ASSOCIATION OF SERUM VITAMIN D LEVELS AND THE SEVERITY GRADE OF A FEMORAL NECK STRESS INJURY IN US MILITARY PERSONNEL

CPT C. Drake Castle, PA-C
MAJ Brandon Carius, DSc, PA-C
MAJ Steven Nardini, MD
Dr James Aden, PhD
MAJ(P) Meghan Joyce, DSc, PA-C

Brooke Army Medical Center (BAMC), San Antonio, TX

Disclaimer

The views expressed are those of the authors and do not reflect the official policy of the Department of the Army, the Department of Defense or the U.S. Government.

The investigators have adhered to the policies for protection of human subjects as prescribed in 45 CFR 46.

I have no potential conflicts with this presentation.

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Key Terms

- Serum 25-hydroxyvitamin D (25OHD)
  - the usual blood measure of vitamin D status (Lai 2010, 2)

Definition	Endocrine Society's 25OHD lab values
Vitamin D Sufficiency	30 to 100 ng/mL
Vitamin D Insufficiency	20 to 29 ng/mL
Vitamin D Deficiency	Less than 20 ng/mL

Key Terms

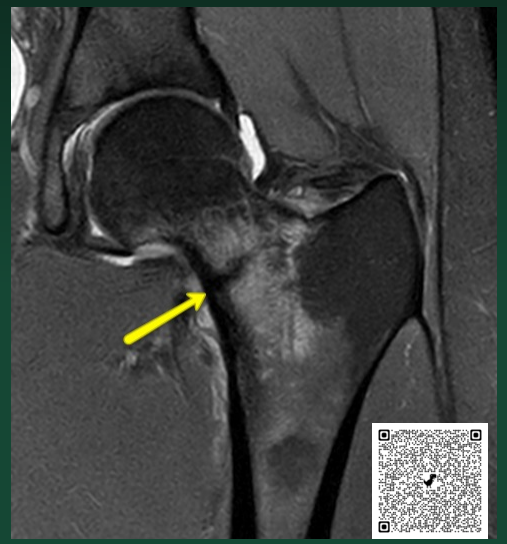
- Bone Mineral Density (BMD)
  - a marker of bone health (Wilson 2020, 15); a low value indicates a potential diagnosis of osteopenia or osteoporosis

- Bone Stress Injury (BSI)
  - an overuse injury of the bone due to repetitive stresses followed by the bones inability to recover

Key Terms

- Femoral Neck
  - the section of bone connecting the shaft of the femur to the head of the femur

- Femoral Neck Stress Injury (FNSI)
  - an overuse injury of the femoral neck due to repetitive stresses followed by the bones inability to recover



Purpose of the Study

- To determine if an association exists between the serum vitamin D value and the severity of a femoral neck stress injury
  - Military service exposes individuals to various activities that increase the risk of BSI

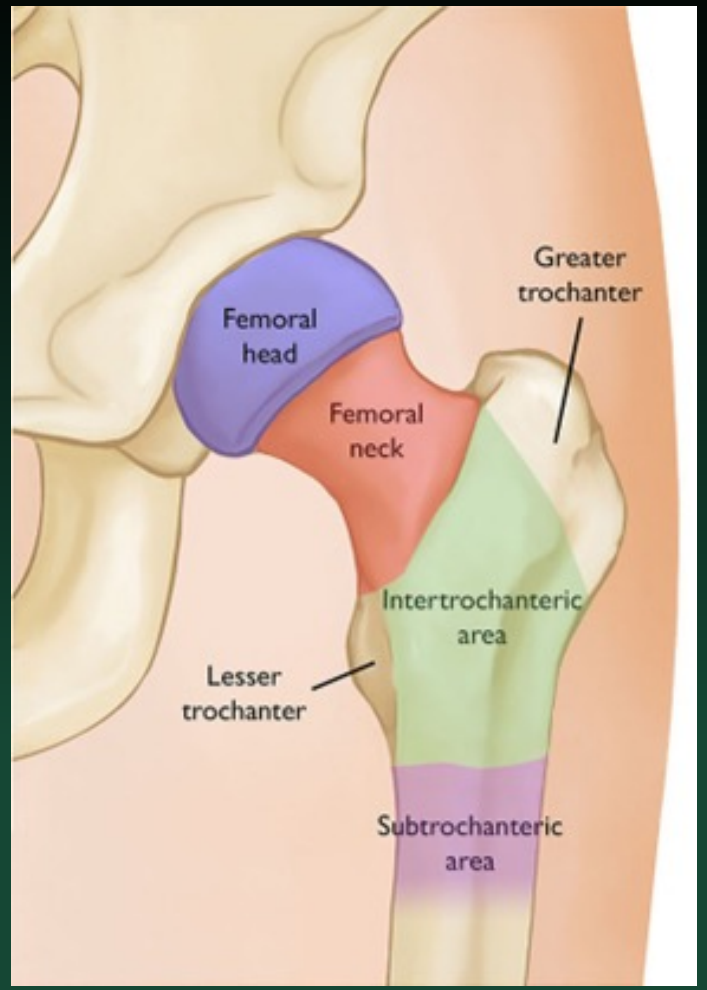
Introduction
(How we get Vitamin D)

- Sun exposure
- Natural foods
- Fortified foods
- Multivitamins

Introduction

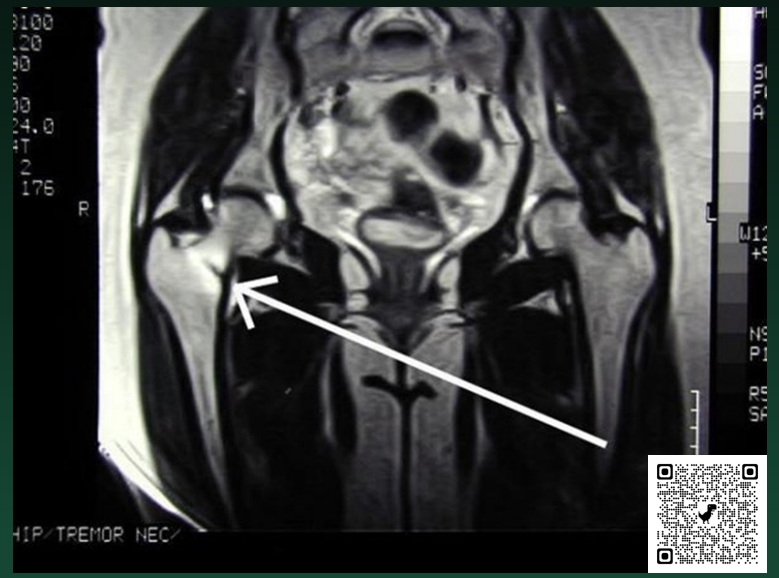
- BSI risks: age, amenorrhea, smoking, female sex, white, and 25OHD (Knechtle et al., 2021; Lappe et al., 2008)
- An inverse correlation exists between 25OHD deficiency and an increased risk of a BSI (Knechtle et al., 2021)
- Over 50% of the 4426 pediatric patients (mean age of 11.6) were found to have a serum 25OHD under 30 ng/mL (Mahen et al., 2020)
- BSI during US Army Basic Combat Training
  - Males with a BSI: 40% attrition rate
  - Females with a BSI: 60% attrition rate (Lappe et al., 2008)

Introduction



Introduction

- Rates of vitamin D deficiency in young, healthy Americans are estimated to be as high as 30-50% (McCabe et al., 2012)
- Over 75% of whites and 90% of African-Americans and Latinos are vitamin D deficient (Shuler et al., 2012)
- New exercise routines: increase in bone turn over in the 1st month
- FNSI are high risk



Literature Review (1)

- Rohena-Quinquilla et al. (2017) proposed a new MRI classification system for FNSI based on a retrospective review of FNSIs in US Army Soldiers over a 24-month period

MRI Classification System for Femoral Neck Stress Injuries (FNSI)	
FNSI Grade	**MRI Findings**
Low Grade	
1	Endosteal marrow edema ≤ 6 mm
2	Endosteal marrow edema > 6 mm and no macroscopic fracture
High Grade	
3	Macroscopic fracture < 50% of femoral neck width
4	Macroscopic fracture ≥ 50% of the femoral neck width

- Strengths: Largest FNSI case, 1st evidence-based support for the use of a 50% fracture cutoff
- Weakness: Retrospective design

Literature Review (2)

- Millward et al. (2020) recognized a 21% risk of a BSI among Division I athletes
  - 40 ng/mL was the cutoff for vitamin D.
  - Athletes with a vitamin D < 40 ng/mL were at a 12% higher risk of a BSI compared to those who maintained or improved their vitamin D to ≥ 40 ng/mL
- Strengths: 497 Males and 305 Females (802 individuals) in a variety of sports
- Limitation: Single university, low number of BSI, and athletes that did not follow up were assumed to have kept the same vitamin D over time

Literature Review (3)

- Lappe et al. (2008) was a double-blind study to determine if supplementation of calcium and vitamin D in female Navy recruits could reduce the incidences of a BSI
  - Occurrence of BSI was 5.9%
  - Supplemented group accounting for a 20% lower incidence of BSIs
- Strengths: 3700 recruits all voluntary
- Limitation: 21.8% females withdrew from the study (7% withdrew to take the supplementation). Did not include males

Literature Review (4)

- Sonneville et al. (2012) a prospective cohort study to determine if calcium and vitamin D intake affected BSI risks in female adolescents
  - An inverse associated existed between vitamin D intake and the risk of a BSI
- Strengths: Study followed 6,712 girls for 7 years
- Weakness: The total sample was not a good representation of the US population

Literature Review (5)

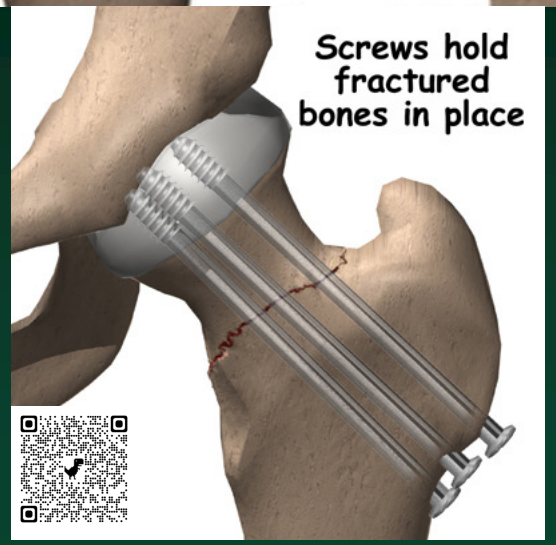
- Williams et al. (2020): a prospective cross-sectional analysis of vitamin D supplementation to reduce BSI risks in Division I collegiate athletes followed by a retrospective chart review of the same sports teams to determine the rates of BSI
  - Blood draws: August and February
  - Individuals with vitamin D levels less <30 ng/mL were treated
- Strengths: First of its kind. Participation was voluntary. Six different teams
- Weakness: Cannot associate the reduction of BSI to the supplementation. No compliance measures in the treatment group

Hypothesis

- Hypothesis: There is an inverse association between serum vitamin D levels and the severity grade of a FNSI

Significance

- No similar studies
- Guide treatment
- Decrease cost for treatment



Methods

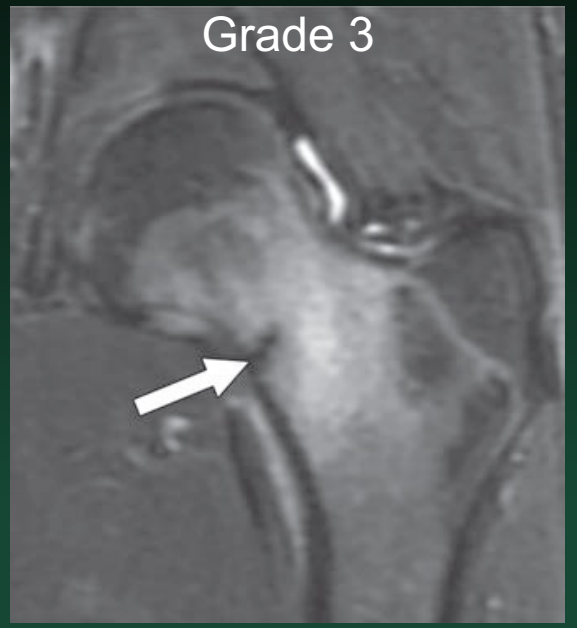
- Primary question: Can pathophysiologic values of vitamin D be associated with a specific grade FNSI?

- Secondary question: Is there a statistically significant vitamin D value that will substantially reduce the risk of a FNSI in military trainees?

Methods

- Primary outcome variables: Identify the vitamin D value based on the severity of a FNSI

FNSI MRI Classification System



Rohena et al. 2018

Methods

- This is a quantitative retrospective study
- Population: US military service members diagnosed with an MRI confirmed FNSI at BAMC located in San Antonio, TX between January 2015 and May 2022

Methods

Inclusion Criteria	Exclusion Criteria
Diagnosed with a FNSI between January 2015 and May 2022	Age < 18 years
Confirmed FNSI by MRI	Age > 60 years
Age: 18 – 60	High Velocity Injury
Military service member	Fall from height above standing
Availability of MRI	Not military
Availability of 25OHD lab values within 28 days of FNSI	Imaging and medical records unavailable

Methods

- Independent variables:
  - 25OHD values (0 ng/mL to 100 ng/mL)
- Dependent variables: FNSI
- Confounding variables:
  - Race, age, sex, body mass index (BMI), alcohol use, tobacco use, and season in which injury occurred

Results

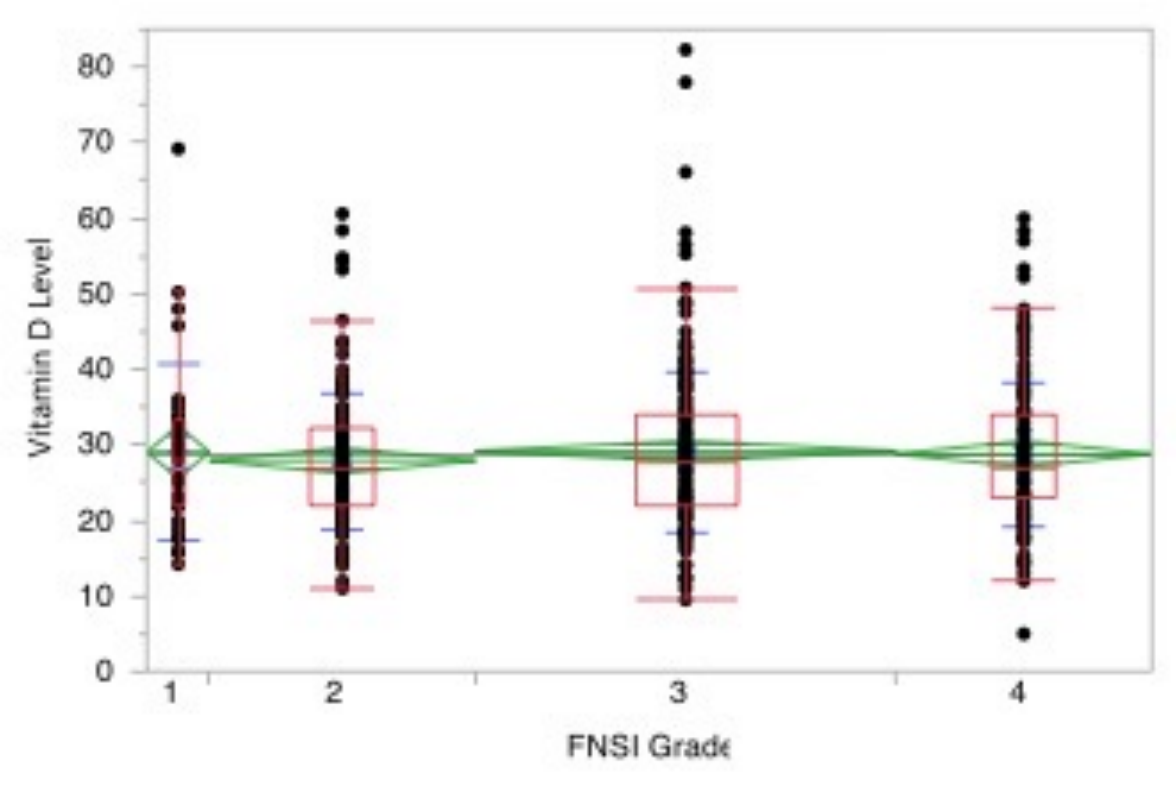
- Identified 680 FNSIs in 514 patients
- Average age was 22.8 (range 18 – 50)
- No difference in age between male and female
- Grades 3 and 4 accounted for ~67% of the injuries

ICD-10 Code
Diagnosed with a fracture of the hip/femur at BAMC from Jan 2015 thru May 2022
(N=9149)

Exclusion Criteria
Not between the ages of 18-60 (N = 6532)
No FNSI (N = 628)
No 25OHD test result (N = 1156)
Not in military (N = 108)
High velocity injury (N = 8)
Injury diagnosed outside the dates (N = 46)
No imaging (N = 8)
Unable to obtain MSK read (N = 123)
Total = 8631

Subjects with an MRI diagnosed FNSI with a 25OHD result within 28 days of diagnosis
(N = 514)

Results (Vitamin D by FNSI)
Primary Outcome



Level	Minimum	25%	Median	75%	Maximum
1	14.2	21.85	28	33.375	69.2
2	11	22	27	32.075	60.6
3	9.5	22	27.6	34	82.3
4	5	23	27	34	60

Nonparametric Comparisons using Wilcoxon Method	
q*	Alpha
1.95996	0.05

Results (Bilateral FNSI by Sex)

Fit Group

Contingency Analysis of Sex by Bilateral

Contingency Table

Bilateral by Sex

Count Col % Row %	Female	Male	Total
Bilateral	61 22.93 36.75	105 42.34 63.25	166
Unilateral	205 77.07 58.91	143 57.66 41.09	348
Total	266	248	514

Fisher's Exact Test	Prob	Alternative Hypothesis
Left	<.0001*	Prob(Sex=Male) is greater for Bilateral=Bilateral than Unilateral
Right	1.0000	Prob(Sex=Male) is greater for Bilateral=Unilateral than Bilateral
2-Tail	<.0001*	Prob(Sex=Male) is different across Bilateral

Test	ChiSquare	Prob>ChiSq
Likelihood Ratio	22.278	<.0001*
Pearson	22.105	<.0001*

Results (Bilateral by Vitamin D)

Level	#	Mean	Std Dev	Lower 95%	Upper 95%
Bilateral	166	26.2902	7.7622	25.101	27.480
Unilateral	348	29.9165	10.7146	28.787	31.046

2-Sample Test, Normal Approximation		
S	Z	Prob>|Z|
37331	-3.43858	0.0006*

Level	10%	25%	Median	75%	90%
Bilateral	17	20.925	25.85	31	36.06
Unilateral	18.89	22.725	27.95	34.1	43.33

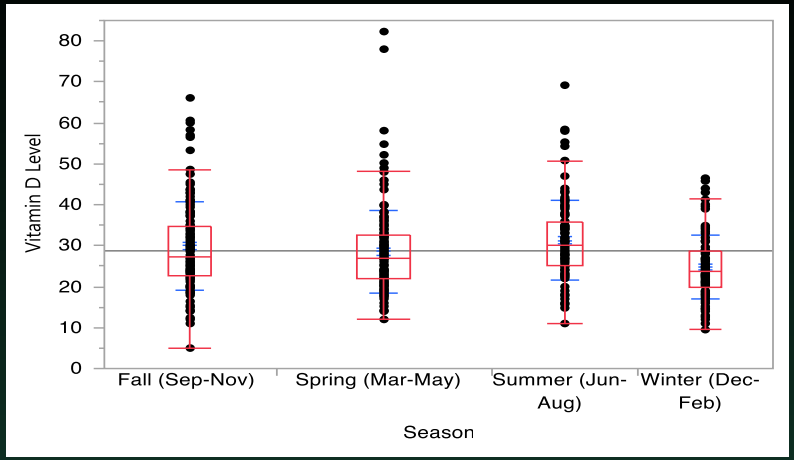
1-Way Test, ChiSquare Approximation		
ChiSquare	DF	Prob>ChiSq
11.8260	1	0.0006*

Results (Race vs Vitamin D)

Level	Minimum	10%	25%	Median	75%	90%	Maximum
White	5	19	23.375	29	34.875	43.06	82.3
Black	11	14.71	19.8	23	28.525	31.97	58.4
Hispanic	9.5	16.19	20.475	25.05	31.6	37.58	69.2
Other	15.2	18	21.6	23.8	30.4	37.9	43.3

Level	- Level	Score Mean Difference	Std Err Dif	Z	p-Value
White	Black	77.6817	14.70249	5.28357	<.0001*
White	Other	46.2576	19.99085	2.31394	0.0207*
White	Hispanic	45.0140	14.86342	3.02851	0.0025*
Hispanic	Black	12.4826	7.23468	1.72538	0.0845
Other	Black	7.6347	6.84838	1.11482	0.2649
Other	Hispanic	-1.8342	6.64617	-0.27597	0.7826

Results (Season vs Vitamin D)



Level	Minimum	Median	Maximum
Fall (Sep-Nov)	5	27.35	66.1
Spring (Mar-May)	12	27	82.3
Summer (Jun-Aug)	11	30	69.2
Winter (Dec-Feb)	9.5	23.9	46.5

ChiSquare	DF	Prob>ChiSq
31.7126	3	<.0001*

Level	- Level	Score Mean Difference	Std Err Dif	p-Value
Summer (Jun-Aug)	Spring (Mar-May)	29.6661	9.82940	0.0025*
Summer (Jun-Aug)	Fall (Sep-Nov)	14.6889	9.06609	0.1052
Spring (Mar-May)	Fall (Sep-Nov)	-12.0631	10.04748	0.2299
Winter (Dec-Feb)	Spring (Mar-May)	-31.4510	9.76369	0.0013*
Winter (Dec-Feb)	Fall (Sep-Nov)	-35.0613	8.95017	<.0001*
Winter (Dec-Feb)	Summer (Jun-Aug)	-45.7479	8.50943	<.0001*

Conclusion

- Statistical significance did not exist to believe that a specific vitamin D value could diagnose a particular grade FNSI

- We can accept the null hypothesis

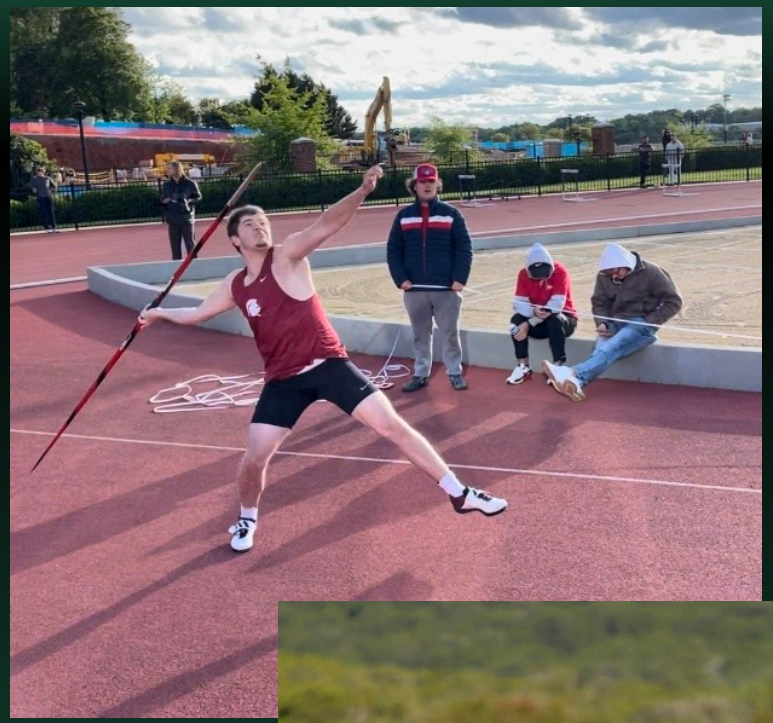
Recommendations

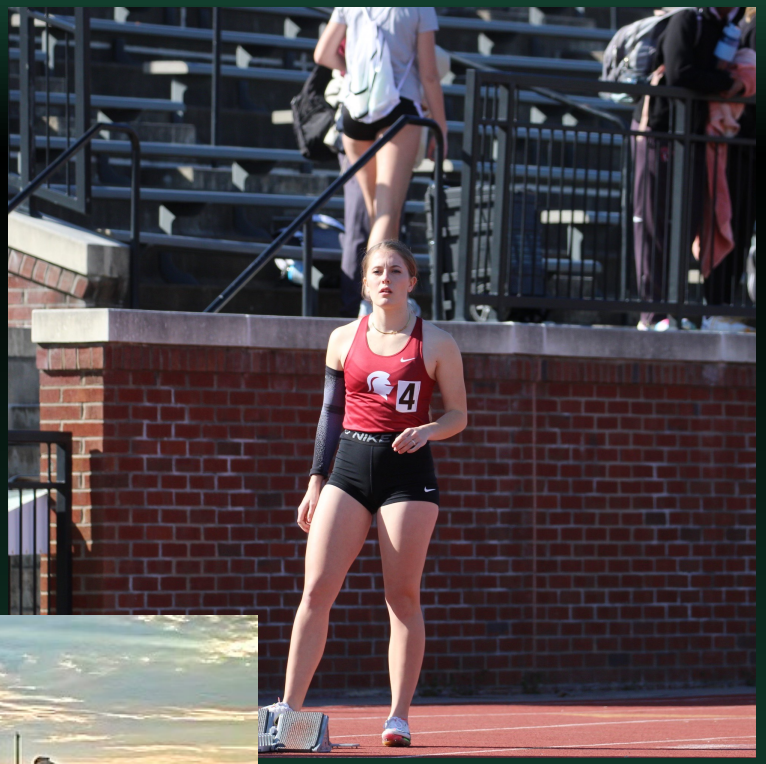
- Consider additional research to determine whether the requirements of vitamin D levels for bone health should diverge based on ethnicity

- Military members with vitamin levels <40 ng/mL should be supplemented
  - Steady state of vitamin D occurs after 90 days of supplementation

- Further research needed to identify the higher rate of bilateral FNSI in males when compared to females

Thank You





Questions?

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