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

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  – AMSSM Foundation Grant
  – UCLA Clinical and Translational Science Institute
Goals & Objectives

• To provide clinical guidelines for physicians for the screening, diagnosis and treatment of the Female Athlete Triad

• To provide recommendations for clearance and return to play for the Female Athlete Triad by using a risk stratification scoring system assessing magnitude of risk
Female Athlete Triad Spectrums

- Optimal Energy Availability
- Reduced Energy Availability with or without Disordered Eating
- Subclinical Menstrual Disorders
- Low BMD
- Low Energy Availability with or without an Eating Disorder
- Functional Hypothalamic Amenorrhea
- Eumenorrhea
- Optimal Bone Health
- Osteoporosis

Female Athlete Triad: A spectrum ranging from optimal energy availability to reduced energy availability, with subclinical menstrual disorders and osteoporosis at the extremes.
Triad Screening Recommendations

• It is the recommendation of the Female Athlete Triad Coalition, that female athletes (high school, college, elite) undergo annual screening with a self-report questionnaire

• Existence of any one of the components should prompt more thorough investigation for the others
Triad Consensus Panel Screening Questions

- Have you ever had a menstrual period?
- How old were you when you had your first menstrual period?
- *When was your most recent menstrual period?
- How many periods have you had in the last 12 months?
- *Are you presently taking any female hormones (estrogen, progesterone, birth control pills)?
- Do you worry about your weight?
- Are you trying to or has anyone recommended that you gain or lose weight?
- Are you on a special diet or do you avoid certain types of foods or food groups?
- Have you ever had an eating disorder?
- Have you ever had a stress fracture?
- Have you ever been told you have low bone density (osteopenia or osteoporosis?)

*The Female Athlete Triad Coalition recommend these questions be asked at the time of PPE; *Not currently in 2010 PPE Monograph
Diagnosis of the Triad

• Low energy availability (with or without an eating disorder or disordered eating)
• Menstrual dysfunction
• Bone mineral density
Low Energy Availability

- Nutrition assessment by a registered sports dietitian
- Energy intake (kcals) – exercise energy expenditure (kcals)/fat free mass (kcals) or lean body mass
- 2011 Compendium of Physical Activities to calculate exercise energy expenditure
- Fat free mass can be obtained from measurement of body weight (kg) and from estimate of percent body fat
- Energy availability calculator (Female Athlete Triad Coalition website: http://www.femaleathletetriad.org/calculators/) to estimate EA
- Female athletes should aim for at least 45 kcal/kg FFM/day of energy intake to ensure adequate EA
Menstrual Dysfunction Screening

• Female athletes presenting with primary amenorrhea, secondary amenorrhea or prolonged oligomenorrhea require an evaluation to rule out pregnancy and endocrinopathies.

• The diagnosis of functional hypothalamic amenorrhea due to low energy availability is a diagnosis of exclusion.
History and Examination

Uterine pathology or outflow tract disorder

Disorders of sexual differentiation

Initial Investigation (based on H&P)
- LH, FSH, hCG
- Prolactin
- TSH, free T4
- Estradiol, testosterone (total and free), DHEA/S ± 8AM 17(OH) progesterone
- Progesterone challenge test
- ± Pelvic ultrasound

Rule out Pregnancy

Low to normal gonadotropins
- Negative progesterone challenge test
- Possibly ↑ prolactin
- Hypothalamic-pituitary etiology
- Rule out outflow tract obstruction if not done so previously
- Consider FHA (prolactin typically not elevated)*

Normal gonadotropins
- Possibly ↑ LH/FSH
- ↑ Total/free testosterone
- Chronic anovulation/PCOS

↑ Gonadotropins
- Positive progesterone challenge test
- Primary ovarian insufficiency

Abnormal TSH, prolactin, DHEA/S or 8 AM 17(OH) progesterone
- Specific investigation of endocrine disorder
Low BMD and Osteoporosis Assessment

• Definitions of low BMD and osteoporosis are different for adolescents, premenopausal women and postmenopausal women

• How often should DXA be obtained for adolescents and premenopausal women?
Low BMD and Osteoporosis in Children and Adolescents < 20 Yrs of Age

• The diagnosis of osteoporosis in children requires a clinically significant fracture history + low BMD or BMC
  – Long bone fracture of lower extremities
  – Vertebral compression fracture
  – Two or more long bone fractures of the upper extremities

• Low BMD or BMC Z-score < -2.0

(Lewiecki et al. ISCD 2007 Adult and Pediatric Positions. Bone 2008; 43: 115-1121)
Low BMD and Osteoporosis in Premenopausal Women

• The diagnosis of osteoporosis requires low BMD + secondary causes of osteoporosis

• BMD Z-score of $< -2.0$ is below expected range for age*

• BMD Z-score above -2.0 is within the expected range for age

(Lewiecki et al. ISCD 2007 Adult and Pediatric Positions. Bone 2008; 43: 115-1121;
Recommendations for DXA Assessment by Triad Risk Stratification*

> 1 “High risk” triad risk factors
- History of DSM V-diagnosed eating disorder
- BMI < 17.5, <85% estimated weight, or recent weight loss of ≥ 10% in 1 month
- Menarche ≥ 16 yrs
- Current or history of < 6 menses over 12 months
- 2 prior stress fractures, 1 high risk stress fracture, or a low energy nontraumatic fracture
- Prior Z-score of < -2.0 (after at least 1 year from baseline DXA)

OR

> 2 “Moderate risk” triad risk factors
- Current or history of disordered eating for 6 months or greater
- BMI between 17.5-18.5, <90% estimated weight, or recent weight loss of 5-10% in 1 month
- Menarche between 15 and 16 years of age
- Current or history of 6-8 menses over 12 months
- One prior stress reaction/fracture
- Prior Z-score between -1.0 and -2.0 (after at least 1 year interval from baseline DXA)

• In addition, in an athlete with ≥ non peripheral or ≥ 2 peripheral long bone traumatic fractures (non stress) + ≥ 1 moderate or high risk triad risk factors
• Athletes on medications for 6 months or more which can impact bone (such as depot medroxyprogesterone acetate, oral prednisone or others)

DXA Screening Site and Frequency

• Children, adolescents and young women < 20 years of age
  – PA spine and whole body less head if possible (otherwise whole body) BMC and areal BMD
• Adult women ≥ 20 years of age
  – PA spine, total hip, femoral neck
  – 33% radius if spine or hip cannot be assessed
• Serial BMD frequency will depend on clinical status and initial BMD; every 1-2 years if meets criteria
Nonpharmacologic Treatment

• Mainstay of triad treatment is increasing energy availability
• Goals include restoration of menses and improved bone health
• Multidisciplinary team is key
• Time course of recovery varies
Recovery of Bone Mineral Density

Recovery of Menstrual Status

Recovery of Energy Status

**PROCESS:** Days or Weeks

**OUTCOMES:**
- Energy status will stimulate anabolic hormones (IGF-1) and bone formation
- Energy status will reverse energy conservation adaptations

**PROCESS:** Months

**OUTCOMES:**
- Reproductive hormones
- Estrogen exerts an anti-resorptive effect on bone

**PROCESS:** Years

**OUTCOMES:**
- Estrogen continues to inhibit bone resorption
- Energy status will stimulate anabolic hormones (IGF-1) and bone formation
Nonpharmacologic Treatment in Athletes with Low EA

- Treatment aims to restore or normalize body weight with improved nutrition and energy status
- Recommend increasing dietary energy intake, decrease exercise energy expenditure or both
- Individual treatment plan should incorporate a variety of considerations such as diet quality, timing, incorporation of energy dense foods, adjustments for training, other considerations
Nonpharmacologic Treatment in Athletes with Low EA

- Increase energy intake gradually by 20-30% over baseline energy needs
- Weight gain of approximately 0.5 kg every 7-10 days
- Regular monitoring of EA by registered sports dietitian recommended
Nonpharmacologic Treatment Targets in Athletes with Low EA

- Reversal of recent weight loss
- Return of body weight associated with normal menses
- Weight gain to achieve a BMI of $\geq 18.5$ or $\geq 90\%$ of predicted weight
Vitamin D and Calcium

- Optimize vitamin D status (32-50 ng/ml)
- Vitamin D replacement if necessary
- Vitamin D, calcium supplementation (IOM)

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<tr>
<th></th>
<th>Vitamin D (IU/d)</th>
<th>Calcium (mg/d)</th>
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<tr>
<td></td>
<td>RDA</td>
<td>Max</td>
</tr>
<tr>
<td>9-18y</td>
<td>600</td>
<td>4000</td>
</tr>
<tr>
<td>19-50y</td>
<td>600</td>
<td>4000</td>
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Pharmacologic Treatment

• Nonpharmacologic treatment constitutes initial management for the triad
• Lack of evidence-based studies to unequivocally recommend pharmacologic treatment for triad disorders
• Consider if lack of response to nonpharmacologic management in an athlete with low BMD + clinically significant fracture history
Pharmacologic Treatment

• Pharmacologic medications other than estrogen and progesterone are not recommended in the absence of a fracture history

• Lack of response to treatment
  – Clinically significant reduction in BMD Z-scores after at least one year of nonpharmacologic management
  – Occurrence of new clinically significant fractures during nonpharmacologic treatment over the course of 1 year
Pharmacologic Treatment Considerations

- BMD Z-score $<-2.0$ with a clinically significant fracture history and lack of response to at least 1 year of nonpharmacologic therapy
- BMD Z-score between $-1.0$ and $-2.0$ with a clinically significant fracture history and $>2$ additional triad risk factors AND lack of response to nonpharmacologic therapy
Pharmacologic Treatment Considerations

- Transdermal estradiol replacement with cyclic progesterone may be considered in young athletes > 16 years of age and < 21 years of age with FHA to prevent further bone loss during critical window of optimal bone accrual considered if:
  - BMD Z-score ≤ -2.0 without a clinically significant fracture history and ≥ 2 additional triad risk factors AND lack of response to at least one year of nonpharmacologic management
Pharmacologic Treatment

• Estrogen administration with cyclic progesterone in female athletes with functional hypothalamic amenorrhea or prolonged oligomenorrhea who have failed nonpharmacologic treatment

• Consider contraceptive needs
Pharmacologic Treatment - OCP

• Combined oral contraceptive therapy 20-35 ug of ethinyl estradiol may *maintain* BMD in those with very low BMD

• No consistent evidence that improves BMD or reduces risk of stress fractures in the amenorrheic athlete or in anorexia nervosa
Pharmacologic Treatment – Transdermal Estrogen

• Transdermal estradiol 100 ug with cyclic progesterone (200 mg micronized progesterone or 5-10 mg medroxyprogesterone acetate) for 12 days a month maintains BMD Z-scores in adolescents with anorexia and is a consideration for low weight amenorrheic athletes who meet criteria for nonpharmacologic treatment

• Can start at 50 ug a day and increase after one month if symptomatic

• Not effective for contraception
Pharmacologic Treatment

• Indications to consider pharmacologic therapy other than estrogen replacement/OCP
  – Contraindication to estrogen
  – Lack of response to estrogen after > 18-24 months
  – Eumenorrheic exerciser who meets criteria for pharmacologic therapy
  – Athletes with multiple debilitating fractures and significant morbidity
Pharmacologic Treatment

• Athletes considered for pharmacologic therapy should undergo a complete metabolic work up

• Consultation with a metabolic bone expert or endocrinologist is advisable
Pharmacologic Treatment - Other

• Other options for pharmacologic therapy include:
  – Bisphosphonates
  – Teriparatide
• Lack of research in the young athlete
• To be considered only if the athlete meets pharmacologic criteria and when no other strategy is effective or when other strategies contraindicated
Bisphosphonates

• Consider only if other strategies are ineffective or contraindicated
• Long $T_{1/2}$, concerns for possible teratogenicity
• Birth control measures for women of reproductive age and counsel
Teriparatide

- Promising, limited data in premenopausal women
- Ongoing studies
- Contraindicated in pregnancy
- Black box warning for those with increased baseline risk for osteosarcoma
  - Open epiphyses
  - Unexplained elevations of ALP
  - Paget’s disease
  - Prior external beam or implant radiation of the skeleton
Denosumab

• No data
• Contraindicated in pregnancy
Triad Clearance & RTP - The Problem

• Clearance
  – Many female athletes with the triad are being cleared without being adequately assessed, managed or treated

• Return to Play
  – Athletes often return to play after triad-related injuries or illness without adequate management and follow up
Why Clearance & RTP Guidelines?

• The female athlete triad is largely preventable
• The prevalence for one or more components is relatively high
• Health consequences are significant
  ➢ Hypothalamic amenorrhea
  ➢ Low BMD
  ➢ Stress fractures
  ➢ Premature osteoporosis
  ➢ Disordered eating precursor to eating disorders
  ➢ High incidence of co-morbid psychiatric disorders in those with DE/ED
Return to Play Goal

• To return an injured or ill athlete to practice or competition without putting the individual at undue risk for injury or illness

(Herring et al. The team physician and the return to play decision: A consensus statement – 2012 update. MSSE, 2012)
The Team Physician’s Role in RTP

• Establish a RTP process
• Evaluate athlete with medical condition
• Treat and rehabilitate the athlete
• Return the athlete to play after it is determined to be safe to do so

(Herring et al. The team physician and the return to play decision: A consensus statement – 2012 update. MSSE, 2012)
Decision-Based Model for Return to Play for the Female Athlete Triad

- Evaluation of health status
  - Medical factors
- Evaluation of participation status
  - Sport risk modifiers
  - Decision modification

Risk Evaluation Process

**Step 1**
Evaluation of Health Status
- Medical Factors
  - Patient Demographics (age, ethnicity)
  - Symptoms (fatigue, lightheadedness, skeletal pain, weight loss/fluctuations)
  - Personal Medical History (Triad risk factors - severity/chronicity, adolescent growth phase, hospitalizations, other medical factors)
  - Family History/Genetics (eating disorders, other psychiatric illnesses, menstrual dysfunction, osteoporosis, fracture history)
  - Signs (Physical Exam) (bradycardia, low BP/orthostatic, low BMI <17.5, low % body fat, lanugo, Russel’s sign, other)
  - Lab Tests/ECG/DXA (metabolic panel, CBC, hormonal work up if oligomenorrhea and/or amenorrhea, 25-OH Vit D if low BMD or bone stress injury, TSH and TFTs, other; ECG if ED or if indicated; DXA if indicated; X-ray and imaging if suspect bone stress injury)
  - Functional Tests (functional movement screen if indicated, other as indicated)
  - Psychological State (depression, anxiety, OCD co-morbidities; severity of illness; athlete’s willingness to participate in treatment; psych testing if indicated)
  - Potential Seriousness (ED, other psych hospitalization, chronicity of each triad spectrum, co-morbidities, bone health eval/DXA)
- Type of Sport (leaness vs non-leaness sport, sport with subjective judging, thin physique felt advantageous, endurance sport, weight class, impact nature/bone loading)
- Position Played (perceived advantage if lean)
- Competitive Level (competitive vs non-competitive, high school, club, college/intercollegiate/division rank, elite, professional, Olympic)
- Timing & Season (in season vs off season, early in season or late)
- Pressure from Athlete (desire to compete and excel)
- External Pressure (coach, family, friends, administration, society)
- Masking the Injury (analgesia, ignoring symptoms)
- Conflict of Interest (scholarship athlete, professional, Olympic athlete, other)

**Step 2**
Evaluation of Participation Risk
- Sport Risk Modifiers
- Cumulative Risk Assessment Score (based on cumulative Triad risk stratification)

**Step 3**
Decision Modification
- Decision Modifiers

*Return-to-Play Decision*
Establishment of a Clearance & RTP Process with Risk Stratification

- Risk stratification utilizing evidence-based risk factors for the triad stratified by magnitude of risk
- Goal to prevent and manage poor outcomes related to the triad
  - Progression of disordered eating to eating disorders
  - Hypothalamic amenorrhea and prolonged oligomenorrhea
  - Low BMD progression to osteoporosis
  - Stress reactions & fractures
Evidence-Based Independent Risk Factors Associated With Poor Triad Outcomes

- Low energy availability with or without disordered eating/eating disorders
- Low BMI
- Delayed menarche
- Oligo/amenorrhea
- Low BMD
- Stress reaction/fracture history
- Leanness sport
Concept of Cumulative Risk

• Evidence that outcomes of low BMD and stress reactions/fractures are greatest with combination of triad risk factors

• Dose-response relationship

Risk Stratification by Cumulative Risk & Magnitude of Risk

- Low Risk
- Moderate Risk
- High Risk
Female Athlete Triad Cumulative Risk Assessment

<table>
<thead>
<tr>
<th>Risk Factors</th>
<th>Low Risk = 0 points each</th>
<th>Moderate Risk = 1 point each</th>
<th>High Risk = 2 points each</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Low EA with or without DE/ED</strong></td>
<td>□ No dietary restriction</td>
<td>□ Some dietary restriction‡; current/past history of DE;</td>
<td>□ Meets DSM V criteria for ED*</td>
</tr>
<tr>
<td><strong>Low BMI</strong></td>
<td>□ BMI ≥ 18.5 or</td>
<td>□ BMI 17.5 &lt; 18.5 or</td>
<td>□ BMI ≤ 17.5 or &lt; 85% EW or</td>
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<tr>
<td></td>
<td>≥ 90% EW** or</td>
<td>&lt; 90% EW or</td>
<td>≥ 10% weight loss/month</td>
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<tr>
<td></td>
<td>weight stable</td>
<td>5 to &lt; 10% weight loss/month</td>
<td></td>
</tr>
<tr>
<td><strong>Delayed Menarche</strong></td>
<td>□ Menarche &lt; 15 years</td>
<td>□ Menarche 15 to &lt; 16 years</td>
<td>□ Menarche ≥16 years</td>
</tr>
<tr>
<td><strong>Oligomenorrhea and/or Amenorrhea</strong></td>
<td>□ &gt; 9 menses in 12 months*</td>
<td>□ 6-9 menses in 12 months*</td>
<td>□ &lt; 6 menses in 12 months*</td>
</tr>
<tr>
<td><strong>Low BMD</strong></td>
<td>□ Z-score ≥ -1.0</td>
<td>□ Z-score -1.0*** &lt; - 2.0</td>
<td>□ Z-score ≤ -2.0</td>
</tr>
<tr>
<td><strong>Stress Reaction/Fracture</strong></td>
<td>□ None</td>
<td>□ 1</td>
<td>□ ≥ 2; ≥ 1 high risk or of trabecular bone sites†</td>
</tr>
</tbody>
</table>

Cumulative Risk (total each column, then add for total score)  
[_____ points] + [_____ points] + [_____ points] = [_____ Total Score]
# Female Athlete Triad Clearance and Return to Play Recommendations by Risk Stratification

<table>
<thead>
<tr>
<th></th>
<th>Cumulative Risk Score*</th>
<th>Low Risk</th>
<th>Moderate Risk</th>
<th>High Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Full Clearance</strong></td>
<td>0 – 1 point</td>
<td>☐</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Provisional/Limited Clearance</strong></td>
<td>2 – 5 points</td>
<td>☐ Provisional Clearance</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>☐ Limited Clearance</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Restricted from Training and Competition</strong></td>
<td>≥ 6 points</td>
<td></td>
<td>☐ Restricted from Training/Competition-Provisional</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>☐ Disqualified</td>
<td></td>
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</table>
Triad Clearance & RTP Decisions

• #1 Full Clearance
  ➢ Low risk
  ➢ Follow up as determined by physician

• #2 Provisional/Limited Clearance (2 categories)
  ➢ Provisional
    ➢ Moderate risk
    ➢ Athlete is cleared, but must follow up with requested members of the multidisciplinary team, as determined by the team physician, and have necessary tests within a defined time period
    ➢ Consider written contract
  ➢ Limited Clearance
    ➢ Athlete is cleared, but team physician determines training/competition is limited, due to current risk factors
    ➢ Must follow up with requested multi-disciplinary team members, as determined by the team physician, and have necessary tests within a defined time period
    ➢ Written contract

• #3 Not Cleared (2 categories)
  ➢ Provisional
    ➢ High risk
    ➢ Athlete is not cleared
    ➢ Management/treatment of triad condition and follow up within defined time period and reassessed for clearance/RTP
    ➢ Written contract
  ➢ Disqualified
    ➢ High risk
    ➢ Athlete unable to safely train/complete
    ➢ Athlete treated for medical condition
Triad Clearance & RTP Decisions

• #1 Full Clearance
  – Low risk
  – Follow up as determined by physician
Triad Clearance & RTP Decisions

• #2 Provisional/Limited Clearance (2 categories)
  – Provisional
    ➢ Moderate risk
    ➢ Athlete is cleared, but must follow up with requested members
      of the multidisciplinary team, as determined by the team
      physician, and have necessary tests within a defined time period
    ➢ Consider written contract
  – Limited Clearance
    ➢ Moderate risk
    ➢ Athlete is cleared, but training/competition limited, due to
      current risk factors
    ➢ Must follow up with multi-disciplinary team members, as
      determined by the team physician, and have necessary tests
      within a defined time period
    ➢ Consider written contract
Triad Clearance & RTP Decisions

• #3 Not Cleared (2 categories)
  – Provisional
    ➢ High risk
    ➢ Athlete is not cleared
    ➢ Management/treatment of triad condition and follow up within defined time period and reassessed for clearance/RTP
    ➢ Written contract
  – Disqualified
    ➢ High risk
    ➢ Athlete unable to safely train/compete
    ➢ Athlete treated for medical condition(s)
Female Athlete Triad Clearance & RTP Multidisciplinary Team Referral

• Once athlete is determined to have Provisional/Limited Clearance or Not Cleared, they are referred to the multidisciplinary team members, as determined by the team physician

• Multidisciplinary team members include the physician, dietitian, mental health practitioner if needed; others
Physician Follow Up

• A follow up time interval is established with the physician

• During this time the athlete meets with the selected members of the multidisciplinary team

• The athlete may not be cleared if she does not comply with the recommended follow up
Athlete Contracts

• Valuable tool
• Can be verbal or written (preferred)
• Includes reason for provisional/limited clearance or restriction from training
• Specifies steps necessary for treatment and follow up, and time frame
• Specifies consequences if not followed
Female Athlete Triad Treatment & RTP - Summary

• Young girls and women with the Female Athlete Triad have significant health risks

• The team physician’s responsibility is to assess risk for the Female Athlete Triad at the PPE and determine safe clearance and return to play

• The team physician’s responsibility is to adequately manage and treat female athletes identified with the Female Athlete Triad

• The 2014 Female Athlete Triad Coalition Consensus Statement on Treatment and Return to Play of the Female Athlete Triad provides guidelines for clinicians that implement risk stratification, taking into account magnitude of risk, and provides recommendations for treatment and return to play
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, CA, May 2012, and 2nd International Conference Held in Indianapolis, IN, May 2013

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Thank you!