Mapping the complexities of Relative Energy Deficiency in Sport (REDs): development of a physiological model by a subgroup of the International Olympic Committee (IOC) Consensus on REDs

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ABSTRACT

The 2023 International Olympic Committee (IOC) consensus statement on Relative Energy Deficiency in Sport (REDs) notes that exposure to low energy availability (LEA) exists on a continuum between *adaptable* and *problematic* LEA, with a range of potential effects on both health and performance. However, there is variability in the outcomes of LEA exposure between and among individuals as well as the specific manifestations of REDs. We outline a framework for a 'systems biology' examination of the effect of LEA on individual body systems, with the eventual goal of creating an integrated map of body system interactions. We provide a template that systematically identifies characteristics of LEA exposure (eg, magnitude, duration, origin) and a variety of moderating factors (eg, medical history, diet and training characteristics) that could exacerbate or attenuate the type and severity of impairments to health and performance faced by an individual athlete. The REDs Physiological Model may assist the diagnosis of underlying causes of problems associated with LEA, with a personalised and nuanced treatment plan promoting compliance and treatment efficacy. It could also be used in the strategic prevention of REDs by drawing attention to scenarios of LEA in which impairments of health and performance are most likely, based on knowledge of the characteristics of the LEA exposure or moderating factors that may increase the risk of harmful outcomes. We challenge researchers and practitioners to create a unifying and dynamic physiological model for each body system that can be continuously updated and mapped as knowledge is gained.

INTRODUCTION

As far back as historical records can be found, humans have been driven to create maps of their understanding of the world around them. The value of maps, then and now, is to provide a visual representation of the nature, magnitude and interrelationships of the features in our environment. Maps show us the landscape and help us to make better informed plans. As new explorations and technologies emerge, expert cartographers update maps with greater detail and precision compared with earlier, cruder representations. We are accustomed to the continual evolution of maps. We also accept the coexistence of different visual representations of the same territory, with varying complexity and features according to the end-user's needs.

Such is the 'cartographic' evolution of Relative Energy Deficiency in Sport (REDs).[1] The International Olympic Committee (IOC) first introduced the REDs concept in 2014[2] (updating it in 2018)[3] to describe the range of negative health and performance sequalae of Low Energy Availability (LEA; see Definitions box) in male and female athletes. REDs expanded the Female Athlete Triad model,[4] which focused on the inter-relationship of LEA, menstrual disturbances and compromised bone health in female athletes; this was itself an update on a previous model[5] and was more recently accompanied by the recognition of the proposed Male Athlete Triad.[6 7] New insights, including contributions from the ~180 new REDs-related papers published since 2018, broadened our understanding of the consequences of LEA and informed the 2023 IOC Consensus Statement on REDs,[1] including its updated REDs Health and Performance Conceptual Models (figure 1) and improved, validated Clinical Assessment Tool (REDs CAT2).[8] The 2023 Consensus Statement and its associated papers[8–13] unveil various changes, address some of the challenges of the underpinning science[14] and discuss future research goals. The REDs Conceptual Models for Health and Performance[1] now clarify that LEA is the exposure and REDs is the eventual outcome (see figure 1 and Definitions box). They contain more precise language and recognise more body systems susceptible to LEA-induced impairments.[1] However, it is important to acknowledge a growing body of scientific[15 16] and practical observations of non-uniform outcomes of LEA exposure, noting variations in both the magnitude and duration of LEA between and among individuals, as well as the specific manifestations of REDs. The REDs Conceptual Models now depict the understanding that some scenarios of LEA can be tolerated with modest and/or reversible perturbations to various biological systems or outcomes; we consider this 'adaptable' LEA.[1] Importantly, scientific/clinical attention is drawn to more severe LEA exposure, termed 'problematic LEA'[1] (see Definitions), which

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ The 2023 International Olympic Committee (IOC) Consensus Statement on Relative Energy Deficiency in Sport (REDs) notes that REDs is a syndrome of impaired physiological and/or psychological functioning experienced by female and male athletes that is caused by exposure to problematic (prolonged and/or severe) low energy availability (LEA).

⇒ Some scenarios of LEA can be tolerated with modest and/or reversible perturbations to various biological systems or outcomes (*adaptable* LEA). However, scientific/clinical attention is drawn to more severe LEA exposure (*problematic* LEA), which leads to an increase in the range and magnitude of REDs health and performance concerns.

⇒ The REDs Conceptual Models provide a simple representation that LEA exposure exists on a continuum between adaptable and problematic, with a range of potential outcomes in both health and performance metrics. The models demonstrate that increased exposure to LEA increases the risk of developing a variety of health and performance impairments that form the REDs syndrome.

WHAT THIS STUDY ADDS

⇒ The proposed physiological model of REDs provides a framework to expand our knowledge, now and into the future, of the effects of LEA on various body systems in the individual athlete and their specific moderating risk factors, resulting in various health and performance impairments.

⇒ The REDs Physiological Model takes a 'systems biology' approach to understanding the specific effects of the characteristics of LEA exposure and moderating factors pertinent to the individual athlete, their environment and their lifestyle on REDs outcomes. It notes that energy reallocation during energy scarcity may affect body systems differently, with systems preferred, essential, reducible or expendable in varying ways between and within athletes.

⇒ The REDs Physiological Model could be informed by insights gained from adjacent disciplines, which involve the effect of energy scarcity on human metabolism and health; these include evolutionary biology and the treatment of obesity.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ The REDs Physiological Model includes information about moderating factors and characteristics of LEA exposure that might assist in the diagnosis of underlying causes of these problems and help to create a targeted treatment plan. While correcting underlying LEA is the cornerstone of REDs therapy, a more personalised and nuanced approach can assist compliance and enhance treatment efficacy.

⇒ The REDs Physiological Model could also be used in the strategic prevention of REDs by drawing attention to scenarios of LEA in which impairments of health and performance are most likely, based on knowledge of the characteristics of the LEA exposure or moderating factors that may exacerbate the risk of harmful outcomes. This may help athletes make informed risk versus reward decisions about deliberate scenarios of LEA (eg, increased training load or body composition manipulation) as well as draw attention to scenarios that might inadvertently lead to problems.

leads to an increase in the range and magnitude of REDs health and performance concerns.

Although recognition of the concept of the continuum between adaptable versus problematic LEA adds some nuance to the REDs Conceptual Models and acknowledges the discordance of real-world outcomes versus laboratory manipulations of LEA exposure, it is unable to fully explain the true complexities and various moderators of REDs manifestations. Therefore, while we appreciate that these models provide valuable visualisations of current knowledge and key messages, we recommend that separate templates be constructed to better explore the multiple layers and interactions between and within LEA and various body systems. A more sophisticated exploration of each spoke within the REDs Conceptual Models (figure 1) could serve as an ever-evolving dashboard of our increasing knowledge of the complexity of the causes and outputs of LEA exposure in athletes. We suggest that such expanded diagrams be termed the REDs Physiological Model (see Definitions). Such models can inform, and be informed by, the insights of researchers studying a given body system as well as others working in fields involving metabolic adaptation.

METHODS

This paper emanated from discussions within a subgroup of the IOC working group on REDs to assist the future expansion of scientific knowledge and practice regarding the different outcomes of LEA exposure between and within individual athletes. Our author group consisted of experts with significant clinical and research experience pertaining to LEA—sports physiologists, sports dietitians and a sports endocrinologist. We further consulted with individual members of the full IOC working group on REDs as well as experts in LEA from other disciplines. With multidisciplinary expert consensus, we developed a systematic process for examining LEA exposure's effects on different body systems. This approach included characterising the influence of moderating factors of LEA's effects on health and performance. The aims of an expanded and more nuanced model of LEA exposure were identified, with athlete health and well-being preservation at its core. This model further addresses the concern around scenarios of adaptable LEA to focus attention on exposure to problematic LEA. LEA literature was examined to identify characteristics of LEA exposure, in addition to factors specific to the individual athlete (eg, environment and behaviours), which appear to influence the type and severity of health and performance outcomes. We subsequently produced a standardised template to expand our understanding of the context and complexity of the outcomes of LEA exposure on athletes, including the potential for positive, benign and detrimental effects. The proposed model was tested on a body system (haematological system) that has been less explored in the current LEA and REDs literature, involving a wider group of experts from that field to refine the concept.

Herein we present a potential framework to systematically examine the effects of LEA exposure on individual body systems. With additional research, the eventual goal is to develop a 3-D map that can demonstrate the unique features of each athlete, real-life scenarios of LEA and the interactions within and between body systems; figure 2 demonstrates a template for a 'systems biology' approach to that end. Ideally, the development and production of each individual template will highlight knowledge gaps and inspire further research questions to enhance their accuracy. Our intention is to challenge researchers and practitioners to assist in creating a unifying and dynamic physiological

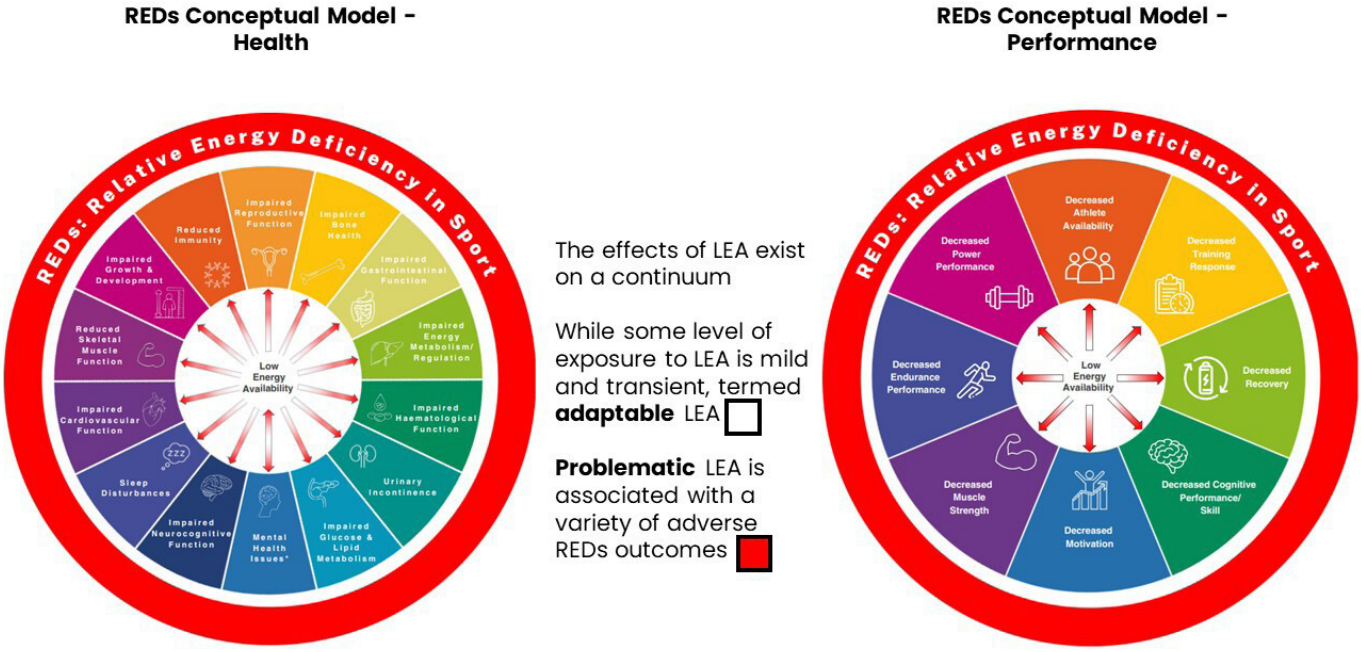

Figure 1 The REDs 2023 conceptual models for health (A) and performance (B). LEA, low energy availability; REDs, relative energy deficiency in sport.

model for each body system or REDs outcome that can be continuously updated and mapped as knowledge is gained.

Equity, diversity and inclusion statement

All contributors to this paper have considerable experience in the research or clinical management of REDs, with skills sets including sports medicine and endocrinology, exercise physiology, nutrition and coaching. The authors include three women and two men, from four different countries.

Recognition of differing responses to LEA exposure: the reproductive system example

The evolution of insights regarding REDs is illustrated by the study of the reproductive system response to LEA. The initial Female Athlete Triad model and REDs Conceptual Models presented simple causal relationships between LEA and functional impairments of individual body systems. Evidence for these relationships was provided by investigations of biomarker perturbations following short-term (~5 to 7 day), strictly-controlled EA manipulations in sedentary females,[17–20] paired with cross-sectional studies of athletes in which biomarkers of LEA were found in association with impairments to these body systems.[21–23] In the case of the reproductive system, concentrations and pulsatility of luteinising hormone (LH) following LEA exposure in females were robustly demonstrated in short-term investigations in laboratory[18 24] and field settings.[25 26] Meanwhile, differences in LH pulsatility were demonstrated between EA replete/eumenorrheic and LEA/amenorrheic cohorts,[27] with an increased prevalence of functional hypothalamic amenorrhea (FHA) and other menstrual disturbances (eg, oligomenorrhea, luteal phase defects, anovulation) in athletes with LEA that was either directly estimated or determined via measurement of LEA surrogates (eg, decreased resting metabolic rate).[28 29]

The results of a laboratory study[24] involving a stepwise approach to EA reduction supported the development of the narrative that LEA could be tolerated until it reached a specific, universal LEA threshold (eg, 30 kcal/kg FFM/day); below which, LEA would lead to REDs outcomes, such as menstrual dysfunction. However, other data failed to support the experience of a uniform LEA threshold.[30] For example, older premenopausal, females (28.7±2.3 years, 14–18 years postmenarche) failed to show the alterations in LH pulsatility observed in younger premenopausal females (20.5±0.9 years, 5–8 y post-menarche) in response to 5 days of a laboratory-controlled reduction in EA (45 vs 10 kcal/kg FFM/day).[15] Such a finding is consistent with the Life History theory that available energy is likely allocated to the various body systems with differing priorities at different phases of life.[31 32] However, even within a narrow age group of females (18–24 years), a longer term intervention with graded reductions in energy balance/availability over three menstrual cycles found a relationship between energy restriction and the prevalence of menstrual disturbances but failed to establish a firm LEA threshold[33] or a relationship with the severity of menstrual disturbances.[34] Cross-sectional studies have also reported inconsistent associations between EA and the range of common menstrual disturbances despite a relationship with the most severe outcomes (ie, amenorrhea).[35] Finally, we now know that LEA inhibits the reproductive system of males, as well. Preliminary evidence from studies of males suggests that they seem less susceptible to signs and symptoms of LEA and/or can tolerate a greater restriction of EA before such negative sequelae are observed.[16] Nonetheless, reductions in testosterone, libido and morning erections have been reported in settings of LEA.[36 37]

Of course, even within the narrow scope of LEA and reproductive outcomes in the REDs model, there have been methodological challenges. These include failure to accurately measure menstrual function,[38] inadequate consideration of the differential diagnosis of menstrual disturbances[39] and usage of surrogate markers of LEA.[21 22] There are also limitations and errors associated with direct assessment of EA in free-living populations.[40 41] Yet, it is clear that the outcomes of LEA exposure differ among athletes according to characteristics of the EA reduction as well as other modifying factors.

Definitions from 2023 IOC consensus statement update on REDs [1]

Energy availability

Energy availability is the dietary energy left over and available for optimal function of body systems after accounting for the energy expended from exercise. Energy availability is expressed as kcal/kg FFM/day and is defined in the scientific literature in the form of a mathematical formula:

EA (Energy Availability)={EI [Energy Intake (kcal)]−EEE [Exercise Energy Expenditure (kcal)]}/FFM (Fat-Free Mass (kg))/day

Low Energy Availability

LEA is any mismatch between dietary energy intake (EI) and energy expended in exercise that leaves the body's total energy needs unmet, i.e., there is inadequate energy to support the functions required by the body to maintain optimal health and performance. LEA occurs as a continuum between scenarios in which effects are benign (adaptable LEA) and others in which there are substantial and potentially long-term impairments of health and performance (problematic LEA).

Adaptable LEA

Adaptable LEA is exposure to a reduction in energy availability that is associated with benign effects, including mild and quickly reversible changes in biomarkers of various body systems that signal an adaptive partitioning of energy and the plasticity of human physiology. In some cases, the scenario that underpins the reduction in energy availability (eg, monitored and mindful manipulation of body composition or scheduled period of intensified training or competition) might be associated with acute health or performance benefits (eg, increased relative VO_{2max}). Adaptable LEA is typically a short-term experience with minimal (or no) impact on long-term health, well-being or performance. Moderating factors may also alter the expression of outcomes.

Problematic LEA

Problematic LEA is exposure to LEA that is associated with greater and potentially persistent disruption of various body systems, often presenting with signs and/or symptoms, and represents a maladaptive response. The characteristics of problematic LEA exposure (eg, duration, magnitude, frequency) may vary according to the body system and the individual. They may be further affected by interaction with moderating factors that can amplify the disruption to health, well-being, and performance.

REDs Health Conceptual Model and REDs Performance Conceptual Model

Separate models (see figure 1) which illustrate the relationship between LEA and REDs for a variety of audiences including the athlete's health and performance team and entourage (eg, coaches, parents). The REDs Conceptual Models provide a simple representation that LEA exposure exists on a continuum between adaptable and problematic, with a range of potential outcomes on both health and performance metrics. The models demonstrate that increased exposure to LEA increases the risk of developing a variety of health and performance impairments that form the REDs syndrome.

REDs Physiological Model

Evolving model which explores the complexity of LEA exposure on each of the body systems included in the RED Health Conceptual Model. A template (figure 2) could be used to develop a physiological model for each body system, which notes the effects of characteristics of the LEA exposure as well as a range of moderating factors on the manifestation health and performance impairments. Ideally, the REDs Physiological Model will develop over time to form a 3-D representation of the REDs syndrome in which the interaction and cross-talk between body systems is recognised.

Continued

Definitions from 2023 IOC consensus statement update on REDs 1 Continued

The physiological model overview: commencing with individual body systems

Following consultation and feedback from many REDs experts, we have developed a template to guide the standardised development of a physiological model for each body system (figure 2). This template encourages a systematic approach to understanding how LEA may affect each body system, while incorporating other moderating factors that influence the manifestation of system dysfunction. The goal of this activity is to distinguish between scenarios in which LEA exposure may present as an '*adaptable*' form and those that are '*problematic*' (see Definitions). Indeed, there is little need to focus on brief and benign exposures to LEA. Rather, it is important to prevent and/or treat REDs by addressing circumstances with likely *problematic LEA* exposures, particularly in the presence of negative moderating factors. Furthermore, this activity will help to illustrate that energy reallocation during energy scarcity may affect body systems differently, with systems being considered preferred, essential, reducible or expendable in varying ways between and within athletes.

The development and application of the physiological model templates could provide a major step in fostering strategies to address individual athletes, scenarios or behaviours that represent a potential for damaging or helpful outcomes. There is existing evidence that specific factors are associated with an altered risk of a body system disturbance within distinct cohorts exposed to LEA. For example, in a group of adolescent runners, a prior stress fracture was a common factor for developing another.[42] However, sex-specific risk factors included later menarche, lower body mass index (BMI) and prior involvement in gymnastics for girls; meanwhile boys with a previous history of a multidirectional movement sport (basketball) had a reduced fracture risk.[42] Similarly, we have already noted that a greater gynaecological age may decrease susceptibility to LH pulsatility perturbations when exposed to LEA.[15] The goal of mapping sophisticated physiological models is to extend and standardise the collection of such information to encourage a targeted approach to LEA treatment and prevention.

Our suggested protocol for undertaking a compartmentalised exploration of each body system is not the end goal; we appreciate the considerable overlap and interaction between many body systems, particularly with the endocrine system. Rather, it provides a dynamic, systematic template that supports the construction of a more intricate model by identifying the commonalities and differences between the effects of various characteristics of LEA, as well as intrinsic and extrinsic moderating factors, on body system outcomes. As the map of each system evolves with new insights, it may prompt discussion of other systems. Importantly, cross-talk, hierarchies and interactions among systems will emerge to link the physiological models into a strong network with the individual athlete at its centre.

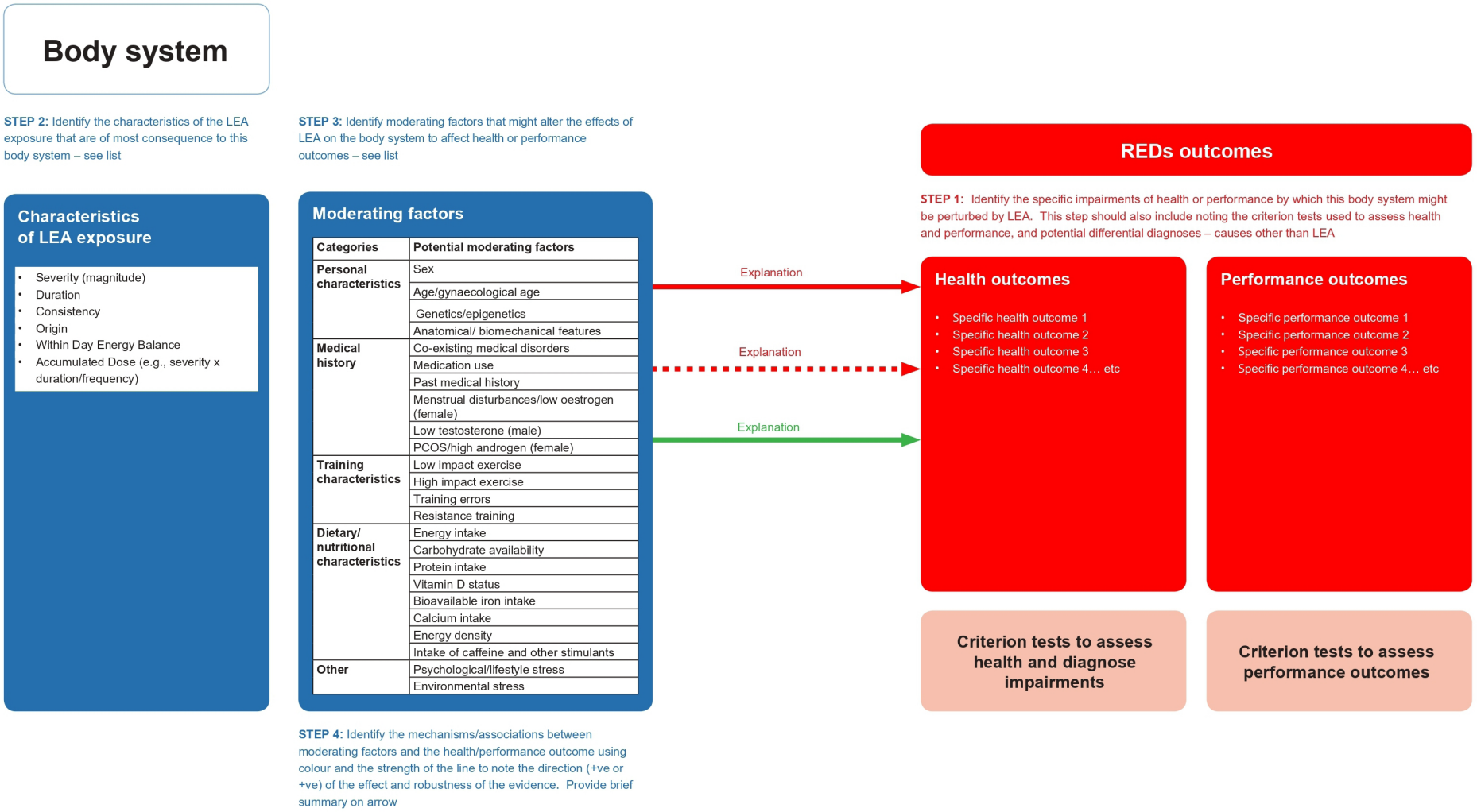

Figure 2 Template for the development of the REDs Physiological Model for each body system identified in the REDs Health Conceptual Model. Each model will show how problematic LEA exposure, with various associated moderating factors, can lead to various REDs outcomes, represented by body system/health dysfunction(s) and potential performance impairment(s). This template outlines four 'actions' (steps) to adapt and update the model as the future science of LEA/REDs evolves. LEA, low energy availability; PCOS, polycystic ovary syndrome; REDs, relative energy deficiency in sport.

Table 1 Characteristics of low energy availability (LEA) exposure that are important in promoting energy partitioning or metabolic adaptation in athletes, differentiating adaptable and problematic LEA exposures

Characteristic	Comment
Magnitude/severity	The severity of acute EA reduction (usually considered over 1 day) from an apparent optimal/'normal' EA of 40–45 kcal/kg FFM/day could be measured, potentially in zones or ranges of interest (eg, ~30 kcal, ~20 kcal, ~10 kcal)
Duration	The duration of a consistent exposure to LEA in terms of days, weeks, months. Ranges of interest might include <1 week, 1–2 weeks, 2–4 weeks, weeks-months, months-years.
Frequency	The frequency of exposure to LEA could be measured with potential zones of interest including frequent intermittent (eg, 5:2 day intermittent fasting, alternate day intensive competition); infrequent intermittent (eg, 1 week within 1–2 months); longer periodic (eg, 1 month within 6 months); or long-term (eg, 3 month competition phase within a 1 year calendar).
Origin	Whether the EA reduction is achieved primarily through a restriction in energy intake, an increase in exercise energy expenditure, or a ratio of both scenarios.
Within day energy deficit	Analysis of the spread/timing of energy intake over the day in relation to exercise energy expenditure (eg, large time periods of energy deficit with 'backloading' or 'catch-up' energy intake (eg, exercise occurs early in the day, but majority of caloric intake is in the evening)).
Accumulated LEA dose	A metric that combines duration, severity and frequency of LEA exposure may allow comparisons between different real-life scenarios: LEA dose = (magnitude × length of exposure/frequency)

Figure 2 displays a proposed protocol for constructing a 'systems biology' approach to each body system or 'spoke' identified on the REDs Health Conceptual Model. To commence the physiological model for each REDs body system, we propose identifying the range of specific health and performance impairments that might occur from LEA exposure, along with details of the criterion tests and metrics that best assess the presence of such disturbances (figure 2, step 1). The full complexity of the model may also be achieved by separately noting the broad differential diagnoses that could be responsible for such impairments (not yet included in the Figure).

Constructing the model: key characteristics for consideration with LEA exposure

Once the functional impairments of each body system are established, the focus should turn to the identification of key features of LEA exposure that may contribute to these. This step notes that energy mismatch is a primary and shared component of LEA, but each athlete's experience may be different (step 2, figure 2). Table 1 provides various LEA characteristics, along with patterns of such characteristics, which have been tested in the lab or observed in the field, within limitations.[40 41]

LEA severity

A series of elegant studies conducted by Professor Anne Loucks and colleagues exposed sedentary females to stepwise reductions in EA (40–45, 25–30, ~20 and ~10 kcal/kg Lean Body Mass (LBM)/day) over~5 days; biomarkers of reproductive health,[24] thyroid function[17] and bone metabolism[20] were measured across the different investigations. Figure 3, which summarises the relative changes in these biomarkers with LEA severity, normalised to their maximal responses, clearly demonstrates that hormonal patterns of specific body systems respond differently to the severity of LEA, at least after a short ~5-day exposure. Unfortunately, most LEA intervention studies have implemented a single high versus low LEA protocol, resulting in possibly dichotomous rather than graded changes.

One of the few longer term observations of graded levels of LEA severity implemented different energy deficits via changes in diet, exercise or both over three menstrual cycles in previously sedentary females.[34] The conditions (approximate energy balance and energy deficits of ~8%, 22% and 42% of daily energy expenditure) were subsequently converted to EA estimations (kcal/FFM/day), allowing comparisons of groups designated by the authors as 'low' EA (23–34 kcal/kg FFM/day), 'moderate' EA (35–41 kcal/kg FFM/day) and 'high' EA (41–50 kcal/kg FFM/day).[33] Another study involved trained male endurance athletes who undertook a stepwise series of 14-day exposures equivalent to 25%, 50% and 75% reduction in their baseline estimated EA, with stages equivalent to overall EA of ~22, 17 and 9 kcal/kg FFM.[43] Most other controlled field-based prospective investigations of EA exposure in athletes or active people have involved comparison of a single, severe[16 44–49] (eg, 10–15 kcal/kg FFM/day) or moderate[50–53] (20-25 kcal/kg FFM/day) restriction of EA compared with 'adequate'/'high' EA or energy balance (40–50 kcal/kg FFM/day), with interventions lasting from 3 to 9 days. Other prospective observational studies[54–56] have identified self-imposed differences in EA in athletes over periods of 5 days to 12 weeks, enabling differences in health or performance outcomes between LEA exposures to be assessed. In short, although there is a continuum in the perturbations of biomarkers of different body systems to varying increases in LEA severity, the responses are not uniform across all cohorts or individual subjects.

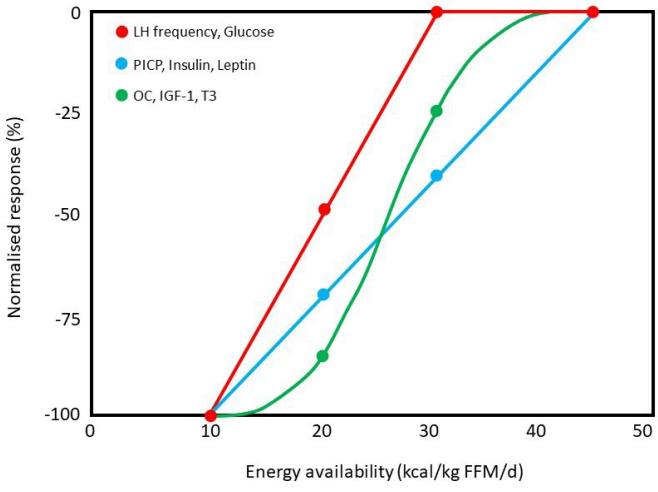

Figure 3 Dose–response effects of energy availability on luteinising hormone (LH) pulse frequency, plasma glucose (Glucose), markers of bone protein synthesis (PICP—procollagen I carboxyterminal propeptide) and mineralisation (OC—osteocalcin), and anabolic hormones that regulate bone formation (insulin, leptin, triiodothyronine (T3), and insulin-like growth factor-1 (IGF-1)). Created from data collected in sedentary women[20 24] and redrawn from Loucks.[109]

Investigation of LEA duration

In real-life scenarios, the *duration* of athletes' energy mismatches may be related to the physiological and psychological sustainability of maintaining energy restriction; the sport's competition calendar, which includes periods that BMI/body fat manipulations may impact performance[57–59] and/or extreme in-event or training blocks with excessive energy expenditures.[60–63] Studies demonstrate that significant perturbations to body systems can occur in as little as 3–4 days of moderate to severe LEA exposures.[17–20] However, systematic time-course studies of longer duration are required to isolate the sequence of the translation of perturbations in biomarkers to functional outcomes of growing severity across the range of body systems. Such investigations are currently unavailable.

Severity and duration

The interaction between the magnitude and duration of EA exposure should be explored. Changes in LH pulsatility and concentrations observed after three menstrual cycles of moderate EA reduction (~30 kcal/kg FFM/day)[64] were found to be similar to changes seen with 4–5 days of severe EA exposure (10 kcal/kg FFM/day).[18 24] Further investigation might warrant the development of a metric that can integrate the interaction of these variables such as an accumulated LEA dose [eg, magnitude×length of exposure (duration×frequency)].

Patterns of accumulation

The pattern of accumulation of EA exposure might also be considered, as real-life scenarios demonstrate a variety of strategies of purposeful (or sometimes non-purposeful) energy restriction and/or increased exercise loads to periodise their body composition over a sporting season or career.[57–59] In addition, extreme exercise energy expenditure (EEE) in competitions or blocks of intensive training, which might pose another risk of LEA despite proactive nutrition support, can be implemented differently even in the same sport (eg, continuous lengthy exposure[61] or intermittent/alternate day racing[62] in road cycling or ultraendurance events ranging from hours to weeks).[60 63] This is likely to have implications for the frequency and characteristics of LEA exposure.

The discrepancies between the typical investigation of LEA and its real-life implementation should be considered. To date, studies of deliberate LEA exposure, both laboratory-controlled and field-based, have employed protocols of daily repetition of an identical energy restriction (and diet characteristics) and/or exercise load.[15–20 24 47–49 51–53 65] Although this strategy provides a practical way to ensure that certain EA conditions are achieved, they do not mimic real-life scenarios in which athletes alter their daily training and dietary practices according to the goals of their micro-, meso- and macrocycles of periodised training.[66 67] We are aware of only one series of studies with a laboratory-controlled EA intervention, implemented in a more ecologically valid protocol in which highly trained athletes continued their periodised training programme (varying the mode, frequency, intensity and duration of daily workouts) while continually adjusting their energy intake (EI) to achieve the daily EA target.[44–46]

EI, EEE or both

Within the studies already noted, exposure to LEA has been usually achieved by a reduction in EI, an increase in EEE or a combination of both. Some investigations have included systematic comparisons of the effects of changing one or other of these components to achieve LEA.[16 18 47] Indeed, such a comparison initiated the birth of the concept of LEA by distinguishing an energy mismatch, rather than low body fatness or high endurance training volumes, as the cause of the Female Athlete Triad symptomology.[68] However, even though these studies have shown that LEA per se creates perturbations to a range of body systems, closer inspection reveals some subtle differences in outcomes according to relative changes in EI or EEE. Indeed, Loucks *et al* reported that LEA achieved via substantial increase in EEE was associated with less disturbance to LH pulsatility than similar LEA achieved through dietary restriction, with the difference attributed to a greater net reduction in glucose availability via the latter strategy.[18] In addition to direct effects on metabolic/hormonal perturbations, the relative contribution of changes in food intake and exercise patterns to LEA exposure may indirectly alter the manifestation of REDs health and performance outcomes due to their association with moderating factors. As noted in table 2 (moderators), characteristics of some forms of exercise may protect specific body systems from the effects of LEA exposure by diverting energy to repair and adaptation, even though this may decrease the energy available to other systems.

Within-day variability

Although EA is typically calculated or averaged across a 24-hour period, there has been distinct interest in within-day energy deficits that might occur at times during the day when there is separation between the periods of exercise and occasions of food intake (eg, exercise is undertaken earlier in the day while substantial eating occasions occur in the evening—'back-loading'). A separate metric, *within day energy balance*, has been developed to audit differences between estimates of EI and EEE in hourly increments, with focus on single or consecutive periods of either positive or negative energy balance, particularly by substantial margins that exceed the estimated energy and blood glucose buffer provided by liver glycogen stores (set at 300–400 kcal for females and males, respectively).[37 69–71] Observational studies applying such an assessment in athletes have reported that a greater duration of substantial within-day energy deficits is associated with perturbations in thyroid hormone,[70] resting metabolic rate,[37 71] oestrogen,[71] cortisol[37 71] and testosterone:-cortisol ratio.[37] However, this concept has been less investigated than other aspects of LEA, with the few studies relying on self-reported data rather than controlled interventions.[37 69–71]

With these issues in mind, we propose that the REDs Physiological Model develops standardised terminology and metrics to identify characteristics of LEA exposure that may have different effects on perturbations of body systems (figure 2). Based on the available literature, the map of each body system can be constructed to note these characteristics' effects and identify the scenarios of greatest potential risk. In addition to contributing to greater insight for current practice, this information will highlight gaps in knowledge that might be systematically investigated in the future research.

Constructing the model: moderating factors that may affect outcomes of LEA exposure

Individual responsiveness in the manifestation of REDs health/performance issues has been a consistent finding in cross-sectional studies of LEA prevalence, with differences in the number and severity of outcomes between and within cohorts.[21 22] Furthermore, prospective investigations have identified differences within[34 48] or between cohorts[15] with respect to immediate physiological/hormonal perturbations or functional outcomes arising from controlled LEA exposure. Therefore, it is logical

Table 2 Examples of moderating factors that may increase or decrease the likelihood that low energy availability (LEA) is associated with a functional impairment of health or performance involving personal characteristics and medical history

Categories	Potential moderating factors	Examples of moderation to (LEA risk), biomarker perturbations or expression of problematic LEA outcomes on (systems) implicated in REDs Health or Performance Conceptual Models
Personal	Sex	Males appear to better tolerate EA reduction: males respond to brief exposure to severe LEA with greater individual responses of bone turnover markers (bone health),[48] and less perturbation to T3 (energy metabolism),[16] testosterone[16] (reproductive system) and IGF-1[16] (growth and development) concentrations. Females are at greater risk of developing stress fractures (bone health).
	Age/gynaecological age	Female: Perturbations of LH pulsatility with brief, severe LEA exposure are seen in females of young (<8 y post-menarche) but not mature (>14 y gynaecological age)[15] (reproductive system). Menopause is associated with a substantial decrease in bone BMD[110 111] (reproductive system). Female/male: Old(er) age is associated with anabolic resistance: that is, lower rates of muscle protein synthesis and muscle gain in response to resistance exercise and protein intake[112] (skeletal muscle function).
	Genetics/epigenetics	Genetic factors that are unrelated to LEA may cause exacerbate several health outcomes identified as possible REDs outcomes, such as FHA[113] (reproductive system), low BMD[114 115] (bone health) and hyperlipidemia[116] (glucose and lipid metabolism).
	Anatomical/ biomechanical features	Poor running biomechanics and certain anatomical features may increase the risk of stress fractures[117] (bone health).
Medical history	Co-existing medical disorders	Coeliac disease can be associated with low BMD[118] (bone health) and iron deficiency[119] (haematological status). Testicular disease can cause male hypogonadism (reproductive system).[120] Traumatic brain injury is associated with hypogonadism in males and females[121] (reproductive system). Some medical conditions found in para-athletes may complicate the assessment of, or require different normative values of, RMR (energy metabolism) or BMD (bone health).[122] The autoimmune condition Hashimoto's Disease is typically associated with hypothyroidism and its various symptoms[123] (energy metabolism/regulation).
	Medication use	Non-steroidal anti-inflammatory drugs can cause gastrointestinal bleeding, contributing to iron loss and poor iron status[124] (haematological status). Glucocorticoid steroid use is associated with reductions in BMD and increased risk of fractures[125] (bone health).
	Past medical history	Previous history of bone stress fractures is a risk factor for future stress fractures[126 127] (bone health). Past history of anorexia nervosa is a risk factor for low BMD and stress fractures[127–129] (bone health).
	Menstrual disturbances/low oestrogen (female)	Low oestrogen concentrations exacerbate the effect of LEA on bone loss via enhanced bone breakdown and suppressed bone formation[80] (bone health). Removal of monthly bleeding in amenorrheic females reduces the risk of iron deficiency[77] (haematological status).
	PCOS/high androgen (female)	Female athletes with FHA and clinical/biochemical signs of hyperandrogenism had lower stress fracture risk than those with FHA alone[130] (bone health) (athlete availability).
Training characteristics	Low impact exercise	Athletes undertaking sports involving low impact, non-weight bearing exercise have lower BMD than their counterparts in higher impact sports[131 132] and may even risk losing bone mass annually in the absence of impact loading stimuli[133] (bone health).
	High impact exercise	Repetitive bone strain from dynamic, high impact, weight-bearing modes of exercise increases BMD and bone quality in athletes[131 134] (bone health). Repetitive footstrike (eg, running on hard surfaces) is associated with haemolysis and increased iron losses[135 136] (haematological status).
	Training errors	Increases in bone strain beyond the adaptive capacity of the bone will independently increase the risk of bone stress injuries; factors include training volume/pattern, type of sport, and inappropriate footwear and training surfaces[42 137–139] (bone health).
	Resistance training	Resistance exercise (and protein intake) may rescue the decrease in resting muscle protein synthesis seen with LEA[140] and protect against the loss in lean body mass with an energy deficit[141] (skeletal muscle function).
Dietary/nutritional characteristics	Energy intake	LEA underpinned primarily by restricted/reduced energy intake increases the magnitude of changes to LH pulsatility compared with an increased energy expenditure[18] (reproductive system).
	Carbohydrate (CHO) availability	Acute exposure to low CHO diet increases marker of exercise-associated bone breakdown and reduces marker of bone formation,[142] with these effects being greater than seen with LEA alone[45] (bone health). Acute exposure to low CHO diet increases the hepcidin response to exercise with likely reduction in iron absorption and recycling, with this effect being greater than associated with LEA alone[46] (haematological status). Acute carbohydrate restriction reduces T3 independently of LEA[143] (energy metabolism). Acute carbohydrate restriction reduces testosterone independently of LEA with exercise training[144] (energy metabolism).
	Protein intake	Higher protein intake is required to optimise muscle protein synthesis in response to resistance exercise when exposed to LEA; inadequate protein intake likely results in reduced muscle protein gains[140] (training response).
	Vitamin D status	Vitamin D deficiency/insufficiency may increase the risk of bone stress fractures[145–147] while a higher vitamin D intake/status may be associated with higher BMD and reduced risk of stress fractures[148 149] (bone health) (athlete availability).
	Bioavailable iron intake	Inadequate intake of bioavailable iron is a risk factor for lower iron status/iron deficiency in athletes[150 151] (haematological status).
	Calcium intake	Inadequate calcium intake may increase the risk of bone stress fractures,[152] while higher intake of dairy foods and calcium is associated with higher BMD and lower risk of stress fractures[148] (bone health). Consuming calcium prior to non-weight bearing exercise may reduce the PTH-associated increase in bone turnover during and after exercise[153 154] (bone health).
	Energy density	Diets with low energy density are associated with increased satiety[155] and may reduce energy intake (LEA severity).
	Intake of caffeine and other stimulants	High intake of caffeine and its spread over the day may contribute to sleep disturbances in athletes[156] (sleep quality).

Continued

Table 2 Continued

Categories	Potential moderating factors	Examples of moderation to (LEA risk), biomarker perturbations or expression of problematic LEA outcomes on (systems) implicated in REDs Health or Performance Conceptual Models
Other	Psychological/lifestyle stress	Psychological stress may lead to FHA independent of physiological stress[157 158] (reproductive function).
	Environmental stress	Training/competing at moderate altitude may increase resting metabolic rate[159]exacerbating risk of LEA unless adjustments are made to energy intake [LEA severity] and potentially reducing physiological adaptation[160] [training response] Training/competing at moderate altitude increases iron requirements exacerbatingrisks to iron status[161] [hematological status], with poor iron status reducingphysiological adaptation to the training/altitude stimulus[162] [training response].

BMD, bone mineral density; FHA, functional hypothalamic amenorrhea; IGF-1, insulin-like growth factor 1; LH, luteinizing hormone; PCOS, polycystic ovary syndrome; PTH, parathyroid hormone; REDs, Relative Energy Deficiency in Sport; RMR, resting metabolic rate; T3, triiodothyronine.

that an individual possesses intrinsic and experiences extrinsic factors that may moderate the manifestation of outcomes to LEA exposure on various body systems (ie, *moderating factors*). The mechanisms may aggravate the risk or effects (or interactive effects) of LEA on the body system, exacerbating or attenuating the perturbations or functional endpoints. Examples of such moderating factors and their interaction with various systems are summarised in table 2, noting their potential effects on LEA and/or body system outcomes.

To further develop the REDs Physiological Model, we propose that factors that may moderate the risk of LEA per se or amplify/reduce its impact on each of the body systems or performance outcomes, be identified in a systematic way (figure 2: step 3). The figure displays how moderating factors could be integrated into the physiological model for each body system, linking factors of specific interest to each identified health or performance outcome (step 4) in the REDs Conceptual Models and noting the direction of the effect. Again, a standardised approach to such activity would contribute insights into the prevention, diagnosis and treatment of REDs and promote a systematic programme of targeted research.

Using the physiological model to predict LEA risks or explain outcomes

As the map of the physiological model for each body system becomes more sophisticated, it could be used to assess the contribution of LEA to the presentation of body system impairments, as well as develop hypotheses regarding the potential for such impairments before they occur. In the case of the athlete who has incurred health or performance decrements, the physiological model includes information about moderating factors and characteristics of LEA exposure that might assist in the diagnosis of underlying causes of these problems. Furthermore, these details could assist in clinical treatment by reducing/removing negative factors and introducing changes that are beneficial as part of a wholistic, multidisciplinary treatment plan. While correcting underlying LEA is the cornerstone of REDs therapy, a more personalised and nuanced approach can assist compliance and enhance treatment efficacy.

The physiological model could also be used in the strategic prevention of REDs. Disordered eating/eating disorders represent pathological conditions that frequently underpin LEA and REDs, with primary, secondary and tertiary prevention (treatment) requiring significant commitment from all within the sporting environment (eg, athlete, coach, performance and medical staff, parents, etc).[72] However, as previously discussed, some scenarios of LEA are integral to the athlete experience (particularly at the elite level) and may sometimes be associated with benefits to performance.[59 73 74] Furthermore, EA mismatches can occur inadvertently due to a variety of factors (eg, food insecurity, poor food availability in the local environment, inadequate nutrition knowledge and practical skills, suppressed appetite and excessive exercise expenditures).[73] Although each of these scenarios can pose health and performance risks, understanding how each might cause a signature type of LEA of greater or lesser concern might prioritise efforts to educate athletes or organise activities that address the most pressing issues and underlying factors.[12]

The future: integrating the model to recognise interactions between body systems

Interorgan cross-talk and interactions among various body systems, including in response to exercise, are both a historically recognised phenomenon as well as an area of evolving science.[75 76] Although the REDs Conceptual Models (figure 1) are drawn in two-dimensional simplicity, the reality of the overlay and interaction among body systems is recognised in research and practice. After complexity is better depicted via the theoretical mapping of the physiological models for each body system, digital online data visualisation skills might be employed to create presentation styles that better integrate the separate models. Features have already been built into this proposal for the REDs Physiological Model to aid this step. These include the interrogation of each body system using a standardised list of *moderating factors* that may assist in identifying the similarities and overlaps of some responses. Furthermore, the inclusion of some features of body systems into the list of *potential moderating factors* for another body system also accentuates the interaction. For example, the list of suggested moderating factors acknowledges that the cessation of menstrual periods (reproductive system) reduces iron losses[77] and is, therefore, a moderating (attenuating) factor for low iron status (haematological system) in females. Similarly, reproductive dysfunction and low levels of sex hormones (reproductive system) are associated with low BMD or bone stress injuries in both men[78 79] and women[80–84] (bone health) and represent a moderating (amplifying) factor to the effects of LEA. Opportunities to establish the hierarchy of energy allocation to different body systems and how this can differ between and within individuals in different scenarios may also be explored. This process of integrating the separate physiological models will challenge both the currently published science as well as provide visualisation opportunities; it will benefit from interdisciplinary input, including expertise and insights from adjacent fields pertaining to energy constraint and energy allocation during scenarios of energy scarcity.

Learning from other perspectives of energy scarcity

Interest in the health and performance effects of LEA is a relatively new theme within the field of sports science/sports medicine. Although impairments of reproductive and/or bone status

were identified as far back as the 1980s in both male[85–88] and female athletes,[89 90] and the 'Female Athlete Triad' (Triad) was coined in 1993[91] and officially described in 1997,[5] the specific involvement of LEA was not recognised until the Triad update in 2007.[4] Since then, the evolution of Triad and REDs models has occurred largely via insights gained within sports science/sports medicine research and practice. Only recently have other perspectives on responses to energy mismatches been considered within the sports domain, with forays into evolutionary biology[92–94] enabled by recognition that "nothing in biology makes sense except in the light of evolution".[95] Additionally, anthropologists have developed the reverse interest in athletes as a modern cohort with unique profiles of energy expenditure.[60 96 97]

Life History Theory proposes that humans have finite energy resources for which various biological processes related to growth, health, activity and reproduction compete with different outcomes over their life span.[31 32 92] During periods of energy scarcity, which occur for numerous reasons over our individual and collective history, energy insufficiency is managed by allocating it to tissues and functions in a hierarchical manner, with priority afforded to those that offer the greatest immediate survival value. Such dynamic energy trade-offs are context specific, varying according to factors such as sex, life stage, environment, severity/duration of energy scarcity and other stressors; our capacity to dynamically redistribute energy resources derives from phenotypic plasticity shaped by human history.[31 32 92] Aspects of life history theory explain many of the features of the updated REDs Conceptual Models: energy partitioning can occur at different levels and timescales across and within athletes; it can range from transient and reversible, representing a normal and necessary, adaptive response through to more severe impairments to body systems that nevertheless represent survival priorities.[92] These perspectives reinforce the caveats identified in the updated REDs Conceptual Models,[1] emphasising that LEA and the response to it are not uniform and always negative,[92–94] and confirming that the focus should be on *problematic LEA* exposure. Observations on athletes via the life history lens have included commentary on priorities of energy allocation during energetic stress, noting considerable reliance on the context of both the energy restriction and the individual athlete/environment,[92–94] but also the apparent importance of preserving physical capacity.[98]

Athletes have allowed a further examination of the constrained energy model of Pontzer and colleagues.[99 100] The constrained energy model proposes that humans share a set of evolved mechanisms to maintain total energy expenditure (TEE) within a narrow range, and to dynamically reduce behavioural and non-behavioural (mainly basal metabolic rate; BMR) components of energy expenditure to compensate for increases in physical activity.[99 100] While compensation may include adjustment to other activities in the day, reduction in whole body BMR via decreased metabolic expenditure on various body systems may occur to limit TEE.[99] This hypothesis opposes the additive energy model in which deliberate high levels of physical activity in athletes, hunter gatherers, labourers and other populations are simply added to the other components of their energy expenditure. The constrained energy model is intriguing and explains REDs as a necessary reduction in metabolic rate in athletes with high EEE. However, it has been noted that its support comes from cross-sectional observational data and statistical models that compare extremely varied populations.[101] It is likely that the level of Constraint vs Addition with respect to physical activity varies across populations, according to factors such as individual characteristics, the level of energy expenditure and the presence of energy balance vs energy deficit.[96 101] Indeed, insights from endurance athletes have contributed to a model that predicts that at low activity levels, exercise is added to total energy expenditure, with moderate to high EEE leading to some partial compensation to achieve energy savings, including behavioural changes to reduce non-exercise activity thermogenesis (NEAT).[94] Meanwhile, very high activity levels that increase TEE beyond alimentary limits to cause LEA will accrue the greatest energy compensations and energy reallocation among biological processes.[94]

The study of obesity also provides insight into REDs-related issues; weight loss is often accompanied by metabolic adaptation or adaptive thermogenesis, as displayed by a reduction in TEE and resting metabolic rate that exceeds that predicted from reduced BM/FFM and decreases in thermic effect of food intake and BM-associated EEE.[102–104] Because this reduction in TEE may contribute to failure to maintain weight loss in the long-term,[102–104] there is interest in understanding and combatting adaptive thermogenesis and its components.[105 106] In the obesity literature, there is also evidence of phenotypic and genetic differences in the presence and components of adaptive thermogenesis.[105 106] Ultimately, a better understanding of REDs will be gained from interdisciplinary expertise and insights from outside the sports medicine/sports science environment. Of course, we recognise the complex differences between obese populations, current and past hunter gatherer populations and athletes, but also some overlaps. Indeed, understanding differences as well as similarities in responses to energy mismatches may help to refine the physiological model of LEA in athletes.

CONCLUSION

Our understanding and presentation of REDs have evolved from the concept first introduced in 2014,[2] with the REDs Conceptual Models for Health and Performance from the 2023 REDs Consensus Statement[1] showcasing a more nuanced and rigorous depiction of the science and practical experiences of the syndrome. Nevertheless, continued development of the knowledge and messaging around REDs to support prevention, diagnosis[107] and treatment strategies[12] that accommodate the range of real-life outcomes seen in athletes is needed. Recognising that REDs entails the accumulation of health and performance outcomes stemming from problematic exposure to LEA, the field requires greater insights into the continuum between *adaptable* LEA vs p*roblematic* LEA exposure. We have proposed the development of a more complex physiological model approach for each body system implicated in REDs, underpinned by a 'systems biology mindset'. We encourage a sequence of activities to develop individual maps for each body system, which could then be integrated to acknowledge interrelationships and cross-talk among organs/systems. This approach will enable a more nuanced assessment of the individual athlete—considering their specific combination of LEA exposure and secondary moderators to determine if the outcome is likely to be positive, neutral or negative. In short, the evolution of the scientific and practical REDs concept requires an interdisciplinary field of study that integrates complex biological interactions and uses a holistic approach towards functional outcomes.[108] We hope that the development and continued evolution of these individual body system, physiologically-based models will enhance the understanding and exploration of the complex science underpinning REDs; that they assist clinicians in providing better education, prevention and treatment programmes for REDs; and most

importantly, that they aid athletes in improving how they manage their own training and nutrition.

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