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Relative Energy Deficiency in Sport (RED-S) in Adolescents – A Practical Review

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ABSTRACT

There are many immediate and longer-term physical, psychological and metabolic benefits of being active during adolescence. These benefits exist when exercise and physical activity are undertaken in a state of energy balance. When exercise occurs in an environment of low energy availability, this is currently termed relative energy deficiency in sport and there are potential significant negative effects on mental well-being, bone, endocrine and metabolic health. Therefore, relative energy deficiency in sport may present to many different specialists or allied health professionals depending upon the symptoms or reasons for seeking help, which include injury, such as bone stress or soft tissue problems, irregular or absent menstruation, stress, anxiety or low mood, or sporting underperformance as examples. The promotion of physical activity in adolescence is a critical part of public health strategy. In parallel with this positive public health message, there needs to be an increase in the awareness of, and education about, relative energy deficiency in sport for those working with and looking after adolescents.This review provides an up to date, practical evidenced based guide on the recognition, investigation and management of relative energy deficiency in sport in the adolescent, both male and female.

Search Strategy

Medline, SPORTDiscus and CINAHL databases were searched from 1 January 2016 to 8 June 2021 and included all study designs and was limited to English language. The search was based around the terms ([adolescent OR young adult OR student OR teen OR child OR minor OR youth] AND [relative energy deficienc * OR RED-S OR REDS OR female athlete triad OR male athlete triad OR energy intake deficienc * OR low energy availability OR bone density OR ((bone or skelet *) AND (mass OR health OR density OR metabolism)). 759 unique articles were identified, and all were assessed for relevance to this narrative review. References of included papers were also assessed for other relevant papers.

Introduction

Relative energy deficiency in sport (RED-S)

The International Olympic Committee (IOC) defined RED-S as a syndrome of health and performance impairments resulting from an energy deficit [1]. Previously, the limited definition of the female athlete triad, consisting of low energy availability (in early literature limited to anorexia), osteoporosis and amenorrhoea, restricted the identification of the multi-system problems and presentations that can arise from a consistent negative energy balance. Importantly, it also did not address the occurrence within males. RED-S has achieved greater recognition in recent years since the original IOC consensus statement and subsequent update [1, 2]. A consensus statement for male athletes (the male athlete triad) has also been produced [3, 4]. The full RED-S syndrome is now recognised as encompassing effects on metabolic rate, menstrual, bone, cardiovascular and gastroenterological health, immunity and mental well-being.

Low energy availability (LEA)

LEA is the foundation for development of RED-S. It occurs when there is insufficient energy available for optimum health and to support sport performance, after exercise energy expenditure (EEE) is subtracted from the total energy intake (EI) and normalized to fat free mass (FFM) [5]. LEA has been defined as < 30 kcal/kg/FFM/day, with optimal energy availability thought to be 45 kcal/kg/FFM/day, however there is significant individual variability [6]. Studying energy availability has many practical difficulties, there is no standardized way of measuring EA outside of the laboratory setting [7]. Energy intake can be estimated from dietary records (typically done over three to seven days) and exercise energy expenditure from activity records, heart rate and/or accelerometry (for example wearable devices), however, under- or over-estimates can arise from inaccuracies in both self reporting and accelerometry data. FFM can be estimated by skin fold measurement or bio-electrical impedance analysis. Dual-energy X-ray absorptiometry (DXA) is considered a more accurate estimate of FFM [7] but may not be available to measure FFM alone in the clinical setting.

Most published research in this area relates to adult females, rather than adult males or the adolescent population specifically. However, during adolescence, nutritional requirements are probably at their greatest compared to any other stage of life [8]. Adolescent metabolism encompasses the energy cost of growth, basal metabolic rate and active/exercise energy expenditure. If the total energy intake falls below the threshold of requirement it may cause growth stunting, pubertal delay and affect bone mass accrual. The calorie requirements for adolescent males are higher than for females to fulfill the higher rate of growth and increased lean body mass [8]. Emerging evidence suggests that in males, greater energy restriction is required to cause compensatory metabolic adaptations to this energy deficit [3].

Physical activity in adolescence

Adolescence is the time of development spanning the onset of puberty until adulthood. It encompasses biological and social maturation from 10–19 years old [9], and is a key time for developing healthy behaviours that will continue in adult life. The benefits of exercise in adolescence are broad and well recognised. Physical activity in adolescence correlates with healthier body composition (including in overweight/obese children and adolescents [10]), increased bone mineral density (BMD) and improved physical performance in adulthood [11], and can mitigate the risks of long-term medical conditions. Healthy male and female adolescent athletes have significantly greater BMD than their normal peers [12, 13]. Physical activity also has a positive effect on mental health and wellbeing in adolescents, and conversely sedentary behaviour is associated with reduced wellbeing and depression [14].

Recognition of RED-S in adolescence

Since the IOC definition of RED-S [1] there has been more research looking at the prevalence of the condition and its components. It is likely that, due to its highly variable presentation, under reporting, and previous lack of recognition that males could also be affected, that the true prevalence is underestimated. RED-S is frequently inadvertent and caused by a lack of knowledge about the fuelling needs of a highly active and growing adolescent. The consequences of this negative energy balance are compounded by sporting myths, including the effects of exercise on menstruation, and exacerbated within sports with a certain aesthetic and real or perceived weight restrictions.

In both males and females, the risk of LEA is higher in sports where leanness or weight targets are important for performance, aesthetics or meeting a weight category. Higher rates have been reported in elite athletes compared to recreational athletes [15], but other studies have concluded that intensity and training volume, independent of competition level, are more important [16]. In a multi-sport cohort of elite young female athletes (age 15–32 years, mean age 19 years), 80 % of 112 athletes had a least one symptom within the RED-S model [17]. Although the cause could not specifically be attributed to LEA, it should be considered as an underlying factor in the wide variety of clinical and psychological symptoms that were highly prevalent in this young group. This is consistent with previous work where the presence of at least one component of the female athlete triad was reported as up to 60 % in female high school athletes [18].

As with females, males participating in sports which require sustained high energy expenditure, such as cycling, soccer, rowing, and endurance running, or those participating in sports with weight classes such as combat sports or jockeys, are thought to be at increased risk of LEA [2, 19–22].

Knowledge and Perceptions of RED-S in Adolescents

What are adolescent athletes' perceptions of RED-S?

Despite the high numbers of adolescent athletes being at risk of, LEA and its consequences, knowledge is low [23]. A survey of 712 adolescent and young adult runners, dancers and figure skaters found that only 12 % had heard of the female athlete triad and only 7 % were able to name 2 of the 3 components of the triad [24]. Misconceptions surrounding menstruation are common, with surveys identifying that 28–56 % of female adolescent athletes think that losing periods is a normal response to a high level of athletic training [23, 25, 26]. A qualitative study in current and former United States (US) collegiate female distance runners highlighted a culture that supports the pursuit of the ideal 'runner body' through restrictive eating and excessive training, and a 'lighter is faster' mentality that is learnt early in careers. The coach-athlete relationship and power dynamic may have a substantial impact on athlete behaviour, mental health and wellbeing [27].

How much do coaches of adolescent athletes know about RED-S?

Knowledge of RED-S, the athlete triads or consequences of LEA, amongst coaches and those working with adolescent athletes is generally low. Misconceptions amongst coaches regarding menstruation, nutrition and body weight/shape are seen frequently [28–30]. One survey in the US found only 8 % of coaches and 38 % of athletic trainers were able to correctly identify all components of the triad [31]. Similar findings were present in a survey of 123 US high school coaches, with 24 % aware of the female athlete triad but only 14 % able to identify all three components [28], and in a study of 106 coaches in Singapore only 2 were able to identify the three components. 85 % had not heard of the female athlete triad at all, and 89 % were not able to identify at least one component [29]. A survey of US Collegiate Head Athletic Trainers found that 98.6 % of respondents had heard of the female athlete triad but only 32 % had heard of RED-S [32].

Contributing factors may include the perceived low priority of RED-S amongst coaches and within organisations, as well as lack of coach education [33]. Many high school coaches in the US lack formal health education [28], and a review of five national sporting organisations in Australia found only one (rowing) had formal education on RED-S within their coach accreditation pathways [34]. Only 7 % of Summer Olympic International Sports Federations undertake health-related programmes, guidelines or research activity into RED-S [35].

What do health professionals know about RED-S?

Knowledge and confidence in managing RED-S is generally low amongst health professionals. A study from 2006 in US physicians from various specialties found that overall, 48 % were able to correctly identify the three components of the female athlete triad whereas only 9 % felt comfortable managing it. Gynaecologists and paediatricians had lower rates of knowledge and comfort in management compared to orthopaedics surgeons and physical medicine and rehabilitation physicians [31]. A more recent survey found that 37 % of physicians, again from a variety of specialties, had heard of the female athlete triad and 51 % reported feeling comfortable treating or referring on a patient with female athlete triad [36]. Amongst physicians and allied health professionals attending a US sports medicine conference, 76 % were aware of the female athlete triad and 29 % aware of RED-S, but less than a third were comfortable managing these athletes [37]. Additionally, in a study of 370 US high school nurses, less than a third had heard of the female athlete triad and only 19 % were able to identify its three components [38]. Taken together these studies demonstrate a need for improving education and training across the multi-professional sporting environment.

Health Consequences of Low Energy Availability

The physiological changes in RED-S reflect a hypometabolic state related to LEA, conserving energy for essential body systems. Consequences of this may be broad [2], with suppressed function of energy-requiring physiological systems such as the menstrual cycle, bone health, decreased resting metabolic rate, implications for growth and immunological impairment. The gastrointestinal and cardiovascular systems may also be affected. Psychological health and wellbeing are closely intertwined with RED-S, with psychological symptoms occurring both before and after development of a low energy state.

Menstrual function

Menstrual function is a vital sign of adolescent female health and wellbeing [39] and is a key part of any female adolescent medical history. Menstruation typically starts between the ages of 11–14 years. Primary amenorrhea is the absence of menses by age 15, and has a prevalence of 0.3 % [40, 41]. Secondary amenorrhea is the absence of menses for 3 consecutive cycles in previously normally menstruating females, or 6 months with previously irregular periods, and affects 3–4 % of reproductive aged women [42, 43]. Menstrual irregularity in the first few years after menarche is common and can be normal, unlike amenorrhoea which requires investigation.

Functional hypothalamic amenorrhea (FHA) is suppression of the normal hypothalamic-pituitary-gonadal (HPG) axis, causing amenorrhoea with no other demonstrable anatomical or medical cause, and is therefore a diagnosis of exclusion. It is the most common cause of primary and secondary amenorrhoea in adolescent females [44]. LEA, rather than the exercise load itself [45], results in suppression of gonadotrophin-releasing hormone (GnRH) pulsatility. Less than 30 kcal/FFM/day is associated with low or low/normal luteinising hormone (LH) and follicle-stimulating hormone (FSH) and reduced ovarian oestradiol production [46]. In longer-term reduced energy availability (EA), there is a more linear relationship between energy availability below 45 kcal/FFM day and HPG axis disturbances (including luteal phase defects, oligomenorrhoea and amenorrhoea) [47]. FHA is often multifactorial, caused by LEA and additionally influenced by medication and psychosocial stressors. It is an adaptive response of the human body to preserve reduced energy availability for essential physiological processes and is therefore a reversible and treatable state [43].

Bone mineral density (BMD) and achieving peak bone mass (PBM)

Osteoporotic fractures are a major public health burden. There were an estimated 158 million people aged over 50 years at high risk of osteoporotic fracture in 2010, and this is thought to double by 2040 [48]. Almost 90 % of peak bone mass is achieved by the age of 18 [49], and maintaining this into adulthood can reduce fracture risk by 50–80 % [50]. If PBM is not achieved, this cannot be compensated for in later life. Genetics remain the largest predictor of PBM, but LEA, hypoestrogenism, menstrual dysfunction, poor calcium intake, significant weight loss, subclinical eating disorders and depot-medroxyprogesterone acetate (DMPA) contraception use can prevent an individual from reaching this genetically determined PBM [51–54]. Physical activity that involves high impact activity in adolescence is well recognised as having positive effects on BMD [55] but only in the presence of energy balance. Young wrestling/judo participants and sprinters have been identified as having higher BMD than endurance athletes and swimmers, and those who are inactive [56–58]. A low BMD has been associated with adolescents who have specialised early into endurance running [59], and risk factors for low BMD in male adolescent runners include body weight < 85 % expected, weekly mileage > 30 miles, history of stress fracture and less than one serving of calcium per day [60]. Horse racing is a weight restricted sport and 29 % of entry level male flat jockeys (mean age 18.5 years) were identified as having Z scores < 2 [61], compared to 13 % of male jump jockeys where the weight restriction is less.

Endocrine Effects

The endocrine changes that occur within LEA reflect a hypometabolic state and physiological stress through interlinked pathways. In female adolescent athletes there are changes in appetite-regulatory hormones, thyroid function, suppression of the hypothalamic-pituitary-adrenal (HPA) axis, increased cortisol, and reduction in the bone stimulatory growth hormone (GH) and insulin like growth factor-1 (IGF-1). The underlying and reversible driver for all these changes is LEA. There is suppression of the normal diurnal rhythm of the anorexigenic hormone leptin, which is independent of exercise stress [62], adiponectin is raised in dancers with LEA [63], the orexigenic hormone ghrelin is raised in low energy states [64], and the appetite suppressant Peptide YY is raised in amenorrhoeic athletes [63]. These changes in appetite-regulatory hormones disrupt the HPA axis resulting in reduced LH pulsatility, low FSH and hypogonadism [64–66]. In LEA the lower levels of insulin, IGF-1, and GH result in reduced muscle and bone anabolic effects [67]. Normally these are raised during the developmental adolescent period of life. Cortisol is raised in LEA, and amenorrheic athletes can demonstrated a blunted response to adrenocorticotrophic hormone (ACTH) stimulation. Thyroid function is disrupted with the most consistent changes identified with low triiodothyronine (T3) levels [63].There is similar but less extensive research in male adolescent athletes, but emerging data demonstrating similar effects on leptin, IGF-1, insulin, disruption of the HPG/HPA axis and testosterone, and changes in spermatogenesis [3, 63, 68, 69].

Psychological Factors in LEA

Psychological comorbidity may occur before or after RED-S is established. Disordered eating, which often coexists with other mental health conditions, is more common in adolescent elite athletes than non-athletes, with studies suggesting the personality traits of athletes convey increased risk [70]. Adolescent females with FHA have a higher incidence of mild depressive traits, psychosomatic disorders, decreased ability to manage stress [2], and social insecurity, concerns about body image and fear of gaining weight. These traits overlap with those found more profoundly in adolescents with eating disorders [71]. In the assessment of RED-S it is critical that the psychological factors are recognised and addressed within the multidisciplinary team (MDT) approach.

Performance Consequences and Injury Risk of RED-S

Low energy states convey increased risk of nutrient deficiency, fatigue and illness, as well as impaired performance [72]. Both the range of physiological systems affected, and the psychological impacts of LEA have a significant impact on performance by increasing time loss from training due to illness and injury, and impaired recovery and adaptation to training.

Performance consequences

Ten potential performance consequences of RED-S were highlighted in the IOC consensus statement [1], encompassing the multiple physiological systems affected by LEA and RED-S. More recently, decreased training and endurance response, decreased coordination, impaired judgement and concentration, irritability and depression has been demonstrated in adolescent and young adult female athletes (n = 1000, mean age 18.9 years) with self-reported LEA compared with those with adequate EA [72]. There is emerging data from a few small studies reporting links between reduced performance and adaptation to training, and the presence of menstrual irregularity and amenorrhoea when compared to eumenorrhoeic peers. This may prove an important driver for restoration of energy balance [73–75].

Injury risk

Injury rates for adolescent athletes are high, with up to 40 % suffering an injury in a 12-month period [76, 77]. There is evidence for increased risk of bone and soft tissue musculoskeletal injury for adolescents with amenorrhoea or other proxy indicators for LEA. Gram et al. demonstrated that amenorrhoeic gymnasts (mean age 14.5 years) had a higher risk of injury compared to their eumenorrhoeic counterparts [78]. Another surrogate marker, the Drive for Thinness (a subscale of the Eating Disorder Inventory (EDI)) has been correlated with increased musculoskeletal injury rates in a college population (18–22 years) [79] and female high school athletes with disordered eating were identified as twice as likely to have an injury during a season (n = 311) [80]. LEA is one of the modifiable risk factors for injury in adolescents.

Clinical Presentation of RED-S in Adolescents

Clinical assessment for RED-S must be broad and thorough, with a a high index of clinical suspicion for adolescent athletes at risk of LEA and RED-S. Adolescents with RED-S may present to a variety of medical and surgical specialties, physiotherapy, psychology or general practice, and features may also become apparent to sports coaches or teachers with awareness of the condition and its risks.

We describe the common clinical presentations of adolescents with RED-S in ▶ **Table 1**. The potential health consequences (ex-

▶ **Table 1** Common clinical presentations of RED-S in adolescents.

Common presentations of RED-S in adolescents
Amenorrhoea (primary/secondary); oligomenorrhoea *
Musculoskeletal injury – bone stress injury/stress fracture; recurrent soft tissue injury
Weight loss, changes in BMI centile or trajectory of height and/or weight gain
Underperformance in sport
Exercise-related symptoms (e.g. dizziness, palpitations, syncope – with normal specialist investigations)
Fatigue; poor sleep
Psychological – low mood, anxiety, stress, compulsive behaviours, disordered eating, pre-occupation with body image
Gastrointestinal – constipation; diarrhoea
* females only; BMI, basal mass index.

panding upon the original Female Athlete Triad) are described in further detail in the 2018 updated IOC Consensus Statement [2]. This has since been further consolidated, including a self-reported questionnaire study associating LEA with menstrual dysfunction, poor bone health, cardiovascular and gastrointestinal issues, metabolic, haematological and psychological conditions in young adult (15–30 years) female athletes [72].

Assessment of RED-S in Adolescents

History

Due to the detailed, and sometimes sensitive, nature of the questioning required, the history should be explored in a safe and confidential environment. The history covers contributory factors of underfuelling, as well as any external stressors, including illness, school, family life and difficult relationships within home or sporting environments. A summary of the key components of the history is in ▶ **Table 2**.

A full medical history should include any current symptoms and a thorough systems review reflecting the broad range of potential clinical presentations. This includes fatigue, gastrointestinal symptoms such as changes in bowel habit, weight loss, and cardiovascular symptoms such as palpitations, dizziness, and syncope (which can be a direct result of LEA and its consequences). Coeliac disease should be considered, as it is linked to fatigue, reduced BMD and bone stress injury [81, 82] as well as the more typical gastrointestinal symptoms. Females should be asked about their past and current menstrual history. Past medical history should be sought along with history of musculoskeletal injury (soft tissue and bony; traumatic or bone stress injuries), a full developmental and pubertal history, and family medical history. Drug history should include prescribed and independently purchased medications, hormonal contraceptives, supplements and recreational drugs. It is worth remembering the side-effects of medication and the potential consequences on energy expenditure, appetite or menstrual pattern, that are seen, for example, with drugs for depression, anxiety or attention deficit hyperactivity disorder and biologics for chronic inflammatory conditions.

▶ **Table 2** Summary guide to history taking in adolescents at risk of RED-S.

History Taking in Adolescents at Risk of RED-S
Current symptoms/timeline
Systems review (including fatigue)
Past medical history
History of musculoskeletal injuries
Growth, developmental & pubertal history
Family medical history
Drug history (including over the counter and internet purchases; contraception; supplements & recreational drugs)
Physical activity history
Dietary history
Psychological symptoms and external stressors (including symptoms associated with disordered eating)
Menstrual history *
* females only

A thorough physical activity history is required to ascertain the volume and intensity of school activities, club training and home exercise. A dietary history should include food intake (meals/snacks), timing of fuel intake around exercise and any restrictive or avoidant eating patterns. Sleep quality and sleep hygiene should be assessed (as key components of well-being and recovery from training). Psychological assessment should include screening for depression and anxiety, as well as dietary cognitive restraint, drive for thinness and purging behaviours, which may be more common in adolescents with amenorrhea and RED-S. The prevalence of eating disorders is higher in elite adolescent athletes (especially females), than controls [83]. If an adolescent has suggestion of a significant eating disorder, such as rapid weight loss, significant concern from carers, purging behaviours, or physical consequences of malnutrition such as bradycardia, fainting or additional mental health problems, referral to a specialist child and adolescent mental health service is suggested [84].

Self-Reported Questionnaires

The practical challenges associated with accurate measure of EA have led to the use of self-reported and surrogate measures. A large review of questionnaire-based reporting in athletes demonstrated that, while intentional energy restriction and disordered eating can be identified, it is more challenging to identify those with unintentional energy deficiency. The most commonly used validated questionnaires were Low Energy Availability in Females Questionnaire (LEAF-Q) and Eating Disorder Examination Questionnaire (EDE-Q). The authors concluded that such questionnaires can be used in screening for RED-S, but not diagnosis, and that their effectiveness may be reduced due to unintentional under-fueling [85]. High drive for thinness (a subscale of the EDI questionnaire) has been shown to be a surrogate marker for energy availability correlating with resting metabolic rate and total T3 levels [86]. More recently it has also been associated with increased rate of musculoskeletal injuries in 18–22 years female athletes [79]. The drive for thinness subscale is used in both female and male athletes [87], and is a quick and simple questionnaire to use in a clinical out-patient setting.

Examination

A thorough physical examination should be undertaken looking at the signs for RED-S and its differential diagnoses.

Height, weight and centile body mass index (BMI) can be measured and plotted on a growth chart. RED-S can occur in the presence of a normal BMI, however attenuation of expected growth or low body weight (< 85 % expected body weight for adolescents) [88] should raise suspicions of RED-S or other conditions associated with weight loss

Physical signs to look for include, signs of androgen excess and hypo- or hyperthyroidism, signs of an eating disorder (anorexia nervosa), purging behavouir, malnutrition, and signs of psychological distress such as self harm.

Heart rate, lying and standing blood pressure measurements and temperature can also be considered, particularly in the presence of anorexia nervosa or other severe eating disorder, and other high risk scenarios such as rapid weight loss or purging behaviour [84].

▶ **Table 3** Initial investigations in RED-S.

Initial investigations in RED-S	
Initial blood tests	**Rationale**
FBC, U + E, LFT, CRP, ESR	Routine blood tests for general health and for other causes of symptoms such as weight loss, fatigue.
Ferritin	Iron deficiency affects bone health, via the GH/IGF-1 axis, hypoxia and hypothyroidism, and other metabolic pathways including thyroid, reproductive function and wellbeing [108]. Low ferritin and iron-deficiency anaemia have been correlated with LEA in adolescent female athletes [2].
TFT	Impaired thyroid function (particularly reduced T3 levels [63] has been demonstrated, sometimes more marked with ovarian suppression) [75].
	Thyroid function status should also be checked in amenorrhoeic females, and may help to guide specialist referral [40].
LH[1], FSH[1], prolactin[1]	In primary and secondary amenorrhoea, prolactin, FSH & LH can help guide specialist referral.
Total testosterone[1/2]	In females, if signs of androgen excess (as part of investigation for primary amenorrhoea) [40].
	Testosterone can be reduced in males with energy deficiency [67].
Pregnancy test[1] (if sexually active)	To exclude pregnancy as a cause of amenorrhoea [40]. Can also be performed as a urine test.
Other tests to consider	
Bone profile; 25(OH)D	25(OH)D status during adolescence is an independent factor for bone mass gain, muscle force and hand grip strength [109]. Increasing observational data propose roles extending beyond musculoskeletal health and performance; this hormone has an important role in immunity, cardiovascular health, neurological function, glucose metabolism and insulin sensitivity.
B12, calcium, folate, glucose, inorganic phosphate, magnesium	In addition to routine blood tests above if concerns of severe eating disorder, rapid weight loss or severe purging behaviour. However, it may be more appropriate in these circumstances to seek urgent specialist advice [84].
IgA and IgA TTG antibody (should have been taking a gluten-containing diet for > 6 weeks)	Children & adolescents with coeliac disease have lower bone mass and density [81] and a the prevalence of coeliac disease was 5 % in 100 patients with bone stress injuries (approximately 5x higher than population estimates) [82].
DXA	We primarily use DXA as part of assessment in bone stress injuries but can also give information on body composition and FFM. In adolescents, spine and total body less head are the preferred skeletal sites. A Z-score of ≤ 2 defines low BMD for chronological age [110]. DXA is recommended if presenting with recurrent bone stress injuries, to provide a baseline for longitudinal monitoring of bone density and response to treatment (important because the BMD distribution may be significantly different to age and gender-specific reference ranges for the general population [12].

[1] – females only; [2] – males only; 25(OH)D, 25-hydroxy-vitamin D; BMD, bone mineral density; CRP, C-reactive protein; DXA, dual-energy X-ray absorptiometry; ESR, erythrocyte sedimentation rate; FBC, full blood count; FFM, fat free mass; FSH, follicular stimulating hormone; GH, growth hormone; IgA, immunoglobulin A; IGF-1, insulin-like growth factor-1; LEA, low energy availability; LFT, liver function tests; LH, luteinising hormone; SHBG, sex-hormone blinding globulin; T3, triiodothyronine; TFT, thyroid function test; TTG, tissue transglutaminase; U + E, urea and electrolytes

Investigations

An initial estimate of FFM can help with the initial assessment and subsequent nutritional recommendations, if the equipment and expertise is available. However, in order to optimize a positive body image in adolescent athletes, routine body composition measurements are not recommended [89].

A pragmatic attempt should be made to estimate energy availability (i.e. do you think the athlete is energy replete and consuming ≥ 45 kcal/kg FFM/day?). If information on physical activity and dietary intake is insufficient from the history, consider a food and activity diary (including records from wearable devices) for three to seven days.

The standard blood tests and other initial investigations specific to RED-S, and its differential diagnoses that we consider, are presented in ▶ **Table 3** along with their rational.

An ECG should be considered if high risk of electrolyte abnormalities, for example anorexia nervosa, rapid weight loss or purging behaviour.

Gynaecological referral is indicated for females with primary amenorrhoea, and it may be appropriate to consider referral to a gynaecologist or endocrinologist for secondary amenorrhoea, if a non RED-S aetiology is suspected [40]. Ultrasound scan and sex-hormone binding globulin could be performed if polycystic ovarian syndrome (PCOS) is suspected. Estradiol, anti-mullerian hormone and dehydroepiandrosterone (DHEA) sulfate (if hyperandrogenism present) are not part of standard clinical practice for investigating amenorrhea in the United Kingdom but are recommended by other guidelines [90]. Additonal specialist investigations for ammenorrhea, guided by clinical findings, may include 17-hydroxyprogesterone (late-onset congenital adrenal hyperplasia), insulin-like growth factor-1 (acromegaly, can also be used in the assessment of low energy availability but may not be available in all settings) and brain magnetic resonance imaging (pituitary tumour or other pathology)

Management of RED-S in Adolescents

Prevention and education

The presentation of RED-S in adolescents can be complex and multifactorial. Individuals may present to a variety of medical specialties, as well as sporting coaches and team staff before a unifying diagnosis is identified. As the development of this condition can reflect a period of under-fueling and LEA before specific symptoms appear, there is also a critical window of opportunity for identification and reversal of these risk factors before RED-S becomes established. It is very important to develop a healthy environment around exercise, nutrition and body image in adolescence as this will define the life-long relationship with food [91].

It has been proposed that education of athletes, team staff and healthcare professionals should take place to raise awareness of RED-S and its consequences, improve recognition of at-risk individuals and sports, and reinforce positive messaging around nutrition, body image and, in females, menstrual cycles [89].Education sessions may also provide an opportunity to challenge misconceptions and negative cultures in sport such as those around thinness and performance. At-risk individuals may be identified with validated questionnaires at pre-participation screening [85].

Peer education [92] and brief video educational interventions [93] have been shown to increase knowledge of RED-S in high-school athletes, but the effect of this on behavior and longer-term outcomes is unknown. Mobile technology interventions have been shown to be acceptable and feasible in a population of adolescent and young adult females [94]. Positive behavioral change at 18-month follow-up was maintained with a short eating disorder intervention in female college athletes [95]. Encompassing a broader age range, educational nutritional and skeletal health interventions were associated with improved bone health, wellbeing, and race performance in competitive male road cyclists (18.5–72 years) [96]. These results show promise for the use of technological interventions in the future, a format that is both familiar and acceptable to the adolescent and young adult population.

Management of established RED-S

Once RED-S is established, the broad aim of treatment is to restore energy balance by increasing energy intake and/or reducing energy expenditure. The underlying aetiology of LEA should be identified. We advocate using the expertise of a MDT, tailored to the needs of the athlete. This is likely to be coordinated by a sport and exercise medicine physician with input from dieticians, psychologists, coaches, physiotherapists, and other medical specialties (such as endocrinology, gastroenterology, gynaecology and psychiatry), as required. Management is long-term with energy balance typically taking days to weeks to restore, menstruation weeks to months and bone density years [2].

Increasing energy intake

For those athletes who are inadvertently under-fueling, education and practical advice on increasing energy intake may be all that is required to restore energy balance. It is worth remembering that in adolescent athletes, energy needs may be higher due to the additional energy demands of growth and development [2]. The increases in energy intake required will differ between athletes, but it has been shown that increasing calorie intake by 250–360 kcal/day is sufficient to restore menses in female athletes with FHA [97, 98]. A 'food first' approach should be used (rather than supplements) and increases in energy intake could be achieved by adding snacks between meals (for example 3 meals and 3 snacks throughout the day), increasing portion sizes and/or increasing the energy-density of meals. The timing of meals and snacks are important to avoid prolonged periods of within-day energy deficit, concentrating on times of energy expenditure such as around training and competition [99]. In addition to providing energy, the consumption of higher amounts of carbohydrate may have an additional positive impact on bone health through attenuation of the post-exercise increase in β-C-terminal telopeptide of type 1 collagen (CTx) [100], and increases in leptin [101].

Consider input from a dietician in athletes with high energy requirements, dietary restrictions, more marked disordered eating or other difficulties increasing energy intake. Athletes with an eating disorder should be referred to a specialised eating disorder service [102].

Vitamin D and calcium supplementation should be considered alongside the management of RED-S to optimise bone and musculoskeletal health. Recommendations for Vitamin D intake in adolescence varies between 5–25 mg daily, however, intakes at the higher end of this range (15–25 mg/day) are likely to be required to achieve and maintain 25(OH)D concentrations > 50nmol/L [103, 104]. Supplementation can take place at daily or weekly intervals [105] and if Vitamin D deficiency is present higher dose replacement may be required. The recommended calcium intake for adolescents is 1300 mg/day [8]. Caution should be used when recommending supplements, such as Vitamin D, due to the risk of contamination, for young elite athletes who may undergo anti-doping testing.

Reducing energy expenditure

If increasing energy intake alone is insufficient to restore energy balance, then energy expenditure can be reduced by altering training and/or competition load. Many adolescent athletes play multiple sports, as well as participating in physical activity at school and active travel. Discussions with the athlete, parents and coaches can be helpful to understand the overall physical activity demands on the athlete and their views. It is important to emphasise the benefits of good recovery and the need for one or two rest days per week. Training and competition loads may need to be reduced, and the athlete should be the main decision maker on which activities they wish to prioritise. Reducing energy expenditure should be considered in athletes with disordered eating or eating disorder but may not be necessary in all cases [102].

Hormonal interventions in female athletes

The use of the combined oral contraceptives (COCPs) for improving BMD in RED-S is not recommended as the evidence of their effects on bone density is inconsistent and they may mask the return of normal menstruation. The lack of effect of COCPs on BMD is thought to be due to downregulation of IGF-1 [90]. In studies which included adolescent athletes, transdermal oestradiol (E2) (which does not affect IGF-1) given with cyclical oral progestin has been shown to increase bone density, compared to the combined oral contraceptive pill, in normal weight oligo-amenorrheic athletes [106] and in amenorrheic athletes with low body weight [107]. However, in the Nose-Aguro study an even greater improvement in bone density was seen in athletes who improved their energy availability and restored normal menstruation. Short-term use of transdermal estradiol with cyclical oral progestin could be consid-

▶ **Table 4** Take home points.

Take Home Points
RED-S affects male and female adolescent athletes
RED-S may present to many different medical specialties, as well as sporting coaches and team staff
Awareness of RED-S amongst coaches and health care professionals is low
Restoration of energy balance, through a MDT educational approach, is the core of management
Resumption of menses is the aim in female athletes
Use of the COCP is not advised in the management of RED-S
Adjunctive novel therapies are not currently recommended
COCP, combined oral contraceptive pill; MDT, multi-disciplinary team; RED-S, relative energy deficit in sport.

ered if other non-pharmacological interventions to improve EA are unsuccessful [90].

Other pharmacological interventions

The use of bisphosphonates, denosumab, testosterone or leptin are not recommended in adolescents due to a lack of data on effectiveness and safety [4, 90]. Recombinant parathyroid hormone may be considered for delayed fracture healing or very low BMD in adult women [90] but should be avoided in adolescents and young adults with open growth plates [2].

Conclusion

Low energy availability, frequently due to inadvertent underfuelling, is common in female and male adolescents. Clinical presentation can be broad and may initially seem quite non-specific, so athletes may present to several medical professionals before the unifying diagnosis is identified. Regular screening during the season, or at times of impaired performance, injury, illness, or other changes may highlight athletes with features of low energy availability before the condition becomes established. Promoting awareness and supporting education amongst adolescent athletes themselves, and in both sporting and medical professionals is key for prevention, early recognition, and management of low energy availability and RED-S. Treatment, ideally within the structure of a multidisciplinary team, should concentrate on restoration of energy balance and individualised management of specific features. Our take home points are summarized in ▶ **Table 4**.

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Conflict of Interest

The authors declare that they have no conflict of interest.

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