widespread in AD soldiers. Clinicians must intervene early in preventable health conditions impacting warfighter performance and readiness and recommend appropriate self-care strategies.

INTRODUCTION

Between the abundance of public health reports[1–3] and the military significance regarding compromised vitamin D status,[4–8] more research is needed to advance the nation's health care agenda and to inform Department of Defense (DoD) policies addressing health promotion and disease prevention. Low vitamin D status is common in individuals who regularly perform extreme physical exertion, particularly when combined with psychological stress, inadequate nutrition, or sleep disruption.[6,9] This places military personnel in a high risk category with significant negative consequences to musculoskeletal[7] and mental health,[10] and thus, resilience. Vitamin D deficiency negatively affects bone health at all ages,[11] contributes to accelerated bone loss during adulthood,[12] and has been linked to a growing list of conditions including musculoskeletal injuries,[13,14] inflammatory and metabolic disorders,[15,16] depression,[17] cancer,[18] and cardiovascular disease,[19,20] with a high likelihood of degradation of warfighter resilience and readiness.[21,22]

Health promotion priorities of the Defense Health Agency, and the Army Surgeon General in particular, are embodied in the framework of the Performance Triad, comprised of three foundational elements, activity, nutrition, and sleep.[23] The Performance Triad has evolved to represent the most unified approach by senior leaders to prioritize and integrate performance optimization and injury prevention strategies to sustain the nation's warfighting capability.[21] In the Survey of Health-Related Behaviors Among Active Duty Military Personnel (2011), physical activity rates exceeded the Healthy People 2020 objective of greater than 47.9% with 74.9% of active duty personnel reporting moderate or vigorous physical activity in the previous month.[5] However, DoD reports and statistics consistently reveal that the lack of physical fitness, particularly in new recruits, leads to musculoskeletal injuries (MSI) which are the number one cause of lost duty days among service members.[4] One annual surveillance report has shown consistent rates of MSI over the past decade; the greatest number of limited duty days is related to upper and lower extremity fractures, as well as extremity and back strains and sprains.[4] The lower extremity injuries are typically classified as overuse injuries and account for over 3 million days of limited duty for the military.[4] In addition, MSI led to the most frequent medical visits with over 2 million medical encounters in 2012, the greatest number of theater evacuations for non-combat injuries, and the most likely reason for disability discharge from the military.[2] According to the most recent Health of the Force Report (2016), 17% of soldiers were medically non-deployable for reasons linked to injuries and overweight status.[2] In addition, cardiovascular-related conditions were documented in over 10% of respondents.

In addition to physical activity, nutrition is a component of the Performance Triad critical to warfighter health and

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performance.[22] The Survey of Health-Related Behaviors Among Active Duty Military Personnel (2013) reported a significant shortfall in meeting U.S. dietary goals with only 11–13% consuming 3 or more servings of fruits, vegetables, and whole grains per day.[5] It is a little known fact that consuming sufficient vitamin D from the diet is also difficult given that so few foods actually contain D_2 or D_3,[12] and fortified foods like grains, cereal, yogurt, and milk may not be diet staples, particularly with wheat or dairy sensitivities. These data suggest that healthy dietary intake behaviors and physical activity are intricately linked with all dimensions of health and individual and population-level interventions are warranted to reduce excessive health care costs,[24] engage soldiers in self-care activities, and lower chronic disease risk.

The large scope of this problem, with ~68% of soldiers insufficient or deficient in vitamin D stores,[25] demands attention from the research community. The significance of the problem has caught the attention of military health care providers who have increased their vitamin D prescriptions in the active duty population by 454% in a 5-year period.[26] A simple "prescription" for midday sun exposure under a cloudless sky with 90% skin exposure wearing no sunscreen in a non-urban, minimally polluted environment would be an ideal treatment, but remains a challenge for almost every American, and even more so for soldiers. While supplements do not stimulate the immune response resulting from natural sunlight exposure and have a variable dose–response across body types,[27] they are the primary treatment available. There remains a lack of knowledge about the non-skeletal health benefits of vitamin D status, the optimal blood level for such benefits, and the most therapeutic dose to achieve these benefits.[28,29] The objective of phase 1 of this two-phase trial was to determine if there is a risk profile of symptoms, biomarkers, or behaviors associated with deficiency states, and examine response to vitamin D supplementation over 3 months in active duty warfighters. Phase 2 will report on results of the gene expression analysis that was undertaken to further evaluate molecular response to no dose, low dose, and high-dose of vitamin D_3 supplementation.

METHODS

Study Design and Participants

This prospective, cohort longitudinal, double-blind, randomized controlled trial addressed vitamin D supplementation in a convenience sample of soldiers recruited from Joint Base Lewis-McChord (JBLM) in the Pacific Northwest where over 25,000 male and female service members live and work every day. The study received funding from the TriService Nursing Research Program (#HU0001-15-TS09; N15-009) and approval from the Western Regional Medical Center-Pacific and the Uniformed Services University of Health Sciences Institutional Review Boards.

To qualify for the study, participants had to be active duty, over 18 years of age, able to read and understand English, not scheduled to deploy in the next 15 months, not taking vitamin D supplements currently, and subjectively in good health. We excluded anyone with chronic health problems (e.g., eating disorders, kidney disease, intestinal malabsorption), current or healing stress fractures, medications for an endocrine disorder, such as synthroid, or medications that may present a harmful or interactive effect if taken with vitamin D (i.e., anti-seizure medications, cyclosporine, and indinavir). Women who were less than 6 months postpartum or who were breastfeeding were excluded from participating as their baseline hormonal status was presumed altered, and safe levels of higher doses of vitamin D have not been fully established.

The study team recruited participants from several authorized venues including the outpatient setting at Madigan Army Medical Center (AMC) and its satellite Soldier-Centered Medical Home clinics on JBLM. Approved flyers, poster boards, and social media postings also proved effective as marketing tools. In most cases, interested volunteers contacted the team at their convenience and arranged to meet in person to learn additional study details. The research staff also discussed privacy and confidentiality of study data and files prior to obtaining written informed consent. Upon enrollment, each volunteer was sent to the Madigan AMC outpatient laboratory for the initial blood draw for 25 hydroxyvitamin (OH) D, calcium, parathyroid hormone (PTH), osteocalcin, sex-hormone binding globulin, Interleukin (IL)-6, and insulin-like growth hormone (IGF)-1. Volunteers received a $25 Army and Air Force Exchange Service gift card once the blood samples were collected and results were recorded. The results for serum 25(OH) D were used to make the assignment to either the no-treatment control group (CG) (equal to or greater than 30 ng/mL) or the treatment group (TG) (less than 30 ng/mL). The Madigan AMC Department of Pathology adheres to the Endocrine Society Clinical Practice Guidelines[29] reporting a level of sufficiency as ≥30 ng/mL. Treatment group participants were randomized to a low or high-dose supplement; randomization was performed by the research pharmacist to include six groups; three categories of race (white, black, other) and two for gender. This was done in an attempt to achieve a diverse sample with a variable response in vitamin D production, which is known to be affected by age, race, gender, skin type, sun exposure, and body fat.[30,31] If assigned to the TG, the participant received a 90-day supply of D_3, either 1,000 IU (low dose) or 5,000 IU (high-dose) gel capsules. Supplementation with D_3 was used because it has been shown to more effectively raise 25(OH)D levels through the winter season when compared to a D_2 preparation[32] and it was available in the desired doses. Participants in the CG received no supplementation; standard practice is not to supplement individuals with a serum 25(OH)D level of 30 ng/mL or greater. In addition, randomizing these participants to a supplement, as high as 5000 IU daily, may have subjected them to harm. Neither the research team nor the subject knew the dose of vitamin D dispensed by the research pharmacist for TG participants. The research assistant sent text messages every other week to remind participants to take the supplement daily and to return bottles with any remaining capsules at the 3-month follow-up appointment. The pharmacist maintained a dispensing log throughout the intervention period.

Measures

A demographic questionnaire was administered at baseline to capture relevant personal and family health history (e.g., hypertension, weak or broken bones) as well as age, gender, race, ethnicity, military occupational specialty, rank, marital status, weight history, alcohol and tobacco use, sun exposure, and usual physical activity. (Table I).

A Vitamin D and Calcium Intake and Frequency Questionnaire (National Center for Research Resources, 2009) was used on two visits during an in-person interview with a registered dietitian or registered nurse to record average daily and weekly servings of foods containing vitamin D and/or calcium. The tool has been validated for use in young adults.[33] The authors report strong correlations for daily vitamin D intake derived from the Food Frequency Questionnaire versus the food record, particularly in girls with anorexia nervosa ($r = 0.78$, $p < 0.0001$). Less robust correlations were observed for calcium intake ($r = 0.65$, $p < 0.0001$). We obtained permission from the author to modify/use it with appropriate acknowledgment of the original research publication.[33]

The National Institutes of Health Patient-Reported Outcomes Measurement Information System (PROMIS)[34] was used for symptom assessment in order to help create a future participant phenotype. This web-based repository contains valid and reliable tools for outcome measures of health concepts that are relevant to research and clinical care. Several questionnaires were identified for this study to create a profile of vitamin D deficiency and its impact on daily living to include concept domains of cognitive function, fatigue, pain, sleep, physical function, and global health.

TABLE I. Summary of Data Collection Time Points

	Time 1 (T1) Baseline	Time 2 (T2) 3 months
Demographic Questionnaire Part I and II	X	
Demographic Questionnaire Part II only	X	X
Nutrition assessment/body composition	X	X
General Health (PROMIS) surveys	X	X
DXA	X	X
Biomarkers (bone, immune, endocrine status)	X	X
Gene expression analyses	X	X
Vitamin D supplementation for 25(OH)D <30 ng/mL	3-month intervention to begin following baseline measures	

PROMIS, patient-reported outcomes measurement system; DXA, dual energy X-ray absorptiometry; 25(OH)D 25-Hydroxyvitamin D; ng nanograms; mL, milliliters.

Upon enrollment, anthropometric measurements were obtained from participants dressed in Army physical training uniform of shorts, t-shirt, and socks. Body composition included height (inches) measured by stadiometer (Seca 213, Portable Stadiometer Height Rod, China, CA, USA) and body weight (pounds and kilograms) using the InBody 230 device (Biospace America, Los Angeles, CA, USA); no shoes were worn for these measurements. The InBody 230 device utilizes bioelectrical impedance to measure body composition and is comparable to Dual Energy Xray Absorptiometry (DXA), the gold standard for measuring lean and fat mass.[35,36] Interrater reliability checks were performed by the two study team members who performed all body composition measurements achieving 94% agreement. Blood pressure (BP) was taken at baseline (T1) and three months (T2) using a Dinamap Procare automated non-invasive BP and heart rate machine that received biomedical maintenance and calibration annually. Blood pressure readings were taken according to a published protocol[37] and documented for comparison with the U.S. Preventive Services Task Force guidelines for hypertension.[38]

Serum biomarkers were carefully selected with the assistance of the team endocrine consultant who identified blood tests representative of bone health, immune system health, and overall endocrine health. There is consensus among clinical and laboratory experts that serum 25(OH)D is the best biomarker to reflect circulating vitamin D status.[29,39] In addition, the most successful approach in past research was to have samples drawn by outpatient phlebotomists and processed in the hospital laboratory with no requirement for special preparation by volunteers, such as fasting. The biomarkers included 25(OH)D, PTH, calcium, IGF-1, IL-6, osteocalcin, and sex-hormone binding globulin (SHBG). The Roche Cobas 6000 instrument used electrochemiluminescence technology to measure calcium and 25(OH)D, PTH and IGF-1 were analyzed using an immunochemiluminometric assay (ICMA), and IL-6 and osteocalcin were measured with the enzyme-linked immunosorbent assay (ELISA) method (Personal communication Madigan AMC Laboratory Officer, RJN, October 12, 2018). Results were obtained electronically with normal ranges separated by age and gender when appropriate.

Statistical analyses

Statistical analyses were conducted using R v3.4.[40] Categorical variables are presented as frequencies (percentages), continuous variables are described using means and standard deviations (SD). Between-group comparisons were performed using both parametric and non-parametric tests. Comparison of categorical data between groups was performed using Chi-square test. Conclusions were extracted using effect sizes according to Cohen's d statistic[41] and significance tests at a False Discovery

Rate of 10%.[42] The *lsr* package[43] was used to run the Cohen's d statistic. Statistical significance was set at the $p < 0.05$ level.

RESULTS

The final cohort of 131 soldiers, 50 females and 81 males, was predominantly white (58%) with a significant difference in racial distribution between normal vitamin D status (77% white) and deficient status (50% white), $p < 0.001$. Fitzpatrick skin type category was not different between CG and TG with the following distribution: Fair (score 1–2) 10%, Moderate (score 3-4) 63%, and Dark (score 5-6) 26%. Demographic data are presented in Table II. Mean (SD) 25(OH)D levels were 37.8 (5.6) ng/mL, 22.2 (5.0) ng/mL, and 22.9 (4.7) ng/mL for the CG, low dose TG, and high-dose TG at baseline (T1), respectively. Following 3 months of treatment, one-way ANOVA indicated a statistically significant difference between groups ($F_{5,246} = 44.37$; $p < 0.0001$). Further analysis with Tukey's pairwise comparison procedure to control for multiple testing revealed that the mean 25(OH)D (± SD) of high-dose TG (40.15 ng/mL ± 7.5) was significantly greater than that of low dose TG (30.80 ng/mL ± 10.0) and that of the CG (34.46 ng/mL ± 9.9) with an overall alpha level of $p < 0.001$. Of note is that there was no appreciable change in PTH levels for any group. For the entire cohort, PROMIS scores for mental health and cognitive function demonstrated improvement between T1 and T2 ($p = 0.06$), and were significant for improvement in fatigue ($p < 0.001$) and sleep ($p = 0.01$) (Table III). Pre-hypertension was documented in over one-third of the entire cohort at T1 and at T2. Biomarker results for the TG reflected a significant decrease in IL-6 from 1.88 (6.2) to 1.17 (1.3), $p = 0.04$ (Table IV). As 25(OH)D levels increased and IL-6 levels decreased, the number of missed work days also declined overall from 1.5 (0.16 SE) days to 1.0 (0.18 SE) days, $p = 0.046$, across time but not by group. Dietary vitamin D intake met the recommended dietary allowance (RDA) of 600 IU for only 10% of both the CG and TG, at T1 and T2. Average intake was 265–275 IU/day or 44% of the RDA. Dietary calcium intake met 92–99% of the RDA (1,000 mg) for ~50% of the enrolled population at T1 and T2. Average calcium intake was 924–990 mg/day. At baseline, 18% of enrolled soldiers reported previous overuse injuries that required a duty profile for 1 week up to 12 weeks in duration (Table V). At T2, no new overuse injuries were reported.

TABLE II. Demographic Variables by Group Assignment

Variable	Control Group		Treatment Group	
	N	%*	*N*	%
Sex				
Male	25	31	55	69
Black	4	9.3	10	11.6
White	17	39.5	30	34.9
Other**	4	9.3	15	17.4
Female	18	36	32	64
Black	2	4.6	4	4.7
White	16	37.2	13	15.1
Other	0	0	14	16.3
Officer rank	18	53	19	29
Age (years)	32.8 (10.5)		31.6 (8.2)	
Married	18	53	42	64
Medical history				
High blood pressure	4	12	4	6
Broken bones	16	47	20	30
Family history of bone disorders	7	21	9	14
Overuse injury/stress fracture	7	5.4	16	12.4
Taking vitamins	7	21	9	14
Tobacco use = never	22	65	43	65
Alcohol use = 0–1 times/mo	13	38	39	59
Exercise (minutes)				
Moderate	33	97	64	97
Vigorous	29	85	59	89
Muscle strengthening	34	100	61	92
Sun exposure				
Days in sun/week	4.1(1.6)		3.8 (2.0)	
Minutes per week in sun	86 (87.5)		80.8 (84.6)	
Sunscreen use = rarely/never	15	44	36	55

*Equals % of assigned group.

**Includes American Indian, Asian, Native Hawaiian, Hispanic.

DISCUSSION

Vitamin D insufficiency and deficiency are widespread in active duty soldiers, not unlike young adults worldwide.[44,45] As in other research trials conducted by this team,[25,46] prevalence of low serum 25(OH)D was high, reaching 67% for this cohort. A review of the demographic data, health history, and behaviors revealed a representative group of military men and women who reported typical alcohol and tobacco use, performed regular physical activity, were infrequently exposed to the sun, and described a modest rate of previous overuse injuries. However, some differences exist in this cohort from previous cohorts, such as a greater percentage of officers (28.5%), older age of volunteers (mean 32.2 years), and over 50% married in both the CG and TG, all of which raise new questions for researchers. Results in this study suggest that perhaps the military environment is not unlike other community living conditions and older, married, educated officers are equally susceptible to health risks from low vitamin D status. Rates of moderate and vigorous exercise indicated probable participation in Unit level physical training and good compliance with the Centers for Disease Control and Prevention recommendations for 150 minutes of moderate intensity aerobic exercise and 75 minutes of vigorous exercise each week, balanced with muscle strengthening activities.[47] This likely contributed to normal BMD levels (not reported), the lack of new stress fractures, and body fat levels that met military standards. However, the suboptimal intake of dietary vitamin D, at 44% of the RDA, may be a contributing factor to changes in levels of fatigue, sleep, and cognitive function reported on the PROMIS tools. For cognitive function, females in the low dose (1000 IU D_3) TG had the lowest scores at T1 and

TABLE III. Standardized PROMIS Scores for Full Cohort at Baseline (T1) and Follow-up (T2)

	T1 *n* = 129		T2 *n* = 124				
Domain	M	SD	M	SD	*t*	*df*	*p*
Cognitive function	49.05	8.2	50.8	7.95	−1.74	251	0.06
Sleep-related impairment	50.98	8.1	48.04	8.8	2.76	251	0.01
Fatigue	50.2	7.8	47.3	8.2	2.85	251	<0.001
Pain interference	47.6	7.2	47.03	7.7	0.6	251	0.48
Physical function	53.99	6.3	54.7	5.9	−1.0	251	0.29
Global health physical	53.5	7.0	52.5	7.0	1.39	127	0.20
Global health mental	55.2	8.4	53.8	8.4	1.76	127	0.06

T1, baseline; T2, 3 month follow-up; M, mean; SD, standard deviation

TABLE IV. Results for Treatment Group (TG) After 3-Month Supplementation

Variable	T1 (M) *n* = 88	SD	T2 (M) *n* = 79	SD	*t*	*df*	*p*
Il-6	1.88	6.2	1.17	1.32	0.98082	164	**0.04**
Osteocalcin	19.04	8.3	20.0	9.3	−0.7479	165	0.45
IGF-1	189.7	52.9	197.1	57.1	−0.87228	165	0.38
SHBG	48.3	37.1	53.25	42.8	−0.79971	165	0.42
Calcium	9.3	0.32	9.28	0.3	−0.48027	165	0.63
25(OH)D	22.6	4.8	35.4	9.9	−10.7686	165	**<0.001**
PTH	41.8	12.4	41.7	14.8	0.010419	165	0.99
Weight	174.3	35.7	172.6	35.2	0.303023	163	0.76
BMI	26.9	3.8	26.7	3.9	0.239299	163	0.81
Body Fat	25.5	7.9	25.69	7.9	−0.10632	163	0.91
BP sys	116.4	11.8	115.2	12.8	0.593633	163	0.55
BP dias	67.3	8.8	68	9.8	−0.51061	163	0.61
FFQ Ca	1,039.5	583.1	990.1	519.3	0.575127	164	0.56
FFQ Vit D	283.9	185.3	273.8	186.8	0.348891	164	0.73

T1, baseline; T2, 3 month follow-up; M, mean; SD, standard deviation; IL, interleukin-6; IGF, insulin-like growth factor-1; SHBG, sex-hormone binding globulin; 25(OH)D, 25-hydroxyvitamin D, PTH, parathyroid hormone; BMI, body mass index; BP sys, blood pressure systolic; BP dias, blood pressure diastolic; FFQ Ca, Food Frequency Questionnaire Calcium; FFQ Vit D Food Frequency Questionnaire vitamin D.

TABLE V. Baseline Biomarkers, Body Composition, and Dietary Intake by Vitamin D Status

Variable	Sufficient *n* = 43 Mean (SD)	Deficient *n* = 88 Mean (SD)	*t*	*df*	*p*	Cohen's *d*
Calcium	9.2 (0.35)	9.3 (0.32)	−0.78	129	NS	0.14
25(OH)D	37.8 (5.6)	22.6 (4.9)	16.02	129	<0.0001	2.98
IGF-1	187.2 (52)	189.7 (53)	−0.25	129	NS	0.05
IL-6	1.4 (1.9)	1.9 (6.2)	−0.47	128	NS	0.09
Osteocalcin	26.7 (27.4)	19.0 (8.3)	2.35	128	0.02	0.44
Parathyroid hormone	39.5 (11.9)	41.8 (12.4)	−1.02	129	NS	0.19
SHBG			−0.94			0.15
	M 33.5 (15)	M 35.9 (16.5)		79	0.35	
	F 117.7 (65.6)	F 78.5 (44.1)		49	$p < 0.05$	
Body fat %			0.03			0.004
	M 21.3 (6.2)	M 21.7 (6.3)		79	NS	
	F 30.6 (7.3)	F 30.7 (7.1)		49	NS	
BMI	26.3 (3.6)	26.9 (3.8)	−0.83	127	NS	0.15
Weight (lbs)	M 190.0 (33.3)	M 189.0 (32.7)	0.19	79	NS	0.03
	F 149.2 (19.0)	F 149.4 (20.8)	−0.05	49	NS	0.01
Calcium intake, mg/d	894.6 (618.1)	1,039.5 (583.1)	−1.3	127	NS	0.24
Vitamin D intake, IU/d	253.8 (193.3)	283.9 (185.3)	−0.85	127	NS	0.16

mg, milligrams; ng, nanograms; IU, international units; pg, picograms; mL, milliliters; nmol, nanomole; d, day; M, male; F, female.

showed the most positive change by T2, although their scores remained the lowest of all 3 groups. Similarly, females in the low dose TG had the worst score for fatigue at T1 with statistically significant improvement at T2. Recent studies have also reported an association between vitamin D deficiency and self-reported symptoms including musculoskeletal pain and sleep disorders, manifested by high levels of IL-6, a pro-inflammatory cytokine.[48] The biomarker Interleukin (IL)-6 was used as a proxy for immune health; one study in athletes deficient in 25(OH)D demonstrated a significantly lower *in vitro* antigen-stimulated production of pro-inflammatory cytokines, including Il-6, by whole blood culture than in athletes with high vitamin D status. Furthermore, the athletes with the higher vitamin D status experienced fewer upper respiratory illness episodes over a 4-month winter period.[49] Similarly, in a study of mice, the IL-6 concentrations in serum were 50% lower following *in vivo* administration of lipopolysaccharide in a vitamin D deficient cohort, indicating that low vitamin D status results in a defect in cytokine production with diminished protection against pathogenic microorganisms.[50] There is unrefuted evidence that 1,25$(OH)_2D$, the active form of vitamin D, interacts with the vitamin D receptor on activated T and B lymphocytes to enhance the immune system's response to infection and to reduce the risk of self-recognition that leads to autoimmune diseases, such as type I diabetes, multiple sclerosis, rheumatoid arthritis, or Crohn's disease.[9] It is important to further explore correlations between vitamin D status, IL-6, and the PROMIS symptoms as this constellation of signals may have a direct impact on warfighter immune health and performance.

It is apparent from data pre- and post-supplementation that warfighters are subject to the same risk factors for low serum 25(OH)D levels as most adults living in the USA; some risks are modifiable and others are not. Sunlight exposure remains the most significant source of vitamin D[44,45] which is very challenging for soldiers who are fully covered in the Army Combat Uniform throughout the day whether their job is inside or outdoors. Most of the ultraviolet B (UVB) radiation (290–320) nm from the sun is absorbed by the ozone layer; approximately 0.1% reaches the earth's surface at noon at the equator in the summer.[44] Clothing, melanin, and sunscreen also present barriers to skin penetration. Clothing absorbs all UVB radiation, highly pigmented skin may require several times the normal exposure to produce sufficient vitamin D, and sunscreen of Skin Protection Factor 30 efficiently absorbs 97.5% of UVB radiation decreasing vitamin D production and minimizing damage to skin cells.[44,45] Demographic data reflect the heterogeneity of the cohort; most participants were Caucasian (59%), followed by Asian (18.5%), African American (15.4%), and Hispanic (4.6%). The CG and TG volunteers reported similar amounts of sun exposure with ~4 days a week for a total of 80–86 minutes/day, and ~50% stated they rarely or never apply sunscreen (Table II). Joint Base Lewis-McChord is situated at latitude 47.1 degrees[51] which, along with season and time of day, greatly influences the sun's zenith angle and thus ability to stimulate sufficient quantities of vitamin D in the skin. Sun exposure above 33 degrees latitude in the winter, and before 9 am or after 3 pm, does not yield any appreciable production of vitamin D.[44,45] While certainly a contributor to the problem, food sources of vitamin D have always been limited so this has not been recommended as the primary mode of replenishment in any population. There are reports that farmers are adding 25$(OH)D_3$ into animal feeds in order to increase the muscle content of vitamin D, rendering chickens, cows, and pigs a potential substantial source in the future.[44] One last modifiable factor involves BMI or body fat mass. Individuals with a BMI > 30, classified as obese, require 2–3 times more vitamin D to treat and prevent deficiency.[44] This is because vitamin D is a fat soluble vitamin that becomes diluted in adipose tissue and bioavailability is lost for physiologic processes.[44] One would not expect military men and women to be classified as obese, yet the last Health of the Force Report[2] stated 17% of service members do indeed meet this classification. This leads to the health and readiness challenges previously discussed regarding musculoskeletal injuries, Army Physical Fitness Test failure, and non-deployable status. Mean BMI and body fat percent for males and females in this trial met Army Regulation 600-9[52] body weight, BMI, and maximum body fat standards. However, at T1, the TG cohort with lower baseline 25(OH)D, had increased body fat compared with the CG, 25.6 (7.9)% vs 23.3 (8.0)%, although this was not statistically significant. Body fat remained unchanged at 3-month follow-up (T2). Army leaders must continue to strive to enforce the weight and body fat standards in order to ensure a fit and ready warfighter; one who will not become one of the first preventable casualties of war.

Limitations of this study include the fact that it is a single center trial in a geographic location known for low levels of sunlight for ~6 months of the year with only a modest sample size.[45] Warfighters are a highly mobile population and previous assignments and deployments, as well as childhood home location, may be factors important in data analyses. Other limitations include the fact that we did not interrupt enrollment for seasonal considerations but data were collected on season of enrollment and thus, season of blood collection. The computer generated randomization was only applied to the treatment group in an attempt to balance race and gender between the low- and high-dose supplement. A more rigorous design should include randomization of all volunteers regardless of vitamin D sufficiency status. Strengths of this study include the representativeness of the sample, blinding of study personnel to vitamin D3 treatment dose, high retention of active duty participants with an attrition rate of ~14%, and the fact that all measurement tools had established validity and reliability. Finally, multiple opportunities presented for study personnel to engage warfighters in self-care activities related to preliminary findings of pre-hypertension and low vitamin D intake, in order to support the overarching goal of health promotion.

CONCLUSIONS

The results thus far are congruent with current literature describing a high prevalence of vitamin D insufficiency and deficiency globally.[30,44] The list of acute and chronic conditions linked to vitamin D status is growing at an alarming rate. We anticipate further analyses will elucidate more clearly the role of vitamin D supplementation in bone health, cardiovascular health, and immune function. In the meantime, experts recommend advising adults to establish daily habits of consuming vitamin D-containing foods and beverages or taking a daily supplement of at least 1,000 IU D_3, and incorporating sensible sun exposure. This advice will help ensure active duty military are proactive in their go-to-war preparations of medical readiness and nutritional resilience for performance optimization.

PREVIOUS PRESENTATIONS

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