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

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Abstract
The female athlete triad is a medical condition often observed in physically active girls and women and involves three components: 1) low energy availability with or without disordered eating, 2) menstrual dysfunction, and 3) low bone mineral density. Female athletes often present with one or more of the three triad components, and early intervention is essential to prevent its progression to serious end points that include clinical eating disorders, amenorrhea, and osteoporosis. This consensus statement presents a set of recommendations developed following the first (San Francisco, CA) and second (Indianapolis, IN) International Symposia on the Female Athlete Triad. This consensus statement was intended to provide clinical guidelines for physicians, athletic trainers, and other health care providers for the screening, diagnosis, and treatment of the female athlete triad and to provide clear recommendations for return to play. The expert panel has proposed a risk stratification point system that takes into account magnitude of risk to assist the physician in decision making regarding sport participation, clearance, and return to play. Guidelines are offered for clearance categories, management by a multidisciplinary team, and implementation of treatment contracts.

Introduction
What follows is a summary of the Female Athlete Triad Consensus Statement on Treatment and Return to Play, first published in the British Journal of Sports Medicine in February 2014 (25) and subsequently in the Clinical Journal of Sports Medicine in March 2014 (24). The consensus statement is the first of its kind and represents a set of recommendations developed following the first (San Francisco, CA) and second (Indianapolis, IN) International Consensus Conference on the female athlete triad (triad). It is intended to provide clinical guidelines for physicians, athletic trainers, and other providers for the treatment of the triad and to provide clear recommendations for return to play (RTP). This consensus statement serves as a supplement to the American College of Sports Medicine (ACSM)’s revised Position Stand on the triad published in 2007 (86).

While agreement exists concerning the primary guidelines and recommendations communicated in this document, the authors acknowledge that the underlying levels of scientific evidence regarding some elements of the triad, particularly those related to treatment strategies, still are evolving. The treatment guidelines and RTP recommendations proposed herein are based on published literature available to date, with consensus from the international team of experts convened at the two consensus conferences. As such, management and RTP decisions should be based on informed clinical judgment, keeping in mind individual risk factors and concerns as described herein.
Definition of the Triad Model
The triad is a medical condition often observed in physically active girls and women and involves any one of the three components: 1) low energy availability (EA) with or without disordered eating (DE), 2) menstrual dysfunction, and 3) low bone mineral density (BMD) (86) (Fig. 1). Female athletes often present with one or more of the three triad components, and early intervention is essential to prevent its progression to serious end points that include clinical eating disorders (ED), amenorrhea, and osteoporosis (86).

The goal of ACSM’s Position Stand in presenting the triad along a spectrum was to highlight the importance of recognizing athletes who exhibit subclinical abnormalities and thus allow for early intervention. Prevention and early intervention remain keys to avoid the more serious clinical end points of the triad (i.e., ED, amenorrhea, or osteoporosis) (86).

Health Consequences Associated with the Triad
Why Is the Triad Harmful to an Athlete’s Health?
Chronic low EA can have significant effects on health and physical performance, particularly when a clinical ED is present (27). Low EA plays a causal role in the induction of exercise-associated menstrual disturbances (17,118). Hypoestrogenemia associated with prolonged reproductive suppression can impact musculoskeletal and cardiovascular health negatively (26,89,96). Low EA also can have negative musculoskeletal effects independent of hypoestrogenism (26,28). Bone stress injuries, including the spectrum of stress reactions and stress fractures, are more common in female athletes with menstrual irregularities and/or low BMD (11,32,36,57,85,108) as well as in female military recruits (60,93). Bone stress injuries also sideline female athletes and reduce their competitive performance. Junior elite swimmers with amenorrhea experience poor sport performance when compared with their normally cycling counterparts (112). Other medical complications of triad disorders can extend to the endocrine, gastrointestinal, renal, and neuropsychiatric systems (14,42,86,98).

A complete discussion of the health consequences of the triad is beyond the scope of this article and can be found elsewhere (10,86).

Screening, Risk Stratification, and Diagnosis of the Triad
What Are the Best Tools to Screen for the Triad?
Early detection of athletes at risk is critical to prevent the triad. Screening for the triad should be undertaken as part of the preparticipation physical evaluation (PPE) (65,100,101). The PPE should include questions that address all aspects of the triad spectrums. Although there is limited evidence related to the efficacy of screening questions (77), it is recommended that female athletes undergo annual screening with the triad-specific self-report questionnaire displayed in Table 1, followed by a more in-depth evaluation of whether the athlete has, or is at risk for, any triad component. Screening for the triad should be performed in both collegiate and high school athletes (94,109). It is important to note that existence of any one of the triad components should prompt more thorough investigation for the others. Screening for components of the triad in female adolescents, along with early intervention, is especially important, given that 90% of peak bone mass is attained by 18 years of age (76), thereby providing a window of opportunity for optimizing bone health.

Diagnosis of the Triad
How Are Triad Conditions Diagnosed?
Following screening, accurate diagnosis of any of the triad disorders is dependent on a thorough evaluation of the athlete by the physician and other members of an experienced multidisciplinary health care team. Members of the multidisciplinary team should include a physician, a sports dietitian (a registered dietitian, who preferably is a board-certified specialist in sports dietetics) (97,103), and a mental health professional if the athlete has DE or clinical ED. Other members of the team may include an exercise physiologist, certified athletic trainer, and medical consultants.

Essential to the process of screening, evaluation, diagnosis, and treatment are the athlete’s honesty and willingness to participate in each of these steps. Each member of the multidisciplinary team must develop a therapeutic alliance with the athlete. The process of engagement and active participation in treatment often is ongoing, reflecting the challenges of restoring adequate EA. Written policies regarding screening, evaluation, and treatment of the triad need to be reviewed with athletes and, when appropriate, with their parents, and supported by coaches and administrators (Fig. 3).

How Is Low EA Diagnosed?
Overt signs of low EA include a body mass index (BMI) <17.5 kg/m² or <85% of expected body weight in adolescents (86). When body weight is not particularly low, more detailed information regarding food intake and energy expenditure is necessary to diagnose low EA. Other markers...
of low EA in the absence of DE and recent weight loss include reduced fat mass and physiological signs of adaptation to chronic energy deficiency such as reduced resting metabolic rate (RMR) (23,88), low triiodothyronine (23,88), and a ratio of measured RMR/predicted RMR less than 0.90 (22,39,102).

It is important to note that methods for assessing EA, dietary intake, and energy expenditure are improving but are imprecise. An experienced sports dietitian or an exercise physiologist can help provide expertise on completing these assessments. An index of daily EA is defined as energy intake (kcal) minus exercise energy expenditure (kcal) divided by fat-free mass (FFM) or lean body mass (kg) (66). A threshold below which detrimental physiological changes in reproductive function, metabolism, and bone occur has been identified as 30 kcal·kg\(^{-1}\)·FFM\(^{-1}\)·d\(^{-1}\) (67). Strategies to estimate dietary intake include 3-, 4- and 7-d dietary logs, 24-h dietary recall, and food frequency questionnaires. Regardless of the method chosen, accurate assessment of dietary intake can be challenging due to a number of factors such as underreporting of intake, modified intake during the period of reporting, and imprecise recording of portion sizes (45). Ideally athletes thought to be at risk for nutritional deficiencies should undergo a comprehensive nutrition assessment by a registered sports dietitian (97).

Practical estimates of exercise energy expenditure are largely dependent on self-report. The 2011 Compendium of Physical Activities (2) can be used to calculate exercise energy expenditure, whereby kilocalories of energy expenditure = metabolic equivalent of task × weight in kilograms × duration of activity in hours. The third component of the EA equation is kilograms of FFM, which is obtained from measurement of body weight in kilograms and from an estimate of body fatness. Various methods can be used to estimate body fat. Dual-energy x-ray absorptiometry (DXA) is a precise method and is widely available (110); other clinically accessible methods commonly used among athletes include air displacement plethysmography, skinfold measurements, and bioelectrical impedance (78). Having gathered the aforementioned data, one can access the EA calculator provided on the Triad Coalition Web site (http://www.femaleathletetriad.org/calculators/) to estimate EA. Ideally physically active women should aim for at least 45 kcal·kg\(^{-1}\)·FFM\(^{-1}\)·d\(^{-1}\) of energy intake to ensure adequate EA for all physiological functions (66,86).

How Is Amenorrhea Diagnosed?

Athletes and physically active women presenting with primary or secondary amenorrhea require evaluation to rule out pregnancy, systemic diseases, and endocrinopathies as no single blood test can confirm a diagnosis. The diagnosis of functional hypothalamic amenorrhea (FHA) in athletes secondary to low EA is a diagnosis of exclusion. In the setting of low EA, reproductive physiology is suppressed as a “functional” strategy to prevent pregnancy and further energy drain. FHA is manifest through a decrease in the pulsatile release of gonadotropin-releasing hormone from the hypothalamus. In turn, this results in diminished pulsatility in the release of gonadotropins from the pituitary gland, ultimately resulting in low circulating estrogen levels. An algorithm for the diagnosis of primary/secondary amenorrhea, modified from the Jameson and De Groot textbook of endocrinology (50), can be viewed in Figure 2.

How Is Low BMD Diagnosed?

Definitions published by the International Society of Clinical Densitometry for low BMD and osteoporosis in children and adolescents (Table 2) and for premenopausal women (Table 3) (64) as well as ACSM-suggested criteria for female athletes involved in regular weight-bearing sports should be utilized in making a diagnosis of low BMD (86). Criteria for who should undergo DXA scan for BMD assessment, which anatomical site(s) should be considered for a DXA scan, and how often DXA scans should be performed are described as follows.

Who Should Get DXA Scans for BMD Testing?

Indications for DXA testing in an athlete include the following:

- ≥1 “high-risk” triad risk factors
  - History of a Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-V) diagnosed ED (6)
  - BMI ≤17.5 kg·m\(^{-2}\), <85% estimated weight, or recent weight loss of ≥10% in 1 month
  - Menarche at ≥16 years of age
  - Currently experiencing or history of <6 menses over 12 months
  - Two prior stress reactions/fractures, one high-risk stress reaction/fracture (Fig. 4), or a low-energy nontraumatic fracture (16,72,85)
  - Prior z-score of less than −2.0 (after at least 1 year from baseline DXA); or
- ≥2 “moderate-risk” triad risk factors
  - Currently experiencing or history of DE for 6 months or longer
Table 2. Definition of low BMD and osteoporosis in children and adolescents (aged 5 to 19).

<table>
<thead>
<tr>
<th>The diagnosis of osteoporosis in children and adolescents requires the presence of both a clinically significant fracture history and low BMC or low BMD.</th>
</tr>
</thead>
<tbody>
<tr>
<td>A clinically significant fracture history is one or more of the following:</td>
</tr>
<tr>
<td>- Long bone fracture of the lower extremities</td>
</tr>
<tr>
<td>- Vertebral compression fracture</td>
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<tr>
<td>- Two or more long-bone fractures of the upper extremities</td>
</tr>
<tr>
<td>- Low BMC or BMD is defined as a BMC or areal BMD z-score that is less than or equal to −2.0, adjusted for age, gender, and body size, as appropriate.</td>
</tr>
</tbody>
</table>

Source: Lewiecki et al. (64).

The ACSM defines low BMC or BMD as a z-score that is less than −1.0 in female athletes in weight-bearing sports (86).

Table 3. Definition of low BMD and osteoporosis in premenopausal women.

<table>
<thead>
<tr>
<th>The diagnosis of osteoporosis in premenopausal women cannot be diagnosed on the basis of BMD alone.</th>
</tr>
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<tbody>
<tr>
<td>A BMD z-score of less than or equal to −2.0 is defined as “below the expected range for age.”</td>
</tr>
<tr>
<td>A BMD z-score above −2.0 is “within the expected range for age.”</td>
</tr>
<tr>
<td>Osteoporosis is diagnosed if there is a BMD z-score of less than or equal to −2.0 plus secondary causes of osteoporosis.</td>
</tr>
</tbody>
</table>

Source: Lewiecki et al. (64).

The ACSM defines low BMC or BMD as a z-score that is less than −1.0 in female athletes in weight-bearing sports (86).
on medications for 6 months or longer that may impact bone (such as depot medroxyprogesterone acetate, oral prednisone, and others) (106), also should be considered for DXA testing.

How Often Should Athletes Get DXA Testing?

The frequency of BMD assessment by DXA will depend on the initial BMD and ongoing clinical status of the athlete. Those with definitive indications for DXA testing may require BMD testing every 1 to 2 years to determine whether there is ongoing bone loss and to evaluate treatment.

Which Sites Should Be Screened with a DXA Scan?

BMD z-scores (and not T-scores) should be reported for all children, adolescents, and premenopausal women.

1) Adult women ≥20 years old
- Weight-bearing sites (posteroanterior spine, total hip, and femoral neck)

<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>Low EA with or without DE/ED</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>Low BMI</td>
<td>☐ BMI ≥ 18.5 or ≥90% EW** or weight stable</td>
<td>☐ BMI 17.5 &lt; 18.5 or &lt;90% EW or 5 to &lt;10% weight loss/month</td>
<td>☐ BMI &lt;17.5 or &lt;85% EW or ≥10% weight loss/month</td>
</tr>
<tr>
<td>Delayed Menarche</td>
<td>☐ Menarche &lt;15 years</td>
<td>☐ Menarche 15 to &lt;16 years</td>
<td>☐ Menarche ≥16 years</td>
</tr>
<tr>
<td>Oligomenorrhea and/or Amenorrhea</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>Low BMD</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>Stress Reaction/Fracture</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

Figure 3: Treatment of the triad. The three components of the triad recovery at different rates with the appropriate treatment. Recovery of energy status is observed typically after days or weeks of increased energy intake and/or decreased energy expenditure. Recovery of menstrual status is observed typically after months of increased energy intake and/or decreased energy expenditure, which improves energy status. Recovery of BMD may not be observed until years after recovery of energy status and until menstrual status has been achieved.

Figure 4: Triad: cumulative risk assessment. The cumulative risk assessment provides an objective method of determining an athlete’s risk using risk stratification and evidence-based risk factors for the triad (11,38,108). This assessment then is used to determine an athlete’s clearance for sport participation (Fig. 5). * Currently experiencing or has a history (3,29). ** ≥90% EW (30,41,61,104); absolute BMI cut-offs should be not used for adolescents. *** Weight-bearing sport (86). † High-risk skeletal sites associated with low BMD and delay in RTP in athletes with one or more components of the triad include stress reaction/fracture of trabecular sites (femoral neck, sacrum, and pelvis) (72,85). ‡ Some dietary restriction as evidenced by self-report or low/inadequate energy intake on diet logs. EW, expected weight.
• Non-weight-bearing sites, namely the radius, if weight-bearing sites cannot be assessed for any reason

2) Children, adolescents, and young women <20 years
• Posteroanterior lumbar spine bone mineral content (BMC) and areal BMD
• Whole body less head if possible (otherwise, whole body) BMC and areal BMD (64)
• Adjust for growth delay (with height or height age) or maturational delay (with bone age)
• Use pediatric reference data, and when possible, report height-adjusted z-scores (43).

Nonpharmacological Treatment Guidelines for the Clinical Sequelae Associated with the Triad
What Are the Components of Nonpharmacological Treatment for Each Triad Condition?
Due to the multifactorial etiology of the triad, an optimal treatment approach must address the underlying cause of the triad, that is, low EA (86). Energy status must be normalized primarily through modifications of diet and exercise training with the goal of increasing EA (27,86). Restoration or normalization of body weight is the best strategy for successful resumption of menses and improved bone health (4–8,84,86). It is important to emphasize that the amount of weight gain that typically leads to resumption of menses is variable among individuals (33,59,69).

In studies thus far, a range of approximately 5% to 10% of body weight or 1 to 4 kg of weight gain has been associated with resumption of menses (33,59,69). The development of any triad treatment plan should include consideration of goals of the athlete, her unique diet and training practices, coexisting conditions, and a systematic approach for monitoring changes (e.g., regular meetings with treatment team members, use of written contracts).

Specific Nonpharmacological Recommendations for Interventions in Athletes with Low EA
Specific treatment recommendations depend on identifying how low EA developed in the athlete. There may be four unique pathways to low EA and, as such, four unique treatment recommendations.

1. If the cause of low EA is inadvertent undereating, then referral for nutritional education is sufficient. Nutrition education ideally should include a sports dietitian. Either a sports dietitian or an exercise physiologist should complete an assessment of energy expenditure and EA.

2. If the cause of low EA is DE, the referral should be to a physician and for nutritional counseling with a sports dietitian.

3. If the cause of low EA is intentional weight loss without DE, then referral for nutritional education is likely sufficient.

4. If the cause of low EA involves clinical ED, treatment should include evaluation and management with a physician, nutritional counseling with a sports dietitian, and referral to a mental health practitioner for psychological treatment (86,107). In this case, the reversal of low EA will be not possible without psychological treatment (13,53,86,104,107).

Since the treatment goal is to restore or normalize body weight, it is recommended that athletes increase dietary energy intake, decrease exercise energy expenditure, or both. Recommendations should consider individual preferences and may depend on where the athlete is in the competitive season (e.g., reductions in training volume may be not feasible in season, acceptance of increased energy intake better may be received vs reduction in training volume). Prescribed changes in energy intake to achieve increased BMI and/or body weight goal should be gradual, beginning with an approximately 20% to 30% increase in caloric intake over baseline energy needs or the amount of energy required to gain approximately 0.5 kg every 7 to 10 d (33,59,69). For an athlete consuming 2,000 kcal·d⁻¹, this would represent a gradual increase of 200 to 600 kcal·d⁻¹ accomplished over several months. If EA (intake (kcal) − exercise (kcal·kg⁻¹FFM·d⁻¹)) can be estimated reliably, the target should be ≥45 kcal·kg⁻¹FFM·d⁻¹.

A successful treatment plan requires standardized periodic monitoring of body weight. Athletes should be weighed on the same scale while wearing minimal clothing, such as shorts and a T-shirt, to reduce the likelihood of falsifying their weight (51). The frequency of weight monitoring depends on the degree to which weight determines health and eligibility to participate in sport. A reasonable frequency is weekly when initiating a treatment program. The goal of treatment for athletes with ED is to normalize pathological eating behaviors, reduce dieting attempts, and alter negative emotions and beliefs associated with food and body image (122).

Specific Recommendations That Target Low BMD
The etiology of bone loss among women with amenorrhea includes energy deficiency-related factors and estrogen deficiency (26,49,82). Thus, weight gain and subsequent resumption of menses are keys to prevent further loss of bone mass (79,84). It is estimated that women with amenorrhea will lose approximately 2% to 3% of bone mass per year if the condition remains untreated (8,79,84). In exercising women with low BMD, treatment recommendations include increasing EA and optimizing weight gain in order to promote the resumption of menses (37,79). In addition, calcium and vitamin D status should be optimized.

Weight-bearing exercise is a primary nonpharmacological strategy for increasing and maintaining BMD and geometry across the life-span (9). Bone tissue is highly responsive to dynamic and high-magnitude loading (87), high-impact loading (12,55,111,119), and resistance training (71,113). To date, prospective studies are lacking wherein investigators explore the impact of resistance training and high-magnitude loading on the bone health of athletes with amenorrhea. However lean mass has been reported to be a strong predictor of hip BMD among anorexic adolescents (83) and also adolescent athletes and nonathletes (19). Realizing that high-impact activity in females with low BMD (± fractures), in fact, may result in fracture (68), further studies are necessary to determine the impact of combined weight-bearing programs on BMD and fracture risk in athletes with low BMD.
What Is the Recommended Time Course of Nonpharmacological Treatment (Including Follow-up)?

Treatment of triad conditions by increasing EA will result in recovery of physiological systems at different rates. Notably the time to resumption of menses may vary among exercising women and is dependent on the severity of the energy deficiency and duration of menstrual dysfunction (7,69,84). An increase in EA can alter metabolic hormone profiles positively within days to weeks, with concomitant changes in body weight occurring over weeks and months. Weight gain has been observed as a clinically positive outcome associated with resumption of menses and enhanced bone health in exercising women (37,59,79,84,123). The recovery of menstrual function with strategies to increase EA can occur within several months (69) but may take longer than 1 year (7). Improvements in BMD will occur more slowly, often over several years. Whether or not BMD can be restored to levels appropriate for age and training status remains unclear (31,52,56).

Pharmacological Treatment Strategies for the Clinical Sequelae of the Triad

Overview

There is no evidence at this time to recommend pharmacological therapy unequivocally for athletes with the triad disorders due to lack of evidenced-based research in this population. Nonpharmacological measures should constitute initial management in female athletes with the triad. For treatment of osteoporosis and/or in those athletes with history of multiple fracture, pharmacological management is to be considered if there is lack of response to nonpharmacological therapy for at least 1 year and if new fractures occur during nonpharmacological management. Pharmacological management also may be necessary in the psychological treatment of ED and DE, especially if there are significant comorbid conditions.

Low EA, DE, and ED

One of the challenges in addressing low EA is that it may be difficult to identify which individuals have an ED that requires more comprehensive treatment. This can be amplified by denial that there is a problem and minimization of the difficulty in changing behaviors, which are common themes for individuals with ED. The team physician should work closely with the multidisciplinary team to determine the best treatment approach for an individual athlete.

Individuals who have unintentional low EA or mild DE may respond well to nutrition education designed to eliminate low EA. Individuals with significant DE may benefit from counseling with a mental health practitioner in addition to nutrition education. In contrast, individuals who have an ED require intensive interdisciplinary attention and treatment. The American Psychiatric Association (APA) Practice Guidelines for the Treatment of Patients with Eating Disorders (5) recommend a multidisciplinary team approach to treatment, including a physician, mental health provider, and sports dietitian. Results of small randomized trials involving treatment approaches that include mindfulness training and dialectical behavior therapy are encouraging (114,120). Antidepressant medications, particularly selective serotonin reuptake inhibitors, can be helpful in the treatment of bulimia nervosa (1). The APA Practice Guidelines (5) describe limited evidence to use medications to restore weight, prevent relapse, or treat chronic anorexia nervosa. Other psychotropic medications can be beneficial in treating comorbid conditions such as anxiety, depression, and obsessive-compulsive behavior.

Menstrual Dysfunction and Low Bone Density

When considering pharmacological strategies to address amenorrhea and hypoestrogenemia in athletes and exercising women, it is essential to acknowledge that combined oral or nonoral routes of contraceptive therapy do not restore spontaneous menses; indeed contraceptive therapy simply creates an exogenous ovarian steroid environment that often provides a false sense of security when induced withdrawal bleeding occurs (15). Moreover combined oral contraceptive (COC) therapy is not associated consistently with improved BMD in athletes with amenorrhea (20,40,115) and, in fact, may compromise bone health further, given first-pass effects on hepatic production of insulin-like growth factor-1 (IGF-1), an important bone trophic hormone (44,63,117).

Replacement of Gonadal Steroids

The major gonadal steroids include estrogen, progesterone, and testosterone, all of which are low in the athlete with amenorrhea.

Estrogen replacement

Given the low endogenous concentration of IGF-1 in athletes with amenorrhea (19), further reduction in IGF-1 levels secondary to the administration of oral estrogen likely limits the beneficial antiresorptive effects of estrogen (62). In addition, the type and dose of estrogen have been implicated in the lack of efficacy of oral estrogen in increasing BMD in energy-deficient states (58). As stated in the 2007 ACSM Triad Position Stand (86), for women with FHA, increases in BMD are associated more closely with increases in weight than with COC administration (20,86), so these treatments likely need to be implemented in combination with nonpharmacological treatment to optimize effectiveness (20).

Transdermal estradiol administration, when given in replacement doses, does not suppress IGF-1 (18,54,81,117). In a randomized controlled trial in adolescent girls with anorexia nervosa, transdermal estradiol administered at doses of 100 mcg twice weekly, with cyclic progesterone (2.5 mg daily for 10 d of every month to prevent unopposed estrogen stimulation of the uterus) increased BMD in this population without a reduction in IGF-1 levels (81). The use of transdermal estradiol warrants further investigation as a strategy to provide hormone replacement therapy safely to women affected by the Triad.

Vaginal estradiol administration also circumvents hepatic first-pass metabolism, and a vaginal estrogen-progesterone combination contraceptive ring is now available. However data regarding the impact of this form of estrogen administration on BMD are conflicting, with one study suggesting maintenance of BMD and another suggesting that it may be deleterious to bone compared with no treatment in premenopausal women (73,74). Thus further research on vaginally applied estrogen is necessary.
In summary, in athletes and exercising women with FHA and prolonged amenorrhea of hypothalamic origin who meet criteria for pharmacological therapy, a reasonable option is estrogen administration with cyclic progesterone after ruling out other causes of amenorrhea. It is also essential to consider the contraceptive needs of the athlete. Before starting therapy, a thorough history and examination should be conducted to rule out contraindications for estrogen therapy.

COC therapy containing 20 to 35 mcg of ethinyl estradiol in addition to progesterone may maintain BMD in those with very low BMD measures, although data are not definitive (58,95). Most studies in adolescents and adults with anorexia nervosa and in athletes with amenorrhea suggest that COC therapies are not effective in increasing BMD (20,40,58,105) or in reducing stress fractures (20), although they are effective for contraceptive needs when used in recommended doses.

Transdermal estradiol (100 mcg of 17β estradiol) with cyclic progesterone maintains BMD Z-scores in adolescents with anorexia nervosa (81) and is a consideration for low-weight, amenorrheic athletes who meet criteria for pharmacological intervention, and as hormone replacement for adolescent amenorrheic athletes (who are at an age when they should be accruing bone rapidly towards attainment of peak bone mass). Athletes who are symptomatic with this dose for estrogen-related side effects such as nausea, bloating, and breast tenderness may be started on a lower dose of the transdermal patch (50 mcg) and the dose increased to 100 mcg after one month. Progesterone may be administered as 5–10 mg of medroxyprogesterone acetate or 100–200 mg of micronized progesterone for 12 days of every month.

Testosterone replacement

There are no data available on testosterone administration in athletes with amenorrhea and exercising women. However a recent study in adult women with anorexia nervosa demonstrated no improvement in BMD with low-dose testosterone administration despite increases in lean mass and initial increases in surrogate markers of bone formation (80).

Pharmacotherapy Other Than Gonadal Steroids for Low Bone Mineral Density

Data regarding the efficacy of other pharmacotherapy in treating low BMD with or without a fracture history in the female athlete are lacking. While pharmacological therapy is recommended for postmenopausal women and men with osteoporosis aged ≥50 years (116), the threshold for pharmacological treatment in the young female athlete with low BMD, stress fractures, and/or impaired bone accrual is less clear.

Caution must be used when considering Food and Drug Administration-approved postmenopausal treatment strategies for use in premenopausal women and children including triad athletes and exercising women. Bisphosphonates have a very long half-life and should be used with extreme caution in women of childbearing age for concerns of teratogenicity (70,91), although data to date are reassuring. The decision to initiate treatment with bisphosphonates in any premenopausal woman should be made on a case-by-case basis. Consideration should include individual fracture risk and potential medication-related adverse effects. Any use of bisphosphonate therapy in young women with the triad should be executed only by or in consultation with a board-certified endocrinologist or specialist in metabolic bone diseases. There are no published studies on bisphosphonate use among exercising and athletic women with triad disorders. Likewise there are no published studies on denosumab or teriparatide use in girls and women with triad disorders. A preliminary report in older women with anorexia nervosa demonstrated that treatment with teriparatide for 6 months increased bone formation (158%) and lumbar spine BMD (anteroposterior spine, 6.0%; lateral spine, 10.5%) compared with placebo (35). There is also a case study that suggests that 4 wk of teriparatide was associated with bone healing, reduced pain, and resumption of normal activities in two premenopausal women with stress fractures (92).

Overall, the decision to treat or not treat with pharmacological therapies does not depend on BMD z-scores alone but also on additional risk factors such as fracture history, genetics (34), cumulative Triad risk factors, which have been associated with an increased risk for low BMD (38) and bone stress injury (11), and rate of bone loss with nonpharmacological management.

Pharmacological therapy may be considered in an athlete with:

- BMD z-scores less than or equal to −2.0 with a clinically significant fracture history (Tables 2 and 3; Fig. 4) and lack of response to at least 1 year of nonpharmacological therapy and
- BMD z-scores between −1.0 and −2.0 with a clinically significant fracture history (Tables 2 and 3) and ≥2 additional triad risk factors (11,38) (Fig. 4) and lack of response to at least 1 year of nonpharmacological therapy.

Transdermal estradiol replacement with cyclic progesterone may be considered in young athletes ≥16 and <21 years of age with FHA to prevent further bone loss during this critical window of optimal bone accrual if they have the following:

- BMD z-scores less than or equal to −2.0 without a clinically significant fracture history (Tables 2 and 3; Fig. 4) and at least one additional Triad risk factor (11,38) (in addition to FHA) (Fig. 4) and lack of response to at least 1 year of nonpharmacological therapy.

Lack of response to therapy has been defined as

- A clinically significant reduction in BMD z-scores after at least 1 year of nonpharmacological therapy or
- Occurrence of new clinically significant fractures during nonpharmacological treatment over the course of 1 year.

Calcium-rich foods should be recommended with optimal calcium intake between 1,000 and 1,300 mg·d⁻¹ (99); Vitamin D status should be optimized. Daily intake of 600 IU of vitamin D is recommended by the Institute of Medicine for adolescents and adults up to age 70 (99). Higher doses may be needed if deficient or insufficient in vitamin D. Vitamin D levels should be maintained between 32 and 50 ng·mL⁻¹ (48).
When Should Pharmacological Options Other than Estrogen Be Considered as Options for Treatment?

In rare instances, pharmacological management other than estrogen replacement/COC therapy can be considered when athletes meet criteria for osteoporosis and have failed non-pharmacological therapy (with recurrent fractures) and meet one of the following criteria:

- Contraindications to estrogen,
- Lack of response to estrogen replacement after ≥18 to 24 months in a compliant patient,
- Eumenorrheic athletes/exercisers (without hypoestrogenism) who meet criteria for therapy, and
- Athletes with multiple debilitating fractures and significant morbidity.

Clearance and RTP

Despite widespread awareness and educational efforts on the triad (86,90,121), there have been no standardized guidelines for clearance and RTP. As a result, many female athletes with the triad are being cleared at their PPE without being assessed, managed, or treated adequately and often return to play without structured follow-up.

More recent studies assessing health outcomes of single and combined risk factors for the triad have demonstrated that there is increased cumulative risk for the outcomes of low BMD (38), stress fracture, and bone stress injury (11,108). For example, female collegiate runners with menstrual dysfunction had more severe bone stress injuries on magnetic resonance imaging (MRI) compared with eumenorrheic runners (85). Low BMD and higher-MRI grade bone stress injuries were independent predictors of delay of RTP (85).

What Is the Role of the Team Physician in the RTP Decision for Triad Athletes?

According to the 2012 consensus statement on The Team Physician and the Return to Play Decision (46), the physician’s duty is “to return an injured or ill athlete to practice or competition without putting the individual at undue risk for injury or illness”. In addition, the team physician’s role is to establish an RTP process, evaluate the athlete with medical conditions, treat and rehabilitate the athlete, and return the athlete to play after he or she is determined to be safe to do so.

With increasing evidence that the athlete’s risk for unfavorable outcomes of low BMD and/or bone stress injuries is greater with cumulative risk factors for the triad (11,38,108), in addition to evidence that triad risk factors may contribute to more severe bone stress injuries and a delay in RTP (85), and due to the lack of standard of care guidelines for the triad, the panel recommends the following risk stratification protocol be implemented (Figs. 4 and 5).

This risk stratification protocol has been translated into a worksheet for the physician (Fig. 4) that incorporates evidence-based risk factors for the triad (11,38,108) and takes into account the magnitude (or severity) of risk, assigning a point value for risk factors in each triad spectrum based on risk severity (low, moderate, and high risk). This cumulative risk stratification protocol then is translated into clearance and RTP guidelines for the triad based on the athlete’s cumulative risk score (Fig. 5). Future research is needed.

<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></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Restricted from Training and Competition</strong></td>
<td>≥ 6 points</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>□</td>
<td>Provisional Clearance</td>
<td>□</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Limited Clearance</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Restrict from Training/Competition-Provisional</td>
<td>□</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Disqualified</td>
<td></td>
</tr>
</tbody>
</table>

*Cumulative risk score determined by summing the score of each risk factor (low, moderate, and high risk) from the cumulative risk assessment (Fig. 4). Clearance/RTP status for athletes at moderate-to-high risk for the triad: provisional clearance/RTP — clearance determined from risk stratification at the time of evaluation (with possibility for status to change over time depending on athlete’s clinical progress); limited clearance/RTP — clearance/RTP granted but with modification in training as specified by a physician (with possibility for status to change depending on clinical progress and new information gathered); restricted from training/competition (provisional) — athlete not cleared or able to RTP at present time, with clearance status reevaluated by a physician and a multidisciplinary team with clinical progress; disqualified — not safe to participate at present time. Clearance status is to be determined in the future depending on clinical progress, if appropriate. It is the recommendation of the consensus panel that athletes diagnosed with anorexia nervosa who have a BMI <16 kg m⁻² or with moderate-to-severe bulimia nervosa (purging >4 times per week) should be restricted from training and competition categorically. Future participation is dependent on treatment of their ED, including ascertainment of BMI >18.5 kg m⁻², cessation of binging and purging, and close interval follow-up with the multidisciplinary team.
to assess whether implementation of a risk stratification model results in improved outcomes for female athletes with triad disorders.

**Risk Stratification and the Multidisciplinary Team**

Who are the members of the multidisciplinary team?

The primary goal of the risk stratification protocol is to optimize health and reduce risk for injury and illness associated with the triad. Best practice for outpatient management of the triad can be accomplished with a multidisciplinary team consisting of the team physician, a sports dietitian, and often a mental health practitioner (53). Other team members may include the athlete’s coach, athletic trainer, family members, and other professionals, depending on the athlete’s unique situation.

What are the recommendations for clearance and RTP based on risk stratification?

The intent of this risk stratification developed for the triad is to determine clearance and RTP recommendations. Athletes at low risk can be cleared fully (assuming otherwise healthy). Athletes at moderate risk for the triad can be cleared provisionally or receive limited clearance. Provisional clearance would include clearance for full training/competition, with the understanding that the athlete will be compliant with the recommendations outlined by the multidisciplinary team. With limited clearance, the athlete is cleared, but there are limitations specified with the athlete’s training and competition based on the athlete’s health status. Athletes determined to be at high risk are restricted from training and competition. In this category, the athlete’s status can be provisional or the athlete may be disqualified. If the health care team determines that the athlete may be able to reach the stated health goals, the status is provisional and a plan is outlined by the multidisciplinary team for a given period and is reevaluated as the athlete’s health status improves. If severity of risk is determined to be too high for the athletic participation at the time of the PPE and prognosis is determined to be poor, the athlete is disqualified and clearance/RTP is reevaluated with clinical progress, if appropriate.

It is hoped that this risk stratification developed for the triad will assist health care providers working with female athletes to minimize risk associated with the triad disorders. With ongoing research, updates to the risk stratification can be implemented in hopes of guiding treatment and decision making for clearance and RTP.

**Treatment Contracts**

How does the team physician utilize contracts?

Athletes in the moderate-risk and high-risk categories should receive a written contract that is reviewed and presented to them by the team physician after their initial evaluation. The goal of the written contract is to specify the

![Figure 6: Decision-based RTP model for the triad. *RTP decision is determined by the primary care or team physician and is based on a complex and comprehensive synthesis of health status, cumulative risk assessment, participation risk, sport, and decision modifiers. 25(OH) Vit D, 25-hydroxyvitamin D; BP, blood pressure; CBC, complete blood count; OCD, obsessive-compulsive disorder; TFT, thyroid function tests; TSH, thyroid-stimulating hormone. [Adapted from Creighton DW, Shrier I, Shultz R., et al. Return-to-play in sport: a decision-based model. Clin J. Sports Med. 2010; 20:379–85. Copyright © 2010. Wolters Kluwer/Lippincott Williams and Wilkins. Used with permission.]

*Return-to-Play Decision*
criteria necessary for ongoing or future clearance and RTP for the female athlete with the multidisciplinary team members and to ensure a shared understanding of how the clinical status of the athlete will be followed with each member of the multidisciplinary team.

The team physician coordinates the treatment goals with each multidisciplinary team member and includes the specific recommendations in the contract in addition to the requested frequency of visits and expectations for each team member. The team physician then reviews the recommendations with the athlete and answers any questions. In the case of the written contract, both athlete and team physician sign the contract after it is discussed. (Please refer to the Appendix on page 232 for an example of a written contract for the triad, which can be modified based on the athlete’s clearance status).

Decision-Based Model for RTP

What other factors play a role in clearance and RTP decision?

In addition to risk stratification, the team physician must take into account the athlete’s unique situation in making the final decision for clearance and RTP (47). The decision-based RTP model developed by Creighton et al. (21) (Fig. 6) points out the complexities in RTP decision making. It is of paramount importance that the team physician has the ultimate say in the decision making process for clearance and RTP (46,47,75). Although the team physician has this authority to make the final decision, the decision is often the product of consultation with the multidisciplinary team and other concerned parties (which may include parents and coaches). The physician always must have the athlete’s health and safety as the first priority in the decision-making process, which should supersede all other pressures or circumstances that may arise.

Conclusions

Young girls and women with the triad have significant health risks. Historically many of these athletes have been cleared for sport participation without appropriate evaluation, management, and treatment. Similarly after medical illness or injury, athletes with the triad often return to play prematurely and without adequate treatment and follow-up. It is the team physician’s responsibility to ensure that each and every athlete that is cleared for participation in sport or RTP after an injury or illness return only when it is determined safe to do so. This evidenced-based risk stratification point system takes into account magnitude of risk to assist the physician regarding sport participation, clearance, and RTP. Guidelines are offered for clearance categories, management by a multidisciplinary team, and implementation of treatment contracts. Future research is needed to study whether risk stratification, clearance, and RTP guidelines are an effective means to optimize health and reduce risk for injury and illness for the triad.

Acknowledgments

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References


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Treatment Contract
(___________ Athlete Name)

The following items are mandatory and must be completed as prescribed. Failure to do so will result in the consequences listed below the requirements. All benefits and consequences are subject to change at any time and at the discretion of the Multidisciplinary Team.

Multidisciplinary Team:

___________ (Physician), ___________ (Mental Health Provider), ___________ (Dietitian).

Requirements:
☐ Meet with _____________ (mental health provider) 1x per week, or as recommended by mental health provider.
☐ Meet with _____________ (dietitian) 1x per week, or as recommended by dietitian.
☐ Meet with Dr. _____________ 1-2x per month, or as recommended by Dr. _____________.
☐ Follow daily meal plan set forth by sports dietician.
☐ Keep daily workout log updated with specific type, length, and effort.
☐ Weight gain of _____ lbs per week.
☐ Weekly weigh-in with _____________ (name team member), or at time intervals of _____ weeks.
☐ Must achieve minimal acceptable body weight of _____ lbs by ______ (date).
☐ After this date, must maintain weight at or above minimal acceptable body weight.
☐ Limit of _____ workout sessions per week with no one session being more than _____ minutes in length. All activity counts (e.g., biking, running, weight lifting, and swimming).

Benefits:

If ALL requirements are met then clearance to participate in team activities and use of athletic facilities will: ☐ be granted ☐ continue.

Consequences:
If ANY requirement(s) are not met then clearance to participate in team activities and use of athletic facilities will be revoked, and re-instatement will be at the discretion of the team physician and multidisciplinary team.

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

_____________________________
Athlete Name

_____________________________
Athlete Signature

_____________________________
Date

_____________________________
Team Physician Name

_____________________________
Team Physician Signature

_____________________________
Date