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REVIEW ARTICLE

Low Energy Availability in Exercising Women: Historical Perspectives and Future Directions

Joanne Slater[1] · Rachel Brown[1] · Rebecca McLay-Cooke[1] · Katherine Black[1]

Abstract Research on the health of female athletes has developed substantially over the past 50 years. This review aims to provide an overview of this research and identify directions for future work. While early cross-sectional studies focused primarily on menstruation, research has progressed to now encompass hormonal changes, bone health and lipid profiles. The seminal work of Loucks and colleagues distinguished that these health concerns were due to low energy availability (LEA) rather than exercise alone. LEA occurs when the body has insufficient energy available to meet the needs of training and normal physiological functioning. While there appears to be agreement that LEA is the underlying cause of this syndrome, controversy regarding terminology has emerged. Originally coined the female athlete triad (Triad), some researchers are now advocating the use of the term relative energy deficiency in sport (RED-S). This group argues that the term Triad excludes male athletes who also have the potential to experience LEA and its associated negative impact on health and performance. At present, implications of LEA among male athletes are poorly understood and should form the basis of future research. Other directions for future research include determination of the prevalence and long-term risks of LEA in junior and developmental athletes, and the development of standardised tools to diagnose LEA. These tools are required to aid comparisons between studies and to develop treatment strategies to attenuate the long-term health consequences of LEA. Continued advances in knowledge on LEA and its associated health consequences will aid development of more effective prevention, early detection and treatment strategies.

Key Points

Research on low energy availability (LEA) and the associated health of athletes has developed substantially over the past 50 years.

There is agreement that LEA is the underlying cause of a series of adverse health outcomes, although controversy among researchers regarding terminology exists.

Continued research and knowledge of LEA and associated health consequences will aid development of more effective prevention, early detection and treatment strategies.

1 Introduction

Historically, women were viewed as somewhat delicate creatures and as a consequence were not encouraged to engage in sport. However, as women were required to take on numerous physically demanding jobs during the two world wars, and as the feminist movement developed during the 1960s and 1970s, there was an increasing acceptance of female participation in sport. As the prevalence of female involvement in sport grew, concern regarding the specific health needs of female athletes was

✉ Katherine Black
katherine.black@otago.ac.nz

[1] Department of Human Nutrition, University of Otago, PO Box 56, Dunedin, New Zealand

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also growing within the scientific community. A new area of research emerged, which initially focused primarily on disruptions in menstrual function, likely due to its obvious manifestations among female athletes. However, investigations in non-athletic populations had already been undertaken by Dr. Rose Frisch and colleagues at the Harvard Center for Population and Development Studies, who noticed delayed menarche amongst poor rural undernourished girls compared with well-nourished counterparts in the late 1960s [1]. These researchers believed that this disruption in reproductive function was due to fat deposits and that body weight was an important predictor of the onset of menarche, which had previously been shown in animal models. This hypothesis was greeted with much scepticism and was widely rejected on the basis of a large body of animal and human research. Although they believed that menstrual dysfunction was due to body fat rather than energy availability (which is now believed to be the cause of menstrual dysfunction), it is some of the earliest work to suggest that nutrition plays a significant role in reproductive function in humans [1].

As knowledge in the area has grown, the terms female athlete triad (Triad) and, more latterly, low energy availability (LEA) have been used to describe the syndrome of negative health consequences observed amongst females. LEA occurs when an energy deficit exists to such an extent that the body has insufficient energy available to meet the needs of training and normal physiological functioning. This is different from energy balance, which takes into account total energy intake compared with all energy expended irrespective of fat-free mass [2]. The brain responds to LEA by altering a range of metabolic hormones that suppress energy-consuming physiological processes, including the suppression of reproductive hormones [2]. LEA does not necessarily equate to negative energy balance, as this involuntary and imperceptible suppression of energy expenditure tends to restore energy balance. LEA can be caused by reducing dietary energy intake or by increasing exercise energy expenditure or a combination of the two, the result being a state where energy intake is inadequate to meet exercise energy expenditure [2].

Physical activity (PA), sport and exercise are promoted as part of a healthy lifestyle enhancing bone health, improving blood lipid profiles and helping to maintain muscle mass [3–5]. However, when in a state of LEA, exercise can have a negative effect on health, specifically bone health [6, 7], lipid profiles (increased low-density lipoproteins and total cholesterol) [8, 9] and hormones (reduced thyroid hormones, luteinising hormone [LH] and estrogen) [10, 11], ironically some of the very beneficial health outcomes that exercise promotes.

Now, with over 50 years of accumulated research in the area, an interesting situation has arisen in which the authors of the recently published International Olympic Committee (IOC) Position Stand propose renaming the syndrome relative energy deficiency in sport (RED-S) [12]. These researchers contend that the term Triad excludes male athletes, who also have the potential to experience LEA and its associated negative impact on health and performance. In contrast, the authors of the also recently published Female Athlete Triad Coalition (FATC) statement argue that the syndrome should remain described as it has been for over 20 years, as the Triad [13]. They contend that the authors of the IOC consensus statement have made mistakes describing the physiology of prolonged energy deficiency. They also feel that the statement has an insufficient research base regarding the effects of LEA on male athletes and has a lack of references for its suggestions regarding treatment of athletes currently experiencing LEA [14]. While debate over terminology continues, it is important to acknowledge that both parties have a common goal, which is to minimise the potential negative health issues amongst male and female athletes, and gain a better understanding of the interplay between energy availability, bone health, the hormonal milieu and associated health problems.

Despite the body of literature on LEA increasing rapidly, our knowledge of its prevalence, aetiology and complexity still requires further investigation. Here we provide an overview of the history of LEA, comment on the current understanding of it and suggest directions for future research.

2 Animal Studies

The effects of energy availability on reproduction in mammals have long been a subject of speculation. In 1939, Selye [15] demonstrated that exercise and insufficient diet can induce ovarian atrophy and adrenal hypertrophy. Both field studies [16–20] and well-controlled laboratory studies [21, 22] in small mammals have shown that food supply influences rates of reproduction. For example, Morin [23] observed that 2 days of energy restriction in Syrian hamsters inhibited follicular development, reduced the plasma estradiol concentration, decreased LH pulsatility and disrupted ovulation.

Others have investigated the effects of exercise on reproductive function to induce LEA in animal models [24, 25]. Young rats that were forced to exercise exhibited a delay in puberty and suppression of LH pulsatility and growth hormone secretion [24, 25]. However, all of these reproductive disruptions were restored by pulsatile infusions of gonadotropin-releasing hormone (GnRH), suggesting that prolonged exercise affects the production of the hypothalamic GnRH-pulse generator signal. In adult

rats forced to exercise, disruptions to the normal 4- to 5-day estrous cycle have been reported [26].

Taken together, these findings suggest that both energy restriction and increased energy expenditure, i.e. decreasing energy availability, can cause reproductive dysfunction in small mammals. This LEA hypothesis is supported by Schneider and Wade [27], who undertook a series of studies, again using Syrian hamsters, manipulating both body weight and energy availability. Hamsters were divided into groups based on body weight (heavy, medium and light) and half the hamsters in each group were deprived of food during the first 2 days of a 4-day estrous cycle. The heaviest group still exhibited vaginal discharge and ovulated, whereas vaginal discharge was only present in 10 % of the starved hamsters in the lightest group. In a follow-up to this experiment, the researchers injected methyl palmoxirate (MP) to inhibit fatty acid transport into the mitochondria with or without food restriction [27]. Neither food deprivation nor MP administration alone led to a disruption in vaginal discharge, but the combination did disrupt estrous cycles. In a final continuation of this experiment, the researchers blocked glucose utilisation with or without MP [27]. The combined inhibition of fuel utilisation disrupted estrous cycles, despite no changes in body mass. These data suggest that fuel availability rather than specific macronutrient availability is key for normal reproductive function. Further, the disruption of cycles with inhibition of fuel utilisation without body weight changes suggests that it is not body weight that is important for reproductive function. Similar findings were reported by Bronson and colleagues [28], who kept prepubescent rats at low body weight and low body fat by energy restriction and/or exercise resulting in decreased LH pulsatility and amplitude. However, when the rats were given ad libitum access to food normal hormonal responses were restored before changes in body weight or body fat occurred, suggesting energy availability was the key component in the hormonal disruption [28].

Williams et al. [29, 30] published two studies in 2001 using female monkeys. In the first study they used exercise to induce amenorrhoea by increasing daily running distance (but maintaining energy intake) whilst documenting changes in menstrual cyclicity and patterns of LH, follicle-stimulating hormone (FSH), estradiol and progesterone [29]. The time lapse before amenorrhoea developed varied from 7 to 24 months, but unlike the study by Schneider and Wade [27], it was not correlated with initial body weight and nor was it related to training distance or food intake. Further, this study was able to show the progression of menstrual dysfunction with LEA prior to amenorrhoea occurring. The process was characterised by an initial suppression of gonadotropin secretion, followed by a lengthening of the period required for the development of a dominant follicle with an impairment of corpus luteum secretory function, and finally a complete absence of menstrual cycles.

In the second study, Williams et al. [30] gradually increased running energy expenditure whilst energy intake remained constant. Following the onset of amenorrhoea, energy intake was increased but the training load remained the same and this increase in energy availability resulted in a restoration of normal reproductive function.

A more prolonged study investigating all aspects of the Triad was undertaken by DiMarco et al. [31] in Sprague–Dawley rats. After baseline data collection, the rats were divided into a restricted group (70 % habitual energy intake) and a group of ad libitum feeding controls for 14 weeks. Energy intake, energy expenditure and energy availability were calculated for each animal and serum estradiol and leptin concentrations were measured. Femoral and tibial bone mineral density (BMD) and bone mineral content (BMC) were also monitored. Food restriction, and thus LEA, resulted in reduced concentrations of serum estradiol and leptin as well as lower ovarian weight and decreased BMC at both the femoral and tibial sites. This indicates that LEA may have negative implications on reproductive and bone health.

3 1960s

By the 1964 Tokyo Olympic Games, women's participation at the Olympic Games had risen from 2.2 % of all athletes in 1900 to 13 %, and it has continued to rise steadily ever since [32]. In concert with this increase in female sports participation, it was during the early 1960s that concerns were first raised in the published literature about the potential negative influence of excessive exercise in combination with low dietary intakes on the health and performance of female athletes [33].

Gyula Erdelyi, a Hungarian medical doctor, undertook the first large cross-sectional study in the area [33] in response to anecdotal observations of female athletes reporting altered menarche. One specific aim of the study was to answer the question "What is the influence of sports activities on the menstrual period and menstrual cycle of the female athletes?" Researchers used questionnaires, personal interviews and menstrual cycle charts to collect data on 729 Hungarian female athletes participating in competitive sport. They observed no alterations in the onset of menarche; however, a subset of athletes ($n = 557$) were asked to report on changes to their menstrual cycle whilst participating in sport and 467 (83.8 %) reported no changes, 28 (5.0 %) 'favourable changes' and 62 (11.1 %) 'unfavourable changes' to their menstrual cycle.

Based on these findings Erdelyi stated that "We should exclude every pathologic factor which may cause these

changes before we should consider sports as the causative factor. However, we may find menstrual disorders that may be associated with too much sports activities". The author suggested that in cases of unfavourable menstrual changes, the athlete should temporarily decrease the training load.

4 1970s

During the 1970s more cross-sectional research was undertaken. Malina and Spirduso [34] investigated the age at onset of menarche in US college athletes ($n = 222$), as well as in high school athletes and non-athletes. These researchers developed a questionnaire that included self-reported information on the participant's menstrual history and training schedule. Contrary to earlier findings by Erdelyi [33]. Malina and Spirduso [34] concluded that high school-, college- and Olympic-level athletes attained menarche significantly later than non-athletes (mean age 13.02, 13.05, 14.18 and 12.29 years, respectively). It is possible this difference in results may be due to changing attitudes towards female involvement in competitive sports, differences in training schedules and the earlier involvement of children in sporting activities over the preceding 16 years. In the USA, the Title IX of the EducationAmendments of 1972 allowed both sexes equal access to sporting opportunities and funding [35]. Although speculative, the equality in terms of access to sporting opportunities and funding afforded by Title IX may have resulted in females increasing the amount and intensity of training at a younger age, and thereby increasing their risk of being in a state of LEA before or at the time of menarche.

Observations from these early studies suggested that female athletes were at risk of experiencing disruption to the development and timing of menstruation. However, due to the cross-sectional nature of these studies it was not possible to determine the mechanism(s) at work. These observational studies stimulated research into the issues surrounding exercise and dietary energy intakes, and investigation of possible concerns for the overall health of female athletes.

5 1980s and 1990s

The 1980s and early 1990s saw a substantial body of evidence published connecting disordered eating behaviours, amenorrhoea and reduced bone mass [6, 36–38]. It was during this period that the first Position Stand on female athletes was published incorporating the major research themes at the time notably disordered eating, bone health and menstrual status [39]. However, by the end of the 1990s criticism of the initial Triad definition was beginning as studies detailing hormonal changes and the aetiology of these changes started to appear in the published literature. It was also during the 1980s and 1990s that researchers became increasingly interested in the health of male athletes.

5.1 The Female Athlete Triad (Triad)

In 1992, the American College of Sports Medicine (ACSM) convened a group to address this area of growing concern within the sporting community. This was a significant milestone as it was during this workshop that the term 'the female athlete triad' (Triad) was coined. The Triad was defined as "the combination of disordered eating, amenorrhoea and osteoporosis found in physically active girls and women". The expert group acknowledged that at this point their understanding of the Triad was limited but recognised it was a complex medical concern that needed to be investigated further. They considered research into the preparation of guidelines and educational material a priority, and specified that it needed to be targeted not only towards sportswomen, but also coaches, management, medical practitioners and other health professionals [40].

The ACSM published the first position stand on the Triad in 1997 [7]. The major aim of this document was to inform physicians, trainers and other healthcare providers about the Triad by providing scientific information related to screening, diagnosis, prevention and treatment.

As discussed at the 1992 ACSM Triad meeting, the diagnostic criteria for having the Triad was the presence of disordered eating behaviours, amenorrhoea and osteoporosis occurring in sequence [40]. Amenorrhoea was defined as a "persistent absence of menstrual cycles" for at least 3 months. Disordered eating was described as occurring on a continuum, ranging from abnormal eating behaviours at a subclinical level through to clinical eating disorders including anorexia nervosa, bulimia nervosa and eating disorders not otherwise specified. Osteoporosis was defined as having a BMD >2.5 standard deviation (SD) below the mean of young adults [39]. Additional intentions of the Position Stand were to highlight the serious short- and long-term health consequences of the Triad for female athletes, and the need for further research investigating the prevalence, causes, prevention and treatment of the syndrome. It should be noted that the use of the oral contraceptive pill is not an appropriate treatment because it will not normalise metabolic factors that impair bone formation, health and performance, as was later pointed out in the 2007 revision of the ACSM Position Stand [84].

However, even by this stage, discussions were emerging in the literature regarding the definitions of the Triad components, and in particular there was concern regarding

the Triad only including the clinical endpoints of each component; many female athletes with less severe manifestations of the Triad components had the potential to go unnoticed, yet still faced potentially significant health implications.

5.2 Bone Mass

In 1984, two case-control studies conducted in the USA investigated the BMD of amenorrhoeic and eumenorrhoeic athletes [7, 41]. Drinkwater et al. [7] compared the BMD of 14 amenorrhoeic female runners and rowers with that of 14 eumenorrhoeic controls matched for sport, age, body mass and height as well as frequency and duration of daily training schedules. Cann et al. [41] did not specifically recruit athletes, instead recruiting 36 amenorrhoeic women from a reproductive endocrinology centre, 11 of whom had functional hypothalamic amenorrhoea (FHA), and ten of these 11 were "regular participants in vigorous exercise programs". The BMD of these amenorrhoeic women was compared with 50 eumenorrhoeic matched controls (according to age but not exercise).

The results of both studies indicated that although the radius, which is mostly comprised of cortical bone, was unaffected by menstrual status, the BMD of the vertebrae, which has a higher trabecular bone content, was significantly lower in amenorrhoeic women (22–29 % lower) than in eumenorrhoeic women: 165.8 (standard error of the mean 4.2) $mg \cdot cc^{-1}$ ($p < 0.01$) in the study by Cann et al. [41]; amenorrhoeic 1.12 (SD 0.04) $mg \cdot cm^{-2}$ versus eumenorrhoeic 1.30 (SD 0.03) $mg \cdot cm^{-2}$ ($p < 0.01$) in the study by Drinkwater et al. [7].

Marcus et al. [38] conducted a follow-up study of 17 female distance runners, 11 of whom had secondary amenorrhoea for 1–7 years. BMD was measured in all women at the lumbar spine and radius. As with the earlier studies, those with secondary amenorrhoea had lower lumbar BMD but normal BMD at the radius. Further, they found that there was a higher frequency of running-related fractures in those with secondary amenorrhoea.

In 1990, Drinkwater and colleagues [6] continued their work on menstrual status and bone health by investigating 97 female American athletes to determine the relationship between previous menstrual irregularities and current menstrual status and current bone density. Participants were asked to complete a self-reported questionnaire to determine their current and past menstrual status. Current menstrual status was confirmed via four blood tests 7 days apart that were assayed for estradiol and progesterone levels [6].

In agreement with their previous study, vertebral bone density was affected by menstrual status, with the investigators observing a significant linear relationship between current vertebral density and past and present menstrual patterns. Athletes with a history of regular menses had significantly higher lumbar densities (1.27 g cm^{-2}; $p < 0.01$) than those with a history of oligomenorrhoea/amenorrhoea combined with regular menses (1.18 g cm^{-2}). Women who never experienced regular menses had significantly lower lumbar densities than those with a history of oligomenorrhoea/amenorrhoea combined with regular menses (1.05 g cm^{-2}; $p < 0.01$). These results suggest that menstrual irregularities were impacting on bone health, which could potentially lead to severe health problems such as increased fracture risk and osteoporosis.

A further finding from the Drinkwater et al. [6] study was a significant positive correlation between body mass and bone density. However, this relationship was also affected by menstrual status, as normal estrogen levels appeared to negate the adverse effect of decreased body mass on bone density. As menstrual irregularities became more severe, the negative association between body mass and bone health became stronger. This was suggestive of an important interaction between menstrual pattern, body mass and vertebral density, and pointed to a potential role for energy balance in menstrual dysfunction [6].

5.3 Eating Disorders

Concurrent with the research on bone mass, others were investigating the prevalence of eating disorders amongst athletes [43, 44]. Unfortunately, the methods used to determine prevalence varied greatly. In addition, there were unclear definitions of study populations, absent or inappropriate control groups, a narrow spectrum of sports included and non-standard diagnostic criteria for an eating disorder, which hindered interpretation of these studies. Some studies investigated the prevalence of pathogenic weight control methods or disordered eating behaviours amongst athletes [44–46], whilst others estimated the prevalence of athletes with clinical eating disorders [45]. Therefore, it is not surprising that the prevalence rates varied substantially between studies, with reports ranging from 1 to 62 % [44, 46].

Despite inconsistencies in the methodology used in these studies, trends were emerging. Many researchers have reported that athletes had comparable frequencies of eating disorders to those of non-athletes [42, 43, 45, 47]. Investigators often grouped athletes from sports with similar characteristics, in particular athletes participating in sports that emphasised leanness or promoted a low body mass, such as aesthetic sports or sports that required body-revealing clothing. It appeared that these athletes had a higher prevalence of disordered eating behaviours than their athletic counterparts competing in sports that did not emphasise leanness [17, 48].

Also consistent with non-athlete literature [49], sex appeared to be a major risk factor in developing an eating disorder, with females having a significantly higher risk than males [43, 50, 51]. In 1991, Wilkins and Boland [50] undertook the first large cross-sectional study investigating eating disorders in male athletes. Researchers investigated male ($n = 99$) and female ($n = 78$) athletes and compared their risk of developing an eating disorder with that of non-athletic controls (39 males, 78 females). Multiple screening tools were used to measure participants' risk of an eating disorder, including using two validated eating disorder questionnaires: the Eating Attitudes Test–26 (EAT-26) and the Eating Disorder Inventory (EDI) drive for thinness scale. The results indicated that sex was the most important variable in predicting indices of eating disorders, with females at significantly higher risk ($p < 0.001$).

In 1993, Sundgot-Borgen [45] invited 603 Norwegian female athletes to participate in a study to determine the prevalence of pathogenic weight control methods and self-reported eating disorders among elite female athletes and non-athlete controls. The 522 athlete participants representing 35 different sports were divided into six groups—technical sports, endurance sports, aesthetic sports, weight-dependent sports, ballgames and power sports—and matched to 448 non-athlete controls. Participants were required to complete a self-administered questionnaire developed by the study investigators alongside the EDI and a subgroup ($n = 193$) participated in an interview and clinical examination to determine the prevalence of eating disorders in this population.

The results of this study showed a non-significant tendency ($p = 0.08$) for athletes (22 %) to be at less risk of an eating disorder than controls (26 %). However, a significantly higher percentage ($p < 0.05$) of athletes competing in aesthetic sports (34 %) and weight-dependent sports (27 %) were found to have an eating disorder compared with athletes competing in ballgames (11 %) and technical sports (13 %) (where leanness may be considered less important) as well as endurance sports (20 %). More athletes than controls reported the use of at least one pathogenic weight control method such as vomiting or inappropriate use of diuretics and laxatives ($p < 0.05$). Specifically, the prevalence of pathogenic weight control methods was significantly higher in athletes participating in the sports that emphasise leanness, including aesthetic sports (16 %) and weight-dependent sports (17 %), than in those competing in ballgames (8 %) and power sports (6 %), as well as compared with non-athlete controls (7 %) ($p < 0.05$).

When reviewing this research it is important to acknowledge that in some instances the sample sizes were very small and consequently may not have been large enough to detect any effect with statistical power, therefore limiting the ability to draw firm conclusions [46, 50, 52–54]. Further, this more general, subjective grouping of sports may not be reliable and may cause these more subtle yet important differences to be lost.

Another later study using the EDI showed no significant difference in the reported rates of eating disorders between amenorrhoeic female runners ($n = 7$), eumenorrhoeic female runners ($n = 9$) and non-athlete controls ($n = 6$) [28]. Similarly, Rosenvinge and Vig [53] found no significant differences in the risk of an eating disorder between 31 elite Norwegian swimmers (19 males and 12 females) and 33 controls (20 males and 13 females) for any of the three EAT-26 scales. Again, because of the small sample size it is difficult to determine whether these are true findings or due to insufficient power to detect a difference.

When discussing disordered eating it must be noted that appetite is affected by exercise [55]. Loucks [55] reported that appetite is not a reliable indicator of energy needs in athletes as exercise can suppress appetite despite an increase in energy needs. This inappropriate stimulation of appetite was demonstrated by Stubbs et al. [56] who allowed eight lean men free access to food throughout 1 week of rest and 1 week of exercise ($\sim$840 kcal·day^{-1}) during which they were resident in a human nutrition unit [56]. The results indicated that there was no associated increase in energy intake despite increased energy expenditure. This is important as it demonstrates that LEA may occur due to an athlete lacking appetite both with or without an underlying eating disorder.

5.4 Menstrual Function

In the early 1980s Boyden et al. [10] investigated the effects of endurance exercise on thyroid function. Thyroid hormones were measured before and after participants were asked to increase their weekly running mileage from a mean of 13.5 miles/week to 30 miles per week for at least 2 weeks. The increase in training volume resulted in decreases in triiodothyronine (T3) and reverse triiodothyronine (rT3) as well as significantly greater thyroid-stimulating hormone (TSH) responses to thyrotropin-releasing hormone (TRH) stimulation [10]. This differed from the responses seen with both acute and chronic starvation [57]. These results suggest that physically active women who undergo additional endurance training have thyroid changes that are indicative of mild thyroidal impairment.

Research on the ovulatory status of exercising females in the late 1980s [58] stimulated interest in the physiological effects of menstrual abnormalities less obvious than amenorrhoea. Bullen et al. [68] progressively increased the training (running) load of 28 untrained college students over a 5-week period. The participants were randomly

assigned to a weight maintenance or weight loss group and menstrual function during this time was assessed. Gonadotropin and sex steroid hormone secretions were measured, and only four participants (three in the weight maintenance group, one in the weight loss group) had normal menstrual cycles throughout. However, normal function resumed in all participants within 6 months of the completion of the study, showing that vigorous activity, especially in combination with weight loss, causes reversible disturbances in reproductive function.

De Souza et al. [59] undertook a prospective observational study on moderately active females (18–36 years) to estimate the prevalence of luteal and ovulatory abnormalities. Participants were included if they had consecutive, asymptomatic, regular menstrual cycles 24–36 days in length. Women with oligomenorrhoea (menstrual cycle 39–90 days) or amenorrhoea were excluded. Participants ($n = 35$) were originally split into two groups: sedentary ($n = 11$) and exercising (recreational runners, $n = 24$). Participants recorded the first and last day of menses for each menstrual cycle throughout the study and collected 8-h urine samples on day 2, 3 or 4 of each menstrual cycle. Urine was analysed for creatinine, FSH, LH, pregnanediol-3-glucuronide and estrogen conjugates. The results showed that 91 % of the sedentary females were ovulatory, with the remaining 9 % demonstrating luteal-phase deficiency. However, less than half (42 %) of the exercising females were ovulatory, with 42 % demonstrating luteal-phase deficiency, and 16 % were anovulatory. This was a pivotal finding in the progression of the understanding of the Triad, as it clearly demonstrated that menstrual cycle length is not an accurate marker of ovarian function in female athletes.

A group of Canadian researchers undertook a cross-sectional study in the early 1990s investigating the association between asymptomatic menstrual disturbances (anovulation and luteal-phase deficiency) and BMD [60]. They recruited 66 premenopausal women aged 21–42 years. The study was carried out over a year and participants were required to provide a blood sample during their first and last menstrual cycle of the study year. These were analysed for LH, FSH, progesterone, testosterone, estradiol, prolactin, cortisol and T3. BMD was measured twice via quantitative computed tomography at a mean ± SD interval of 12.0 ± 1.8 months apart. Results showed subclinical ovulatory disturbances over a 1-year period, including a short luteal phase and anovulation that were associated with loss of spinal trabecular bone (4.3 ± 4.2 mg cm^{-3} year^{-1} [$p < 0.001$] and 6.4 ± 3.8 mg cm^{-3} year^{-1} [$p < 0.001$], respectively). Further, they found that the mean luteal phase length over the year was the best predictor of changes in trabecular bone [60].

5.5 Growing Criticism of the Restrictive Categorisation of the Triad

The finding of an association between sub-clinical menstrual disturbances and bone health, as well as consistently high estimations of the prevalence of more subtle menstrual disturbances in exercising women, raised the question of whether luteal suppression occurred somewhere on the continuum between regular menstrual cycles and amenorrhoea. Similar research investigating the BMD in athletes suggested osteoporosis is very rare in athletes, although the prevalence of osteopenia was increased [61–63]. The very low prevalence of osteoporosis reported in athletes suggests that by including osteoporosis as part of the diagnostic criteria for the Triad, the number of female athletes who can be clearly defined as having the Triad is severely limited, and likely underestimates the magnitude of the problem [64–66]. Furthermore, the definition of the Triad at this time highlighted the role of disordered eating in the development and maintenance of amenorrhoea and associated poor bone health in physically active females. As cross-sectional studies started to incorporate multiple aspects of the Triad, it became evident that menstrual dysfunction and bone health were occurring in female athletes both with and without an eating disorder or disordered eating behaviours [66].

An underlying belief of many researchers in the Triad area at this time, which dated back to the 1960s when Erdelyi [33] first stated that "We may find menstrual disorders that may be associated with too much sports activities", was that strenuous exercise is the factor that can disrupt reproductive function in females [58, 67, 68]. Beginning in 1993, American researchers Loucks and Callister [70] challenged this and proposed the idea that LEA, which can occur with or without an associated eating disorder or disordered eating, may be the driving factor in the development of menstrual disruptions and thus the Triad.

In order to explore this theory, a series of investigations were conducted that manipulated both dietary intake and exercise energy expenditure [69–71]. The results of these studies revealed a close association between energy availability and variation of LH pulses, indicating that energy availability plays a pivotal role in initiating the menstrual disturbances associated with the Triad (Table 1) [69–71].

Loucks and Heath [69] initially investigated the effect of dietary energy restriction on gonadotropins. This was then used as the first phase of a study to differentiate the independent effects of energy availability and exercise stress on LH pulsatility in exercising women [71]. The results showed that LEA disrupted LH pulsatility, causing a reduction in pulse frequency during waking hours. The suppression of LH occurred regardless of whether energy

Table 1 Summary of randomised crossover trials investigating low energy availability as the driving factor in the female athlete triad

Study	Participants	Treatment	Methodology	Results[a]
Loucks and Callister [70]	7 women, 19–27 years Regularly menstruating[b] Habitually sedentary Non-smoking No recent history of dieting 15–30 % BF No medication including OCP Habitual energy intake between 35 and 55 kcal/kg LBM/day <60 min aerobic activity per week	Using a liquid dietary supplement (Ensure) EA was set at either balanced[c] or restricted[d] for 5 days beginning on day 5, 6 or 7 of participant's menstrual cycle Subjects assigned to each intervention in random order ≥ 2 months apart	Fasting blood samples taken for 3 days starting 2 days before treatment started On the 4th–5th day of treatment blood researchers assayed LH and FSH in blood samples drawn at 10- and 60-min intervals, respectively, over 24 h starting on day 9, 10 or 11 of their menstrual cycles 24-h energy expenditure calculated using accelerometer Participants were instructed not to change their exercise patterns Dietary intake was analysed using 7-day diet record	LH pulse frequency (waking)** Balanced diet: 20.6 ± 1.7 Restricted diet: 15.2 ± 1.8 LH pulse frequency (sleeping) Balanced diet: 16.0 ± 1.1 Restricted diet: 13.5 ± 1.9 LH pulse frequency (24 h)* Balanced diet: 19.0 ± 1.5 Restricted diet: 14.6 ± 1.7 LH pulse amplitude (waking) Balanced diet: 1.7 ± 0.2 Restricted diet: 2.0 ± 0.2 LH pulse amplitude (sleeping)* Balanced diet: 2.2 ± 0.3 Restricted diet: 3.6 ± 0.4 LH pulse amplitude (24 h)* Balanced diet: 1.9 ± 0.2 Restricted diet: 2.5 ± 0.3
Loucks et al. [71]	9 women, 18–29 years Otherwise the same criteria as above	Same as above with the addition of requiring participants to expend 30 kcal·kg LBM^{-1}·day^{-1} in exercise at 70 % of their aerobic capacity	Same as above with the following changes: Blood sample taken on days 8, 9 or 10 of the follicular phase of menstrual cycles Total energy expenditure during exercise measured using indirect calorimetry	LH pulse amplitude (waking)* Balanced diet: 1.2 ± 0.1 Restricted diet: 1.6 ± 0.1 LH pulse amplitude (sleeping)* Balanced diet: 1.9 ± 0.2 Restricted diet: 2.6 ± 0.3 LH pulse amplitude (24 h)** Balanced diet: 1.4 ± 0.1 Restricted diet: 1.9 ± 0.1 LH pulse frequency (24 h)** Balanced diet: 18.9 ± 0.3 Restricted diet: 17.1 ± 0.6 LH pulse frequency (waking)* Balanced diet: 20.4 ± 0.7 Restricted diet: 18.1 ± 0.8 LH pulse frequency (sleeping) Balanced diet: 16.0 ± 1.3 Restricted diet: 15.4 ± 1.5

Values are given as mean ± standard error, expressed in units of IU/l

BF body fat, *EA* energy availability, *FSH* follicle-stimulating hormone, *LBM* lean body mass, *LH* luteinising hormone, *OCP* oral contraceptive pill

* $p < 0.05$, ** $p < 0.001$

[a] In Loucks et al. [71], four participants received a 'restricted' EA of 15 kcal kg LBM^{-1} day^{-1} and two received a 'balanced' EA of 50 kcal·kg LBM^{-1} day^{-1}

[b] ≥3 months of menstrual cycles 26–32 days in length

[c] Restricted EA: 10 kcal·kg LBM^{-1} day^{-1}

[d] Balanced EA: 45 kcal·kg LBM^{-1} day^{-1}

availability was reduced by dietary restriction alone or by exercise energy expenditure. In the exercising women, LEA significantly increased LH amplitude during waking and sleeping hours [71], a similar result to the previous study where LEA caused by dietary restriction also significantly increased LH amplitude [69]. These findings marked a significant turning point in the direction of future research into the Triad and led to the understanding that LEA is the driving factor in this highly complex syndrome.

A further study, which employed a dietary intervention, produced results consistent with the studies previously outlined [72]. A small sample size of four amenorrhoeic females between the ages of 18 and 34 years were recruited. Each participant performed at least 7 h of exercise per week. Participants completed a questionnaire developed by the study investigators regarding health, exercise and diet as well as self-reported menstrual and weight history [72]. Blood samples were drawn for hormone analysis. Participants then began a 20-week diet and exercise intervention. The intervention required participants to decrease energy expenditure by adding one rest day to their current exercise programme, and increase energy intake by adding a daily serve (360 kcal) of Gatorade Pro® to their current diet. The results showed that not only did this intervention significantly improve energy balance, but menstruation resumed in three of the four participants during or just after the 20-week intervention programme, again suggesting athletic amenorrhoea is controlled by energy availability [72]. However, as no control group was included, the degree to which the observed changes were related to the intervention or other factors cannot be conclusively determined.

Collectively, results from the studies outlined in this section provide evidence that the Triad is more fluid and complex than the original 1997 ACSM model had described [14].

5.6 Male Athletes

During the 1980s and 1990s, the body of literature on LEA largely focused on females; however, some researchers also investigated the health of male athletes [73–75]. In the late 1980s, Bilanin and colleagues [73] carried out a small study comparing the BMD of long distance runners with that of non-runners: runners had significantly lower vertebral BMD (1.2 ± 0.03 g cm^{-2}) than non-runners (1.25 ± 0.04 g cm^{-2}). A similar study was carried out in 1993 in which Hetland et al. [74] investigated 120 men who ran between 0 and 160 km per week. In this study researchers investigated bone health as well as reproductive hormone status. Although no statistical difference in reproductive hormones and level of training was found, there was a significant negative correlation between running volume and BMD of the lumbar spine ($r = -0.37$; $p < 0.0001$) [74]. These results conflict with findings from a study carried out a year earlier in which no statistical difference was found in the spinal BMD or testosterone levels of six groups of men running between 0 and 120 km per week [75]. Therefore, further research is necessary in this area before any firm conclusion can be drawn.

6 2000s

The FATC was formed in 2002. This not-for-profit coalition consists of representatives from organisations around the world, including the ACSM, the American Medical Society for Sports Medicine and the American Dietetic Association (ADA). The FATC is dedicated to improving knowledge of the Triad and decreasing the prevalence of this syndrome through education, international leadership, public policy and research.

A year later in 2003, Loucks and Thurma employed a crossover study to investigate whether LH pulsatility in females is disrupted at a certain threshold of energy availability (Table 1) [76]. The results indicated that energy availability relative to lean body mass (LBM) of 30 kcal·kg LBM^{-1} day^{-1} had no effect on LH pulsatility. However, at energy availability below 30 kcal kg LBM^{-1} day^{-1}, LH frequency decreased and LH amplitude increased. Furthermore, participants with shorter luteal phases appeared to be most sensitive to decreases in energy availability, showing the largest disruption in LH pulses.

In 2005, the IOC released their first Position Stand on the Triad [77]. This position stand added to the ACSM 1997 Position Stand by outlining definitions of the Triad components along with their subclinical presentations. They also included risk factors and prevention strategies for each of the three components of the Triad. This Position Stand had a detailed appendix that included a diagnostic tool for identifying athletes with an eating disorder.

In response to mounting evidence that the diagnostic criteria of the Triad (namely disordered eating, amenorrhoea and osteoporosis) were likely to be too restrictive, a writing team had been assembled in 2003 by the ACSM to update the original 1997 position stand. A year later, in 2004, De Souza and Williams [78] proposed an expansion of the Triad to also include subclinical presentations of the clinical endpoints disordered eating, amenorrhea and osteoporosis [78]. They also proposed including increased cardiovascular risk as a health consequence and suggested including recreationally physically active females as well as 'athletes' per se. However, conflicting opinions within the scientific community meant this new expansion of the Triad was not universally accepted at this time and also resulted in delay of the publication of the new Position

Stand until 2007 [79–83]. Those opposed to the promotion of the Triad as a major health issue for female athletes argued that women should be encouraged to be physically active [80]. They reasoned that publicising potential negative outcomes from PA could contravene global efforts to increase PA as part of the fight to combat the rising prevalence of obesity [80]. It was thought this could cause confusion for active females and compromise public health programmes designed to encourage females to lead an active lifestyle in order to derive the associated health benefits [80]. Opponents also stressed the efforts that had gone into allowing females to reach the same level of accessibility in competitive sports as males, and fears that promotion of the Triad would hinder this progress [81]. Opponents also suggested that redefining the components of the Triad and describing its components on a continuum would allow a large percentage of females both athletes and non-athletes to be classified as 'at risk' of this supposedly 'life-threatening' syndrome by just having subclinical symptoms of one component [80].

In response to this challenging opinion, the updated 2007 ACSM Position Stand clearly re-states that the benefits of exercise far outweigh the risks, and emphasises that women should be encouraged to participate in exercise [84]. The Position Stand outlines that energy availability is reduced by extreme dietary restriction, extreme exercise expenditure or a combination of these factors, and because LEA has been shown to have adverse effects on reproductive function and bone health, female athletes need to take care to avoid LEA.

In the 2007 Position Stand the descriptions of the Triad components were modified to energy availability (with or without an associated eating disorder/disordered eating behaviours), menstrual function and BMD [84]. A new model presenting the Triad as a three-dimensional sliding scale, where the athlete can fall anywhere between the disease state (osteoporosis, disordered eating/energy deficiency and/or amenorrhoea) and good health (good bone health, healthy eating habits/energy status and normal ovulatory menstrual cycles) was also developed. The updated model recognised an important feature of the Triad: an athlete can fall anywhere along the continuum for each separate condition at any one time.

Meanwhile, research continued to expand the academic community's knowledge of LEA and its effect on the health of athletes. Using data from a previous controlled laboratory study [71], Ihle and Loucks [85] investigated bone turnover in 29 female college students after manipulating energy availability. Blood samples were assayed for markers of bone turnover (plasma osteocalcin, procollagen carboxy-terminal propeptide [markers of bone formation] and urinary N-telopeptide [a marker of bone resorption]). Results showed that the 10 kcal·kg LBM^{-1} day^{-1} treatment caused N-telopeptide concentrations to increase ($p < 0.01$). It was also found that whilst procollagen carboxy-terminal propeptide declined linearly with energy availability, the majority of the suppression of osteocalcin occurred between 20 and 30 kcal·kg LBM^{-1} day^{-1} ($p < 0.05$). These results indicate that restricted energy availability resulting in the uncoupling of bone formation and resorption may result in irreversible reductions in bone mass. Further, less severe energy availability resulting in reduction of bone formation may inhibit young females' ability to reach their peak bone mass.

By the 2000s, researchers were becoming increasingly interested in the health of male athletes [86–91]. Research during this time continued to produce conflicting results, with some studies finding decreased BMD or reproductive hormone levels in male athletes [86, 87], and others finding increased levels of total body and regional BMD in male athletes and no difference in testosterone levels [88]. For example a cross-sectional study in the USA investigated bone health among male recreational cyclists and runners. Researchers found as many as 63 % were classified as having osteopenia and male cyclists were three times more likely to have osteopenia of the spine than long-distance runners [86]. Another cross-sectional study carried out in the USA estimated the prevalence of osteopenia and osteoporosis in competitive male cyclists to be 25 and 9 %, respectively [87]. This study also compared testosterone levels of untrained controls with those of elite male cyclists [87]. The total testosterone levels of both groups were within the reference range ($\geq$0.28 nmol L^{-1}) for healthy males, but 12.5 % of cyclists versus 6.7 % of controls had free testosterone levels below the reference range ($\geq$0.62 pmol L^{-1}). Reviewing the available literature on male athletes indicates that there is a need for further research in this area, particularly investigating the potential relationship between LEA bone health and reproductive hormone status.

7 2010s

In 2014, a comprehensive consensus statement on diagnosis, treatment and return to play of the Triad was published by the FATC [13], which has been endorsed by the ACSM and the American Bone Health Alliance. Very soon after, the IOC published their latest consensus statement [12]. While both groups aimed to supplement the ACSM 2007 revised Position Stand on the Triad, they highlight a divide and difference of opinion that has developed amongst well-respected researchers in this area. A major modification included within the updated IOC consensus statement is the proposal of a new name to replace the term the Triad [12]. RED-S describes the wide range of adverse

effects on various body systems beyond those described by the Triad. These include the immune, gastrointestinal, cardiac and endocrine systems among others [12], although there is very little evidence, if any, to support a direct relationship between LEA and many of these body systems [14]. It also recognises that males can suffer the negative health and performance implications of LEA. The authors of the updated IOC consensus statement proposed a traffic light system to assess risk and readiness of athletes to return to play [12]. The authors of the FATC statement also proposed a tool for risk assessment and return to play [13]. However, they refute the concept of RED-S and argue that the original model of the Triad should continue as there is a lack of research in males and the few studies that have been carried out indicate the consequences for females are more severe than for males [14]. Further, it is clear that LEA has a causal relationship with menstrual dysfunction and impaired bone health in females. The effect of exercise and diet restriction on reproductive hormones was again demonstrated by Williams et al. [92], with the area under the curve for urinary estrone-1-glucuronides deficit significantly related to daily energy deficit.

Both the IOC and FATC consensus statements propose treatment strategies, which mainly include increasing energy status through increasing energy intake, decreasing exercise energy expenditure or a combination of the two. Details of the specific treatment strategies are outside the scope of this paper; for more detail, refer to these position statements [12, 13].

The inclusion of males in the IOC consensus statement is of interest. At present, there is very little research regarding the health effects of LEA in men. In an applied setting it is harder to identify males with LEA, as they do not have the obvious menstrual irregularities apparent in females. Further, many of the potential negative effects of LEA in females are due to alterations in their hormonal profiles, notably estrogen and progesterone. Given the hormonal sex differences, it is important to address whether the same level of LEA in males results in the same negative health outcomes. More research is required amongst male athletes in order to obtain a better understanding of the aetiology of LEA in males. Additionally, when energy availability is low, it is likely energy intake as well as micronutrient and macronutrient intakes are also low [91, 93]. As a consequence, this could have adverse effects on certain aspects of humoral and cell-mediated immunity, thereby weakening the immune system and causing athletes to become more susceptible to illness and infection, in particular respiratory tract infection [94–97]. The link between impaired immune function and LEA has not been fully established and the interplay between all aspects identified by RED-S means that the diagram is overly simplified. However, for ease of understanding, especially in the applied setting, this may have benefits. The debate between proponents of the IOC perspective and proponents of the FATC perspective is likely to continue, but all parties have a common goal, which is to minimise the potential negative health issues amongst male and female athletes, and gain a better understanding of the interplay between energy availability, bone health, the hormonal milieu and associated health problems.

8 Conclusion

It is possible that athletes may present with subclinical symptoms of LEA. The long-term effects of LEA can be debilitating and potentially irreversible, although, if diagnosed early, they are preventable. Although intervention studies are required to obtain more information on the identification and early treatment of LEA, studies are firstly needed that continue the work of Loucks and colleagues [58, 69–71] to assess the level of energy availability that causes negative health effects in different populations.

There is emerging evidence that males can also suffer from LEA [86, 87, 97]. Vogt et al. [97] investigated 11 professional male cyclists to compare their exercise energy expenditure with their energy intake over 6 days [97]. Results indicated that athletes were in negative energy balance as low as -7.9 ± 1.1 MJ (energy availability of 5 kcal·kg FFM^{-1} day^{-1}) on training days, but unfortunately the investigators did not measure any health effects [97]. Despite documentation of LEA existing in males, the full health consequences and hormonal changes of LEA are unknown for the male athlete and non-athlete populations; this research area needs to be addressed. Unfortunately, the use of the original Triad terminology may have unintentionally hindered the progression of research in males. It therefore remains unclear whether LEA affects males to the same extent and severity as females, and whether the prevalence is as high. It may be premature to advocate that males suffer from the same syndrome as females, as the term RED-S suggests. One thing is certain, researchers do agree the underlying driving factor resulting in this complex clinical syndrome is LEA.

Further standardisation of methods to identify those as risk of LEA needs to occur before moving forward. With the recent publication of the Low Energy Availability in Females Questionnaire (LEAF-Q) and the Brief Eating Disorder in Athletes Questionnaire (BEDA-Q), the variation in screening tools continues to grow [98, 99]. Although these tools are validated in an athletic population they still exclude men, athletes with a disability and are validated in European populations without diverse ethnicity. These are important limitations to be considered when revised editions of these questionnaires or new screening

tools are being developed. This will help to ensure that particular athlete groups are not inadvertently omitted from the screening process and will also allow health professionals, as well as coaches, parents and athletes themselves, to be consistent in identifying the signs and symptoms of LEA and to seek the appropriate treatment before serious health consequences can occur.

Continued advancement using vigorous research practices to enhance our knowledge and understanding of LEA and its associated health consequences will aid development of more effective prevention, early detection and treatment strategies. This will allow athletes of all demographics to enjoy exercise, whilst maintaining good health and maximising their sporting performance.

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