Vitamin D Supplementation in Military Personnel: A Systematic Review of Randomized Controlled Trials

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Context: Vitamin D supplementation is important in military research because of its role in musculoskeletal health.

Objective: This systematic review examined the effects of vitamin D supplementation on serum 25-hydroxyvitamin D (25(OH)D) concentrations and musculoskeletal health outcomes in military personnel.

Data Sources: A comprehensive search was conducted using MEDLINE, EMBASE, CINAHL, SportDiscus, and the Cochrane Library databases and the reference lists of existing review articles and relevant studies.

Study Selection: Reviewers independently screened titles, abstracts, and full texts of the articles using predefined criteria.

Study Design: Systematic review of randomized controlled trials (RCTs) using the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) statement.

Level of Evidence: Level 3.

Data Extraction: Three reviewers independently extracted data and assessed the methodological quality. Mean differences with 95% CI in serum 25(OH)D concentrations between the vitamin D and placebo arms were calculated.

Results: Four RCTs were included in the qualitative analyses. The 25(OH)D concentrations were improved with 2000 IU/d supplementation (mean difference, 3.90 ng/mL; 95% CI, 0.22-7.58). A trial on female Navy recruits showed a significant decrease in stress fractures (risk ratio, 0.77; 95% CI, 0.62-0.95), particularly tibial fractures, from daily supplementation of 800 IU vitamin D and 2000 mg calcium.

Conclusion: There was a positive trend in 25(OH)D concentrations from higher doses of supplementary vitamin D in military submariners and a possible benefit to bone health when vitamin D was combined with calcium.

Keywords: military personnel; vitamin D; 25(OH)D

Across the Army, Navy, and Air Force sectors, military personnel experience a broad spectrum of physical activity ranging from intense Army basic combat training to sedentary submarine patrol missions.^{5,8} The environmental conditions are also unique, as submarines and specifically designed military uniform requirements can limit sunlight exposure, placing soldiers at a higher risk for vitamin D insufficiency.^{13,18}

Vitamin D plays a vital role in promoting calcium absorption and maintaining normal bone homeostasis.^{3,13} Under normal conditions, bone remodeling is an intricate balance between osteoblastic reconstruction and osteoclastic resorption.¹³

Unaccustomed exercise protocols such as initial basic training typically promote bone remodeling and high bone turnover.^{7,15,19} However, mechanical loading of the skeleton in the setting of vitamin D insufficiency can lead to prolonged recovery times from microinjuries and increased incidence of stress fractures as the bone becomes less resilient to structural overload.³ Stress fractures are one of the most expensive injuries in the context of medical bills, lost training days, and increased recruitment costs.^{7,16}

Vitamin D can be synthesized within the cutaneous layer of the skin from sun-derived ultraviolet B radiation or from dietary sources such as egg yolk, fatty fish, vitamin supplements, and

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fortified foods, including milk, yogurt, and cereals.¹⁵ Currently, serum 25-hydroxyvitamin D (25(OH)D) is considered to be the most accurate indicator of vitamin D status.³ The Endocrine Society Committee (ESC) Task Force recommends 1500 to 2000 IU vitamin D daily intake with an upper limit of 10,000 IU for adults aged 19 years and older.¹² The corresponding serum 25(OH)D concentration needed to promote sufficient bone health is at least 50 nmol/L (20 ng/mL) with the ideal status being in the 90 to 100 nmol/L range (36–40 ng/mL).¹⁵ The 2016 global recommendations suggested 30–50 nmol/L (12–20 ng/mL) as insufficient and <30 nmol/L (<12 ng/mL) as deficient in vitamin D levels.¹⁹ The relationship between low serum 25(OH)D concentrations and stress fractures has been demonstrated in Israeli and Finnish military recruits.^{7,20} However, there is a paucity of data examining these outcomes among military soldiers that warrants further research on nonskeletal outcomes.¹⁶

Limited access to nutritional foods and sun deprivation in submarines, high-latitude field duty, and protective military clothing and gear predisposes military personnel to vitamin D insufficiency. A systematic review⁴ reported a high prevalence of vitamin D insufficiency in military personnel and showed an association between lower extremity stress fractures and low concentrations of serum 25-hydroxyvitamin D. No systematic reviews have been conducted on vitamin D supplementation. Therefore, we assessed (1) the effect of vitamin D supplementation on serum 25(OH)D concentrations in military personnel and (2) the impact of vitamin D supplementation on musculoskeletal health outcomes.

METHODS

The study used the Cochrane Reviews, the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) criteria,¹⁷ and Covidence online platform.¹¹

The eligibility criteria included (1) active military participants across all branches (Army, Marine Corps, Navy, or Air Force); (2) vitamin D supplementation (pharmaceutical or fortified food) with or without calcium; and (3) randomized controlled trial design. The exclusion criteria included veterans, discharged military personnel, and participants with morbidities other than vitamin D insufficiency.

The MEDLINE, EMBASE, CINAHL, SportDiscus, and the Cochrane Library electronic databases were searched from inception to June 2016. Combinations of keywords and Medical Subject Headings (MeSH) were used to find relevant studies such as “military personnel,” “submarine,” “naval,” “Army,” “soldier,” “vitamin D,” “25-hydroxyvitamin D” (Appendix Table 1, available in the online version of this article). Duplications were removed, and references of the review articles were manually searched for relevant articles. The search was updated in July 2017.

Three reviewers independently screened the titles, abstracts, and full-text articles for eligibility using the Covidence platform. Furthermore, the 3 reviewers independently assessed the methodological quality of the studies using the Cochrane risk of

bias and extracted data on demographics and study characteristics (geographic location, latitude, and season). The disagreements were resolved by consensus.

The primary outcome measure was change in the serum 25(OH)D concentrations. Secondary outcome measures included fractures and stress fractures. The dosages of the vitamin D supplements were reported in international units (IU) and serum 25(OH)D concentrations in nanogram per milliliter (ng/mL) and nanomoles per liter (nmol/L).⁶ A cutoff of >30 ng/mL (>75 nmol/L) recommended by the ESC,¹² also used in our recent publication,⁶ was chosen for vitamin D sufficiency.

Because of the small number of eligible trials and heterogeneity among study populations and interventions, the data were qualitatively synthesized. The mean differences (MDs) with 95% CIs between vitamin D and placebo groups were calculated for 25(OH)D concentrations and other outcomes, adjusting for preintervention levels. The pooled MDs with 95% CIs were reported when appropriate. The risk ratios with 95% CIs for stress fractures were calculated. A *P* value of 0.05 was considered for statistical significance. Review manager (RevMan 5.3) was used for analysis.

RESULTS

Study Selection

A total of 1423 publications were identified after combining the results from all databases (Figure 1). Five placebo-controlled randomized controlled trials (RCTs) met the eligibility criteria. One article was excluded due to duplicate publication.¹⁰ Three studies monitored serum 25(OH)D concentrations^{5,8,9} and bone health and 1 study assessed stress fractures.¹⁴ The findings of the methodological quality and risk of bias assessment are shown in Figure 2.

Baseline Characteristics

Studies meeting the inclusion criteria were composed of 2 RCTs observing US Navy submariners,^{5,9} with 1 study focusing on basic combat training personnel,⁸ and the other on Navy recruits.¹⁴ (Table 1). Eligible RCTs did not evaluate the Air Force or Coast Guard personnel. All participants were males with a mean age of 28 (±5) years. Duplessis et al⁵ supplemented 400 IU/d of vitamin D, whereas Gasier et al⁹ provided doses of both 1000 IU/d and 2000 IU/d in the form of tablets. The placebo in the study by Duplessis et al⁵ consisted of a vitamin B₆ tablet (50 mg/d). The submariners were on patrol for 92 days (with 5 underway replenishments) in the study by Gasier et al⁹ and 76 days with a 6-day port of call in Pearl Harbor (21.3°N) in the study by Duplessis et al.⁵ In the submarine environment, the crew members had reduced physical activity, spending a significant amount of time in the semirecumbent, recumbent, and sitting positions.⁵ Gaffney-Stomberg et al⁸ included Army basic combat trainees, with a mean age of 21.4 (±3.7) years, composed of men (62.5%) and women (37.5%) who received daily supplements of 1000 IU/d vitamin D₃ with 2000 mg of calcium in the form of snack bars (Table 1). Physical training

Figure 1. PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flow diagram.

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Intention-to-treat approach	Incomplete outcome data (attrition bias)
Duplessis et al., 2005	+	+	+	+		+
Gaffney-Stomberg et al., 2014	+	+	+	+		-
Gasier et al., 2014		+	+	+	+	+
Lappe et al., 2008			+	+	+	-

Figure 2. CONSORT (Consolidated Standards of Reporting Trials) risk of bias assessment.

included exercises such as foot marching, obstacle courses, sprinting, and muscle strength training. The baseline serum 25(OH)D concentrations across all interventional groups were insufficient in the 3 aforementioned RCTs (Table 2).^{5,8,9}

Lappe et al¹⁴ included female naval basic trainees with a median age of 19 years (range 17-35 years) who received 800 IU/d vitamin D and 2000 mg/d calcium or placebo in the form of tablets for 8 weeks (Table 1). The participants had 1 hour of daily physical exercise and traveled by foot between the base and food galley for 6 weeks. They had an intense "Battle Stations" training exercise program in week 7. All participants were vitamin D deficient at baseline.

Table 3 shows the MD in 25(OH)D concentration and other outcomes between vitamin D supplementation and placebo up to 12 weeks of intervention.

Serum 25(OH)D Concentrations

Duplessis et al⁵ found a significant decrease in 25(OH)D levels during submerged patrol phases in both groups, with no benefit from 12 weeks of 400 IU/d vitamin D supplementation (MD, -0.60 ng/mL; 95% CI, -6.95 to 5.75; $P = 0.85$). Gasier et al⁹ found a significant increase in serum vitamin D levels from 12 weeks of 2000 IU/d vitamin D (MD, 3.90 ng/mL; 95% CI, 0.22-7.58; $P = 0.04$) but not from 1000 IU/d vitamin D (MD, 0.50 ng/mL; 95% CI, -2.72 to 3.72; $P = 0.76$) in Navy submarines. The benefit from 1000 IU/d vitamin D and 2000 mg calcium was minimal (MD, 0.8 ng/mL; 95% CI, -2.03 to 3.63; $P = 0.58$)⁸ in Army basic combat trainees.

Table 1. Characteristics of the 4 included randomized controlled trials

Authors, Year	Country	N	Latitude	Season	Activity	Dosage	Duration	Type	Product
Duplessis et al, 2005 ⁵	USA	51	47.7°N	Early spring/winter	Navy submariners (sailors)	400 IU/d	11 weeks	D ₃ tablet	Nature's Bounty Inc
Gasier et al, 2014 ⁹	USA	53	47.7°N	Fall/early winter	Navy submariners (sailors)	2000 IU/d 1000 IU/d	13 weeks	D ₃ tablet	Compounded Solutions in Pharmacy, LLC
Gaffney-Stomberg et al, 2014 ⁸	USA	247	34.7°N	Early spring/winter	Army (Basic Combat Training Personnel)	1000 IU/d + 2000 mg calcium/d	9 weeks	D ₃ snack bar	Combat Feeding Directorate
Lappe et al, 2008 ¹⁴	USA	5201	41.0°N	Unclear	Navy recruits	800 IU/d + 2000 mg calcium/d	8 weeks	D ₃ tablet	NR

NR, not reported.

Table 2. Baseline measurements (mean and SD) of participants^a

Authors, Year	N	Vitamin D Dosage	Gender, %	Age, y	Serum 25(OH) D, ng/mL	Serum 25(OH) D, nmol/L	Serum 25(OH) D Method of Analysis	Loss to Follow-up, % (Lost/Total)
Duplessis et al, 2005 ⁵	26 25	400 IU/d Placebo	Males (100) Females (0)	28.0 (NR)	28.3 (15.0) 26.3 (10.0)	70.64 (37.44) 65.64 (24.96)	RIA (Quest Diagnostics)	0 (0/51)
Gasier et al, 2014 ⁹	17 20 16	2000 IU/d 1000 IU/d Placebo	Males (100) Females (0)	28.1 (5.4) 29.4 (5.0) 28.3 (4.7)	21.4 (6.8) 20.99 (5.61) 20.0 (7.04)	53.44 (16.86) 52.39 (14.01) 49.92 (17.56)	RIA (DiaSorin Inc)	0 (0/53)
Gaffney-Stomberg et al, 2014 ⁸	83 85	1000 IU/d + 2000 mg calcium/d Placebo	Males (62.5) Females (37.5)	21.4 (3.8) 21.4 (3.7)	23.2 (10.3) 20.6 (8.1)	57.91 (25.71) 51.42 (20.22)	RIA (DiaSorin Inc)	32 (79/247)
Lappe et al, 2008 ¹⁴	1852 1848	800 IU/d + 2000 mg calcium/d Placebo	Males (0) Females (100)	19 (17, 35) ^b	NR	NR	NR	28.9 (1501/5201)

NR, not reported; RIA, radioimmunoassay.

^aThe values for age, serum 25(OH)D are presented as mean (SD).^bMedian (minimum, maximum).

Fractures

The results from Lappe et al¹⁴ revealed 21% relative reduction in stress fractures from 800 IU/d vitamin D and 2000 mg/d calcium supplementation (6.8%) compared with placebo (8.6%) ($P = 0.02$). The majority of the reduced fractures were fibular and tibial fractures (risk ratio, 0.77; 95% CI, 0.62-0.95; $P = 0.02$) (Figure 3).

DISCUSSION

Submariners included in this systematic review did not show significant improvements in serum vitamin D levels from ≤ 2000 IU/d vitamin D supplementation.^{5,9} The only significant increase in serum 25(OH)D concentrations was from 2000 IU/d vitamin D supplementation.⁹ A recent meta-analysis demonstrated that

Table 3. Mean difference in outcome measures at 12 weeks

Outcome at 12 Weeks	Vitamin D Supplementation, N	Placebo, N	MD [95% CI]	P
Serum 25(OH)D (ng/mL)				
400 IU/d Duplessis et al, 2005	26	25	-0.60 [-6.95, 5.75]	0.85
1000 IU/d Gasier et al, 2014	20	16	0.50 [-2.72, 3.72]	0.76
2000 IU/d Gasier et al, 2014	17	16	3.90 [0.22, 7.58]	0.04
100 IU + 2000 mg Ca Gaffney-Stomberg et al, 2014	82	83	0.80 [-2.03, 3.63]	0.58

MD, between-group mean difference adjusted for baseline values.

Figure 3. Overall and location-specific stress fractures risk ratios (Lappe et al¹⁴). M-H, Mantel-Haenszel.

athletes required ≥ 3000 IU/d to achieve sufficiency in vitamin D concentration. Such higher doses required in athletes may be attributed to the demanding intensive nature of their training and physical activity.⁶ Although military personnel are different from athletes, professional athletes are now more commonly utilizing tactical strength and conditioning adopted from military and police forces to optimize their fitness programming. As such, insights from military personnel may become increasingly relevant to the athletic population and can provide further knowledge to optimize athletic performance and physical health. Submarines, however, provide a controlled environment for research as all crew members experience sun deprivation, artificial breathing atmospheres, and restricted physical activity.⁵

In Army basic combat trainees, there was a significant increase in 25(OH)D levels from baseline in both the placebo and treatment group that had received 1000 IU/d vitamin D with 2000 mg calcium/d⁸ for 8 weeks. This might have likely been due to sun exposure and other factors as there were no significant differences in increased 25(OH)D levels between the placebo and treatment groups.

Lappe et al¹⁴ found a significant decrease in stress fractures from 800 IU/d vitamin D with 2000 mg/d calcium supplementation in 5000 Navy recruits.¹⁴ Seafarers at work experience limited opportunity to exercise, and have sleep deprivation due to long working hours, noise, or irregular movement of the ship, as well as restricted food choices due to storage conditions.²¹ Sedentary conditions, in conjunction with poor access to nutritious foods, have attributed to obesity in Navy recruits. The protective effect of the supplementation on stress fracture was robust regardless of these risk factors.¹⁴ The calcium component of the supplement is an important point of discussion as optimal calcium levels are necessary to facilitate the repair of microdamage to bone that occurs in the intense exercise protocols during military training.¹⁴ Lappe et al¹⁴ were the first to show decreased stress fracture from calcium and vitamin D supplementation. The study had a 29% loss to follow-up, including discharges, withdrawals, and fracture incidences. In addition, given the fact that the study focused on female Navy recruits alone, the generalizability of the findings may be limited; females are more prone to stress fractures² with a fracture rate of 1.6% to 21% compared with 0.2% to 5.2% in males.¹⁴ However, researchers of this study did not measure serum 25(OH)D concentrations to quantify its association with stress fractures.

Consistent with our findings, a review by McCabe et al¹⁵ showed the benefits of combining vitamin D with calcium in fracture prevention, while a meta-analysis of 7 RCTs did not show benefit from 400 to 800 IU/d of vitamin D supplementation related to the prevention of stress fractures.¹ In agreement with the literature, Lappe et al¹⁴ and Gaffney-Stomberg et al⁸ were the only trials that demonstrated a protective benefit of supplementing both vitamin D and calcium in the context of bone health with no reports of adverse events.

The present review has specific strengths. First, this review included placebo-controlled double-blinded RCTs. Second, the

homogeneity between submarine environments allows for a better assessment of the effects of varying doses of vitamin D on 25(OH)D in this branch of military personnel. In addition, the authors conducted a rigorous methodology as the literature search was comprehensive and study selection and data collection were robust.

The main limitation of this review, however, is the small number of studies. Furthermore, there was considerable heterogeneity between the dose and duration of the interventions, environmental factors, and diverse military populations. In addition, there was a lack of studies focusing on Air Force personnel. Similarly, none of the included trials measured muscle strength or performance. Two trials^{8,14} provided supplementation of vitamin D in conjunction with calcium.

Several points should be considered for future investigations:

1. The supplementation of combined vitamin D and calcium because of their synergistic effect on the bone health.¹⁶
2. The timing and duration of supplementation, as it takes longer than 12 weeks for a sustainable increase in 25(OH)D concentrations.^{3,6,16}
3. Assessing exposure to sunlight, as it is associated with increased serum 25(OH)D concentrations.⁸
4. Monitoring of weight loss during basic training for adjustment purposes as a confounding factor among military recruits.⁸
5. Potential outcome measures such as incidence of stress fractures, fractures, and musculoskeletal health biomarkers.

In conclusion, there seems to be a positive linear trend in 25(OH)D concentrations from higher doses (2000 IU/d) of supplementary vitamin D in military submariners. There was also a benefit to bone health, specifically decreased fracture rates, from combined calcium and vitamin D supplementation. Well-designed randomized controlled trials with higher doses of vitamin D in different military populations are needed to accurately evaluate the effects of vitamin D supplementation on serum 25(OH)D concentrations and its impact on musculoskeletal health and injuries.

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