# Relative Energy Deficiency in Sport (RED-S) in Rowers?


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Until every child is well™

HARVARD MEDICAL SCHOOL
TEACHING HOSPITAL

# Disclosures

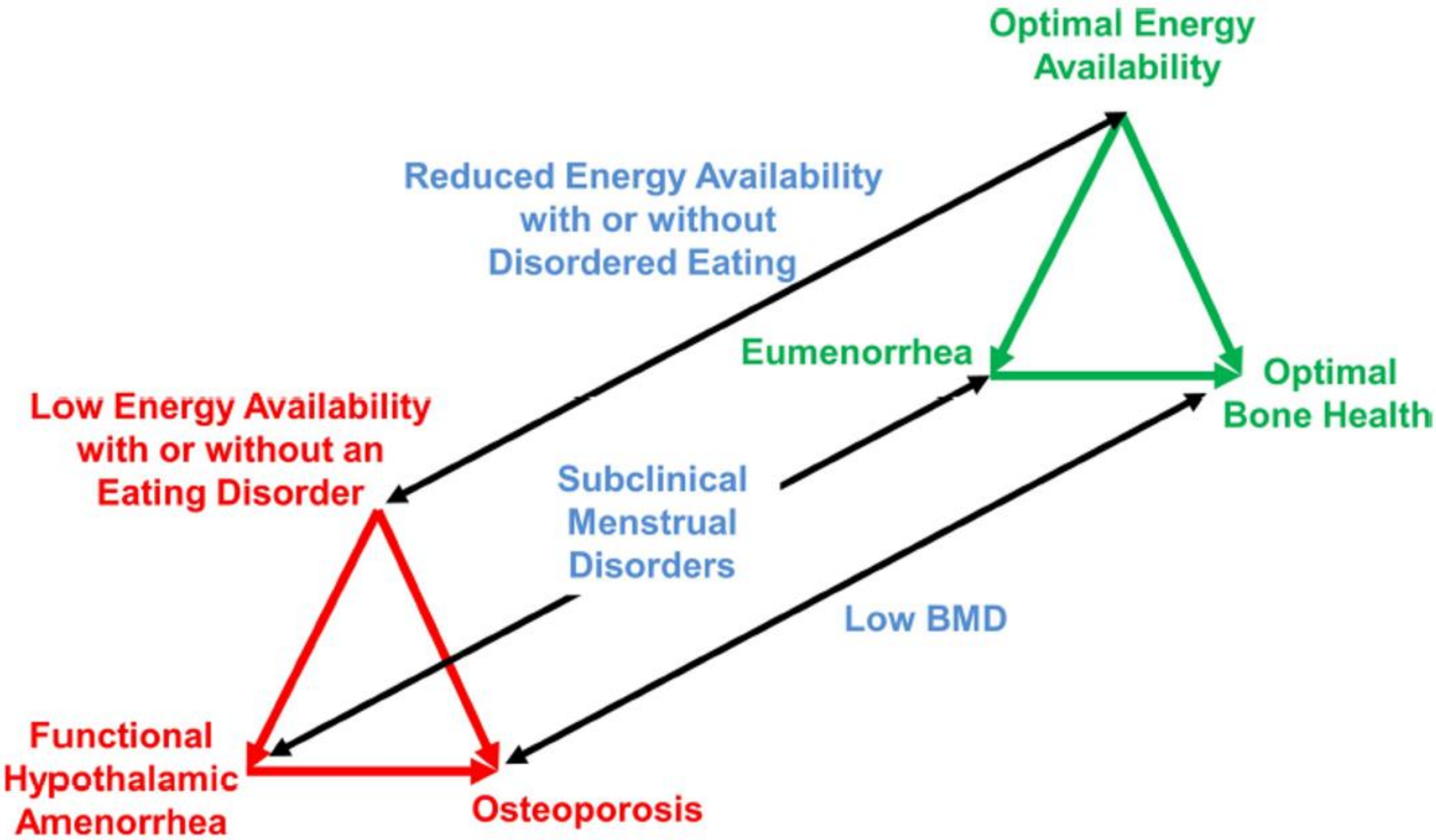
- Member- Female Athlete Triad Coalition (FATC)
- Member- International Olympic Committee's Relative Energy Deficiency in Sport (IOC RED-S) and Female Athlete Working Groups
- Endocrine Consultant- FISA Medical Commission

# Objectives

- Understand the origin of RED-S
- Explain current evidence of the various aspects of RED-S with a focus on rowers
- Describe future directions for RED-S

**WE NEED TO APPROPRIATELY FUEL OUR ATHLETES AND LOOK OUT FOR RED-S!**

# The Female Athlete Triad




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

# The IOC consensus statement: beyond the Female Athlete Triad—Relative Energy Deficiency in Sport (RED-S)

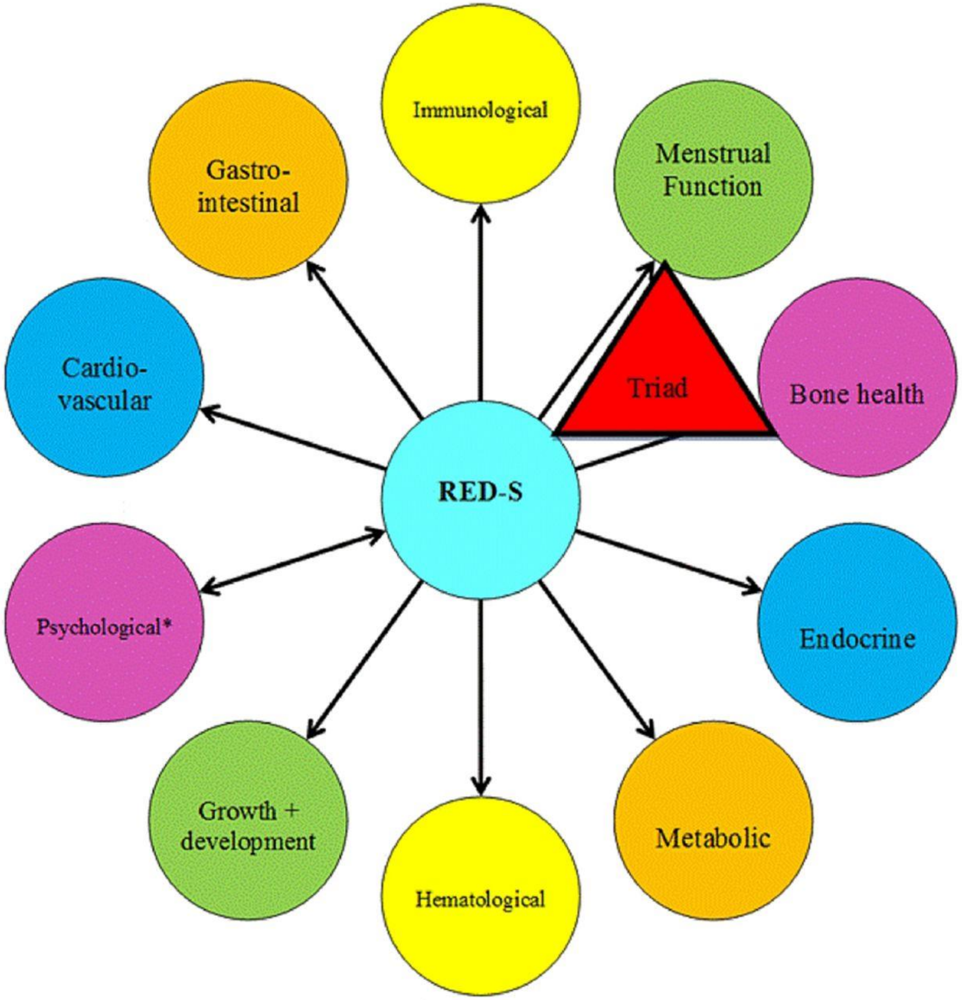
Margo Mountjoy,[1] Jorunn Sundgot-Borgen,[2] Louise Burke,[3] Susan Carter,[4] Naama Constantini,[5] Constance Lebrun,[6] Nanna Meyer,[7] Roberta Sherman,[8] Kathrin Steffen,[2,9] Richard Budgett,[9] Arne Ljungqvist[9]

# IOC consensus statement on relative energy deficiency in sport (RED-S): 2018 update

Margo Mountjoy,[1] Jorunn Kaiander Sundgot-Borgen,[2] Louise M Burke,[3,4] Kathryn E Ackerman,[5,6] Cheri Blauwet,[7] Naama Constantini,[8] Constance Lebrun,[9] Bronwen Lundy,[3] Anna Katarina Melin,[10] Nanna L Meyer,[11] Roberta T Sherman,[12] Adam S Tenforde,[13] Monica Klungland Torstveit,[14] Richard Budgett[15]

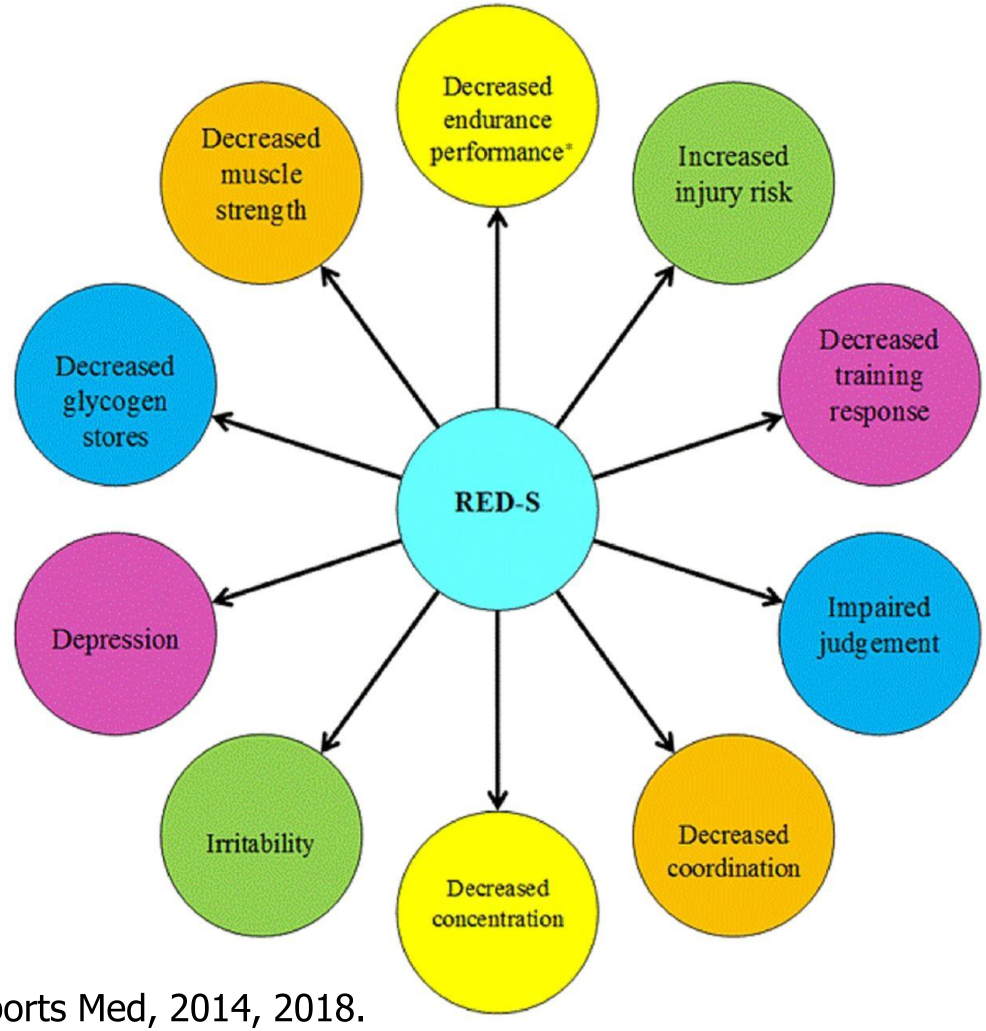
Mountjoy M, et al. Br J Sports Med, 2014, 2018.

# Health Consequences of RED-S




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

# Potential Performance Effects of RED-S




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

# Low Energy Availability

- **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

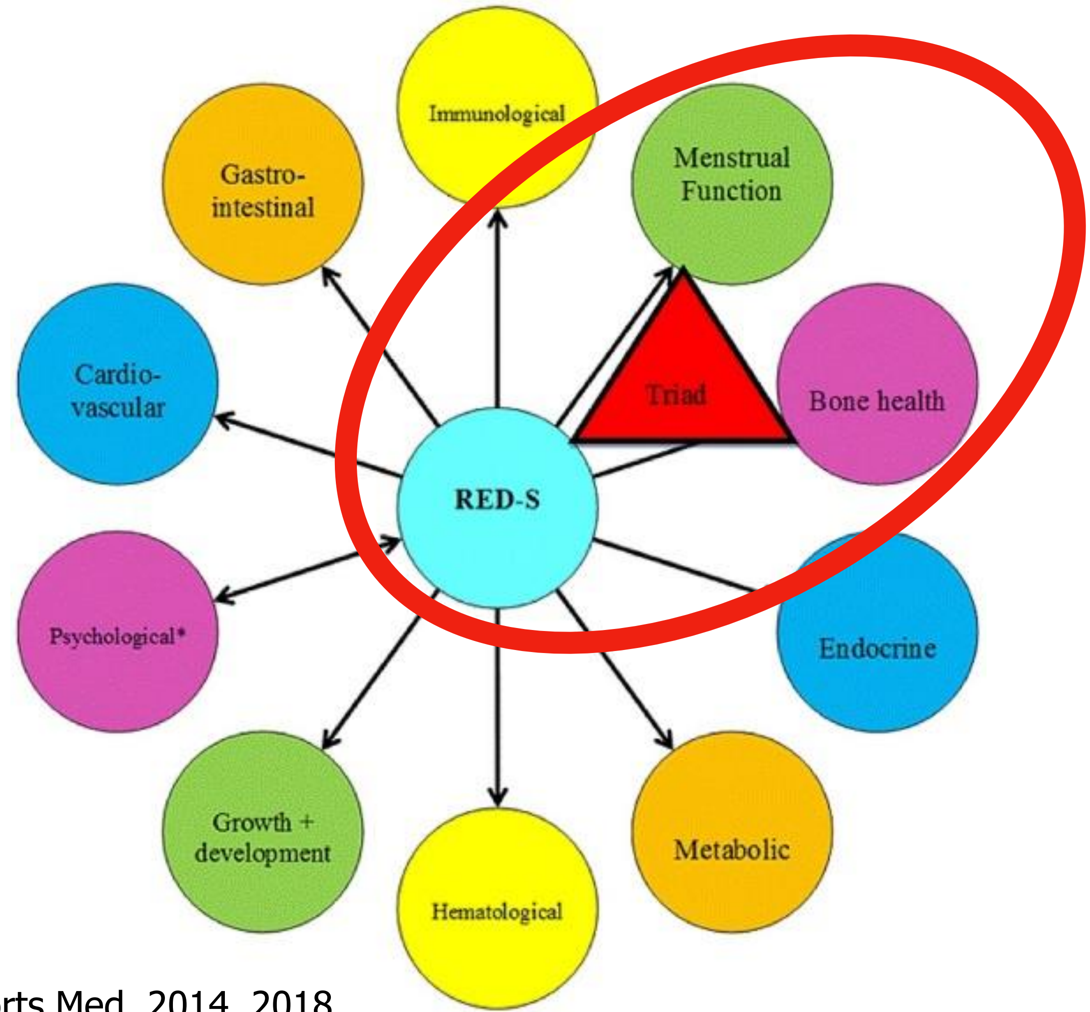
- **Exercise energy expenditure:** energy expended during exercise in excess of energy that would have been expended in non-exercise activity during same time interval

**30 kcal/kg/FFM per day needed at a minimum. 45 may be ideal. Likely personal variation.**

**30**

Loucks AB and Thuma JR. JCEM, 2003.

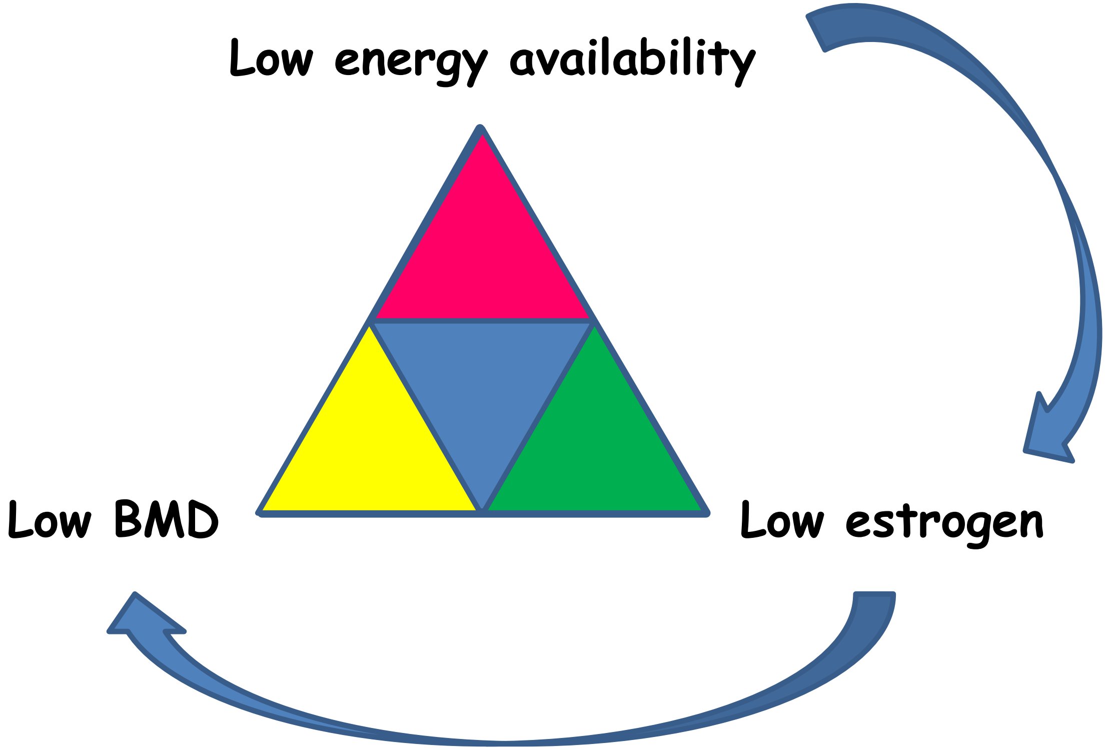
# RED-S/Triad




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

# Interrelationship of Components of the Triad

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



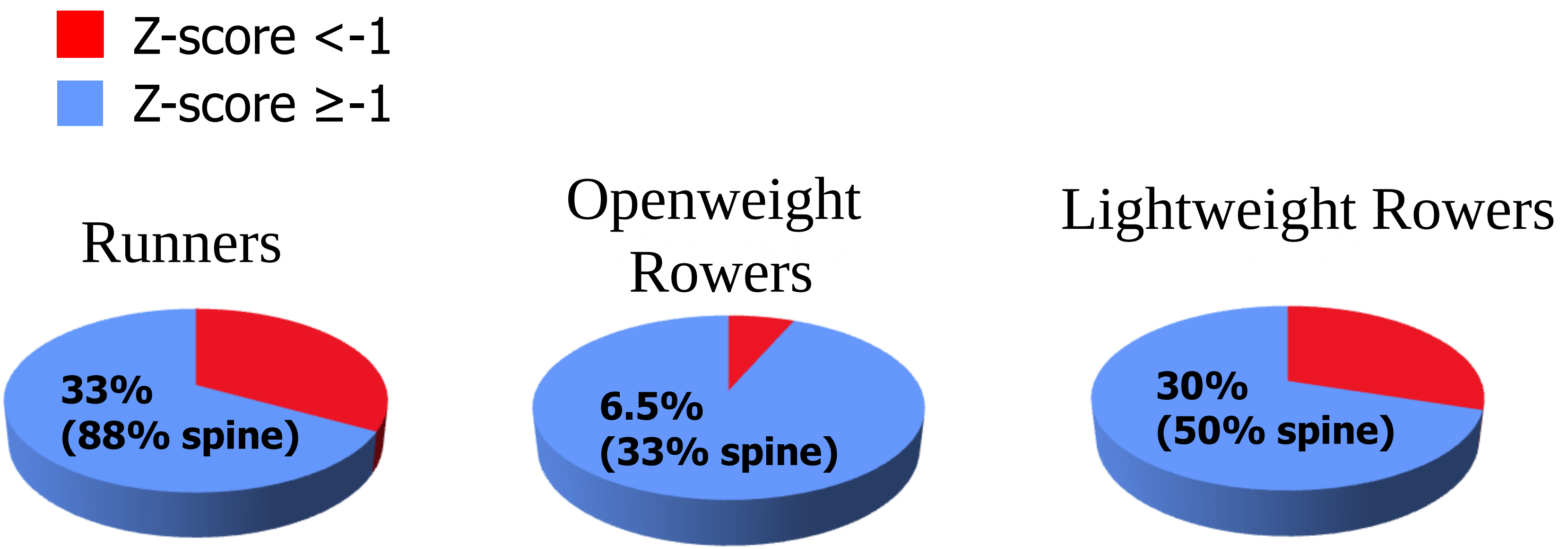
# Interrelationship of Components of the Triad

- 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, Ackerman KE, et al. Functional Hypothalamic Amenorrhea: An Endocrine Society Clinical Practice Guideline. JCEM, 2017.
Ackerman K and Misra M. "Neuroendocrine Abnormalities in Female Athletes" in The Female Athlete Triad- A Clinical Guide, 2015.

# Bone Health in Women Rowers vs. Runners

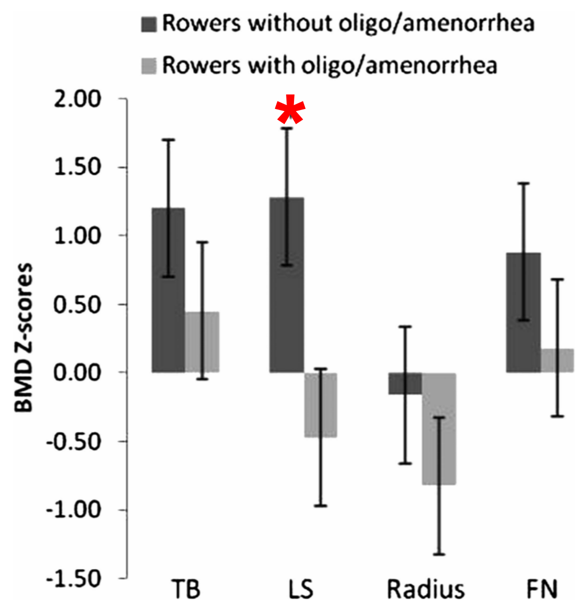
- Study of 51 female runners and 66 rowers (46 openweight and 20 lightweight)
  - Higher rates of menstrual dysfunction in the lightweight rowers (vs. runners and vs. openweight rowers)
  - Bone mineral density:

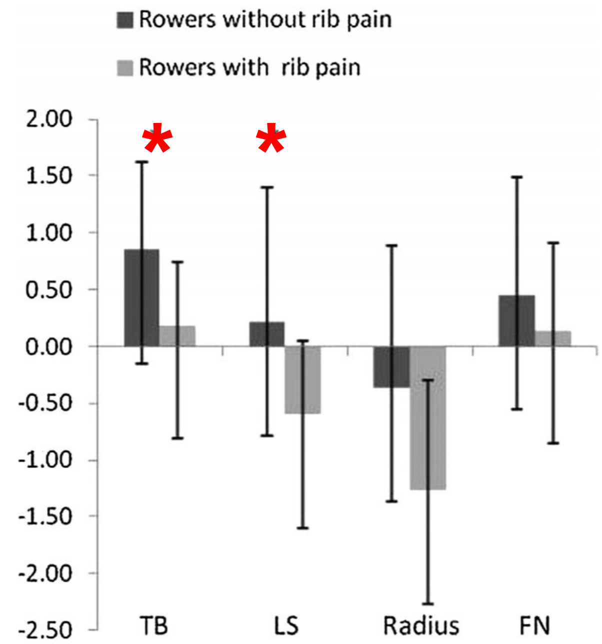



Ackerman KE, et al. Endocrine Society, 2009.

# Bone Health in Lightweight Women Rowers

- 29 Female lightweight rowers (12 active, 9 retired) were surveyed & had DXAs
  - Rowers with DE started rowing younger than those without & their amount of intentional weight loss was associated with EAT-26 score
  - 76% had history of oligomenorrhea/amenorrhea; 32% had history of rib pain
  - 41% had low BMD; 3 at Spine; 1 at Femoral Neck; 8 at Radius



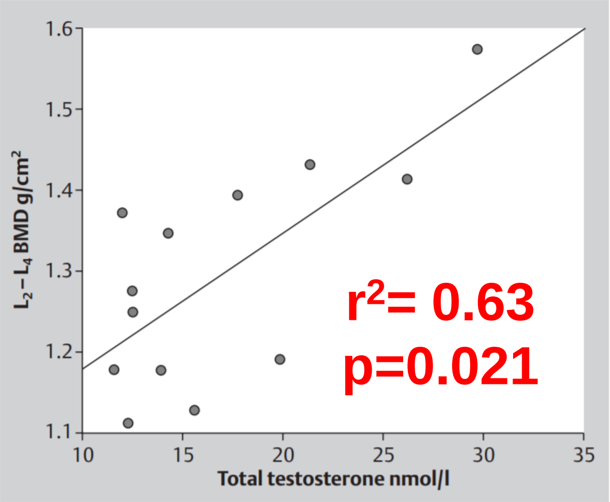



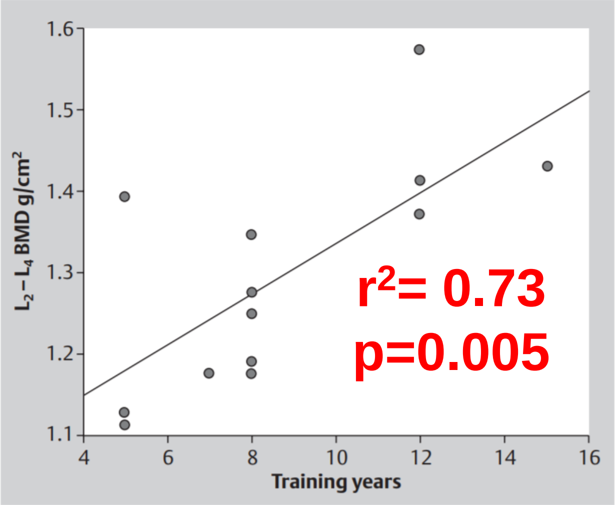

Dimitriou L, et al. BMJ Open, 2014.

# Bone Health in Lightweight Male Rowers

- 13 Danish team lightweight male rowers
  - BMD within normal range

- Lightweight rowers found to have lower testosterone, lower BMD, and increased risk of rib stress fracture compared to openweights





Vinther A, et al. Int J Sports Med, 2008.
Vinther A, et al. Scand J Med Sci Sports, 2006.
Burke LM, et al. Int J Sport Nutr Exerc Metab, 2018.

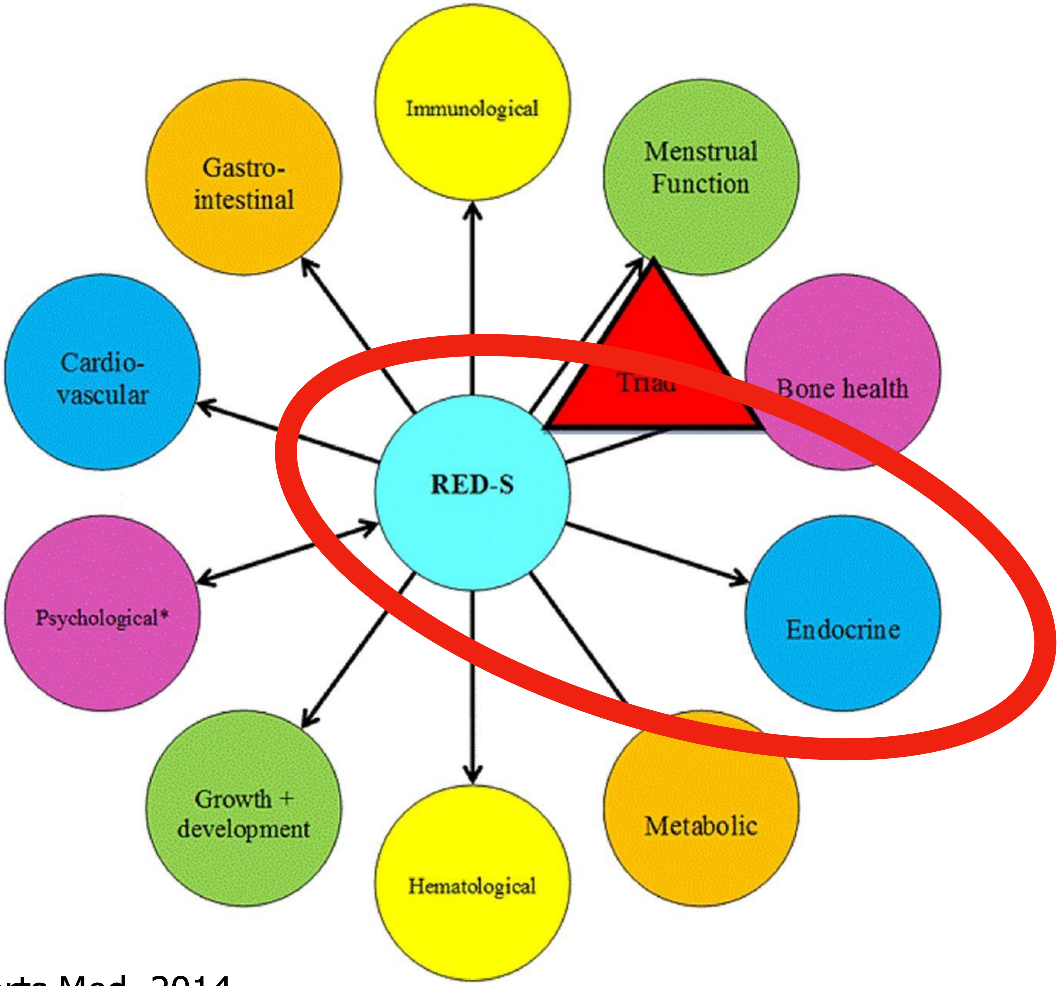
# Australian Rowing Team- *courtesy of Bronwen Lundy*

- 12 openweight men- DXAs 2- 4.5 years apart
  - Lumbar Spine: 10 had decreases (1.3- 11.9% ↓); 2 had increases (0.1- 0.6% ↑), but decreases at the hip (5.0 & 8.2% ↓)

- 6 openweight women
  - More inconsistent results


*Lundy B, unpublished data.*

# RED-S Health Consequences



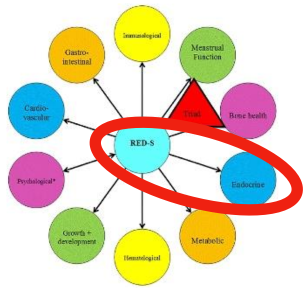

Mountjoy M, et al. Br J Sports Med, 2014.

# Endocrine Changes with RED-S

| | 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 | ↑ | ↑ |

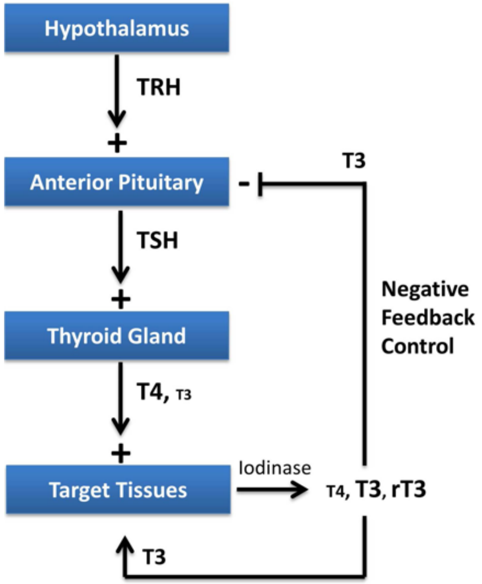
Elliott-Sale K, et al…Ackerman KE. IJSNEM, 2018.



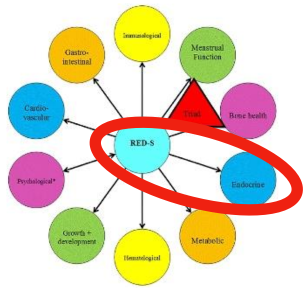

# RED-S → Endocrine

# T3

- Thyroid
  - 32 subject cross-sectional study: **lower** T4 & **T3 in AA** vs. EA and HC
  - 27 subjects: AA, EA, and HC
    - **TSH response to TRH stimulation was blunted in AA** vs. EA
  - 27 eumenorrheic non-athletes:
    - 4 days of exercise but different energy availabilities
    - **↓ in T3 and free T3** between 19 and 25 kcal/kg FFM/day
    - ↑ in T4 and rT3 between 10.8 and 19 kcal/kg FF/day



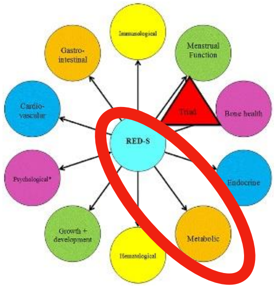

Harber VJ, et al. Can J Appl Physiol, 1998.
Loucks AB and Health EM, A J Phys, 1994.
Loucks AB, et al. J Clin Endocrinol Metab, 1992.




# RED-S → Endocrine (ROWERS)

- 17 collegiate female rowers
  - Labs at baseline and during 20 weeks of training
  - 10 had decreases in **free T3** (responders); 7 had no change
  - In the responders:
    - **free T3 concentrations ↓** from baseline during an intense training period at 5 weeks by -28.2% & at 10 weeks by -24.9%, then returned towards baseline at 20 weeks
    - Similar changes in leptin and TSH
- 6 male rowers
  - high intensity resistance training for 3 weeks
    - Leptin, TSH, & **free T3 ↓**
  - endurance training for 3 weeks
    - TSH ↑
  - Depression of leptin and hypothalamic-thyroid axis associated with training intensity

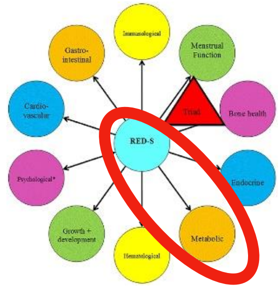
Simsch C, et al. Int J Sports Med, 2002.    Baylor LS, Hackney AC. Eur J Appl Phys, 2003.




# RED-S → Metabolic

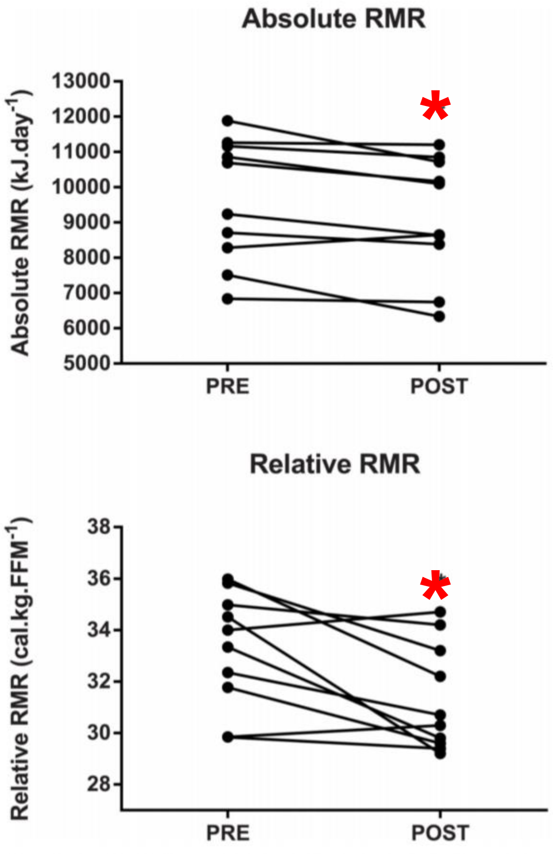
- Metabolic Rate
  - Small study of normal weight women (n=25)
    - different exercise and caloric intake alterations for 3 months
  - **SEV: -1062±80 kcal per day (n=9), MOD: -633±71 kcal per day (n=7), or BAL: (n=9)**
  - Weight loss occurred in SEV (3.7kg) and MOD (2.7kg), but significantly less than predicted (SEV: 11.1kg; MOD: 6.5kg)
  - **RMR ↓ by 6±2% in MOD**
  - In SEV, RMR did not change for entire group, but those whose RMR ↓ lost more weight and had a higher baseline RMR than those whose RMR did not ↓
  - Expected changes in leptin, T3, IGF-1, and ghrelin occurred only in SEV
  - **The energy deficit and adaptive changes in RMR explained 54% of weight loss**

Koehler K, et al. Eur J Clin Nutr, 2017.

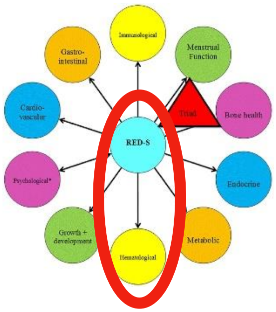



# RED-S → Metabolic (ROWERS)

- 10 Australian Team Rowers
  - 4 weeks of training
  - Training load ↑ 21 ± 7% but caloric intake didn't change

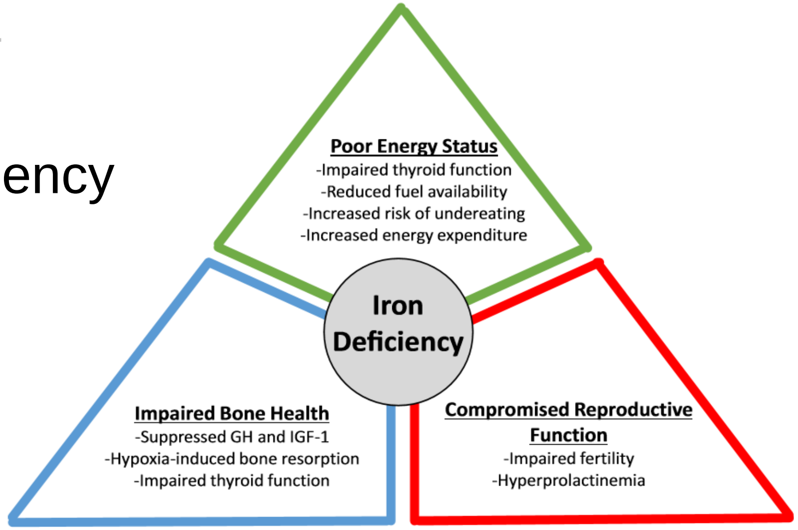




Woods AL, et al. PLoS One, 2017.



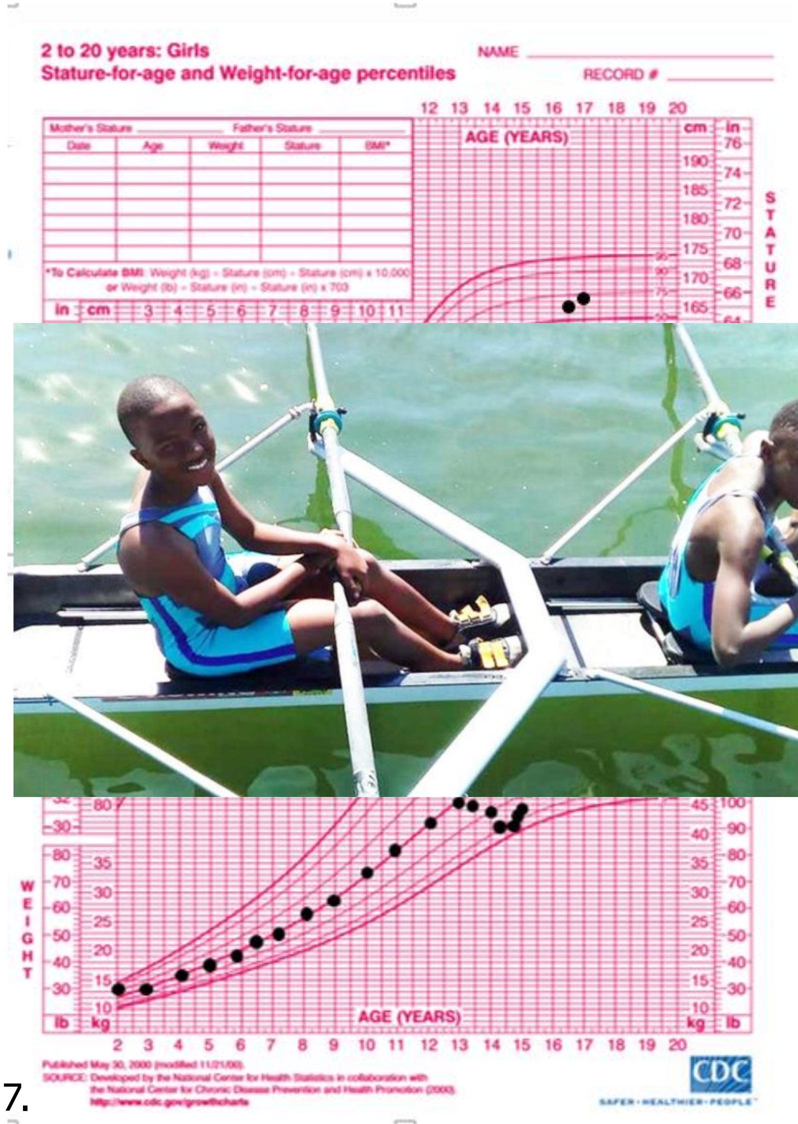

# RED-S → Hematological (↔)

- Many athletes, including rowers, with reduced energy availability have iron deficiency
- Iron deficiency may worsen the hypometabolic state associated with decreased energy availability
  - T4 synthesis & T4→T3 conversion
- Iron deficiency may **promote** energy deficiency
  - Shifts ATP production from oxidative phosphorylation to anaerobic pathways
- Iron needed for reproductive function
  - Follicular development and corpus luteum function
- Bone health may be further impaired by iron deficiency

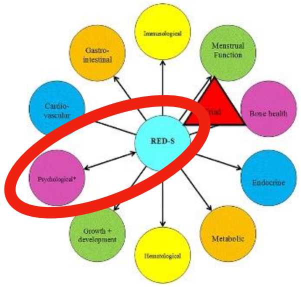



Petkus DL, et al. Sports Med, 2017.


# RED-S → Growth & Development



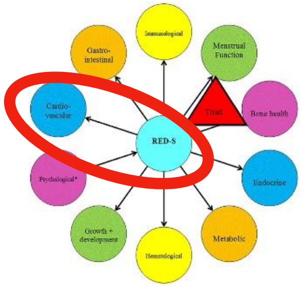

Kapczuk K. Minerva Pediatra, 2017.




# RED-S ↔ Psychological

- **Drive for Thinness (DT)** was assessed in exercising and sedentary women (n=52) using the Eating Disorder Inventory
  - Athletes with high DT (vs. athletes and non-athletes with normal DT)
    - Scored higher on questions re: Bulimia, Inefffectiveness, and Cognitive Restraint
    - Experienced more oligo/amenorrhea vs. other 2 groups
    - Had lower REE (kj/kg of FFM) and actual REE/predicted REE; more were classified as "energy deficient" (66% vs. 27% in the other groups)
    - Had lower total T3 and higher ghrelin
  - Significant negative correlation between DT and Total T3, adjusted REE; positive correlation between DT and ghrelin
- **Adult lightweight male rowers**: High levels of cognitive control of eating accompanied with body dissatisfaction under hunger but not satiety

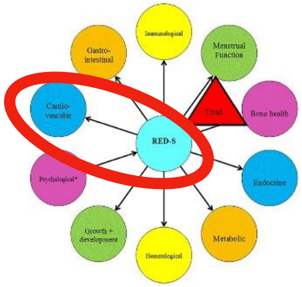
De Souza MJ, et al. Appetite, 2007. Pietrowsky R and Straub K. Eat Weight Disord, 2008.




# RED-S → Cardiovascular

- **Postmenopausal women:** Decreased levels of endogenous estrogen unfavorably modify lipid levels and vascular function
- **Premenopausal women with anorexia nervosa and athletes with amenorrhea**: poor lipid levels
  - Theories include interactions of estrogen deficiency, liver dysfunction, dehydration, reduced cholesterol turnover, ↓T3, and delayed cholesterol metabolism
- Retrospective data suggests development of **early CAD in some older premenopausal women with history of FHA**

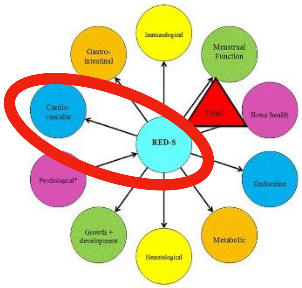
Rickenlund A, et al. J Clin Endocrinol Metab, 2005.
O'Donnell E, et al. J Clin Endocrinol Metab, 2011.
Nakai Y, et al. Intern Med, 2016.




# RED-S → Cardiovascular

- Estrogen stimulates vascular endothelium, leading to increased endothelial-derived nitric oxide (NO) → vasodilation
- NO also has anti-atherosclerotic properties
  - inhibition of platelet aggregation
  - smooth muscle proliferation
  - leukocyte adhesion
  - LDL oxidation
- Estrogen and regular aerobic physical activity are *independently* associated with enhanced synthesis &/or bioavailability of endothelial NO

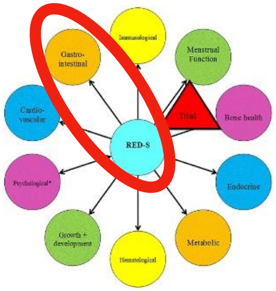
Rickenlund A, et al. J Clin Endocrinol Metab, 2005. O'Donnell E, et al. J Clin Endocrinol Metab, 2011.




# RED-S → Cardiovascular

- Flow-mediated dilation (FMD)
  – can assess endothelial function in the brachial artery
  – 95% positive predictive value of abnormal brachial dilation in predicting coronary endothelial dysfunction
  – **FMD lower in AA vs. OA and EA**
    - Serum estrogen levels positively correlated with vascular function
    - Restored vascular function was associated with ↑ estrogen levels in AA who became eumenorrheic

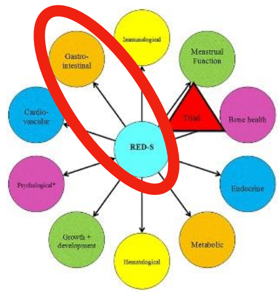
Zeni Hoch A, et al. Med Sci Sports Exerc, 2003.
Rickenlund A, et al. J Clin Endocrinol Metab, 2005.
Yoshida N, et al. Arterioscler Thromb Vasc Biol, 2006.
Hoch AZ, et al. Clin J Sport Med, 2011.




# RED-S → Gastrointestinal

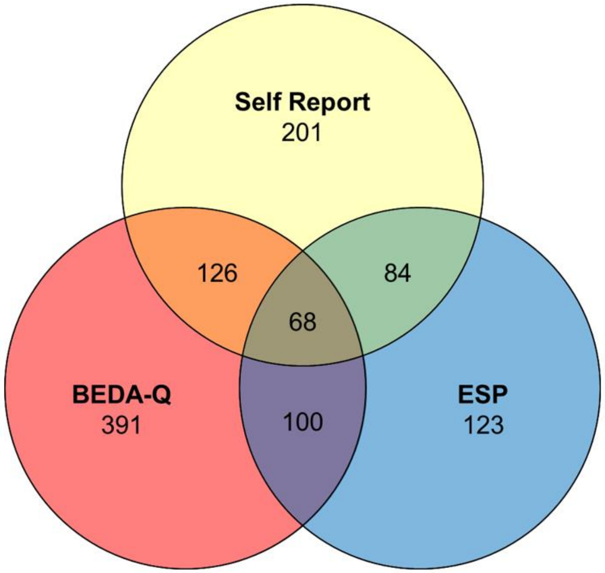
- Systematic Review of 123 articles of patients with anorexia nervosa
  - Delayed gastric emptying, increased intestinal transit time, and constipation
  - Elevated liver enzymes

Norris, ML. Int J Eat Disord, 2016 *Unpublished data

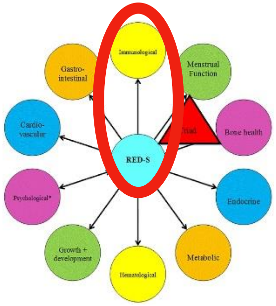



# RED-S → Gastrointestinal

- Survey of 1000 female sport medicine clinic patients (age 15-30 years, ≥4 hrs/wk of exercise)
  - Surrogate markers of Low EA:
    - Self-report or DE/ED, BEDA-Q, ESP
  - 84.5% response rate
  - Low EA 47.3%
    - 1.5x greater odds of GI complaints with Low EA vs. Adequate EA (95% CI 1.19-1.92, $p<0.0001$)




Norris, ML. Int J Eat Disord, 2016. Ackerman KE, et al. Br J Sports Med, 2018.

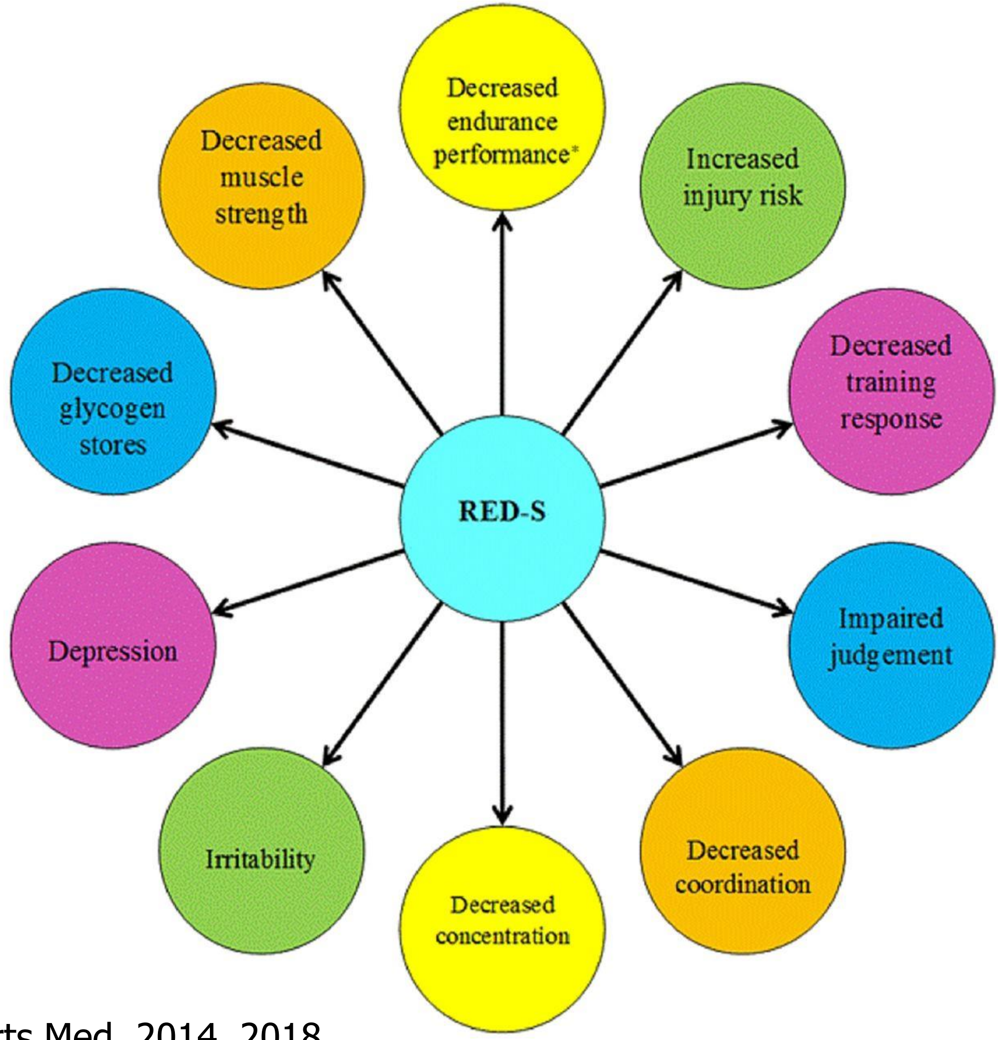



# RED-S → Immunological

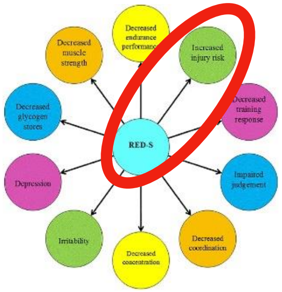
- Athletes with high training loads often experience impaired immune function and frequent URIs
- ↓ salivary IgA correlates to ↑ upper respiratory infections (URIs)
- Salivary IgA correlates with salivary estradiol
- Study of 21 Japanese elite, collegiate runners (13 AA, 8 EA)
  - Salivary IgA levels, serum 17β-estradiol and progesterone, and # of URI symptoms in last month
  - AA had lower levels of serum estradiol and IgA secretion, and more URI symptoms
- Elite Australian athletes prepping for Rio 2016
  - Low EA measured by LEAF-Q
    - ↑ odds of illnesses (e.g.upper respiratory and GI tracts), body aches, and head-related symptoms in prior month

Drew MK, et al. J Sci Med Sport, 2017. Drew M, et al. Br J Sports Med, 2018.

# Potential Performance Effects of RED-S

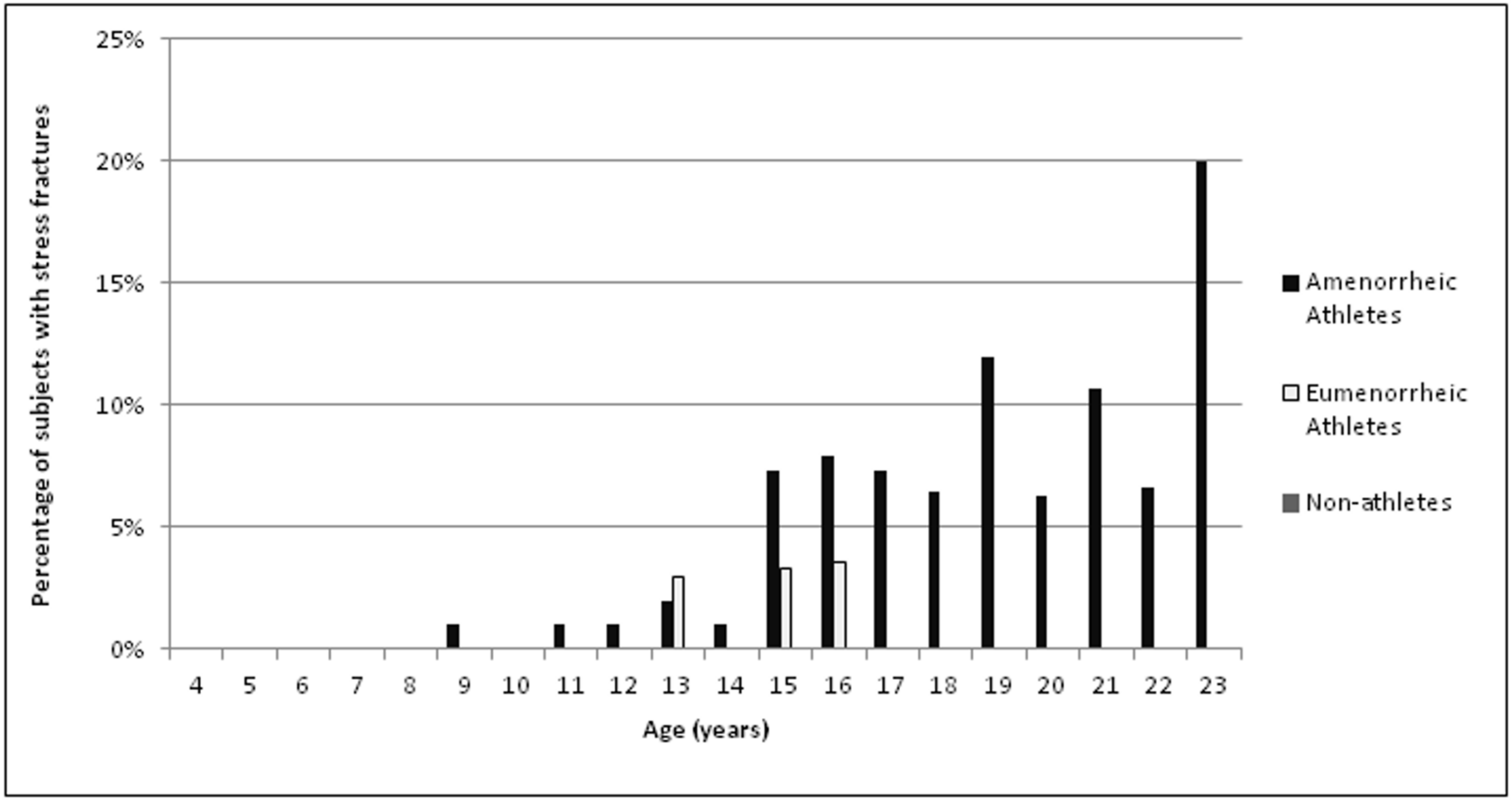



Mountjoy M, et al. Br J Sports Med, 2014, 2018.

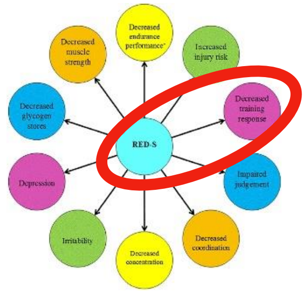



# RED-S → Injury Risk

## Proportion of Subjects with Stress Fracture each Year

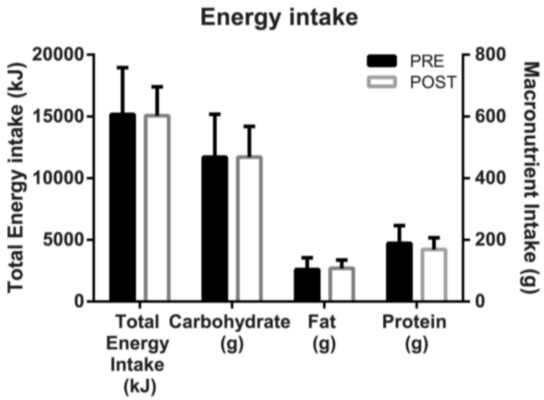


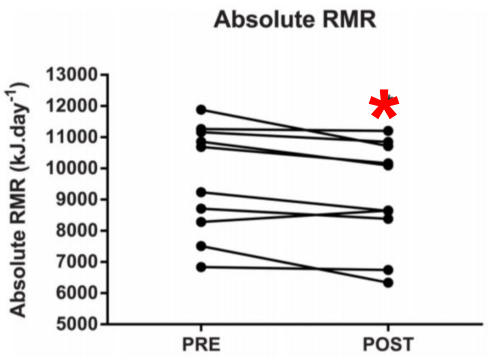

Ackerman KE, et al. Med Sci Sports Exerc, 2015.

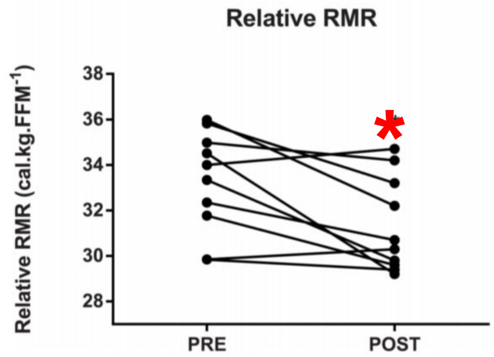



# RED-S → Decreased Training Response (ROWERS)

- 10 Australian Team Rowers
  - 4 weeks of training
  - Training load went up 21 ± 7% but caloric intake didn't change

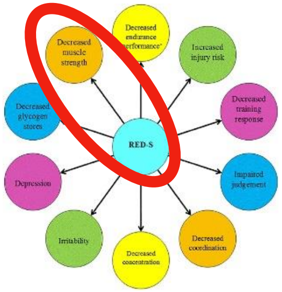




**5K time trial got slower!**

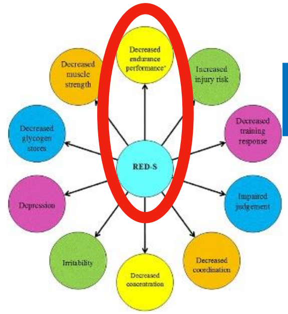
Woods AL, et al. PLoS One, 2017.




# RED-S → Decreased Muscle Strength

- Neuomuscular performance assessed in elite amenorrheic athletes (AA) and eumenorrheic athletes (EA)
  - Knee muscular strength and knee muscular endurance worse in AA (11% and 20% ↓) and reaction time was 7% longer vs. EA
  - ↓ leg FFM, glucose, estrogen, T3, and ↑ cortisol levels correlated with the findings

Tornberg AB, et al. MSSE, 2018.




# RED-S → Decreased Endurance Performance

- 10 junior elite female swimmers (15-17 years)
  - Cyclic (CYC) or Ovarian suppressed (OVS) based on $E_2$ and $P_4$ levels
  - Monitored q2 weeks over 12 weeks
  - OVS had suppressed $E_2$ and $P_4$ levels throughout season and had ↓ T3 and IGF-1 at week 12 vs. CYC
  - Energy intake and energy availability lower in OVS
  - **OVS had a 9.8% ↑ in 400m swim time while CYC had an 8.2% ↓**

- Survey: 1.47x greater odds of decreased endurance performance with Low EA vs. Adequate EA (95% CI 1.08-2.02, p=0.02)

Vanheest JL, et al. Med Sci Sports Exerc, 2014. Ackerman KE, et al. Br J Sports Med, 2018.

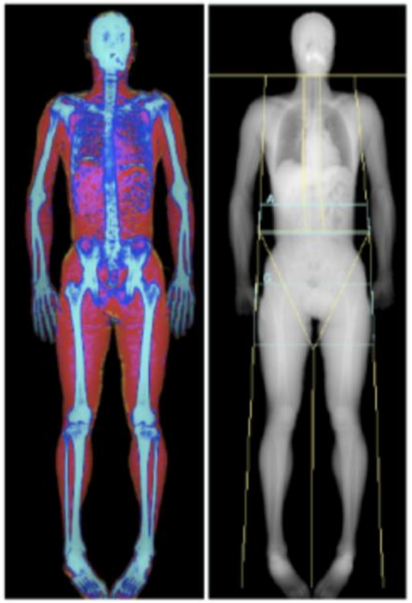
# Rowers and RED-S

- ↑ risk for low EA and resulting health consequences of RED-S:
  - cyclical changes in body mass and composition (“making weight”)
  - prolonged inadequate energy intake to meet high exercise energy expenditure
  - abrupt changes in training volume/intensity
  - participation in strenuous endurance events without changing nutrition
  - inadequate food availability, including food insecurity from cultural practices or lack of financial resources

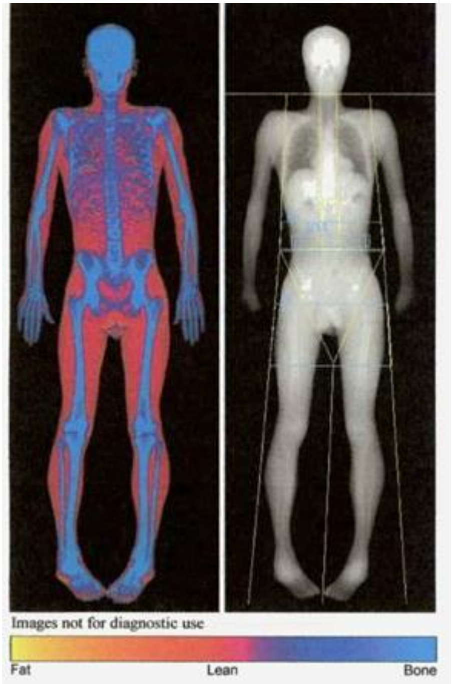
Mountjoy M, et al. Br J Sports Med, 2018.
Burke LM, et al. Int J Sport Nutr Exerc Metab, 2018.

# RED-S

- The medical professional can often spot it, but we need to prove it to the athlete and entourage!
  - Signs, symptoms, etc.



- Amenorrhea (low FSH, LH, estradiol), decreased libido, low testosterone, low WBC, low iron/ferritin, low T3, low Vit D, increased LFTs, altered lipids, decreased performance, decreased BMD, low BMI, low fat mass



| HIGH RISK: NO START RED LIGHT | MODERATE RISK: CAUTION YELLOW LIGHT | LOW RISK: GREEN LIGHT |
|---|---|---|
| - Anorexia nervosa and other serious eating disorders<br>- Other serious medical (psychological and physiological) conditions related to low energy availability<br>- 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<br>- Substantial weight loss (5–10 % body mass in one month)<br>- 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<br>- 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).<br>- 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<br>- Healthy musculoskeletal system |
| - Severe ECG abnormalities (i.e. bradycardia) | - Athletes with physical/ psychological complications related to low EA+/-disordered eating;<br>- Diagnostic testing abnormalities related to low EA +/-disordered eating | |
| | - Prolonged relative energy deficiency<br>- Disordered eating behavior negatively affecting other team members<br>- Lack of progress in treatment and/or non-compliance | |

# RED-S CAT

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

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

# Future Directions

- Studies exploring other health and performance effects of low energy availability in female and male **rowers**!
- Tracking EA in our rowers and prioritizing fueling
- Studies determining efficacy of RTP Protocols
- Definitive hormonal and other therapy studies for RED-S
- More awareness and prevention programs
- More collaborating with the Aussies!
  - and others who want to join us!

# THANK YOU!

- Funding: NIH grant 1 UL1 RR025758 & HD060827-01A1, US Army Medical Research W81XWH-15-C-0024, AMSSM Research Grant

- Boston Children's Hospital Sports Medicine and the Female Athlete Program

- Massachusetts General Hospital Sports Endocrine Research Lab

- Dr. Jürgen Steinacker and FISA

- Our Patients and Rowers

USA

Harvard-Radcliffe Rowing

# THANK YOU

## and Happy Thanksgiving!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