Bone Stress Injuries in Young(ish) Adults

INTERDISCIPLINARY SYMPOSIUM ON OSTEOPOROSIS 19

NATIONAL OSTEOPOROSIS FOUNDATION

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Until every child is well™

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Disclosures

- I have no relevant disclosures.

STRIVE

Stress Fracture Initiative at Harvard

STRIVE at Harvard is a multidisciplinary research group focused on bone stress injury treatment and prevention. Our group is made up of physicians, PhDs and athletes. Our goal is to communicate to the athletic and research community through newsletters with updates on the latest scientific literature on bone health in athletes, and to provide a platform for affiliates to advertise current research studies.

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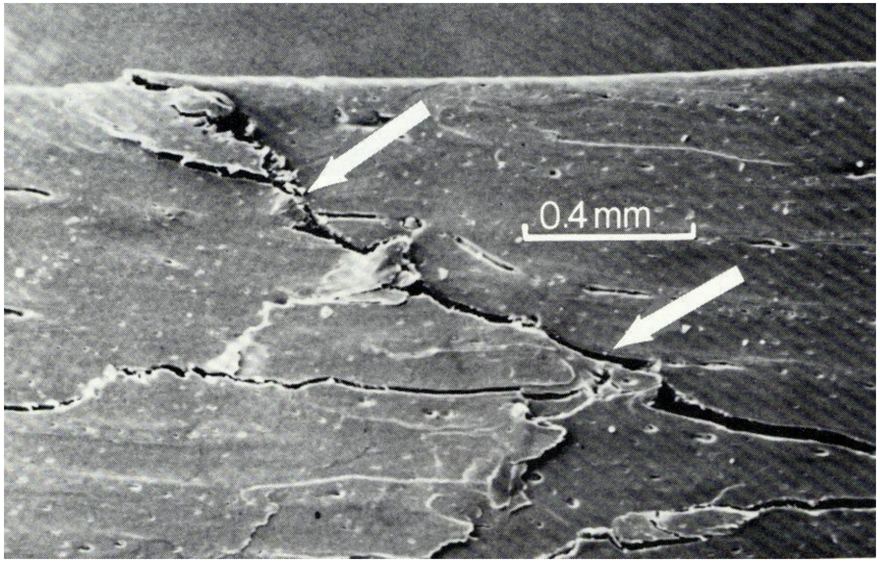
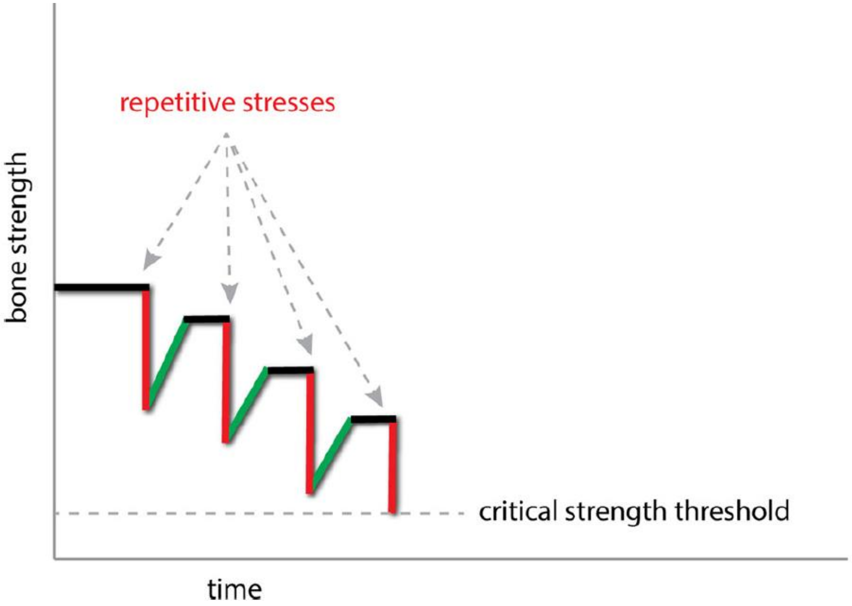
Stress Fractures/Bone Stress Injuries

- Microfractures in cortical bone as a result of abnormal bone remodeling in the setting of repetitive stress impact

- Bone stress injuries account for up to 20% of injuries seen in sports medicine clinics





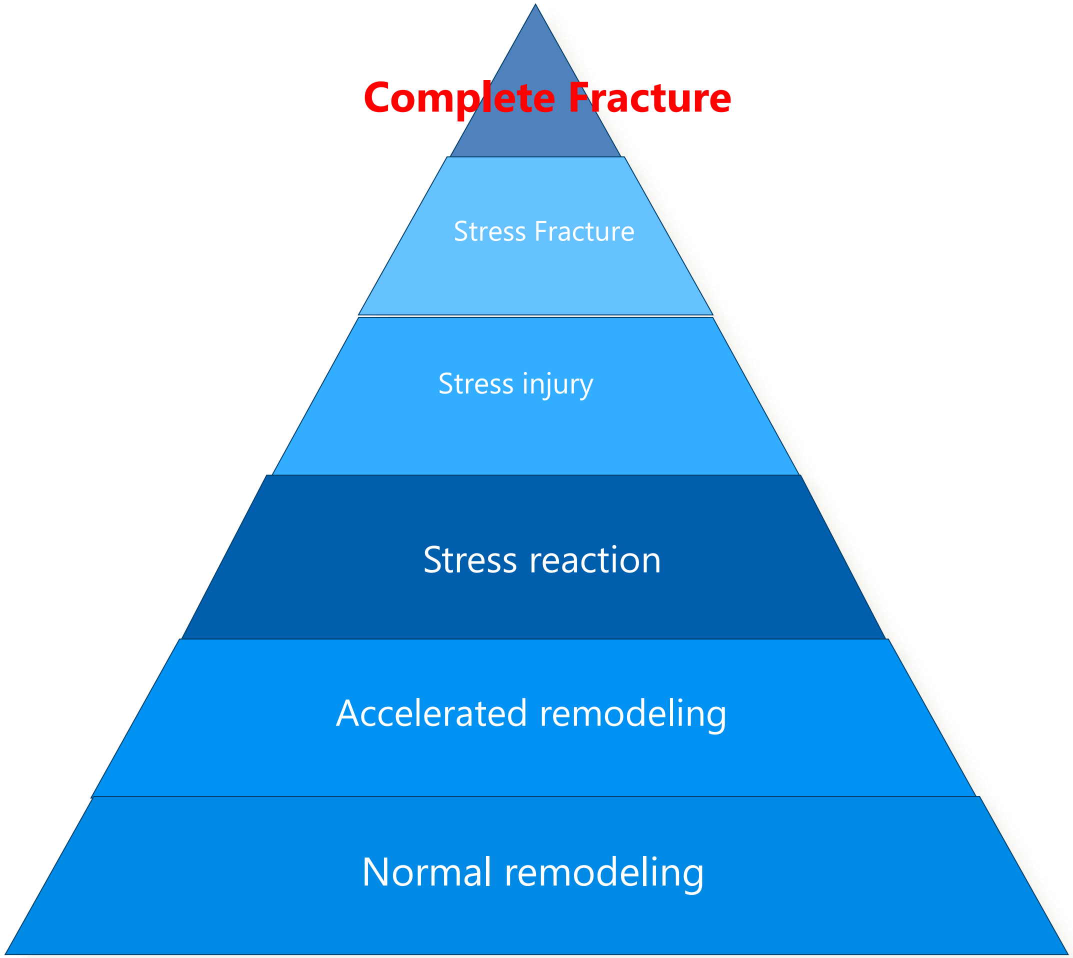
Fredericson M, et al. Top Mag Reson Imag, 2007. Mandell JC, et al. Skeletal Radiol, 2017.

Semantics

- Stress fractures are sometimes divided into fatigue fractures and insufficiency fractures
  - A *fatigue fracture* occurs from repeated stress on a "normal bone"
  - An *insufficiency fracture* occurs with relatively normal activity on a "weakened bone"

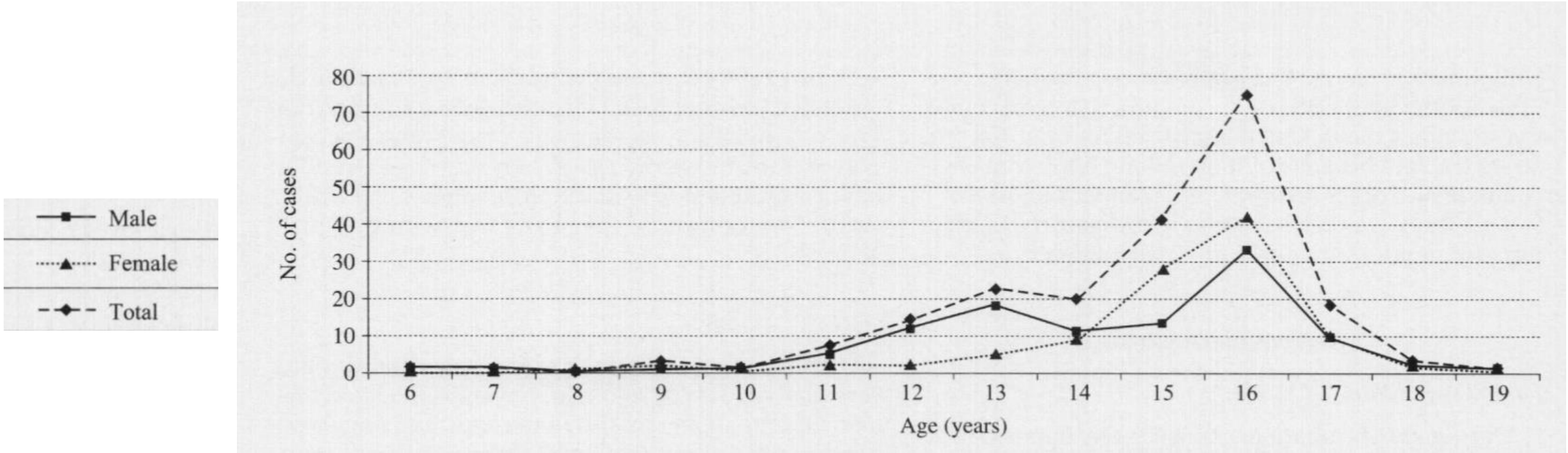
- Stress Fracture/Fatigue Fracture/Bone Stress Injury

Continuum of Bone Stress Injuries



Stress Fractures/Bone Stress Injuries

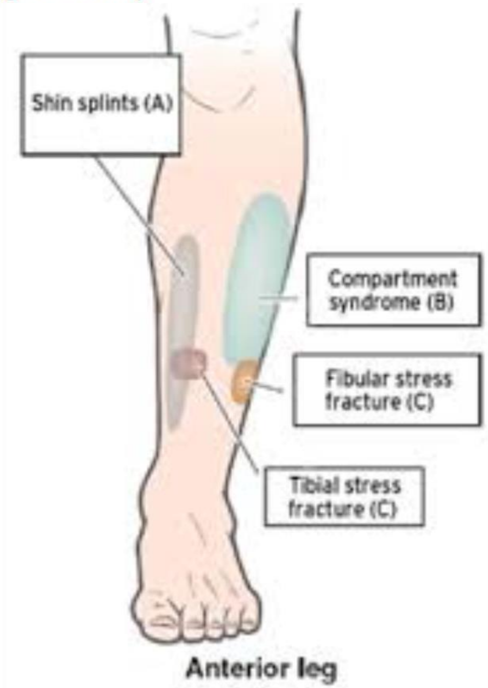
- Runners who average >25 miles per week are at increased risk for stress fractures
- More common in women than men
- The tibia, fibula, and metatarsal bones are the most frequently affected sites
- In children there are peak times of susceptibility



Moreira CA and Bilezikian JP. J Clin Endocrinol Metab, 2017. Ohta-Fukushima M, et al. J Sports Med Phys Fitness, 2002.

Common Locations of BSI

Stress fracture location	Differential diagnosis	History and physical evaluation
Tibia – medial	• Medial tibial stress syndrome • Meniscal pathology (medial tibial condyle) • Ligamentous injury (medial malleoli, tibial condyle) • Malignant tumor (medial tibial condyle)	• Focal pain during weight-bearing/or activity along tibial shaft • Pain with percussion
Tibia – anterior	• Compartment syndrome • Tendinopathy	• Focal pain during weight-bearing/or activity along tibial shaft • Pain with percussion
Fibula	• Meniscal injuries • Lateral ligament sprains	• Focal pain and tenderness • Referred knee pain



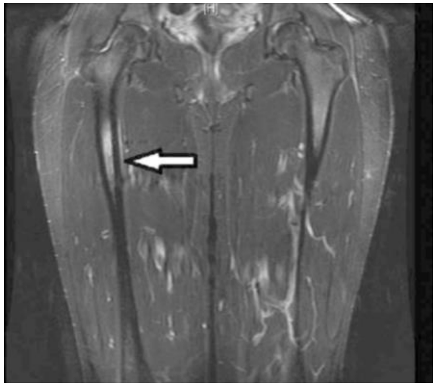
Kahanov L, et al. Open Access J Sports Med, 2015.

Common Locations of BSI

Stress fracture location	Differential diagnosis	History and physical evaluation
Great toe sesamoid	• Sesamoiditis • Avascular necrosis • Synchondrosis • Partite sesamoid • Osteomyelitis • Bursitis	• Focal point tenderness and swelling • Pain on dorsiflexion • Pain during weight bearing and push off • Increasing pain with activity
Metatarsals	• Strain • Plantar fasciitis • Morton's neuroma • Metatarsalgia	• Pain during weight bearing • Focal swelling • Focal tenderness

Kahanov L, et al. Open Access J Sports Med, 2015.

Common Locations of BSI

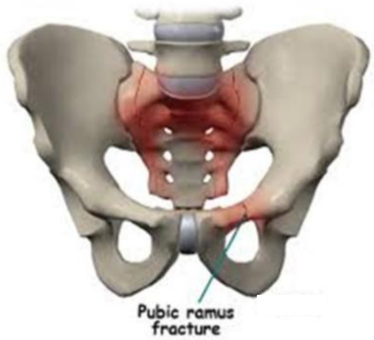


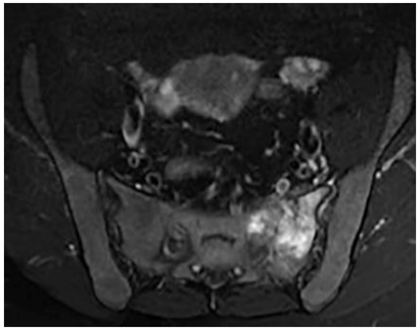
Stress fracture location	Differential diagnosis	History and physical evaluation
Femur/femoral shaft	• Rectus femoris strain • Adductor strain	• Dependent on location of injury o Groin o Anterior thigh o Gluteal o Knee • Activity related pain • Hip pain at end ranges of motion • Pain with one leg hop • No pain on palpation • Night pain may be present
Femoral neck	• Trochanteric bursitis • Strain in hip musculature	• Anterior groin pain • Increasing pain with activity • Pain with straight leg raise • Pain with log roll • Pain with one leg hop

Kahanov L, et al. Open Access J Sports Med, 2015.

Common Locations of BSI

Stress fracture location	Differential diagnosis	History and physical evaluation
Pelvis (pubic rami)	• Strain of adductors • Bursitis	• Groin, buttock, or thigh pain • Focal tenderness • Pain with single leg stance on affected side • Positive hop test • Point tender (may be extreme) on pubic rami
Sacrum	• Sciatica • Disk pathology • Sacroiliac joint pathology • Strain of gluteus maximus • Strain deep external rotators or piriformis • Strain hamstring	• SI and/or buttock pain during palpation and load bearing activity • Low back pain • Radiculopathy • Additional physical examinations are typically unremarkable





Kahanov L, et al. Open Access J Sports Med, 2015.

Low-risk and High-Risk

High Risk	Low Risk
Region of Maximal Tensile Load	Compression Load
Poor natural history: progression to complete fracture	Good natural history
Zone of diminished blood flow	Good blood flow
Chronic Pain	Chronic Pain
Delayed Union / Non Union	Good healing
Predilection for protracted recovery	Good recovery
Complete Fracture needs surgery	Symptomatic: activity modification
Incomplete fracture needs Strict NWB or Surgery	Asymptomatic: need no x-Ray follow up

Kaeding CC, et al. Clin J Sports Med 2005; Diehl JJ, et al. Clin J Sports 2006; McInnis KC & Ramey LC, PM R, 2016. *Courtesy of Dr. Juan Manuel Alonso*

Low-risk and High-Risk

Low Risk	High Risk
Iliac Crest	Sacrum
Pubic Ramii	Femoral Neck
Femoral Shaft	Patella
Fibula	Anterior cortex of tibia
Posteromedial Tibia	Medial Malleolus
Lateral Malleolus	Talus (lateral process)
Calcaneus	Tarsal Navicular
Cuboid	Proximal Diaphysis of MT5
Cuneiforms	Base of MT2-MT4
Diaphysis of MT1-MT4	Great-toe sesamoids

Kaeding CC, et al. Clin J Sports Med 2005; Brukner & Khan´s Clinical Sports Medicine, 2017. *Courtesy of Dr. Juan Manuel Alonso*

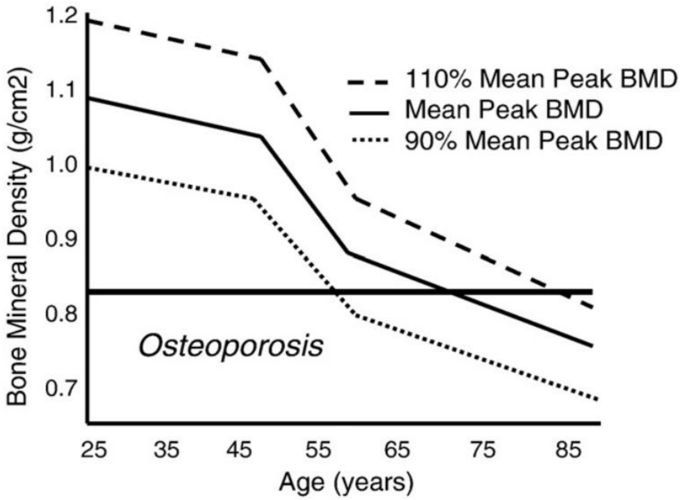
Common MRI Grading (Fredericson with Kijowski modification)

Grade	Illustration	Grade	Illustration
Grade 0: Normal MR		**Grade 3:** Moderate bone marrow edema seen on both T2-weighted images and T1-weighted images *return to sport in mean 39-44 days*	
Grade 1: Periosteal edema only *return to sport in mean 16 days*		**Grade 4a:** Cortical signal abnormality, not linear in morphology *return to sport in mean 39-44 days*	
Grade 2: Mild bone marrow edema seen on T2-weighted images only *return to sport in mean 39-44 days*		**Grade 4b:** Linear cortical signal abnormality *return to sport in mean 71 days*	

Mandell JC et al. Skeletal Radiol, 2017. Fredericson M, et al. Am J Sports Med, 1995. Kijowski R,et al. Am J Roentgenol, 2012.

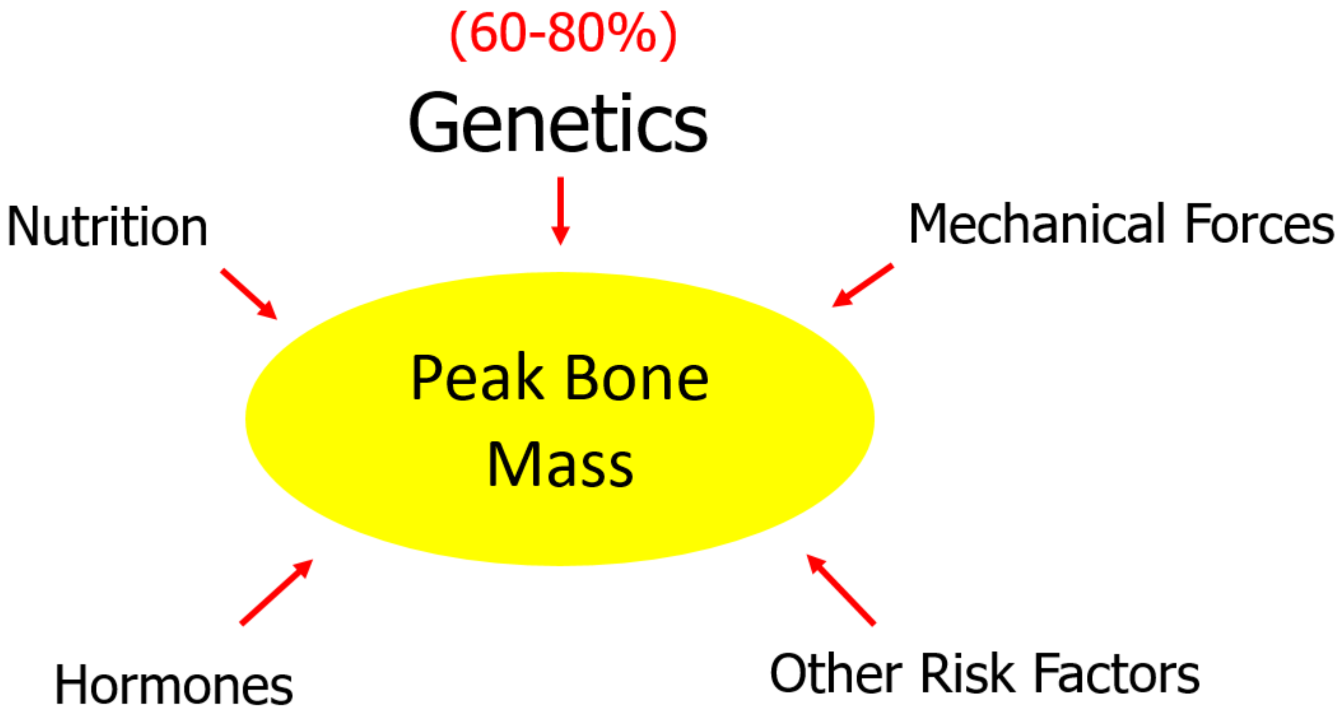
Peak Bone Mass

- Peak Bone Mass attained during childhood and adolescence is a major determinant of bone mass and fracture risk later in life
  - We build 90% of our peak bone mass by age 18
  - If a young adult's BMD is just 10% higher than the mean, it may decrease stress fracture and fracture risk and delay the age of crossing the osteoporosis threshold by 13 years!



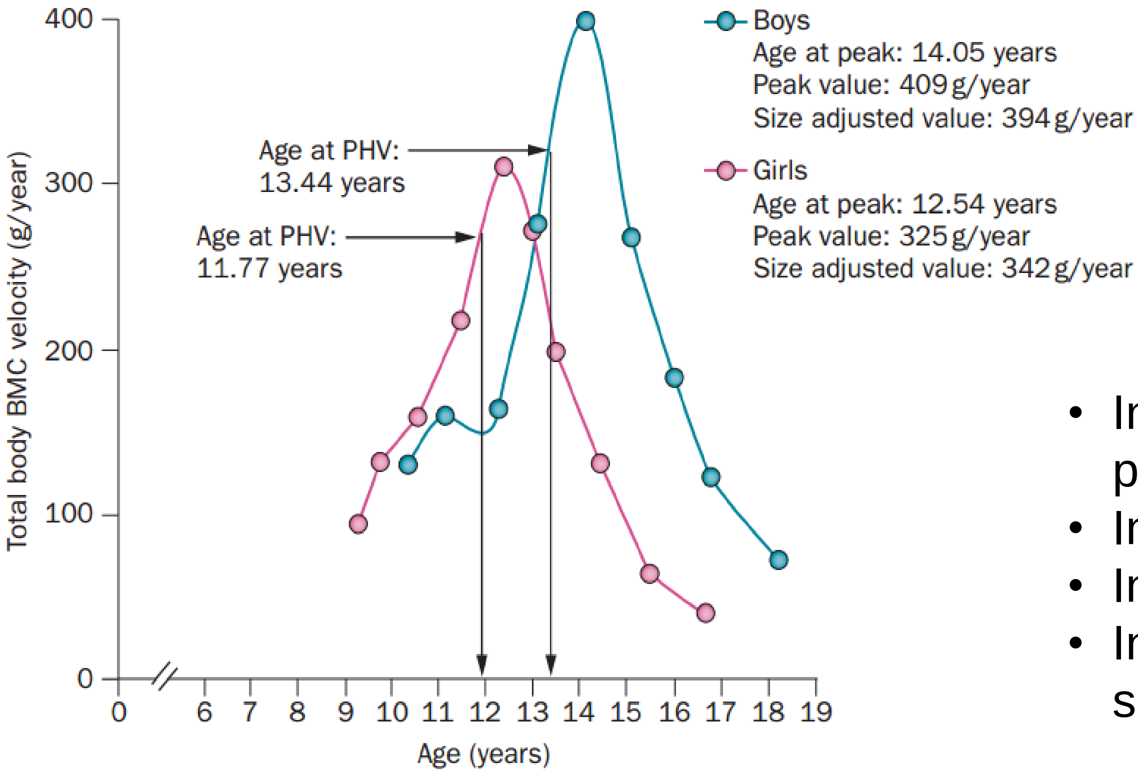
Rizzoli R, et al. Bone, 2010.
Hernandez CJ, et al. Osteoporos Int, 2003.

Determinants of Peak Bone Mass (and Risk of BSI)



Rizzoli R, et al. Bone, 2010.

Bone Accrual and Growth



- Increased cortical porosity
- Increased sports volume
- Increased fragility
- Increased fracture susceptibility

Bailey DA, et al. J Bone Miner Res, 1999.
Farr JM and Khosla S. Nat. Rev. Endocrinol, 2015.

Primary Conditions associated with Bone Fragility

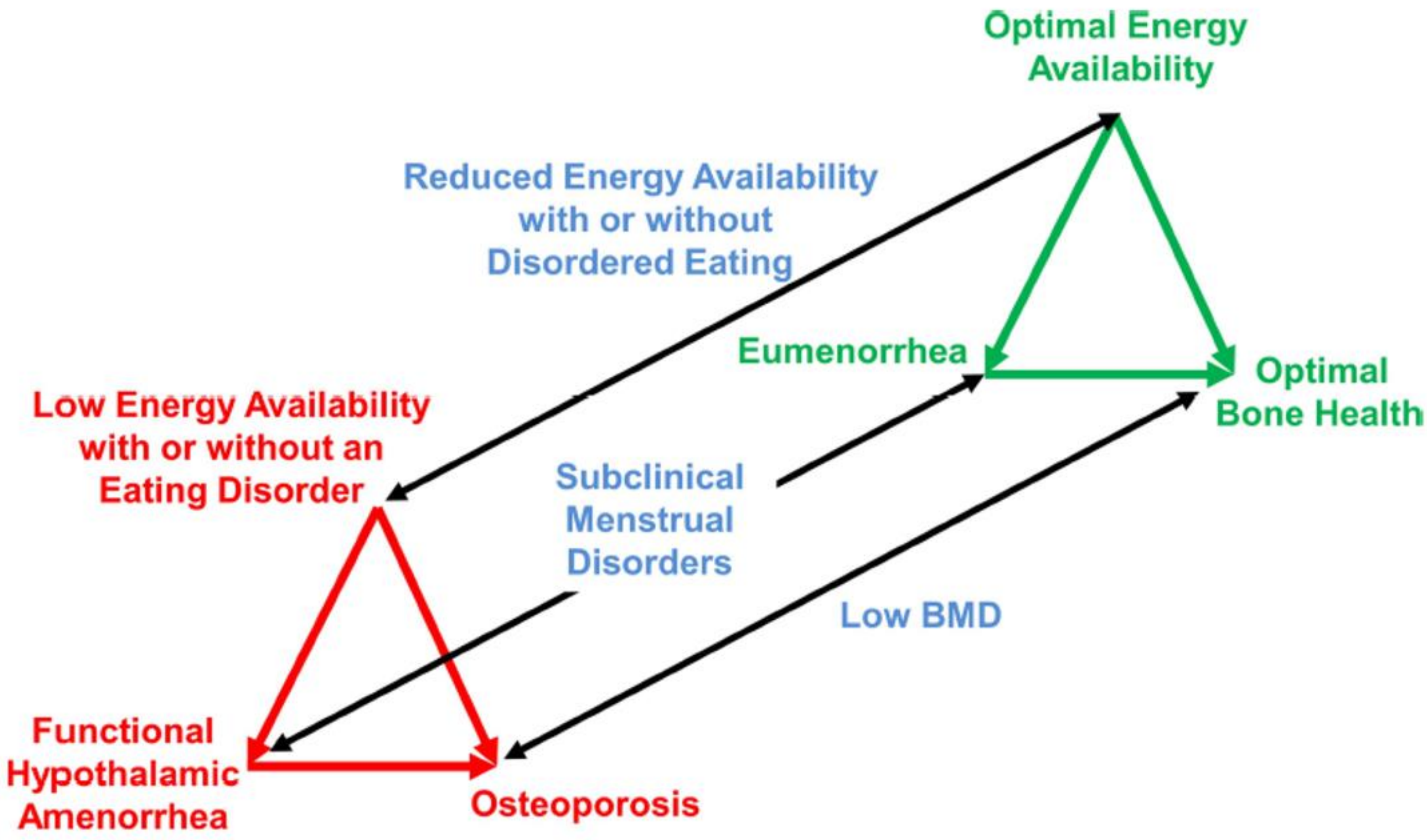
- Impaired collagen gene expression/modification/ cross-link formation
  - Osteogenesis Imperfecta, Bruck syndrome
- Connective tissue defects
  - Ehlers-Danlos syndrome, Marfan syndrome, Homocystinuria
- Defective bone mineralization from low alk phos activity
  - Hypophosphatasia
- Impaired cell signaling and osteoblast function
  - Osteoporosis pseudoglioma syndrome
- Idiopathic Juvenile Osteoporosis

Secondary Conditions associated with Bone Fragility

- Medication induced
  - Glucocorticoids, Antiepileptic meds, Anticoags, Depo-medroxyprogesterone
- Decreased weight-bearing or muscle bulk
  - Duchenne muscular dystrophy, Cerebral palsy
- Infiltrative conditions
  - Leukemia, Thalassemia
- Chronic inflam. conditions
  - Juvenile idiopathic arthritis, Inflam. bowel disease
- Endocrine abnormalities
  - Hypogonadism, GH deficiency, Hyperpara, Hyperthyroidism, Hypercortisolism
- Vitamin and nutritional deficiencies
  - Vit D deficiency, Celiac disease, Eating disorder, Cystic fibrosis
- Renal disease
  - Renal failure w/ 2° hyperpara, Idiopathic hypercalciuria

Harrington J and Sochett E. Pediatr Clin North Am, 2015.

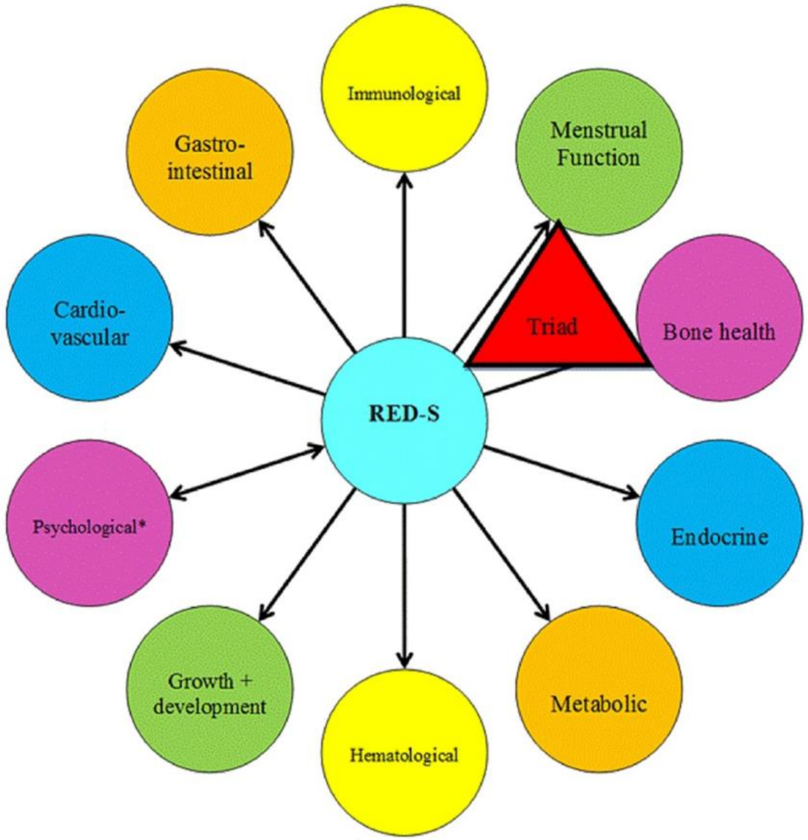
Female Athlete Triad



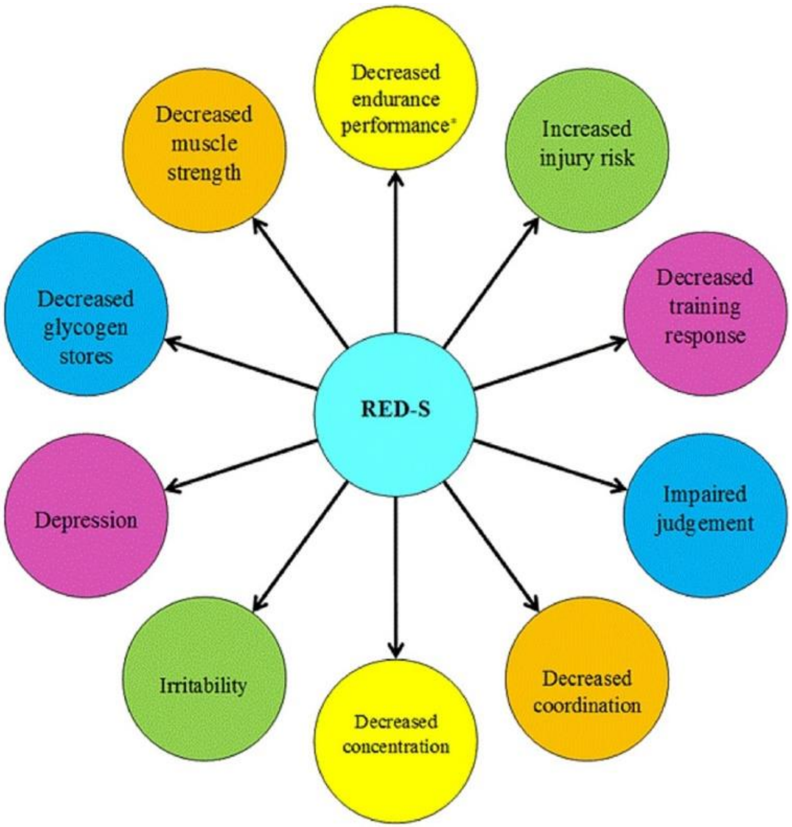
Nattiv A, et al. Med Sci Sports Exerc, 2007.
De Souza MJ, et al. Br J Sports Med, 2014.

Relative Energy Deficiency in Sport (RED-S)

Health



Performance



Mountjoy M, et al. Br J Sports Med, 2014, 2018.

Low energy availability surrogates correlate with health and performance consequences of Relative Energy Deficiency in Sport

Kathryn E Ackerman,[1,2] Bryan Holtzman,[1] Katherine M Cooper,[1] Erin F Flynn,[1] Georgie Bruinvels,[3,4] Adam S Tenforde,[5] Kristin L Popp,[6] Andrew J Simpkin,[4,7] Allyson L Parziale[1]

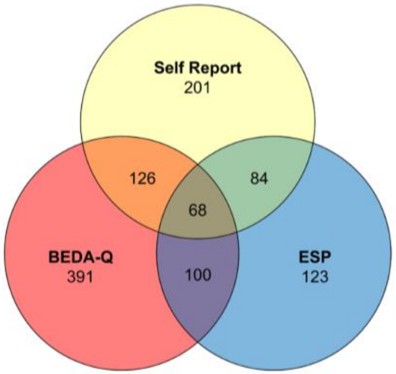


Figure 1 Distribution of participants categorised as low EA by screening tools. Non-overlapping areas represent all participants who were categorised as low EA using that test. Overlapping areas represent the subset of participants who were categorised by two or more tests. Sixty-eight participants met the low EA criteria for all three tests.

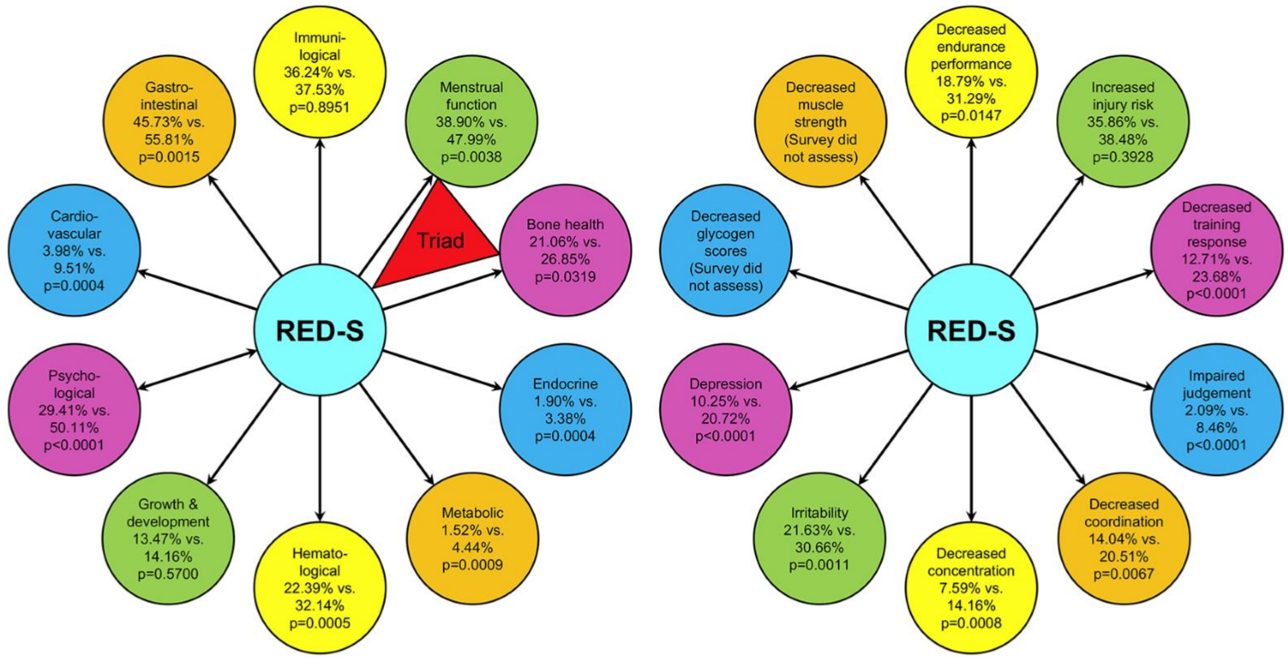


Figure 2 (A) The prevalence of potential health-related RED-S consequences in those with and without ED/DE/high BEDA-Q/ESP score (surrogates for low EA/RED-S). Prevalence expressed as % of adequate EA with health consequence versus % of low EA with health consequence. (B) The prevalence of potential performance-related RED-S effects in those with and without ED/DE/high BEDA-Q/ESP score (surrogates for low EA/RED-S). Prevalence expressed as % of adequate EA with performance consequence versus % of low EA with performance consequence.

Ackerman KE, et al. Br J Sports Med, 2018.

Low Energy Availability

30!

- **Energy Availability (EA):**
  - Dietary energy intake (EI)- Exercise energy expenditure (EEE) normalized to fat-free mass (FFM): **EA= (EI- EEE)/FFM**
  - Ex. **EI**= 2000 kcal/d, **EEE**= 600 kcal/d, **FFM**= 51 kg

    (2000-600)/51 = 27.5 kcal/kg of FFM/d

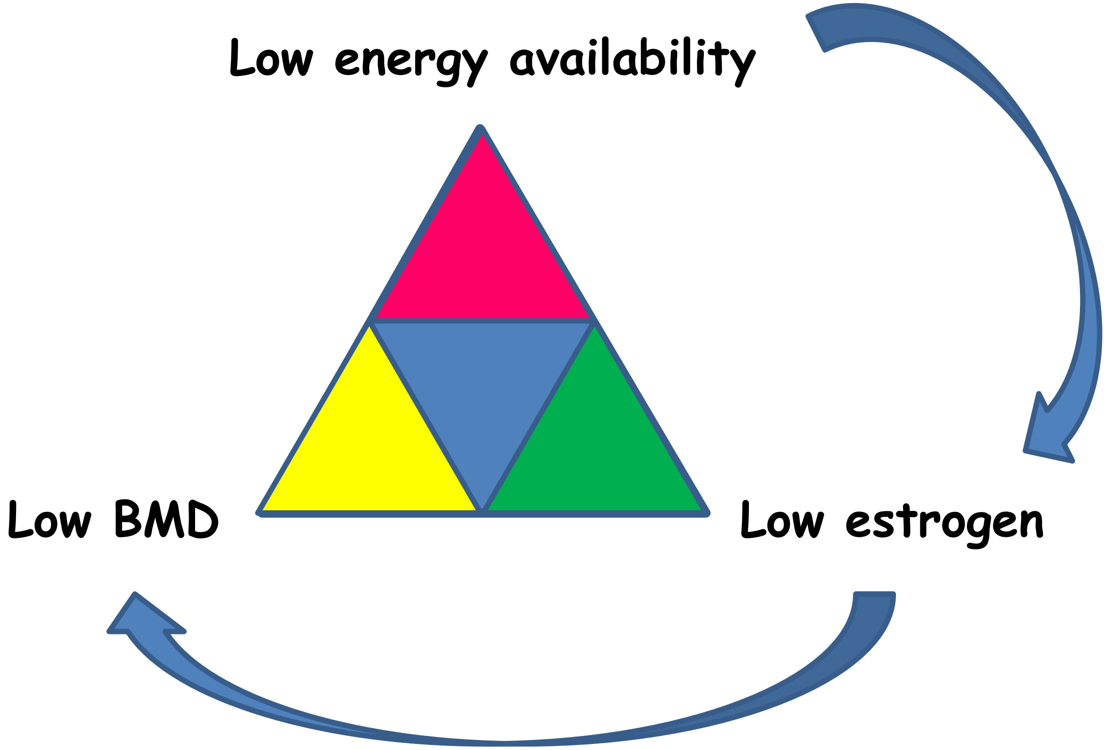
- **Exercise energy expenditure:** energy expended during exercise in excess of energy that would have been expended in non-exercise activity during same time interval

45 may be the target

Loucks AB, Thuma JR. J Clin Endocrinol Metab, 2003.
Nattiv A, et al. Med Sci Sports Exerc, 2007.
Heikura IA, et al. Int J Sport Nutr Exerc Metab, 2018.

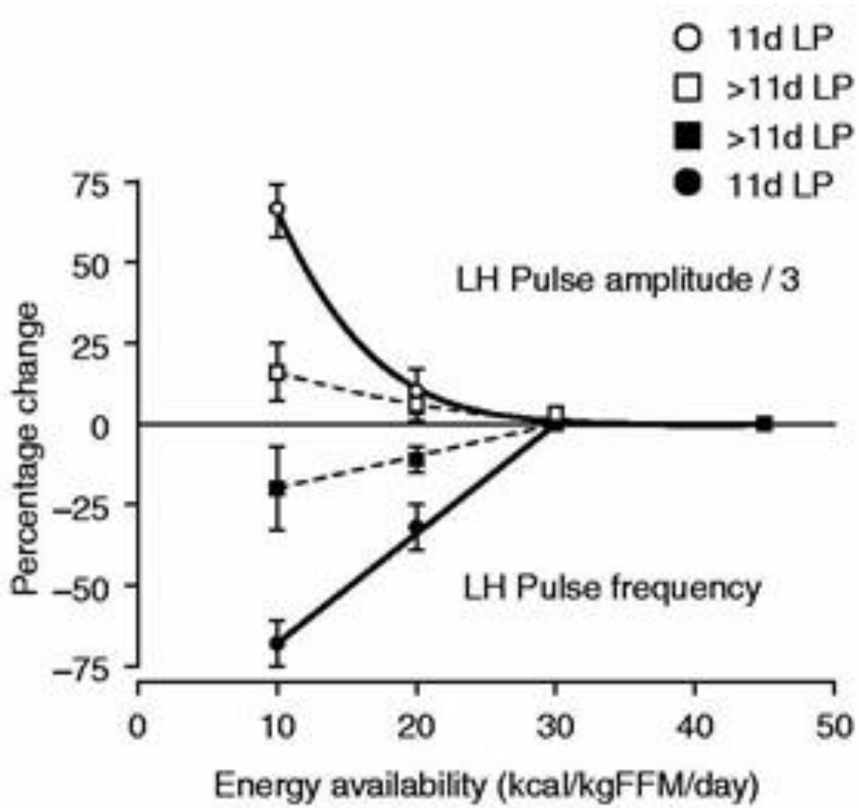
Interrelationship of Components of the Triad

- ***Negative Energy Balance*** **→ Disruption of the Hypothalamic-Pituitary-Ovarian (HPO) axis**



Energy Availability and Menstrual Function

Dose-response relationship between EA and LH pulsatility



Loucks AB, Thuma JR. J Clin Endocrinol Metab, 2003.

Interrelationship of Components of the Triad

- As energy availability ↓ below 30 kcal/kg FFM/day
  - **Bone protein synthesis and mineralization ↓**
  - **Insulin, which enhances amino acid uptake, ↓**
  - **IGF-1 ↓**
  - **T3 ↓**

- These effects occurred within **5 days** of the onset of energy deficiency, and without a reduction in estrogen concentration!

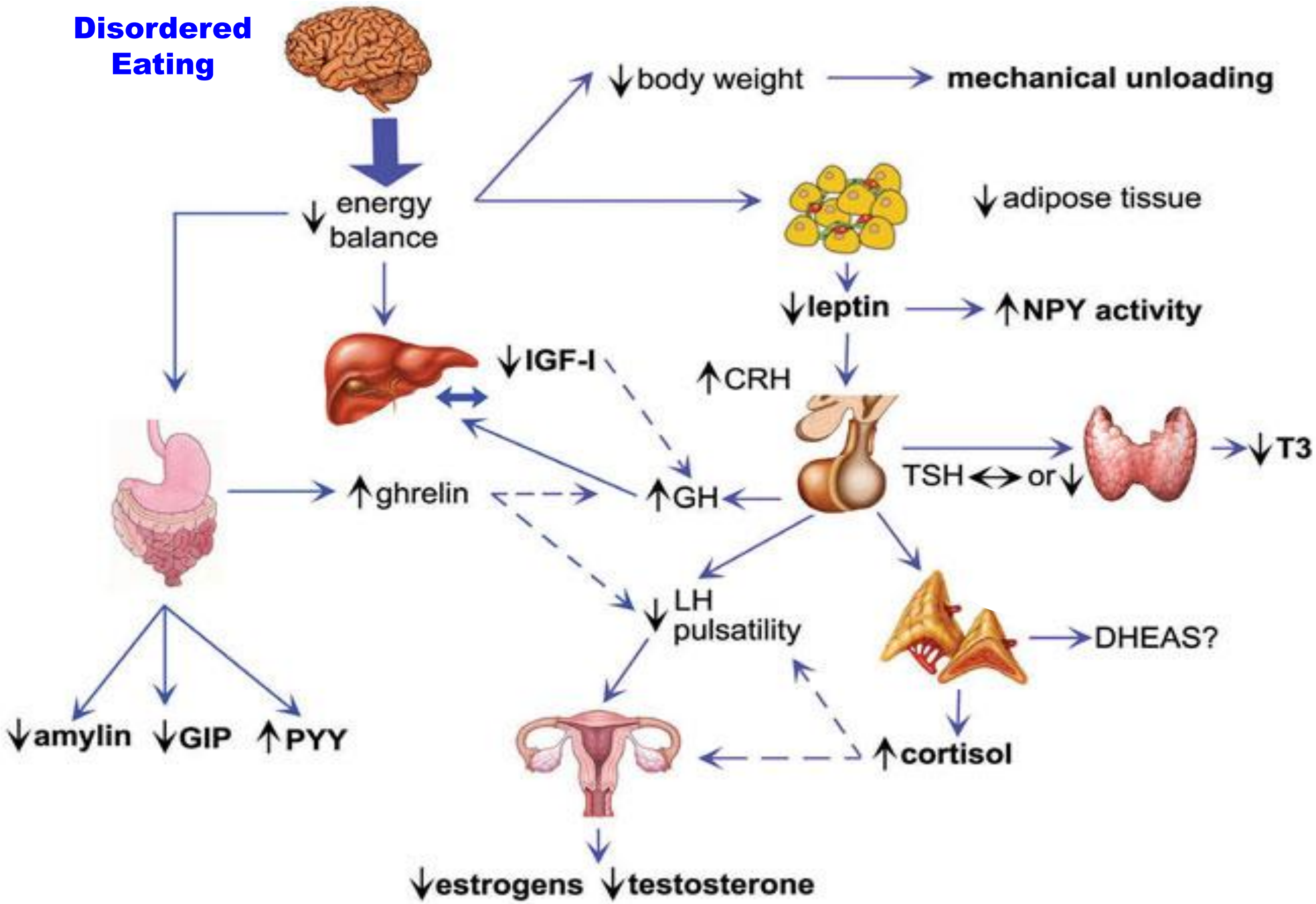
Loucks A, et al. J Sports Sci, 2011.

Interrelationship of Components of the Triad

- Low energy availability
  - ↓ BMI, fat mass, & lean mass
  - ↓ in FSH, LH, estradiol, androgens
  - ↓ insulin, glucose, IGF-1, T_3, and leptin
  - ↑ in fasting PYY, ghrelin, cortisol, and GH resistance

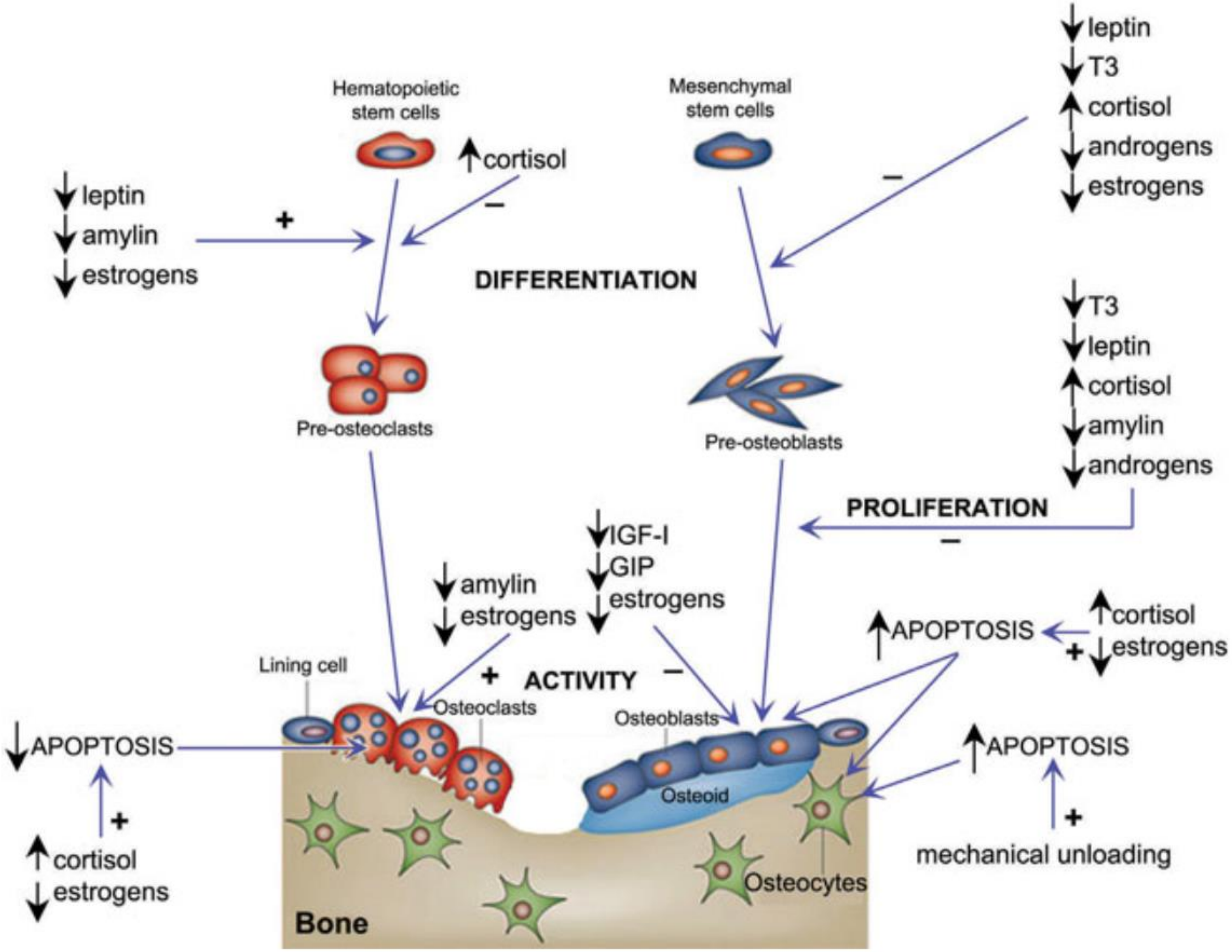
Gordon C, et a. JCEM, 2017.
Ackerman K and Misra M. "Neuroendocrine Abnormalities in Female Athletes" in The Female Athlete Triad- A Clinical Guide, 2015.

Mechanisms of adaptive alterations similar to Anorexia Nervosa



Dede AD, et al. Hormones, 2014.

Hormonal Effects on Bone



Dede AD, et al. Hormones, 2014.

Endocrine Changes with Low EA

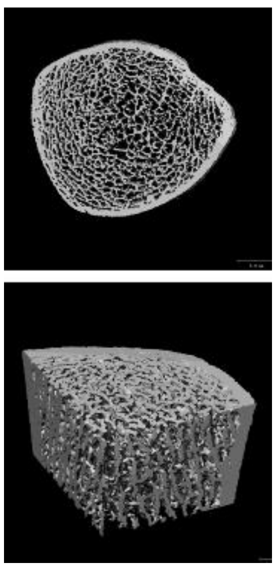
	Females	Males
Hypothalamic-Pituitary-Gonadal Axis		
LH	↔, ↓	↑, ↔, ↓
FSH	↔	↓
Estradiol	↓	↓
Testosterone	↑, ↔, ↓	↔, ↓
Progesterone	↓	
Energy Homeostasis, Appetite		
Resting metabolic rate	↓	↓
Leptin	↓	↓
Adiponectin	↑, ↔	
Ghrelin	↑	↔
Peptide YY	↑	↑
Oxytocin	↓	↓
Insulin	↓	↓
Amylin	↓	

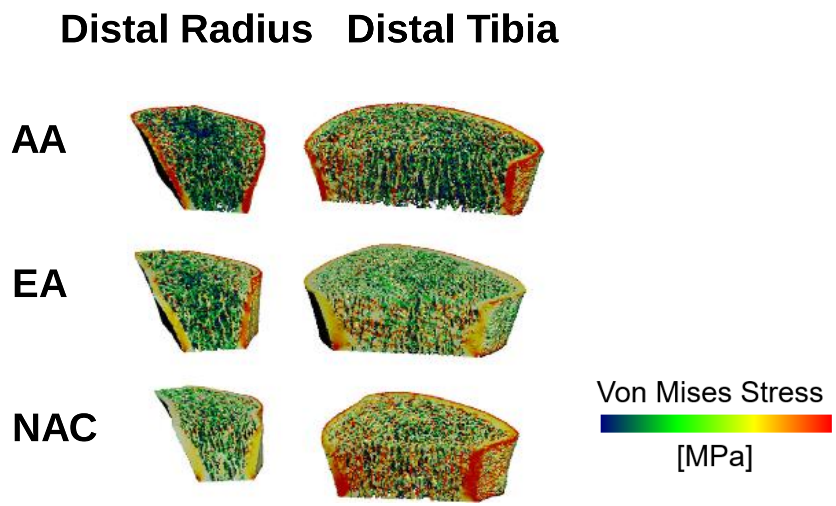
	Females	Males
Hypothalamic-Pituitary-Adrenal Axis		
Cortisol	↑, ↔	↔
Hypothalamic-Pituitary-Thyroid Axis		
TSH	↔	↔
T3	↓	↓
Free T3	↓	↓
T4	↑, ↔, ↓	↓
Free T4	↔, ↓	↓
Growth Hormone and IGF-1 Axis		
GH	↑	↑
IGF-1	↔, ↓	↑, ↓
IGF binding protein-1	↑	↑

Elliott-Sale Elliott-Sale KJ, Tenforde AS, Parziale AL, Holtzman B, Ackerman KE. Int J Sport Nutr Exerc Metab, 2018.

Bone Density and Structure in Adolescent and Young Adult Female Athletes

- Athletic activity → ↑ cross-sectional bone area at tibia
- **Amenorrhea in athletes →**
  ↓ trabecular # & ↓ cortical thickness →↓ trabecular & total BMD → decreased stiffness and failure load **(i.e. weaker bones!)**

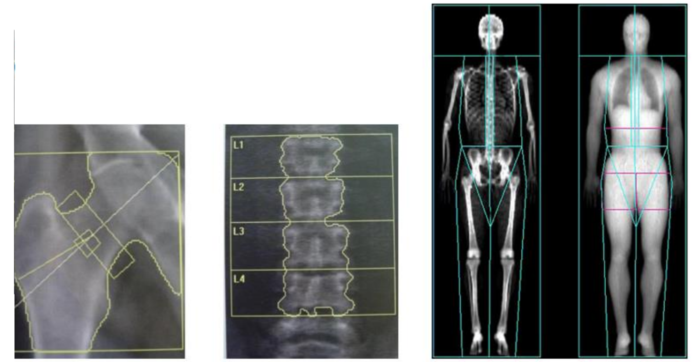




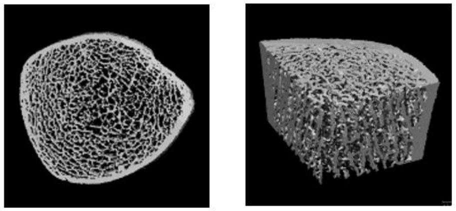
Ackerman KE, et al. J Clin Endocrinol Metab, 2011; Ackerman KE, et al. Bone, 2012.

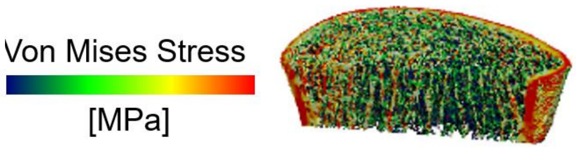
Fractures in Relation to Menstrual Status and Bone Parameters in Young Athletes

- 175 females 14-25 year olds were studied
  - 100 oligo-amenorrheic athletes (AA)
  - 35 eumenorrheic athletes (EA)
  - 40 non-athlete controls (NA)



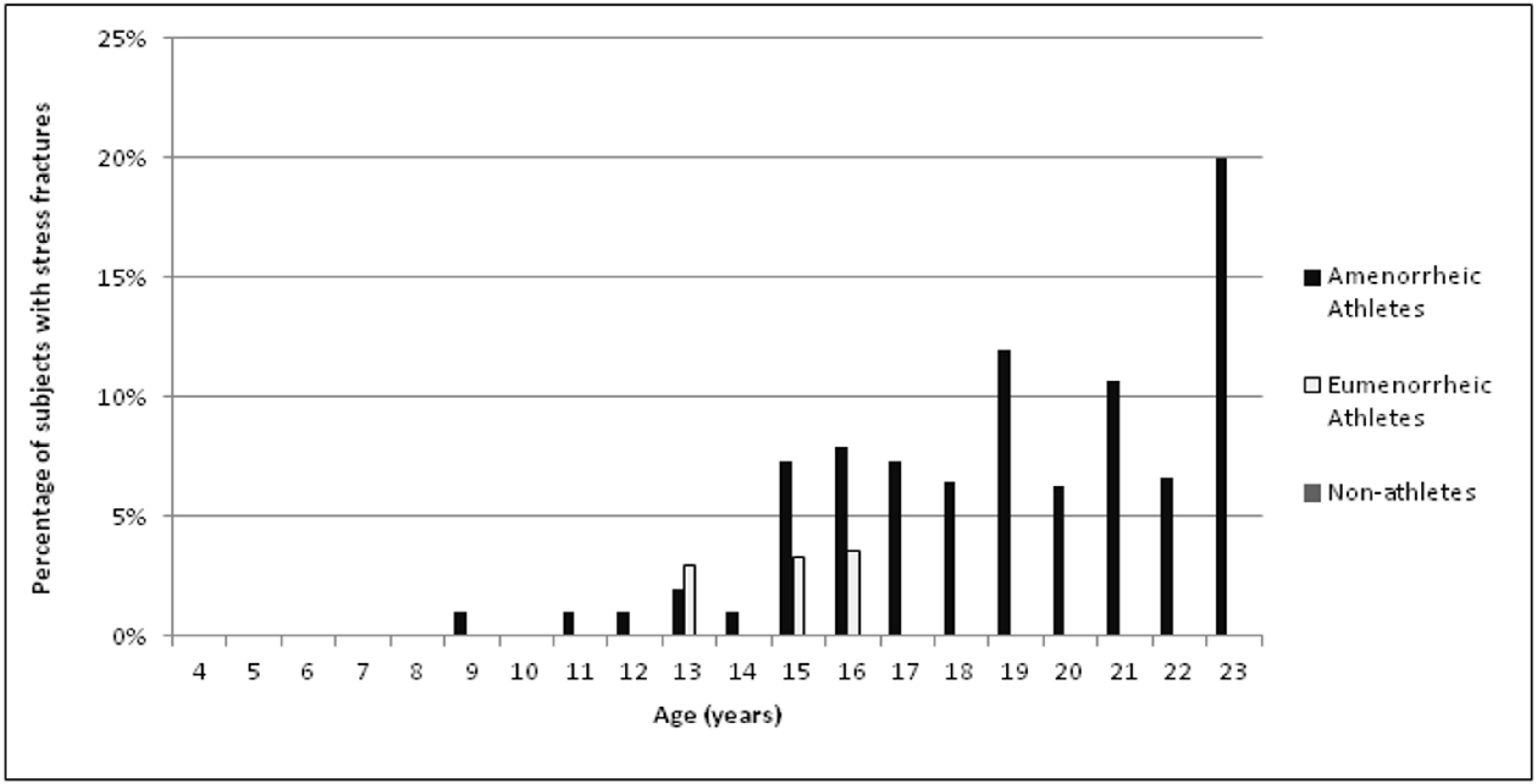
- Lifetime fracture history was obtained through participant interviews
- Areal BMD was assessed by DXA at the spine, hip and whole body
- Bone structure was assessed by HRpQCT at the radius and tibia, and strength by finite element analysis





Ackerman KE, et al. Med Sci Sports Exerc, 2015.

Proportion of Subjects with *Stress Fracture* each Year



Ackerman KE, et al. Med Sci Sports Exerc, 2015.

DXA and HRpQCT Data in AA according to Stress Fracture History

	< 2 Stress Fx	≥2 Stress Fx	P
DXA (BMD Z-scores)	n=84	n=16	
Lumbar Spine	-0.61±1.20	-1.58±0.87	**0.003**
Whole Body	-0.55±1.02	-1.09±0.94	**0.05**
HRpQCT Radius	n=71	n=13	
Total area (mm^2)	267.9±45.8	240.7±32.9	**0.045**
Ct. porosity (%)	1.2±0.9	0.8±0.5	**0.07**
Tb. thickness (mm)	0.071±0.011	0.067±0.009	**0.25**
Tb. vBMD (mg HA/cm^3)	168.5±32.2	148.1±21.2	**0.03**
Outer Tb. vBMD (mg HA/cm^3)	226.8±31.1	204.5±21.0	**0.02**
Inner Tb. vBMD (mg HA/cm^3)	128.3±33.8	109.0±21.9	**0.05**
Stiffness (kN/m)	74.3±13.7	63.0±12.1	**0.007**
Failure load (kN)	3.78±0.68	3.18±0.60	**0.004**
HRpQCT Tibia	n=73	n=14	
Stiffness (kN/m)	230.7±30.3	213.8±28.0	**0.05**
Failure load (kN)	11.5±1.5	10.7±1.4	**0.048**

Ackerman KE, et al. Med Sci Sports Exerc, 2015.

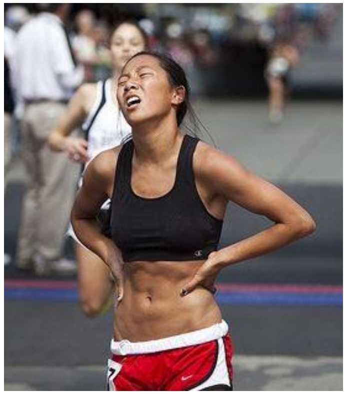
Low BMD in Male Athletes a/w BSIs at Bones with Greater Trabecular Composition

- 28 male athletes (ages 14-36 y) referred for bone health eval after sustaining lower extremity fractures
  - Trabecular-rich locations (pelvis, femoral neck, and calcaneus) vs. cortical-rich locations only (tibia, fibula, femur, metatarsal and tarsal navicular)
  - 12 (43%) had low BMD
  - Athletes with trabecular-rich BSIs had a 4.6X ↑ risk for low BMD vs. those with only cortical-rich BSIs
  - Runners had 6.1X increased risk for low BMD vs non-runners

	Trabecular-Rich BSIs (n = 11)	Cortical-Rich BSIs (n = 17)	*P* Value
Age, y	22.73 ± 7.65	16.78 ± 1.29	.004
Height, cm	176.99 ± 6.92	177.38 ± 5.99	.88
Weight, kg	70.47 ± 7.14	69.44 ± 8.43	.74
BMI, kg/m^2	22.44 ± 1.80	22.04 ± 2.12	.61
LS			
Z-score	–1.06 ± 1.21	0.271 ± 0.89	.002
BMD	0.91 ± 0.17	1.02 ± 0.11	.065
TBLH			
Z-score	–1.63 ± 0.23	–0.34 ± 0.60	.008
BMD	0.85 ± 0.08	1.02 ± 0.06	.007
TH			
Z-score	0.35 ± 0.95	0.58 ± 1.27	.67
BMD	1.08 ± 0.15	1.07 ± 0.21	.95
FN			
Z-score	0.24 ± 1.14	0.48 ± 1.12	.67
BMD	0.95 ± 0.16	1.02 ± 0.16	.39
Vit D, ng/mL	27.89 ± 10.27	35.83 ± 9.83	.64

Tenforde AS…Ackerman KE. Am J Sports Med, 2017.

What questions to ask



- ROS
- Medical hx
  - – fracture hx (location, when, etc.)
  - – growth hx
- Medications
- Pubertal/menstrual hx
- Pregnancy/lactation hx
- Sexual function
- Training hx
- Dietary hx
- Fam hx
  - – fractures, osteoporosis, delayed puberty, endocrine disorders

What to look for on Physical Exam

- Height & weight (BMI)
- BP and pulse (orthostatics prn)
- HEENT: blue sclera, proptosis, gross visual fields, dentition, thyromegaly, LA
- CV
- Lungs
- Abdomen
- Maturation
- Bone pain/deformities
- Reflexes
- Flexibility/laxity
- Skin color
- Tremor?

Imaging to Consider- DXA

- DXA (with bone age in kids/adolescents)

- Z-score < -1.0 in a weight-bearing athlete
  - Investigate further

Labs to Consider

- BASIC:
  - Complete Metabolic Panel
  - Phos
  - Mg
  - PTH
  - 25(OH) Vitamin D
  - CBC
  - Urine Calcium/Creatinine
  - TSH
  - Celiac screen (Total IgA and TTG IgA)
  - ESR, CRP
  - Iron studies
- PRN:

  - Other endocrine labs (prolactin, FSH, estradiol, etc.); Further GI work-up; Myeloma screen; Genetic testing (COL1A1, COL1A2, karyotype, etc.)

At a minimum- What everyone should know about optimizing bone health

- Weight-bearing activity with adequate recovery and caloric intake is important
- General Calcium and D Recommendations

AGE	CALCIUM RDA	VITAMIN D RDA	VITAMIN D LEVEL
4-9	1000 mg in divided doses	600 IU*	30 - 50 ng/mL
9-18	1300 mg in divided doses	600 IU*	30 - 50 mg/dL
19+	1000 mg in divided doses	600 IU*	30 - 50 ng/dL

* May need more vitamin D to reach level > 30, so many bone specialists recommend ≥800-1000 IU/day

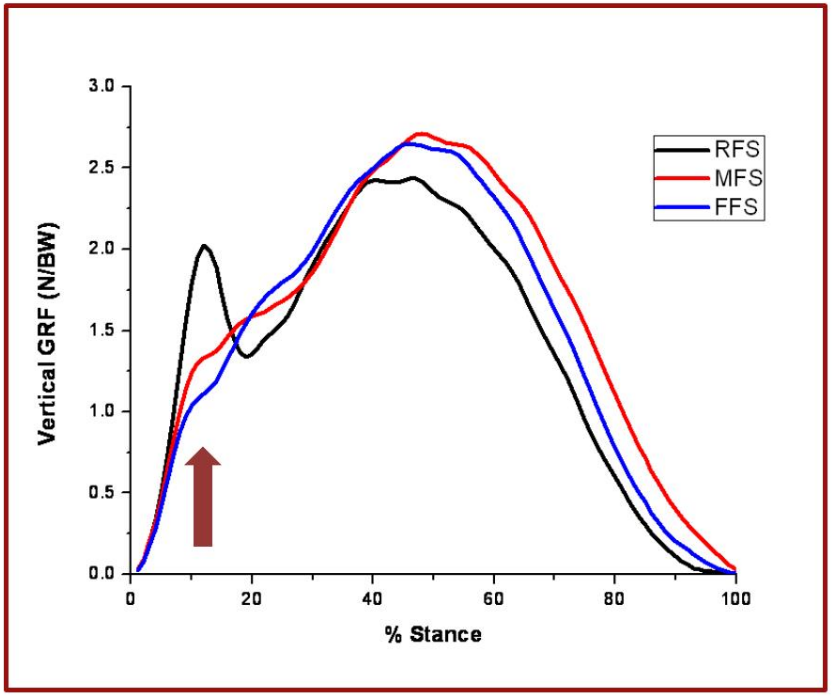
- Some literature suggests that athletes may need higher doses of calcium

Treatment Options

- Interdisciplinary Approach-
  - Address Biomechanical, Behavioral, and Biological Factors

Gordon CM, Ackerman KE, et al. Functional Hypothalamic Amenorrhea:
An Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab; May 2017.

Biomechanics- Strengthening, Stretching, Gait Assessment/Retraining



Images courtesy of A. Tenforde, MD

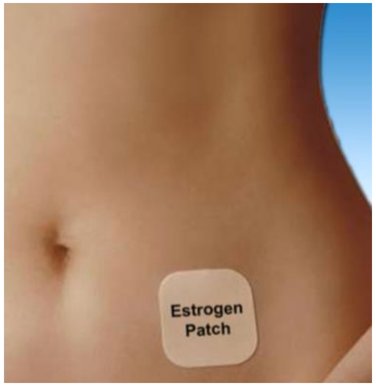
Nutrition and Training Modification

Transdermal Estrogen?

- 121 oligo-amenorrheic athletes 14-25 years old were randomized to receive:
  - 100 mcg 17-β estradiol transdermal patch applied continuously with cyclic oral micronized progesterone (200 mg for 12 days of each month) (PATCH group)

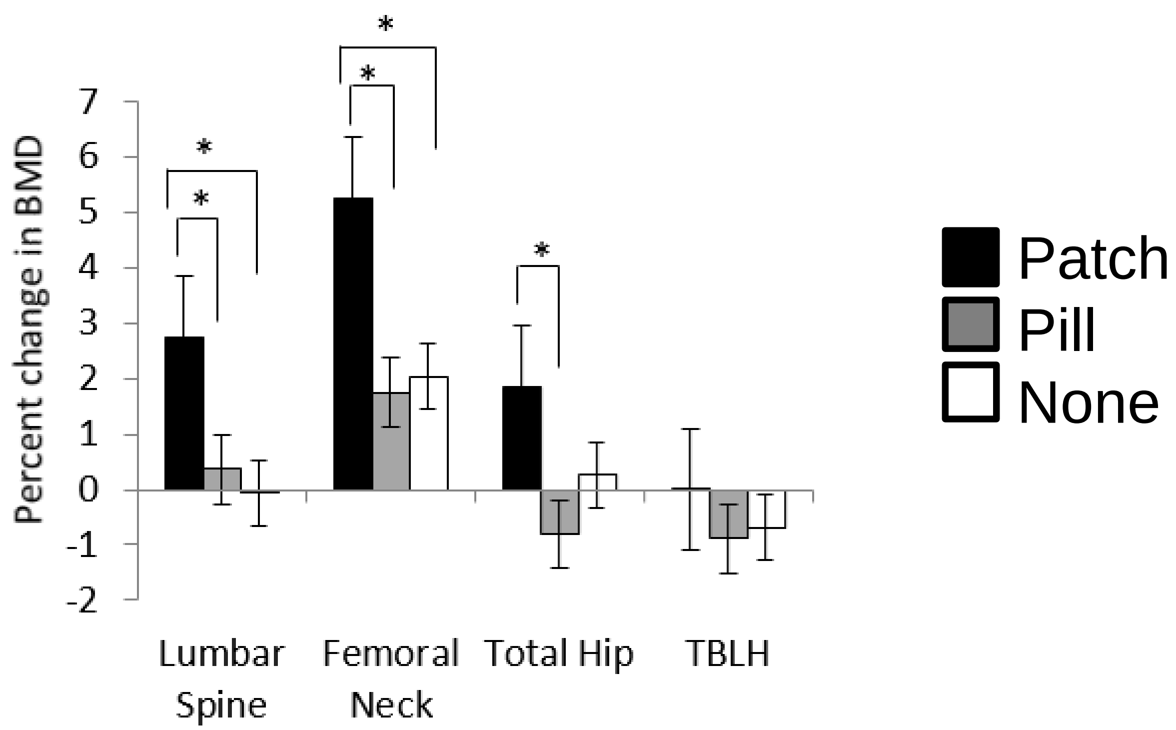
    or
  - 30 mcg ethinyl estradiol oral pill with 0.15 mg desogestrel daily with a week of placebo pills every month (PILL group)

    or
  - no estrogen/progesterone (NONE)



Transdermal Estrogen + Cyclic Oral Progesterone: Greater Increases in BMD

1 year of treatment



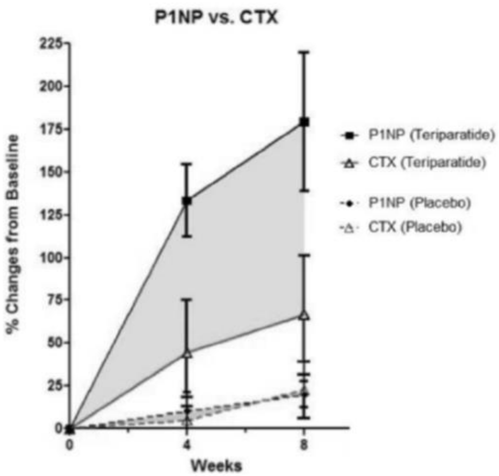
Ackerman KE, et al. Br J Sports Med, 2018.

Bisphosphonates

- Antiresorptive agents that inhibit osteoclast function
- Have been used in case series/case reports
- Used off label in professional athletes
- Low energy availability and amenorrhea can both increases bone loss and suppress formation, but bisphosphonates do not address issue of reduced bone formation
- Not recommended in premenopausal women secondary to the long half-life of these drugs (up to 10 years) and their potential teratogenic effects
- Not FDA-supported

Teriparatide?

- An anabolic agent used in some forms of osteoporosis
- A PTH analog that activates osteoblasts more than osteoclasts when used intermittently (e.g. daily injection)
- Used off-label to accelerate fracture healing
  - Almiral et al.: trial for stress fracture tx in women (6 teriparatide vs. 7 placebo)
    - Better anabolic window
    - larger cortical area and thickness vs. placebo at the tibia (placebo group had a greater total tibia and cortical density
    - MRI: 83.3% of the teriparatide and 57.1% of the placebo-treated group had improved or healed stress fractures ($p = 0.18$).



- Fazeli et al. randomized 21 adult women (mean age 47 y) with anorexia nervosa to teriparatide or placebo:
  - At 6 months, spine BMD increased significantly more with treatment (PA spine, 6.0% $\pm$ 1.4%; lateral spine, 10.5% $\pm$ 2.5%) vs. placebo (PA spine, 0.2% $\pm$ 0.7%; lateral spine, -0.6% $\pm$ 1.0%)
- No studies yet in Triad/RED-S and not appropriate for adolescents
- Not FDA-supported

Almiral EA, et al. J Clin Transl Endocrinol, 2016. Fazeli PK, et al. Clin Endocrinol Metab, 2014.

PREVENTION: FATC's Return to Play Approach

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

De Souza MJ, et al. Br J Sports Med, 2014.

FATC's Return to Play

	Cumulative Risk Score*	Low Risk	Moderate Risk	High Risk
Full Clearance	0 – 1 point	☐		
Provisional/Limited Clearance	2 – 5 points		☐ Provisional Clearance ☐ Limited Clearance	
Restricted from Training and Competition	≥ 6 points			☐ Restricted from Training/ Competition-Provisional ☐ Disqualified

De Souza MJ, et al. Br J Sports Med, 2014.

IOC's RED-S CAT

Mountjoy M. et al. Br J Sports Med. 2015.

HIGH RISK: NO START RED LIGHT	MODERATE RISK: CAUTION YELLOW LIGHT	LOW RISK: GREEN LIGHT
- Anorexia nervosa and other serious eating disorders - Other serious medical (psychological and physiological) conditions related to low energy availability - Use of extreme weight loss techniques leading to dehydration induced hemodynamic instability and other life threatening conditions.	- Prolonged abnormally low % body fat measured by DXA* or anthropometry - Substantial weight loss (5–10 % body mass in one month) - Attenuation of expected growth and development in adolescent athlete	- Appropriate physique that is managed without undue stress or unhealthy diet/exercise strategies
	- Low **EA of prolonged and/or severe nature	- Healthy eating habits with appropriate EA
	- Abnormal menstrual cycle: functional hypothalamic amenorrhea > 3 months - No menarche by age 15y in females	- Healthy functioning endocrine system
	- Reduced bone mineral density (either in comparison to prior DXA or Z-score < -1 SD). - History of 1 or more stress fractures associated with hormonal/menstrual dysfunction and/or low EA	- Healthy bone mineral density as expected for sport, age and ethnicity - Healthy musculoskeletal system
- Severe ECG abnormalities (i.e. bradycardia)	- Athletes with physical/psychological complications related to low EA+/-disordered eating; - Diagnostic testing abnormalities related to low EA +/-disordered eating	
	- Prolonged relative energy deficiency - Disordered eating behavior negatively affecting other team members - Lack of progress in treatment and/or non-compliance	

HIGH RISK RED LIGHT	MODERATE RISK YELLOW LIGHT	LOW RISK GREEN LIGHT
- No competition - No training - Use of written contract	- May train as long as he/she is following the treatment plan - May compete once medically cleared under supervision	- Full sport participation

STEPS	RISK MODIFIERS	CRITERIA	RED-S SPECIFIC CRITERIA
STEP 1 Evaluation of Health Status	MEDICAL FACTORS	- Patient Demographics - Symptoms - Medical History - Signs - Diagnostic Tests - Psychological Health - Potential Seriousness	- Age, sex - See Yellow Light column in RED-S Risk assessment model - Recurrent dieting, menstrual health, bone health - Weight loss/fluctuations, weakness - Hormones, electrolytes, electrocardiogram, DXA - Depression, anxiety, disordered eating/eating disorder - Abnormal hormonal and metabolic function - Cardiac arrhythmia - Stress fracture
STEP 2 Evaluation of Participation Risk	SPORT RISK MODIFIERS	- Type of Sport - Position Played - Competitive Level	- Weight sensitive, leanness sport - Individual vs. team sport - Elite vs. recreational
STEP 3 Decision Modification	DECISION MODIFIERS	- Timing and Season - Pressure from Athlete - External Pressure - Conflict of Interest - Fear of Litigation	- In/out of season, travel, environmental factors - Mental readiness to compete - Coach, team owner, athlete family, sponsors support - If restricted from competition

Sport and Triad Risk Factors Influence Bone Mineral Density in Collegiate Athletes

ADAM S. TENFORDE[1], JENNIFER L. CARLSON[2], KRISTIN L. SAINANI[3], AUDREY O. CHANG[4], JAE HYUNG KIM[5], NEVILLE H. GOLDEN[2], and MICHAEL FREDERICSON[5,6]

- All Triad risk factors were associated with lower BMD Z-scores in univariable analyses
- Only low BMI and oligomenorrhea/amenorrhea were associated with lower BMD in multivariable analyses (all $p<0.05$)

TABLE 4. Influence of sports participation, Triad risk factors, and body composition for low BMD (LS or TB BMD *z*-score < −1.0) reported as rate ratios.

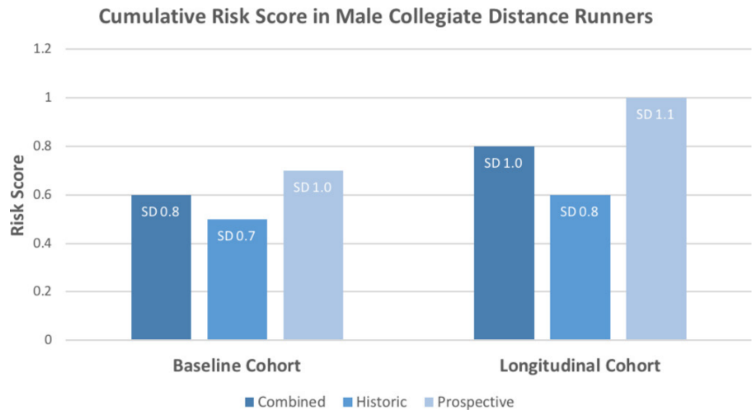
Categories	Unadjusted Model[a]	*P*	Model Adjusted for Triad Risk Factors[a]	*P*	Model Adjusted for Triad Risk Factors and Body Composition[a]	*P*
Sport						
Low-impact (*n* = 47)	1.00 (reference)	—	1.00 (reference)	—	1.00 (reference)	—
Nonimpact (*n* = 81)	0.71 (0.32–1.59)	0.4	1.26 (0.50–3.18)	0.63	1.16 (0.45–2.89)	0.75
Multidirectional (*n* = 58)	0.18 (0.04–0.79)	0.0235	0.31 (0.06–1.53)	0.15	0.20 (0.03–1.48)	0.115
High-impact (*n* = 53)	0.10 (0.01–0.75)	0.0251	0.15 (0.02–1.18)	0.072	0.17 (0.03–1.33)	0.092
Triad risk factors						
Oligomenorrhea/amenorrhea, per point added risk[b]			2.05 (1.27–3.31)	0.0031	2.12 (1.34–3.35)	0.0013
Low BMI, per point added risk[b]			2.01 (1.15–3.51)	0.0145	0.98 (0.59–1.65)	0.95
Body composition						
Lean mass (kg)					0.92 (0.87–0.98)	0.0057
Height (in)					1.21 (0.98–1.48)	0.071

[a]Values represent rate ratio (95% confidence interval).
[b]Quantified risk factor additional point in risk assessment score per De Souza et al. (10).

Tenforde AS, et al. Med Sci Sports Exerc, 2018.

Bone stress injuries in male distance runners: higher modified Female Athlete Triad Cumulative Risk Assessment scores predict increased rates of injury

Emily Kraus,[1] Adam S Tenforde,[2] Aurelia Nattiv,[3] Kristin L Sainani,[1] Andrea Kussman,[1] Megan Deakins-Roche,[1] Sonal Singh,[3] Brian Young Kim,[4] Michelle T Barrack,[5] Michael Fredericson[1]



- The cumulative risk assessment score was associated with higher risk for prospective BSI.
- The baseline model demonstrated each risk assessment point was associated with 37% increased risk for BSI (p=0.0079).
- The longitudinal model found an elevated risk of 27% for each point (p=0.05).
- In the baseline model, prior BSI was associated with 1.57-fold increased risk for BSI (p=0.0042).

Kraus E, et al. Br J Sports Med, 2018.

Characterization of risk quantification differences using Female Athlete Triad Cumulative Risk Assessment and Relative Energy Deficiency in Sport Clinical Assessment Tool

- 1000 female athletes ages 15-30 yrs
- Most of the sample was assigned moderate or high risk for Triad CRA and RED-S CAT (Triad: 54.7% moderate and 7.9% high; RED-S: 63.2% moderate and 33.0% high)
- The tools agreed on risk for 55.5% of athletes. Agreement increased to 64.3% when only athletes with DXA measurements were considered.
- Triad CRA and RED-S CAT provide consensus on the majority of athletes at elevated (moderate or high) risk for low EA, but have less agreement on the specific risk level assigned.

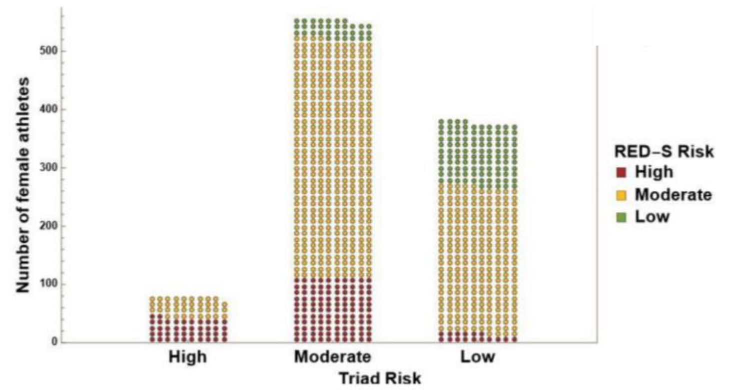


Figure 1: Comparison and overlap of risk level assigned by Triad CRA and RED-S CAT. RED-S CAT identified more athletes as at risk for energy deficiency than Triad CRA.

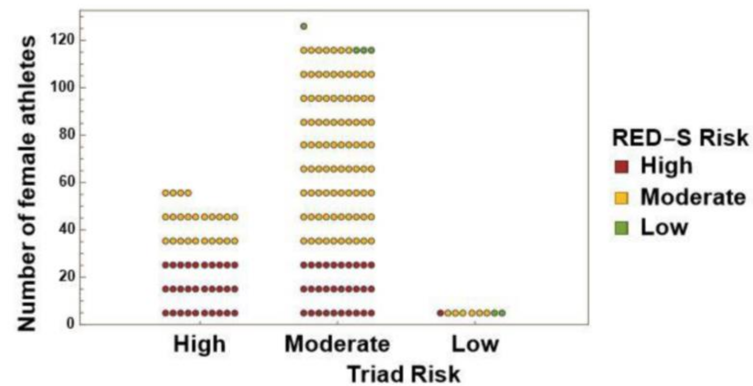


Figure 2: Comparison and overlap of risk level assigned by Triad CRA and RED-S CAT for athletes with DXA BMD measurements available. Triad CRA and RED-S CAT had increased agreement level when compared to the general sample.

Holtzman B, Tenforde AS, Parziale AL, Ackerman KE. Int J Sport Nutr Exerc Metab, 2019.

Conclusions

- Bone Stress Injuries happen and have intrinsic and extrinsic factors
- We need an interdisciplinary approach to address biological, biomechanical, and behavioral issues for treatment and prevention
- Enhanced knowledge of athletes, providers, and coaches is needed
- Currently hormonal treatments are off-label and not recommended
- Screening tools may be helpful
- More research is needed

Thank you!   Question?

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