An IOC consensus group has recently introduced a new umbrella term, that is, ‘Relative Energy Deficiency in Sport’ (RED-S) to describe the physiological and pathophysiological effects of energy deficiency in male and female athletes. The authors assert that “new terminology is required to more accurately describe the clinical syndrome originally known as the Female Athlete Triad” that is “a more comprehensive, broader term for the overall syndrome, which includes what has so far been called the ‘Female Athlete Triad’.” This new terminology (RED-S) is insufficiently supported by scientific research to warrant adoption at this time. The Female Athlete Triad has more than 30 years of published evidence to support its existence in the scientific literature with strong evidence for its clinical sequelae and should remain a focus of scientific inquiry and translation. In contrast, research on the ‘energy deficiency’ and its effects in men, non-Caucasians and disabled individuals is in its infancy and is not sufficiently developed to warrant a new theoretical construct. The complex interactions of physiological factors with a causal link to low energy availability have been described and experimentally manipulated in studies which provide the scientific foundation for the most severe clinical outcomes identified in the triangle diagram illustrating the Female Athlete Triad. At the centre of the RED-S hub and spoke diagram is the term ‘relative energy deficiency’, which, according to the IOC authors, refers to the aetiological factor underlying RED-S, that is, “an energy deficiency relative to the balance between dietary energy intake (EI) and the energy expenditure required to support homeostasis, health and the activities of daily living, growth, and sporting activities.” This definition of the ‘energy deficiency’ component of RED-S in terms of energy balance is incongruent with the definition of ‘energy availability’ used throughout the rest of the IOC paper. Energy balance and availability are not synonymous. Careful work by researchers has demonstrated that Triad conditions can be present in women who are in ‘energy balance’ and thus do not exhibit ‘energy deficiency’ as defined in the
IOC paper, but likely exhibit ‘low energy availability’ as defined and supported in work by Loucks and colleagues12–17 20 and included (albeit defined incorrectly) in the IOC paper. The psychological portion of the diagram also appears independent of all other factors, another alarming misrepresentation, as decades of research in the field of eating disorders (ED) and the Triad would substantiate.21–23

Another error presented in the IOC paper and its figure is the simplistic and underdeveloped approach to understanding the ‘Triad’ by implying that the ‘Triad platform is limited to reproductive and skeletal issues, and that the IOC RED-S idea is more comprehensive. The 2007 position stand on the Triad and the 2014 consensus paper6 include a discussion of other medical issues, to include cardiovascular issues such as impaired endothelial vasodilation, impaired perfusion to working muscles, impaired skeletal muscle oxidative metabolism, lipid dysfunction, problems with the central nervous system, gastrointestinal system and renal system. Certainly the psychological concerns are highlighted in all of these publications on the Female Athlete Triad25 when discussing disordered eating (DE) and ED. Stress fractures are a component of the Triad even though they are not specifically listed in the diagram of the Triad; likewise, metabolic and endocrine perturbations are mechanisms of the components of the Triad. Clearly, the most serious clinical sequelae of the Female Athlete Triad include ED, reproductive disorders and skeletal outcomes. In particular, negative bone outcomes are especially concerning since they are questionably irreversible.26–28 and as such, are highlighted in the framing of the terminology of the Triad. Such a highlight on the most serious clinical sequelae benefits many athletes who suffer from these clinical outcomes, and does not exclude other outcomes. The Triad framework is also most favourable for knowledge translation to the most frequently affected population, namely young female athletes and exercising women. Alternatively, the introduction of a new term (RED-S), and a new (flawed) illustration of the physiology of the syndrome diffuses the messaging about the heightened susceptibility to and severity of effects of the Triad in girls and women, and places too much emphasis on ‘sport’, thus overshadowing the many recreational athletes that are similarly affected.29–32

The IOC paper incorrectly claims the recognition that energy deficiency can impact male athletes as something new; this is not new and Triad researchers and others have been alluding to this concern since 1993. The first 1993 ACSM workshop paper4 and the 19977 as well as the 2007 versions of the ACSM Triad position stand indicates that further research is necessary to explore clinical outcomes in male athletes. Although several studies have documented the existence of Triad-like conditions in male cyclists,26 27 judoists,28 and horse jockeys,29 almost two decades later few data exist to support the existence of serious clinical sequelae in men relative to those in women that result from energy deficiency.

Meanwhile, there is good reason to suspect that sex differences protect men against the serious clinical consequences of energy deficiency that afflict women. Testosterone promotes bone as well as muscle growth, and effects of low testosterone on bone formation are different from the effects of low oestrogen on bone resorption.30–32 Testosterone endows men with wider bones that are less susceptible to fracture.33 Furthermore, the energetic costs of reproduction are much lower in men than in women.34 Men do not have to ‘fuel’ ovarian and menstrual cycles, let alone gestation and lactation. Evidence of effects of low energy availability on sperm count and motility is largely non-existent, in part because egg cells mature by growing in size, whereas sperm cells mature by shrinking. Sperm do not store large quantities of energy derived from the male body, and inside women they derive their fuel for motility from the female body. For these and other reasons, reproductive and skeletal disorders may occur in men in extreme energy deficiency, but a prevalence as high as that in women at less severe levels of energy deficiency is doubtful.

Many more studies should document a concerning prevalence of physiological and clinical consequences of low energy availability in male athletes before a new term is introduced for those specific conditions in men. Moreover, the recent studies documenting ED and low bone density in men34–36 deserve to be extended without bias stemming from existing literature in women. It has taken decades to learn that important sex differences exist in male and female physiology, and we should not repeat previous mistakes by establishing clinical guidelines for both sexes when there are data primarily only for one sex. It is misleading in this regard that the risk stratification and return-to-play guidelines in the IOC paper are developed mostly from studies in women,3 include few male-specific end points and ignore that implementation problems will exist if applied to male athletes. The preceding concerns of lack of data and the errors in applying clinical guidelines to more than one population are magnified when other issues such as race, ethnicity and ability are considered. The point made by the IOC authors that low energy availability has serious consequences in male athletes, non-Caucasians and individuals with disabilities is important, but there is no evidence for their recommendation. Indeed, their recommendations should have stopped at advocating for more research and should not have extended to screening, treatment and return-to-play recommendations.

The IOC authors propose a new risk assessment and return-to-play model, ‘Red Light–Yellow Light–Green Light’, representing high-risk, moderate-risk and low-risk athletes, respectively.1 Concerning is both the lack of evidence and lack of quantification behind some of the risk factors noted within this framework. For example, the lack of clarity and quantification of ‘yellow light’ risk factors, such as ‘prolonged abnormally low per cent body fat’, ‘prolonged energy deficiency’ and ‘lack of progress in treatment’, makes each one of them difficult to interpret in the return-to-play schema. Likewise, this framework does not take into account cumulative risk in a quantitative way that can be measured over time to assess improvement or decline. Similarly, the return-to-play categories noted in table 3 do not provide the clinician any guidance as to the number of risk factors within each category that warrant the return-to-play recommendations. As such, adopting the IOC return-to-play model will lead to ambiguous decision-making.

The IOC paper is also weakened by the authors’ disregard for accuracy when referencing scientific literature. The IOC paper1 is fraught with fundamental errors and misinterpretations of the literature. Several of these errors are described below. Generally speaking, the paper is poorly referenced throughout. There are many instances where inaccurate references are used, several instances where statements are not referenced and many instances where original research is not referenced. The most important and blatant errors are listed below.

**HORMONAL AND METABOLIC IMBALANCE SECTION**

1. The authors state that “Abnormal levels of hormones, LH pulsatility, inadequately stored body fat stores, low energy availability (EA) and exercise stress may be aetiological factors in menstrual disorders in athletes.” Marked reduction in EA
may disrupt the LH pulsatility by affecting the hypothalamic hormone gonadotropin-releasing hormone (GnRH) output which subsequently alters the menstrual cycle.” These statements are incorrect. The hypothalamus can make GnRH in varying amounts or patterns (GnRH output) in different states of energy availability, but it is specifically abnormal GnRH pulsatility that impacts gonadotropin pulsatility, as opposed to GnRH output, and that leads to amenorrhea.32

2. The authors state that “Subtle menstrual dysfunction, such as very light bleeding, mildly extended menstrual interval and premenstrual and postmenstrual spotting may occur, and may be underestimated by routine screening.” De Souza et al24 is cited for this statement. Although De Souza et al24 reported that subtle menstrual disturbances are prevalent among physically active women, it was highlighted that these subtle menstrual disturbances are difficult to detect clinically. In addition, there is no mention of light bleeding or spotting in the De Souza et al24 paper.

HEALTH AND PERFORMANCE SECTION

1. The authors state that “hormonal and metabolic abnormalities caused by RED-S and carbohydrate deficiency can result in a decreased production of growth hormone.” This statement is incorrect. Low EA is associated with an increase in growth hormone, which is most likely a result of reduced circulating insulin-like growth factor 1 (IGF1) concentrations and hepatic growth hormone resistance.38 39

2. The authors state that “Oestrogen increases uptake of calcium into blood and deposition into bone, while progesterone facilitates the actions of oestrogen through multiple complex mechanisms.” This is also inaccurate. Oestrogen acts by inhibiting osteoclast activity, not by increasing uptake of calcium into blood and deposition in bone.40 Calcium absorption from the gut is driven by 1,25(OH)2 vitamin D.41 It is not clear what (if any) bone effects of oestrogen are facilitated by progesterone and how. No original research references are provided to support the proposed progesterone effects on bone in the IOC paper.

3. The authors state that testosterone stimulates osteoclast activity. Testosterone does not stimulate osteoclast activity. Testosterone directly stimulates osteoclast activity thereby upregulating bone formation.40 42 and may inhibit osteoclast activity through its aromatisation to oestrogen (which has primarily anti-resorptive effects).

4. The authors state that “DE/ED in male jockeys are associated with low BMD” and cite Dolan et al29 as a reference for this statement. This is an inaccurate reference for this statement. Dolan et al29 did not assess DE or ED in their study. Rather, Dolan et al29 report that low BMD in jockeys was associated with low IGF-1 and elevated sex hormone-binding globulin concentrations.

SCREENING AND DIAGNOSIS SECTION

Bone health

The authors state that “In the adolescent, DXA should include the whole body (head excluded) in addition to the lumbar spine... A value below −2.0 SD is considered as osteoporosis with the presence of secondary clinical risk factors.” This statement requires clarification. The International Society of Clinical Densitometry (ISCD) recommends assessment of lumbar spine or whole body sites for assessment of bone density in adolescents, and while it prefers the assessment of whole body less head (to whole body), when technically feasible, it does not indicate that whole body BMD assessment should not be performed.43 In addition, the ISCD defines osteoporosis in adolescents as low bone density z-scores (≤−2) with a history of clinically significant fracture43 and not a low bone density z-score alone. This stand has been reiterated in the 2013 position statement from the ISCD.44 45 It is important to clarify this and to indicate what conditions constitute secondary clinical risk factors.

TREATMENT SECTION

1. For the section regarding weight gain and improvement in bone density, the authors state “However, full recovery may not be feasible, as bone microarchitecture is also impaired.” The reason for lack of full recovery is not that bone architecture is also impaired. Impaired bone architecture is a consequence of many of the same factors that lead to low bone density.46 47 Lack of full recovery of bone parameters is likely consequent to incomplete recovery of certain hormonal changes (such as cortisol elevation) despite an improvement in energy status.48

2. The authors recommend that the “athlete diet should include 1500 mg/day of calcium.” The reference that is cited for that statement49 does not directly state that 1500 mg/day is the appropriate calcium intake for athletes. Rather, the article provides guidelines for how to counsel individuals about appropriate calcium intake, but does not recommend a certain intake. Furthermore, the appropriate calcium intake for athletes is not mentioned in the article.49 The current recommended dietary allowance for calcium from the 2011 Institute of Medicine guidelines is 1300 mg/day for adolescents and 1000 mg/day for young adults.50 51

According to the American Academy of Pediatrics Committee on Sports Medicine and Fitness,52 and others,53 it is recommended that amenorrheic athletes intake 1500 mg of calcium per day. As such, this is an example of a statement that uses imprecise wording and is not properly referenced.

3. The authors state that “Programmes of high-impact loading and resistance training should be implemented at least 2–3 days/week for athletes in non-weight bearing sports and/or those with decreased BMD.” This statement is not supported by any reference. In fact, one may argue that high-impact loading activity may precipitate fractures in amenorrhoeic women with very low bone density. This issue is not discussed.

4. The authors state that leptin “can be used to stimulate appetite.” On the contrary, leptin is an anorexigenic hormone and therefore suppresses appetite54–56 and, in fact, recombinant leptin administration is associated with suppression of appetite and weight loss in women with functional hypothalamic amenorrhea.57 58

5. The authors state that “The Endocrine Society Guideline (2011) recommends maintaining vitamin D [25(OH)D] blood levels above 32–50 ng/mL, with 1500–2000 IU/day of vitamin D.” This is inaccurate. The guidelines are as follows59: “We recommend using the serum circulating 25(OH)D level, measured by a reliable assay, to evaluate vitamin D status in patients who are at risk for vitamin D deficiency. Vitamin D deficiency is defined as a 25(OH)D below 20 ng/mL (50 nmol/liter), and vitamin D insufficiency as a 25(OH)D of 21–29 ng/mL (525–725 nmol/liter), and “We suggest that adults aged 19–50 yr require at least 600 IU/d of vitamin D to maximize bone health and muscle function. It is unknown whether
600 IU/d is enough to provide all the potential non-skeletal health benefits associated with vitamin D. However, to raise the blood level of 25(OH)D consistently above 30 ng/ml may require at least 1500–2000 IU/d of vitamin D.” The Endocrine Society guidelines do not provide a recommended target range for vitamin D.

6. The authors state that “use of the oral hormonal contraceptive pills in athletes with functional hypothalamic amenorrhea have been reported to have a detrimental effect on BMD through the suppression of androgen secretion and cause premature closure of the epiphyses compromising growth of the long bones in adolescents.” The authors cite Scheid et al.60 Scheid et al60 is the wrong reference as that paper has nothing to do with any of these factors.

7. Throughout the treatment section, no critical analysis of randomised controlled trials versus prospective studies is presented and no source literature is referenced. This is a major flaw as treatment recommendations are included in the IOC paper. In addition, treatment recommendations for bone health in men are not based on studies in male athletes.

SUMMARY

We are concerned that readers of the IOC paper will be confused and misled by the poorly referenced statements and frank (and sometimes dangerous) errors in the paper. The IOC authors should publish a correction of these and other errors noted. Broadening research of low energy availability in other groups, such as the male athlete, athletes of diverse ethnicities and the disabled athlete may help to advance science and may one day warrant introduction of a specific term for whatever serious clinical sequelae of energy deficiency may be discovered in future research on men.

Research on the ‘Female Athlete Triad’ has forged a platform from which a broad array of healthcare providers (eg, physicians, sport dietitians, mental health professionals and athletic trainers) have made great strides in learning how to manage and treat affected women. Research on the ‘Female Athlete Triad’ has also been translated to the lay public such that more and more affected female athletes and exercising women willingly seek education, prevention and treatment.

Meanwhile, subsuming the term ‘Female Athlete Triad’ under the umbrella of the term RED-S has the potential to confuse rather than enlighten, and undo decades of work educating and advocating for awareness, prevention and treatment for the Triad. The individual most impacted by the de-emphasis on the Triad will be the female athlete herself. The overwhelming clinical importance of the Female Athlete Triad compared with other conditions under the proposed RED-S umbrella will continue to make a specific reference for the Triad useful for those who deal with it, including physicians, coaches, sport dietitians, athletics trainers, parents and, most importantly, female athletes. As such, efforts promoting awareness, prevention and treatment of the Female Athlete Triad remain critically important and should not be overshadowed by an ill-conceived and poorly defended new construct.

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