

Female Athlete Triad: Update and Management

Lana Dani, MD


Primary Care Sports Medicine Fellow

University of Maryland






Disclosure

- I have no actual or potential conflict of interest in relation to this program/presentation
- 




Objectives:

- **Review and Definitions**
 - Prevention
 - Screening
 - Non-pharmacological Management
 - Pharmacological Interventions
- 

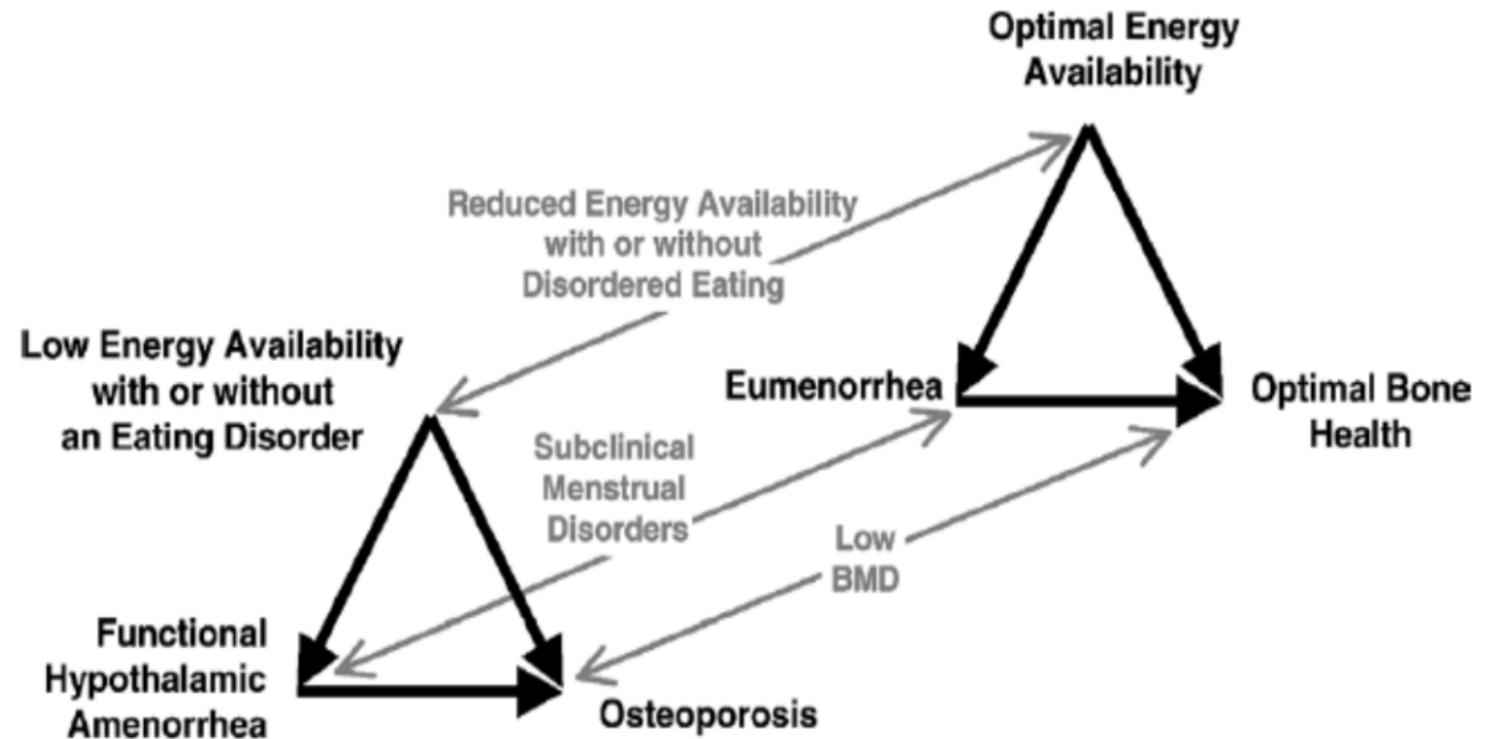


Female Athlete Triad

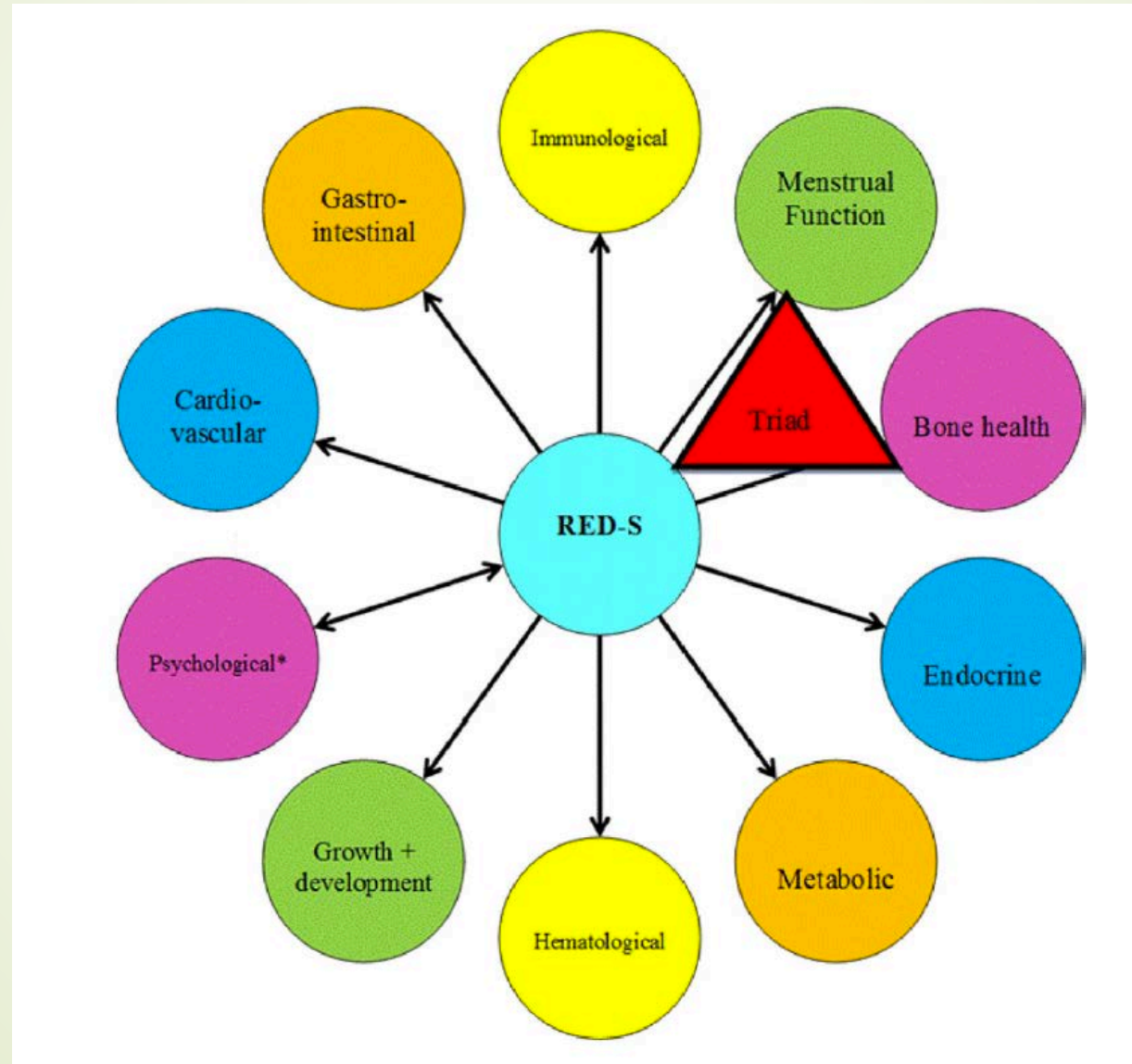
- ▶ One or more of the following criteria:
 - ▶ Low energy availability with or without disordered eating
 - ▶ Menstrual cycle disturbances
 - ▶ Low bone mineral density (BMD)
 - ▶ Sports that emphasize leanness, demand high energy expenditure and/or an aesthetic component (cross country running, gymnastics, figure skating, etc.)
 - ▶ Prevalence of one component of the Triad ranged from 16 to 60% in female athletes.
- 

Female Athlete Triad

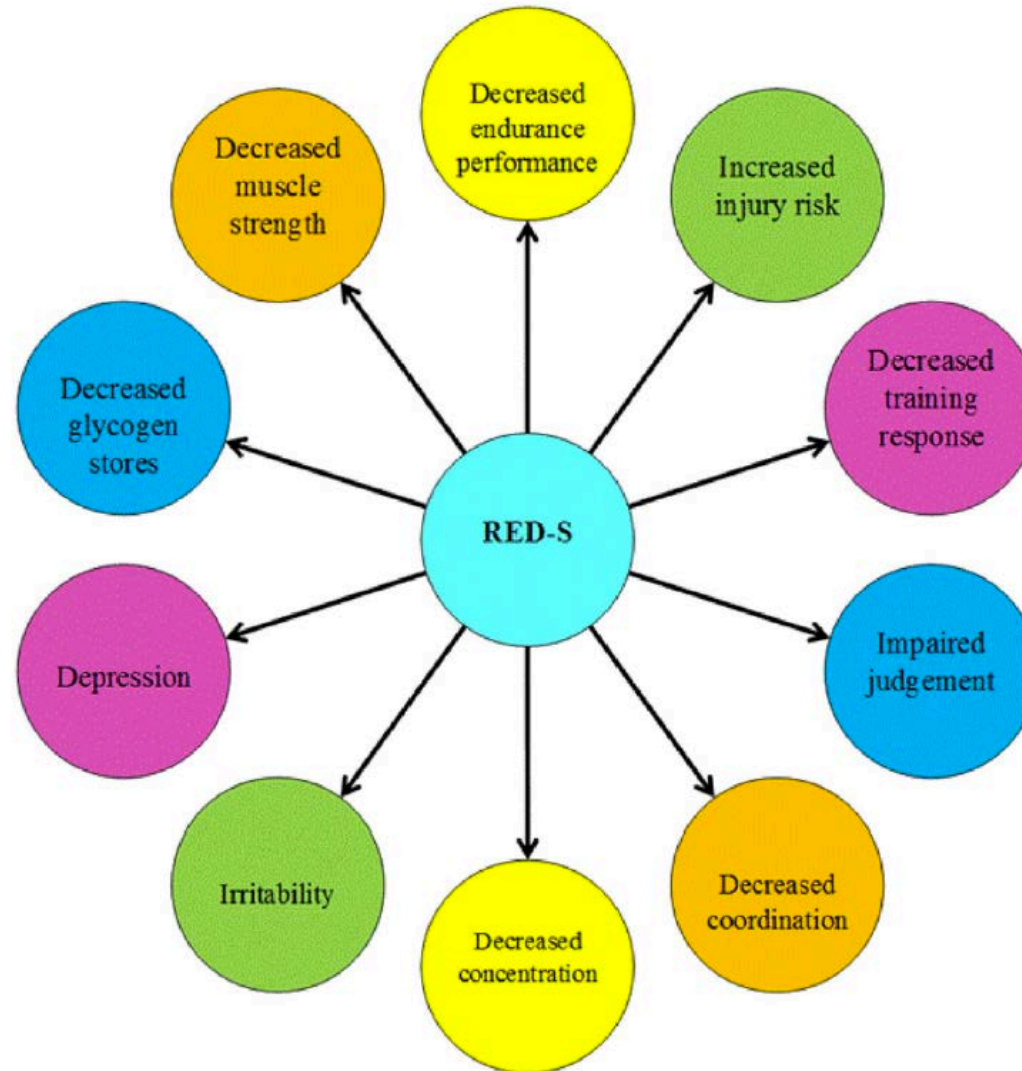
Figure 1



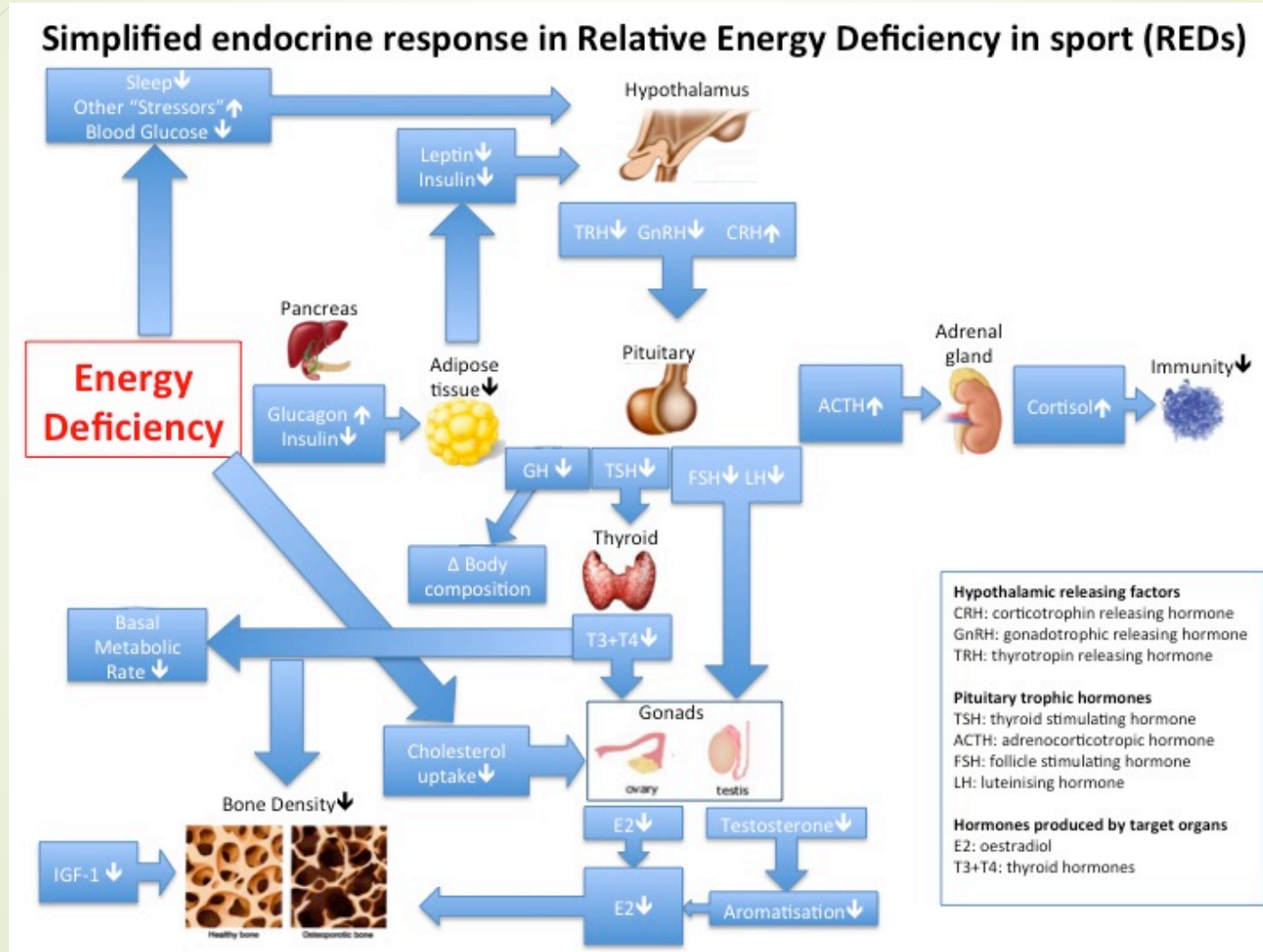
Relative Energy Deficiency in Sports



Relative Energy Deficiency in Sports



Menstrual Function and Bone Health




Energy Availability (EA)

$$\frac{(\text{daily dietary intake (kcal)} - \text{daily exercise energy expenditure (kcal)})}{\text{ffm (kg)}}$$

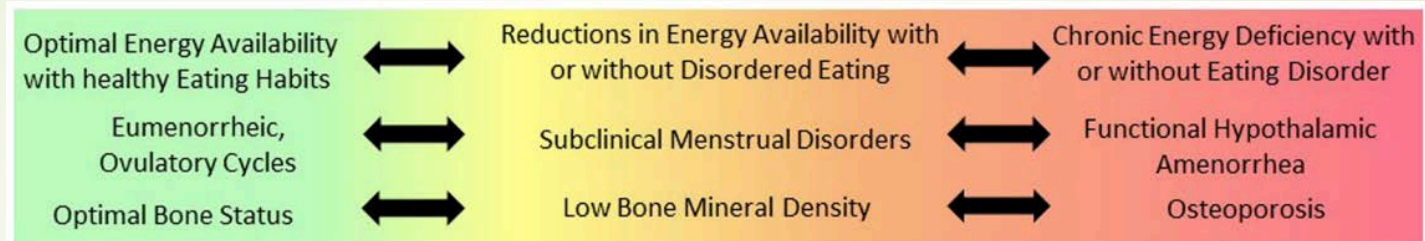
- ▶ Optimal EA for healthy physiological function is achieved at 45 kcal/kg ffm
- ▶ EA < 30 kcal/kg ffm has been shown to affect the hypothalamic-pituitary axis
 - ▶ Slowing of LH pulse frequency → menstrual disturbances
 - ▶ Reduced serum glucose, Ttiiodothyronine, insulin, IGF-1
 - ▶ Decreased GH and cortisol



Measurement of EA

- ▶ How practical and reliable is it?
 - ▶ No standardized or reference protocol for undertaking an EA assessment.
 - ▶ Difficult and expensive to calculate
 - ▶ Will require a lot of equipment and precision to be a stand-alone diagnostic tool
 - ▶ Best surrogate measure is a biomarker.
- 

Measurement of EA



CHANGES IN METABOLIC HORMONE PROFILES ACROSS THE FEMALE ATHLETE TRIAD CONTINUUM

- REE	↓ REE	↓↓ REE
- Total T ₃	↓ Total T ₃	↓↓ Total T ₃
- Ghrelin	- Ghrelin	↑↑ Ghrelin
- PYY	- PYY	↑↑ PYY
- Leptin	↓ Leptin	↓↓ Leptin
- IGF-1	↓ IGF-1	↓↓ IGF-1
- Cortisol	↑ Cortisol	↑↑ Cortisol

CHANGES IN REPRODUCTIVE HORMONE PROFILES ACROSS THE FEMALE ATHLETE TRIAD CONTINUUM


- LH Pulsatility	↓ LH Pulsatility	↓↓ LH Pulsatility
- FSH	↓ FSH	↓↓ FSH
- Estrogen	↓ Estrogen	↓↓ Estrogen
- Progesterone	↓ Progesterone	↓↓ Progesterone

CHANGES IN BMD AND BONE MARKERS ACROSS THE FEMALE ATHLETE TRIAD CONTINUUM

Z-score ≥ -1.0	Z-score -1.0 to -2.0	Z-score ≤ -2.0
- P1NP	↓ P1NP	↓↓ P1NP
- NTx	↓ NTx	↓↓ NTx
- CTX	↓ CTX	↓↓ CTX




Objectives:

- Review and Definitions
 - **Prevention**
 - Screening
 - Non-pharmacological Management
 - Pharmacological Interventions
- 




Prevention of Female Athlete Triad requires increased awareness

- ▶ Feldman, J, et al. "Female Adolescent Athletes' Awareness of the Connection between Menstrual Status and Bone Health" (2011)
 - ▶ 33.3% of 103 adolescent female track athletes reported menstrual irregularity.
 - ▶ High mileage athletes and runners with greater tenure corresponded with more awareness
 - ▶ Higher awareness levels associated with menstrual regularity




Prevention of Female Athlete Triad requires increased awareness

- ▶ Pantano, K, "Current Knowledge, Perceptions and Interventions Used By Collegiate Coaches" (2006)
 - ▶ 64% of 91 NCAA D1 coaches have "heard about the triad".
 - ▶ 43% were able to identify the three components of the triad.
 - ▶ College coaches with a high degree of knowledge had a statistically significant difference in their attitudes and skills.
 - ▶ Knowledge about the triad has no correlation with gender of the coach or years of experience.



Prevention of Female Athlete Triad requires increased awareness

- ▶ Kroschus, E, et. al. "Assessing the Awareness and Behavior of U.S. High School Nurses With Respect to the Female Athlete Triad" (2015)
 - ▶ 28.4% of the 370 nurses had heard of the triad
 - ▶ 13.8% were able to identify the 3 components
 - ▶ 44.5% thought amenorrhea is not normal and requires a medical referral
 - ▶ 40.8% thought amenorrhea was normal but should be reassessed every 3-6 months
 - ▶ 10.8% of responders' schools had policies in place to deal with disordered eating, 0.9% with menstrual irregularity and 4.3% with repeated stress fractures




Prevention of Female Athlete Triad requires increased awareness

- ▶ Curry, E. et al, "Female Athlete Triad Awareness Among Multispecialty Physicians" (2015)
 - ▶ 37% of the responding primary care physicians have heard of the Triad
 - ▶ 51% reported feeling comfortable treating or referring a patient with the Triad
 - ▶ 32% of attendings, 46% of fellows and 44% of resident physicians have heard of the Triad.
 - ▶ Residents and fellows were significantly better at identifying the components of the Triad.
 - ▶ Awareness rates were highest among orthopedists, ob/gyn and PM&R physicians



Objectives:

- Review and Definitions
 - Prevention
 - **Screening**
 - Non-pharmacological Management
 - Pharmacological Interventions
- 



Screening for Female Athlete Triad

- ▶ Female Athlete Coalition Consensus Statement (2014)
 - ▶ Disordered eating
 - ▶ Clinical eating disorder
 - ▶ Intentional weight loss without disordered eating
 - ▶ Inadvertent undereating

Screening for Female Athlete Triad

- Several disordered eating/eating disorder screening tools for the general population

- Eating Disorder Inventory-3

- SCOFF

- ≥ 2 positive answers
- Sensitivity 84.6%-100%
- Specificity 87.5% - 89.6%

- S** Do you make yourself *SICK* (vomit) because you feel uncomfortably full?
- C** Do you worry that you have lost *CONTROL* over how much you eat?
- O** Have you recently lost more than *ONE* stone (15 pounds) in a 3-month period?
- F** Do you believe yourself to be *FAT* when others say you are thin?
- F** Would you say that *FOOD* dominates your life?



Screening for Female Athlete Triad

- ▶ Validated screening tools for the detection of disordered eating behavior in athletes
 - ▶ Athletic Milieu Direct Questionnaire (AMDQ)
 - ▶ Female Athlete Screening Tool (FAST)
 - ▶ American Physiological Screening Test for eating disorders among Female College Athletes.



Screening for Female Athlete Triad

- ▶ Low Energy Availability in Females Questionnaire (LEAF-Q)
 - ▶ Screening tool based on self-reported physiological symptoms
 - ▶ Self-reported physiological symptoms linked to persistent energy deficiency, with or without DE/ED



Screening for Female Athlete Triad

- ▶ Plateau, C. et al., "Female Athlete Experiences of Seeking and Receiving Treatment for an Eating Disorder"
 - ▶ 13 in-person interviews – preliminary study
 - ▶ Challenges to treatment include lack of eating disorder literacy among athletes and coaches
 - ▶ Feeling out of place
 - ▶ Coping with exercise transitions




Screening for Female Athlete Triad

- ▶ In-depth personal interview must be performed to make the diagnosis.
- ▶ Prevalence of energy deficiency is high without the presence of disordered eating.
- ▶ Coaches have difficulty identifying disordered eating and convincing athletes to seek treatment.



Objectives:

- Review and Definitions
 - Prevention
 - Screening
 - **Non-pharmacological Management**
 - Pharmacological Interventions
- 



Non-Pharmacological Management

- ▶ If low energy availability is due to unintentional under eating, nutritional education may suffice (eg, sports dietician).
- ▶ Increased food intake.
- ▶ Changes in food choices.
- ▶ Individualized changes based on athlete's energy expenditure and exercise goals.
- ▶ May need reduction or cessation of exercise.
- ▶ Achieve level of 25-hydroxy vitamin D > 30 ng/mL
- ▶ Adequate consumption of Calcium
- ▶ Cognitive behavioral therapy
- ▶ Non-compliance with therapy may lead to removal of athlete from competition/training

Non-Pharmacological Management

Relative Energy Deficiency in Sport (RED-S) Treatment Contract

RED-S Treatment Contract for _____

Multidisciplinary Team:

- (Physician) _____
- (Psychotherapist/Psychiatrist) _____
- (Exercise physiologist) _____
- (Dietitian) _____
- (Other) _____

Requirements

Meet with:

- The psychotherapist at intervals recommended by the health professional treatment team
- The dietitian at intervals recommended by the health professional treatment team
- The physician at intervals recommended by the health professional treatment team
- Follow daily meal plan developed by the health professional treatment team
- Follow the adapted training plan developed by the health professional treatment team
- If underweight, weight gain expected to be _____ kg per week/weight stable within week _____
- If underweight, must achieve minimal acceptable body weight/fat of _____ kg/percent by _____
- Regular weigh-in at the following time intervals of _____ week (s)
- After this date, _____ (dd/mm/yyyy), must maintain weight and % fat at or above minimal acceptable body weight/fat mass of _____ (kg/%)
- Other _____

If **ALL** requirements are met and the eating behavior (and other severe conditions) are normalized the Team Physician will decide if cleared for competition.

I, _____ have read this contract and all of my questions were answered.

Athlete Name

Athlete Signature

Date

Team Physician Name

Team Physician Signature

Date



Non-Pharmacological Management

- ▶ Mallison, R., "A Case Report of Recovery of Menstrual Function Following a Nutritional Intervention in Two Exercising Women With Amenorrhea of Varying Duration (2013).
 - ▶ 19 yo female with 11 months of amenorrhea.
 - ▶ Menses resumed after 2.5 months of increased daily dietary intake by 500 kcal.
 - ▶ Menses continued to be irregular for several cycles.
 - ▶ Estrogen levels increased 64.3% compared to baseline.
 - ▶ No increase in BMD in 12 months but there was an increase by 49.6% in P1NP, a marker of bone formation



Non-Pharmacological Management

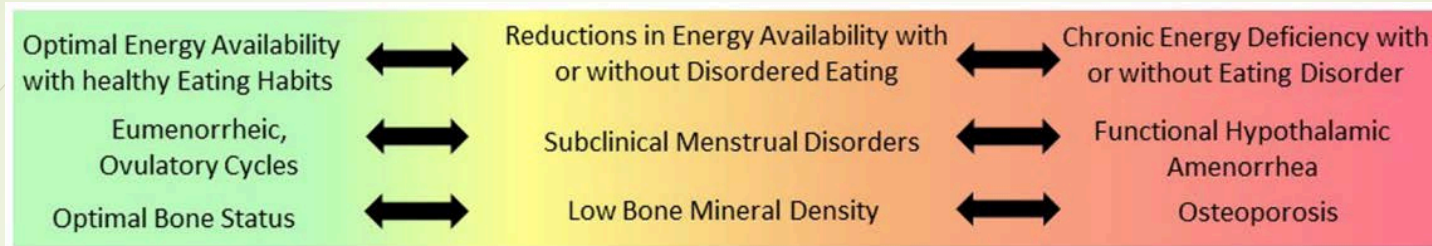
- ▶ Ruohola, J., "Association Between Serum 25(OH)D Concentrations and Bone Stress Fractures in Finnish Young Men (2006).
 - ▶ 756 army recruits
 - ▶ Median serum 25(OH)D of recruits with stress fractures was significantly lower than in the group without stress fracture.
 - ▶ Recruits with serum concentration of 25(OH)D < 30 ng/mL had a significantly higher number of stress fractures.



Non-Pharmacological Management

- ▶ Michopoulos, V., "Neuroendocrine recovery initiated by cognitive behavioral therapy in women with functional hypothalamic amenorrhea: a randomized controlled trial" (2013).
 - ▶ Sample of 8 women in CBT.
 - ▶ 87.5% exhibited a decrease in cortisol levels vs 33% in control arm (9 women).
 - ▶ 75% of women in CBT resumed ovulation vs. 33% in the control arm.
 - ▶ BMI was not affected by CBT
 - ▶ Leptin levels were increased in women who underwent CBT, whereas leptin remained constant in women in the control arm
 - ▶ TSH levels in women who underwent CBT increased, but did not change in women in the control arm

Future of Non-Pharmacological Management



CHANGES IN METABOLIC HORMONE PROFILES ACROSS THE FEMALE ATHLETE TRIAD CONTINUUM

- REE	↓ REE	↓↓ REE
- Total T ₃	↓ Total T ₃	↓↓ Total T ₃
- Ghrelin	- Ghrelin	↑↑ Ghrelin
- PYY	- PYY	↑↑ PYY
- Leptin	↓ Leptin	↓↓ Leptin
- IGF-1	↓ IGF-1	↓↓ IGF-1
- Cortisol	↑ Cortisol	↑↑ Cortisol

CHANGES IN REPRODUCTIVE HORMONE PROFILES ACROSS THE FEMALE ATHLETE TRIAD CONTINUUM


- LH Pulsatility	↓ LH Pulsatility	↓↓ LH Pulsatility
- FSH	↓ FSH	↓↓ FSH
- Estrogen	↓ Estrogen	↓↓ Estrogen
- Progesterone	↓ Progesterone	↓↓ Progesterone

CHANGES IN BMD AND BONE MARKERS ACROSS THE FEMALE ATHLETE TRIAD CONTINUUM

Z-score ≥ -1.0	Z-score -1.0 to -2.0	Z-score ≤ -2.0
- P1NP	↓ P1NP	↓↓ P1NP
- NTx	↓ NTx	↓↓ NTx
- CTX	↓ CTX	↓↓ CTX



Objectives:

- Review and Definitions
 - Prevention
 - Screening
 - Non-pharmacological Management
 - **Pharmacological Interventions**
- 



Pharmacological Interventions

- ▶ Daily calcium (1,200-1,500 mg) and vitamin D (400- 800 IU) will assist the bone with building materials.
- ▶ Combined oral contraceptives are NOT recommended for regaining menses or improving bone mineral density.
- ▶ Transdermal oestradiol (E2) therapy with cyclic oral progestin
 - ▶ Short-term use
 - ▶ If not responding to non-pharmacological management
- ▶ Recombinant parathyroid hormone 1-34 (rPTH)
 - ▶ Short-term use in setting of delayed fracture healing or very low bone mineral density
 - ▶ Contraindicated in adolescents with open growth plates



Pharmacological Interventions

- ▶ Lopez LM, Steroidal contraceptives and bone fractures in women: evidence from observational studies (Cochrane Review, 2015).
 - ▶ Included 6 observational studies examining OCPs effect on risk of fracture in women.
 - ▶ Overall, no relationship between OCPs and risk of fracture.
 - ▶ One cohort study reported OC had increased risk for all fractures.
 - ▶ Another case-control study reported increased risk only for those who had 10 or more prescriptions
 - ▶ Two other studies found little evidence of association between OC use and fracture risk



Pharmacological Interventions

- ▶ Ackerman, K., "Oestrogen replacement improves bone mineral density in oligo-amenorrhoeic athletes: a randomised clinical trial" (2019)
 - ▶ 121 young oligo-amenorrhoeic female athletes.
 - ▶ Compared transdermal birth control vs. OCP vs. no intervention over 12 months.
 - ▶ Transdermal estradiol plus cyclic oral progesterone showed improvement in bone mineral density over the OCPs and arm with no intervention
 - ▶ IGF-1 and P1NP decreased during the study in OCP compared with transdermal arm.
 - ▶ Great adjunct in treatment



Pharmacological Interventions

- ▶ Fazeli, P., et. al., “Teriparatide Increases Bone Formation and Bone Mineral Density in Adult Women With Anorexia Nervosa” (2014).
 - ▶ 21 adult women with anorexia nervosa received PTH for 6 months
 - ▶ Spine bone mineral density increased significantly with PTH (6-10% increase)
 - ▶ No changes in BMD of the hip and femoral neck
 - ▶ Serum P1NP increased after 3 months of PTH and remained the same at 6 months
 - ▶ IGF-1 levels were unchanged
 - ▶ PTH is a great adjunct in treatment



Treatment Strategies

- ▶ Multidisciplinary team approach
 - ▶ Physicians
 - ▶ Athletic trainers
 - ▶ Coaches
 - ▶ Sports dieticians
 - ▶ Mental health support
- ▶ Inpatient treatment for patients with
 - ▶ Bradycardia
 - ▶ Hypotension
 - ▶ Orthostasis
 - ▶ Electrolyte imbalance



Treatment Strategies

- ▶ Resistance to treatment increases with severity of problem
- ▶ Patients see disorders as purposeful and necessary
- ▶ Use sport participation as leverage
- ▶ Concurrent depression, anxiety and substance abuse has to be addressed
- ▶ Athletes with severe eating disorders, participation in competition is not recommended



References

- Ackerman KE, Singhal V, Baskaran C, et al. Oestrogen replacement improves bone mineral density in oligo-amenorrhoeic athletes: a randomised clinical trial. *Br J Sports Med* 2019;53:229–236.
- Curry EJ, Logan C, Ackerman K, et al. Female athlete triad awareness among multispecialty physicians. *Sports Med Open* 2015;1:38.
- De Souza MJ, West SL, Jamal SA, et al. The presence of both an energy deficiency and estrogen deficiency exacerbate alterations of bone metabolism in exercising women. *Bone* 2008;43:140–8.
- De Souza MJ, Nattiv A, Joy E, et al. 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. *Br J Sports Med*. 2014; 48(4):289.doi: 10.1136/bjsports-2013-093218
- Fazeli PK, Wang IS, Miller KK, et al. Teriparatide increases bone formation and bone mineral density in adult women with anorexia nervosa. *The Journal of Clinical Endocrinology & Metabolism* 2014;99:1322–9.
- Feldmann JM, Belsha JP, Eissa MA, et al. Female adolescent athletes' awareness of the connection between menstrual status and bone health. *J Pediatr Adolesc Gynecol* 2011;24:311–4.
- Garner DM, Olmstead MP, Polivy J. Development and validation of a multidimensional eating disorder inventory for anorexia nervosa and bulimia. *Int J Eat Disord* 1983;2:15–34.
- Gibbs JC, Williams NI, Scheid JL, et al. The association of a high drive for thinness with energy deficiency and severe menstrual disturbances: confirmation in a large population of exercising women. *Int J Sport Nutr Exerc Metab* 2011;21:280–90.
- Gordon CM, Ackerman KE, Berga SL, et al. Functional hypothalamic amenorrhea: an endocrine society clinical practice guideline. *J Clin Endocrinol Metab* 2017;102:1413–39.



References

- Hill LS, Reid F, Morgan JF, et al. SCOFF, the development of an eating disorder screening questionnaire. *Int J Eat Disord* 2010;43:344–51.
- Kopp-Woodroffe SA, Manore MM, Dueck CA, et al. Energy and nutrient status of amenorrheic athletes participating in a diet and exercise training intervention program. *Int J Sport Nutr* 1999;9:70–88.
- Kroshus E, Fischer AN, Nichols JF. Assessing the awareness and behaviors of U.S. high school nurses with respect to the female athlete triad. *J Sch Nurs* 2015;31:272–9.
- Loucks AB, Thuma JR. Luteinizing hormone pulsatility is disrupted at a threshold of energy availability in regularly menstruating women. *J Clin Endocr Metab*. 2003; 88(1):297–311. [published Online First: Epub Date] | . DOI: 10.1210/jc.2002-020369 [PubMed: 12519869]
- Mallinson RJ, Williams NI, Olmsted MP, et al. A case report of recovery of menstrual function following a nutritional intervention in two exercising women with amenorrhea of varying duration. *J Int Soc Sports Nutr* 2013;10:34.
- Melin A, Tornberg AB, Skouby S, et al. The LEAF questionnaire: a screening tool for the identification of female athletes at risk for the female athlete triad. *Br J Sports Med* 2014;48:540–5.
- Michopoulos V, Mancini F, Loucks TL, et al. Neuroendocrine recovery initiated by cognitive behavioral therapy in women with functional hypothalamic amenorrhea: a randomized, controlled trial. *Fertil Steril* 2013;99:2084–91.
- Mountjoy M, Sundgot-Borgen J, Burke L, et al. The IOC consensus statement: beyond the Female Athlete Triad – relative energy deficiency in sport (RED-S). *Br J Sports Med* 2014;48:491–7.
- Pantano KJ. Current knowledge, perceptions, and interventions used by collegiate coaches in the U.S. regarding the prevention and treatment of the female athlete triad. *N Am J Sports Phys Ther* 2006;1:195–207.
- Plateau CR, Arcelus J, Leung N, et al. Female athlete experiences of seeking and receiving treatment for an eating disorder. *Eat Disord* 2017;25:273–7.
- Ruohola JP, Laaksi I, Ylikomi T, et al. Association between serum 25(OH)D concentrations and bone stress fractures in Finnish young men. *J Bone Miner Res* 2006;21:1483–8.