

Strategies to Prevent Bone Stress Injuries in Distance Runners

Michael Fredericson, MD

Professor & Director, PM&R Sports Medicine
Stanford University



Disclosures

The research presented in this study was supported by grants from the *American Medical Society for Sports Medicine* and the *Pac-12 Health and Well-Being Initiative*.

Objectives

Discuss the application of current research to optimize bone health and prevent *bone stress injuries* (aka- stress reaction/fracture) in collegiate distance runners.

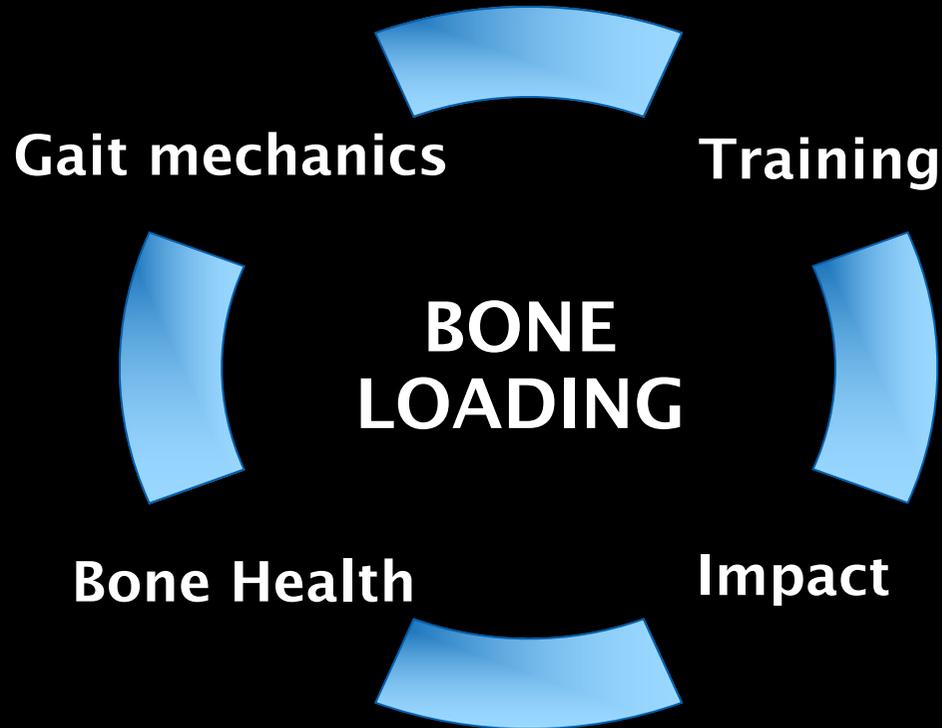
Incidence

Bone stress injuries account for up to 15% of all sports injuries and up to 30% in track and field athletes.



Fredericson et al. Stress Fractures in Athletes. Top Mag Reson Imag, 2007

Risk Factors



Matheson et al. Stress Fractures, 1999



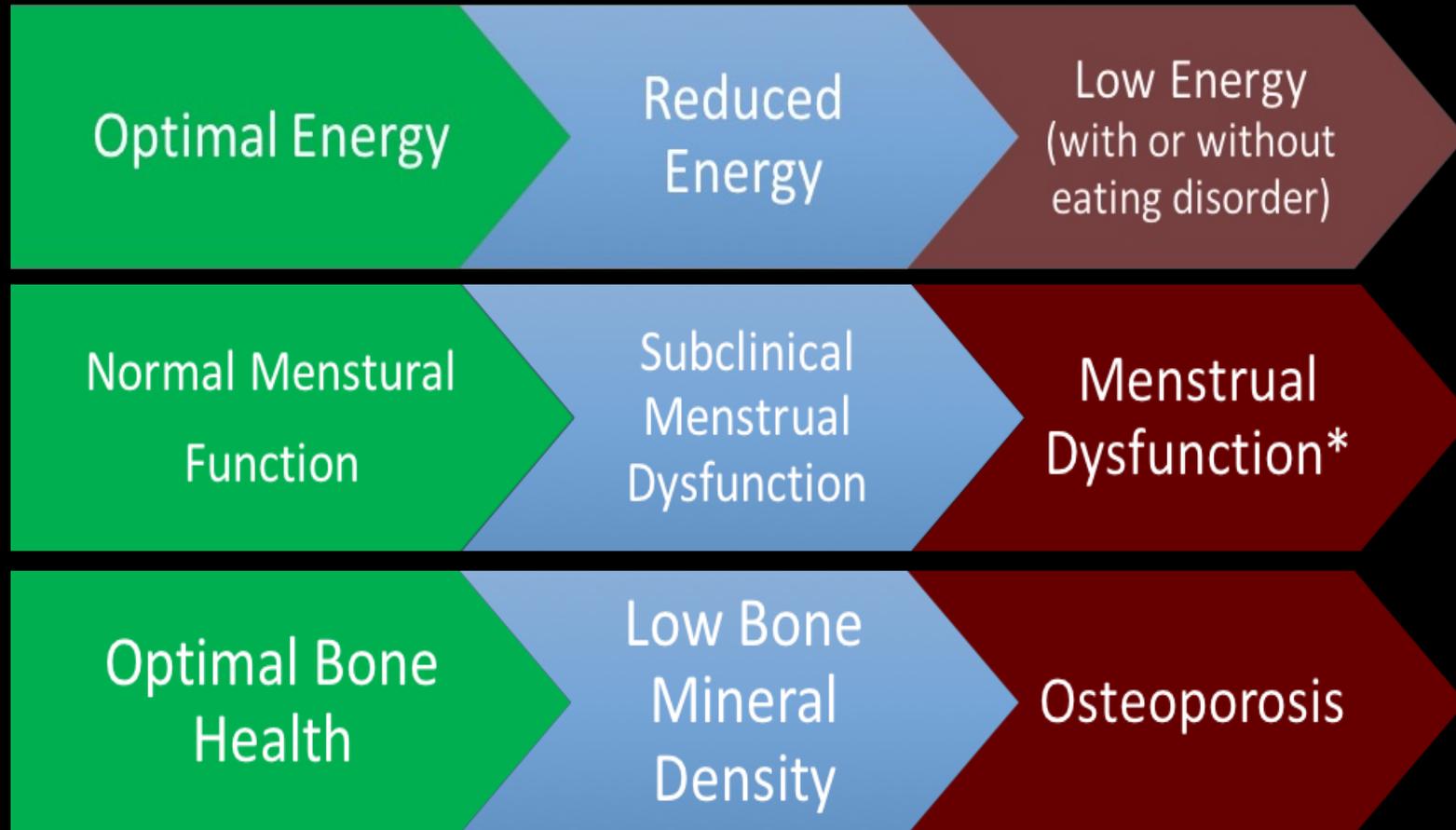
Overuse History



Overuse?



Female Athlete Triad



Low Bone Mineral Density

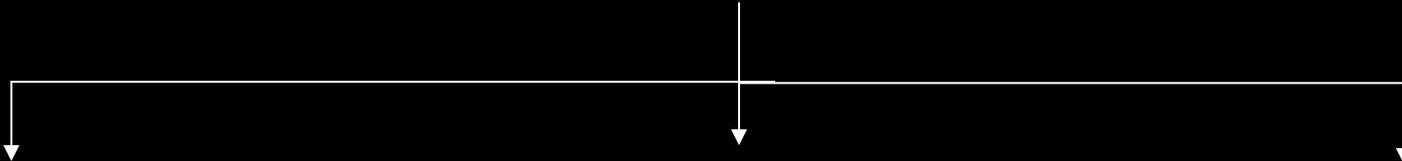
Chronic Low Energy Availability



Menstrual Dysfunction



Decreased Estrogen



Failure to reach peak bone mass

Premature bone loss

Poor mineralization of bone with stress

Prediction of Bone Stress Injuries?

Identifying Sex-Specific Risk Factors for Stress Fractures in Adolescent Runners

ADAM S. TENFORDE¹, LAUREN C. SAYRES², MARY LIZ MCCURDY², KRISTIN L. SAINANI³,
and MICHAEL FREDERICSON¹

Medicine and Science in Sports and Exercise 2013

- Prospective study in 748 high school athletes
- Found risk factors for stress fracture included:
 - prior fracture (6-fold increased risk)
 - late menarche
 - BMI <19 kg/m²
 - participation in sports that emphasize leanness

Identifying Risk Factors

- Each risk factor contributed to 2-3-fold increased risk
- Risk factors are cumulative
 - In females who had **3 of 4 risk factors** there was a 40% likelihood of sustaining a BSI over the next 12 months

Identifying Sex-Specific Risk Factors for Low Bone Mineral Density in Adolescent Runners

Adam Sebastian Tenforde,^{*†} MD, Michael Fredericson,^{†‡} MD, Lauren Carter Sayres,[§] BA, Phil Cutti,[‡] MS, and Kristin Lynn Sainani,^{||} PhD

American Journal of Sports Medicine 2015

- From larger cohort, 136 athletes obtained DEXA scans
- Risk factors for low BMD (defined as Z-score ≤ -1):
 - Boys:
 - BMI ≤ 17.5 kg/m²
 - belief that thinness leads to faster running performances
 - Girls:
 - BMI ≤ 17.5 kg/m²
 - combination of menstrual irregularities and history of fracture

Prevention of Bone Stress Injuries?



THE HEALTHY RUNNER PROJECT

A Multicenter Prospective Interventional Study to Improve Bone Health and Reduce the Incidence of Bone Stress Injuries in Division I Female Collegiate Distance Runners

Primary Aims

- To determine if a nutritional intervention in collegiate distance runners decreases incidence, severity, and return to play time for bone stress injuries prospectively, compared to a historical control group over 4 years.

Secondary Aim

- To assess the effectiveness of the nutrition intervention on bone mineral density, vitamin D 25-OH and other bone biomarkers prospectively

Sub-Analysis

- To assess if the Female Athlete Triad Risk Assessment Tool used prospectively is predictive of bone stress injuries and RTP time

Female Athlete Triad Consensus Statement

2014 Female Athlete Triad Coalition Consensus Statement on Treatment and Return to Play of the Female Athlete Triad:

1st International Conference held in San Francisco, California, May 2012
and 2nd International Conference held in Indianapolis, Indiana, May 2013

Mary Jane De Souza,¹ Aurelia Nattiv,² Elizabeth Joy,³ Madhusmita Misra,⁴
Nancy I Williams,¹ Rebecca J Mallinson,¹ Jenna C Gibbs,⁵ Marion Olmsted,⁶
Marci Goolsby,⁷ Gordon Matheson,⁸ Expert Panel

Cumulative Risk Assessment (CRA)

Risk Factors	Magnitude of Risk		
	Low Risk = 0 points each	Moderate Risk = 1 point each	High Risk = 2 points each
<i>Low EA with or without DE/ED</i>	<input type="checkbox"/> No dietary restriction	<input type="checkbox"/> Some dietary restriction‡; current/past history of DE;	<input type="checkbox"/> Meets DSM-V criteria for ED*
<i>Low BMI</i>	<input type="checkbox"/> BMI ≥ 18.5 or ≥ 90% EW** or weight stable	<input type="checkbox"/> BMI 17.5 < 18.5 or < 90% EW or 5 to < 10% weight loss/month	<input type="checkbox"/> BMI ≤ 17.5 or < 85% EW or ≥ 10% weight loss/month
<i>Delayed Menarche</i>	<input type="checkbox"/> Menarche < 15 years	<input type="checkbox"/> Menarche 15 to < 16 years	<input type="checkbox"/> Menarche ≥ 16 years
<i>Oligomenorrhea and/or Amenorrhea</i>	<input type="checkbox"/> > 9 menses in 12 months*	<input type="checkbox"/> 6-9 menses in 12 months*	<input type="checkbox"/> < 6 menses in 12 months*
<i>Low BMD</i>	<input type="checkbox"/> Z-score ≥ -1.0	<input type="checkbox"/> Z-score -1.0*** < - 2.0	<input type="checkbox"/> Z-score ≤ -2.0
<i>Stress Reaction/Fracture</i>	<input type="checkbox"/> None	<input type="checkbox"/> 1	<input type="checkbox"/> ≥ 2; ≥ 1 high risk or of trabecular bone sites†
Cumulative Risk (total each column, then add for total score)	___ points +	___ points +	___ points = ___ Total Score

	Cumulative Risk Score*	Low Risk	Moderate Risk	High Risk
<i>Full Clearance</i>	0 – 1 point	<input type="checkbox"/>		
<i>Provisional/Limited Clearance</i>	2 – 5 points		<input type="checkbox"/> Provisional Clearance <input type="checkbox"/> Limited Clearance	
<i>Restricted from Training and Competition</i>	≥ 6 points			<input type="checkbox"/> Restricted from Training/ Competition-Provisional <input type="checkbox"/> Disqualified

Consensus Statements-Male Athlete Triad Clin Journal Sports Med 2021

Consensus Statement

The Male Athlete Triad—A Consensus Statement From the Female and Male Athlete Triad Coalition Part 1: Definition and Scientific Basis

Aurelia Nattiv, MD,* Mary Jane De Souza, PhD,† Kristen J. Koltun, PhD,‡ Madhusmita Misra, MD, MPH,§
Andrea Kussman, MD,¶ Nancy I. Williams, ScD,† Michelle T. Barrack, PhD, RD,|| Emily Kraus, MD,¶
Elizabeth Joy, MD, MPH,** and Michael Fredericson, MD¶

Consensus Statement

The Male Athlete Triad—A Consensus Statement From the Female and Male Athlete Triad Coalition Part II: Diagnosis, Treatment, and Return-To-Play

Michael Fredericson, MD,* Andrea Kussman, MD,* Madhusmita Misra, MD, MPH,† Michelle T. Barrack, PhD, RD,‡
Mary Jane De Souza, PhD,§ Emily Kraus, MD,* Kristen J. Koltun, PhD,¶ Nancy I. Williams, ScD,§ Elizabeth Joy, MD,
MPH,|| and Aurelia Nattiv, MD**

Study Protocol

Risk Factor Questionnaire

- Questions on general health, risk factors for fracture and osteoporosis including specific Triad consensus questions

Nutrition Assessment

- Energy availability through dietary recall
- Fat free mass calculation

Run Fueled App

- Two four-week modules providing nutrition handouts, video clips, & educational slides

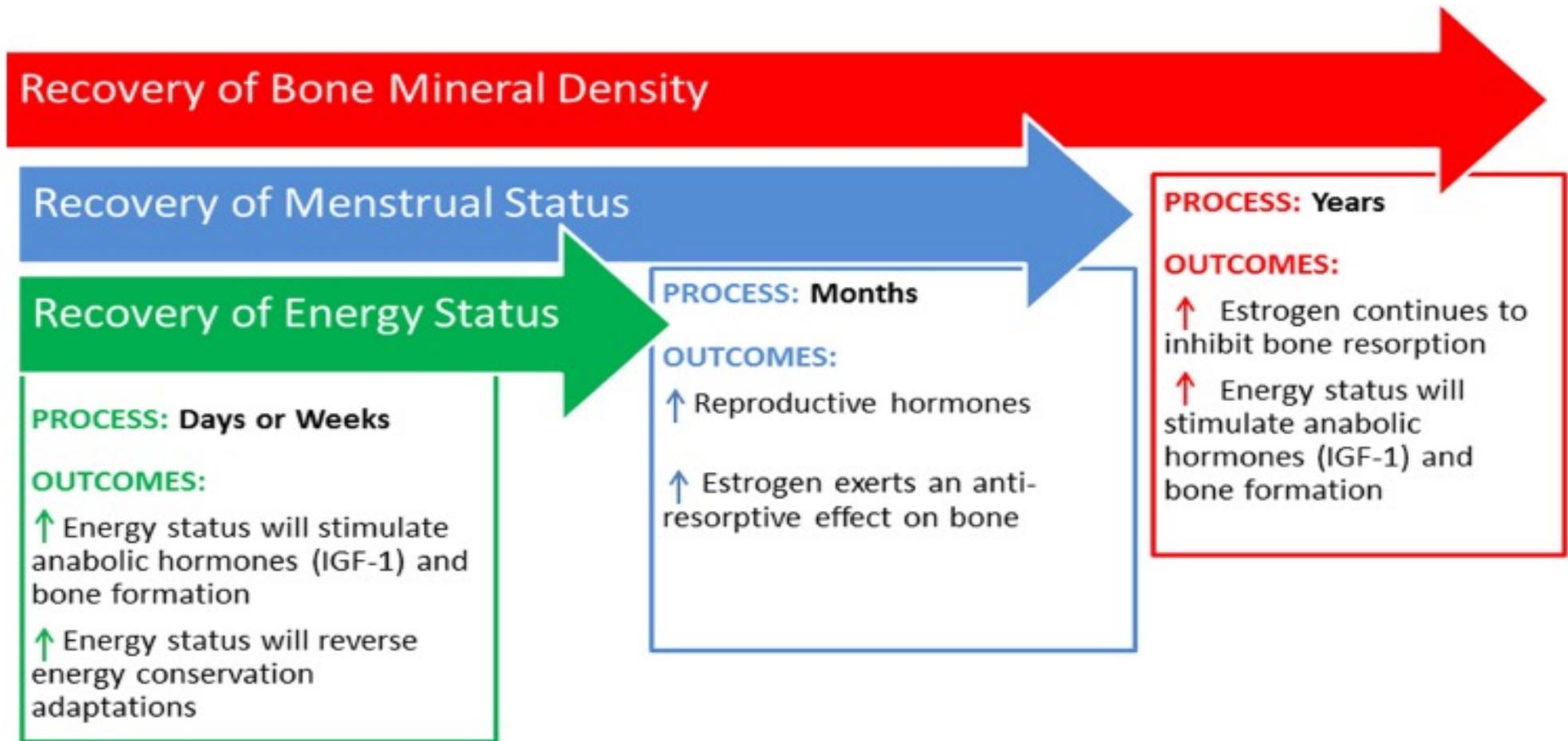
DXA Scan

- Bone density assessment from the lumbar spine, femur, distal radius, and total body.

Lab Evaluation

- Leptin, ghrelin, N-telopeptide, bone alkaline phosphatase, Vit D 25-OH, Free T3 and Total T3

Treatment



Nutrition for Bone Health

$$\text{Energy Availability} = \frac{[\text{Energy Intake} - \text{Exercise Energy Expenditure}]}{[\text{Fat Free Mass}]}$$

Balanced EA* = 45 kcals/kg FFM/day

Low EA* = < 30 kcals/kg FFM/day

*Needs may vary for adolescents and/or male athletes

Nutrition Protocol

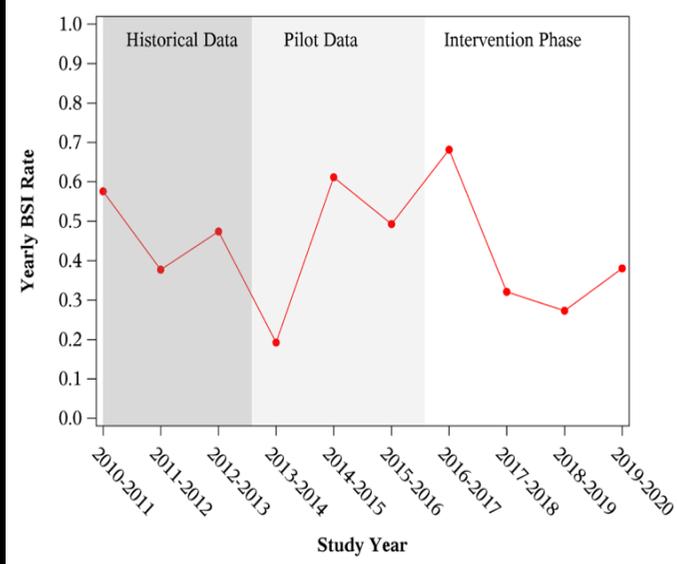
- **Web-based Nutrition Screening survey**
- **One-on-one meeting with Sports Dietitian**
 - Evaluate current intake, risk for low energy availability, other nutrient deficits
 - Choose 1-2 nutrition goals every season
- ***RunFueled* Application**
 - Two four-week modules providing nutrition handouts, video clips, & educational slides

BSI Rates - Results

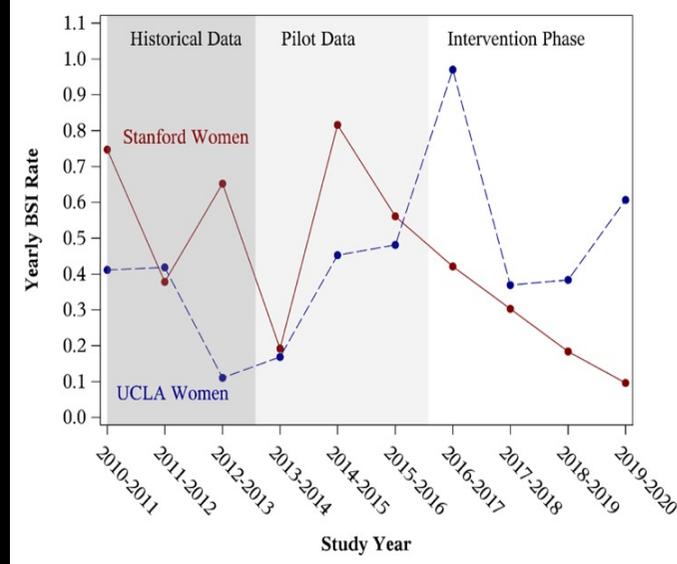
BSI Rates Stratified by School (Women):

- Stanford's women had a significant reduction in BSI rate in the intervention phase (0.27 BSI events per person year) compared to the historical phase (0.62) ($p=.015$)
- UCLA's women had no significant change

Combined Yearly BSI Rate for Women



Stratified Yearly BSI Rate for Women

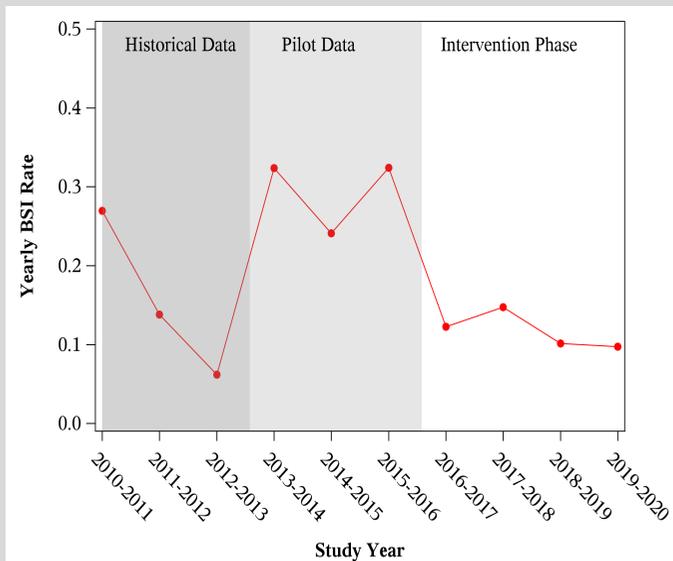


BSI Rates - Results

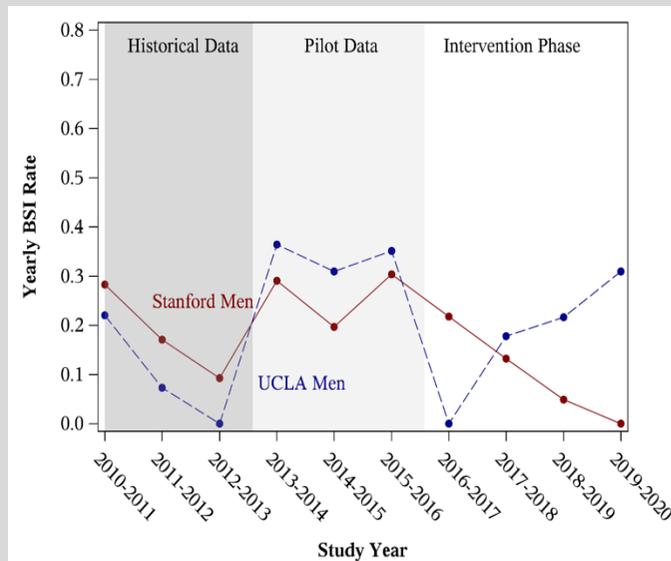
BSI Rates Stratified by School (Men):

- **Stanford's men saw a non-significant reduction in BSI rates from 0.18 events per athlete-year in the historical phase to 0.11 in the intervention phase ($p=.39$)**
- **UCLA's men had no change**

Combined Yearly BSI Rate for Men



Stratified Yearly BSI Rate For Men



Trabecular vs Cortical Bone

Trabecular bone:

- greater surface area more impacted by metabolic bone disease such as that associated with an energy deficit or low estrogen state

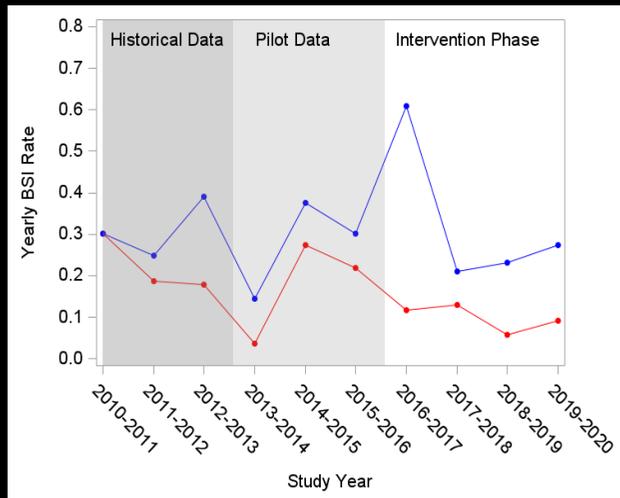
Cortical bone:

- generally more susceptible to impact or shearing biomechanical forces

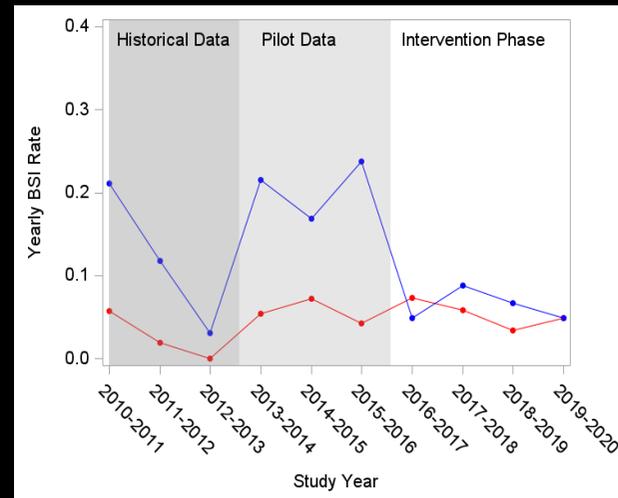
Trabecular vs Cortical BSI Rates

- In women, the rate of trabecular BSI was *halved*
- In men, overall trabecular BSIs were low in all phases
- In women, the rate of cortical BSI was unchanged
- In men, the cortical BSI rate decreased non-significantly

Cortical vs Trabecular, Women



Cortical vs Trabecular, Men



Higher Scores on Cumulative Triad Risk Assessment and Trabecular Bone Stress Injury

In men, high-risk CRA score was associated with an 8.50-fold increased risk for trabecular BSI compared to the low-risk group.

In women, high-risk CRA score was associated with a 4.40-fold increased risk for trabecular BSI.

Characteristic of Risk Group	Person -Years	Rate	Adjusted Rate	Crude Rate Ratio	Adjusted Rate Ratio	p value
Low-risk (59 observations)¹	52.10					
Trabecular BSI (= 3)		0.06	0.07	1.00 (ref)	1.00 (ref)	
Cortical BSI (= 4)		0.27	0.19	1.00 (ref)	1.00 (ref)	
Total BSI (= 17)		0.33	0.30	1.00 (ref)	1.00 (ref)	
Medium-risk (183 observations)	153.50					
Trabecular BSI (= 20)		0.13	0.12	2.17	2.87	0.025
Cortical BSI (= 44)		0.29	0.25	1.07	1.32	0.48
Total BSI (= 66)		0.42	0.40	1.27	1.35	0.37
High-risk (29 observations)	22.86					
Trabecular BSI (= 8)		0.35	0.31	5.83	4.40	0.025
Cortical BSI (= 16)		0.70	0.54	2.59	1.65	0.41
Total BSI (= 24)		1.05	0.94	3.18	3.17	0.0024

Change in Menstrual Irregularity

During the intervention phase, menstrual irregularity decreased from 47.8% to 26.3%.

Women	menstrual irregularity		
	overall	Stanford	UCLA
Pilot phase			
1	47.8%	55.3%	32.7%
2	49.5%	56.2%	38.6%
3	59.1%	59.5%	60.1%
Intervention phase			
1	47.8%	38.9%	56.7%
2	59.6%	64.2%	56.7%
3	20.8%	15.3%	26.0%
4	26.3%	25.5%	26.5%
odds ratio	0.84	0.78	0.91
p-value	0.02	0.03	0.36

Improvements in Bone Mineral Density

Men experienced significant increases in BMD at all sites (hip, femoral, total body, and spine)

Women increased significantly at the spine

Spine	Men		Women	
	N	Z-Score	N	Z-Score
Baseline Z	40	-0.46	36	-0.49
Year 1 – baseline	28	-0.04	29	0.14
Year 2 – baseline	17	0.10	11	0.21
Year 3 – baseline	11	0.30	10	0.41
Year 4 – baseline	4	0.05	2	0.65
Estimated rate of change per year	P=.0006	0.06	P=.0097	.12

Femoral	Men		Women	
	N	Z-Score	N	Z-Score
Baseline Z	25	0.50	23	.54
Year 1 – baseline	21	0.07	18	.04
Year 2 – baseline	7	0.21	4	-0.19
Year 3 – baseline	1	0.00	3	0.13
Year 4 – baseline	0		0	
Estimated rate of change per year	P=.0016	0.09	P=.85	-0.01

Total Body	Men		Women	
	N	Z-Score	N	Z-Score
Baseline Z	41	0.27	40	0.39
Year 1 – baseline	29	0.07	29	0.04
Year 2 – baseline	19	0.22	14	0.11
Year 3 – baseline	12	0.03	10	0.04
Year 4 – baseline	5	0.22	2	-0.20
Estimated rate of change per year	P=.028	0.05	P=.41	0.02

Total Hip	Men		Women	
	N	Z-Score	N	Z-Score
Baseline Z	25	0.43	23	0.57
Year 1 – baseline	21	0.10	18	-0.04
Year 2 – baseline	7	0.43	4	-0.08
Year 3 – baseline	1	-0.30	3	0.20
Year 4 – baseline	0		0	
Estimated rate of change per year	P=.014	0.08	P=.19	0.03

BMD changes by CRA Risk Group

The moderate/high risk group had significant increases at the spine and total hip.

The low risk group had significant increases in femoral BMD.

Spine	Low Risk		Moderate or High Risk	
	N	Z-Score	N	Z-Score
Baseline Z	36	-0.16	40	-0.75
Year 1 – baseline	26	-0.11	31	0.19
Year 2 – baseline	12	0.07	16	0.30
Year 3 – baseline	9	0.32	12	0.38
Year 4 – baseline	4	0.05	2	0.65
Estimated rate of change per year	P=.196	0.03	P=.0005	0.14

Total Hip	Low Risk		Moderate or High Risk	
	N	Z-Score	N	Z-Score
Baseline Z	25	0.71	23	0.27
Year 1 – baseline	22	0.03	17	0.05
Year 2 – baseline	5	0.20	6	0.28
Year 3 – baseline	1	-0.30	3	0.20
Year 4 – baseline	0			
Estimated rate of change per year	P=.45	0.02	P=.0026	0.09

Femoral	Low Risk		Moderate or High Risk	
	N	Z-Score	N	Z-Score
Baseline Z	25	0.71	23	.54
Year 1 – baseline	22	0.10	17	.04
Year 2 – baseline	5	0.04	6	-0.19
Year 3 – baseline	1	0.00	3	0.13
Year 4 – baseline	0			
Estimated rate of change per year	P=.0139	0.07	P=.34	0.03

Total Body	Low Risk		Moderate or High Risk	
	N	Z-Score	N	Z-Score
Baseline Z	39	0.43	42	.24
Year 1 – baseline	26	0.07	32	.04
Year 2 – baseline	11	0.27	18	0.22
Year 3 – baseline	10	0.03	13	0.03
Year 4 – baseline	5	.22	2	-0.20
Estimated rate of change per year	P=.091	0.04	P=.11	0.04

Cumulative risk assessment (CRA) score in females

- CRA score accurately predicted future bone stress injury, with each additional 1-point increasing risk by 13% ($p=0.027$)

Kraus E, Fredericson M, et al. Higher modified female athlete triad cumulative risk assessment score predict increased rates of injury. AMSSM Annual Meeting, 2018

Cumulative risk assessment (CRA) score in males

- Each 1-point increase in cumulative risk score was associated with a 37% increase in risk for future bone stress injury.

Kraus E, Fredericson et al. BJSM 2019

Cumulative Risk Assessment Scores and Delayed Return to Play

- **Higher scores** were associated with a significant delay in *return to play* in collegiate distance runners with BSI
- Each **1-point increase** in cumulative risk score increases the time lost from injury in days by 17%

Summary

- Observed steady year-to-year declines in BSI rates for Stanford's women and men with the nutrition intervention
- BSI rates at UCLA may have been impacted by a 2015 change in the team dietitian, loss of a dietitian during the 2020 season, and a 2018 coaching change



CLINICAL RELEVANCE:

- Importance of communication between physicians, coaching staff, athletic trainers, and athletes
 - *Focus on shifting team culture has major impact*
- Hormonal response and bone health changes after intervention can take time
- Triad Cumulative Risk Assessment Tool can help predict injury and guide clinical decision making



Stanford & UCLA Research Team

- Physicians, Dieticians, Statistician:
 - Dr. Aurelia Nattiv, Dr. Michelle Barrack, Dr. Kristin Sainani, Dr. Emily Kraus, Dr. Andrea Kussman, Sonal Singh, and Dr. Brian Kim, Dr. Adam Tenforde, Kristin Gravani RD, Beth Miller RD
- Other Support:
 - Participants, parents, coaches, school administrators and others who made these studies possible



Thank You!



QUESTIONS?

