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REVIEW ARTICLE

The Influence of Energy Balance and Availability on Resting Metabolic Rate: Implications for Assessment and Future Research Directions

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Abstract

Resting metabolic rate (RMR) is a significant contributor to an individual's total energy expenditure. As such, RMR plays an important role in body weight regulation across populations ranging from inactive individuals to athletes. In addition, RMR may also be used to screen for low energy availability and energy deficiency in athletes, and thus may be useful in identifying individuals at risk for the deleterious consequences of chronic energy deficiency. Given its importance in both clinical and research settings within the fields of exercise physiology, dietetics, and sports medicine, the valid assessment of RMR is critical. However, factors including varying states of energy balance (both short- and long-term energy deficit or surplus), energy availability, and prior food intake or exercise may influence resulting RMR measures, potentially introducing error into observed values. The purpose of this review is to summarize the relationships between short- and long-term changes in energetic status and resulting RMR measures, consider these findings in the context of relevant recommendations for RMR assessment, and provide suggestions for future research.

Key Points

Changes to resting metabolic rate (RMR) that are greater than expected based on change in body mass or composition are more likely to occur following long-term interventions (≥ 14 days) and in the context of negative energy balance.

A ratio of measured to predicted RMR that is below cutoffs defined in the relevant literature (e.g., 0.90) may help identify athletes at risk for the health consequences of chronic energy deficiency.

To the extent possible, researchers investigating RMR via indirect calorimetry should employ a period of weight stabilization (preferably ≥ 2 weeks), a consistent period of abstention from moderate- to vigorous-intensity exercise or physical activity (preferably ≥ 24 h), and a period of fasting (preferably ~ 12 h) prior to assessments.

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1 Introduction

Resting metabolic rate (RMR) is the total amount of energy required to sustain homeostasis in the resting state [1]. A similar but not completely synonymous concept is basal metabolic rate (BMR), which is the energy required for the maintenance of cells and tissues, respiration, circulation of blood, gastrointestinal and renal processing, and the energy costs of remaining awake [2]. Indirect calorimetry, the most common method of BMR and RMR assessment, measures energy expenditure through the volume of oxygen consumed and carbon dioxide produced [1, 3]. However, while BMR represents the energy expended in the period shortly after waking, in a thermoneutral environment, and at least 12 h after consuming food [2], RMR can be assessed at other times of day and with variable durations of fasting, making it a more feasible option in outpatient and clinical settings [1]. Observed values for RMR may be approximately 10–20% higher than for BMR, especially if food has recently been consumed or physical activity undertaken [2]. Despite the less precise definition and implementation of RMR in clinical settings, pre-assessment standardization of RMR assessments in research settings should approach the rigor of that required for estimating BMR. Sleeping metabolic rate (SMR), meanwhile, denotes the energy required for basal physiological functions during sleep, and values may be 5–10% lower than those for BMR [2].

The effects of various diet and exercise interventions on RMR are commonly investigated across diverse populations. As a major contributor to an individual's total energy expenditure [1], RMR plays an important role in body weight regulation across a range of populations. The monitoring of RMR—as well as the application of potential interventions to maintain or optimize it—is also important in populations that must maintain a certain body weight or composition for performance (e.g., for improvement in strength-to-bodyweight ratio in weight-restricted and power athletes or speed and economy in endurance athletes) or aesthetic purposes (e.g., for maintenance of leanness or low bodyweight in aesthetic and physique sports) [4]. RMR may also be used as a non-invasive marker of energetic status in athletes and active individuals [5], providing insight about their risk for the deleterious health effects associated with chronic energy deficiency [6]. In these individuals, dietary intake patterns that do not sufficiently meet the combined energetic demands of formal exercise, everyday tasks, and basic physiological processes may eventually lead to the sequelae of negative health consequences described as the female athlete triad [7] and male athlete triad [8], with a broader syndrome known as relative energy deficiency in sport (RED-S) [9].

Fat-free mass (FFM) is considered the largest contributor to RMR [10], although the various organ and tissue components of FFM (e.g., bone, skeletal muscle, brain, liver, and kidneys) influence RMR to different degrees [11]. Chronic manipulations of energetic status, defined as either energy balance or energy availability, may possibly inflate or diminish observed RMR values beyond what would be expected on the basis of these factors. While energy balance represents the difference between total energy intake and total energy expenditure throughout the day, energy availability considers only the amount of energy expended through formal exercise and standardizes the difference between this value and energy intake to an individual's FFM [12]. As such, it may be a more appropriate metric for athletic individuals. Thus, the purposes of this review are to (1) summarize the relationships between various states of energy balance, energy availability, and RMR within both short-term (< 14 days) and long-term (≥ 14 days) contexts; (2) consider these findings in the context of relevant recommendations for RMR assessment; and (3) provide suggestions for future research.

1.1 Current Recommendations for RMR Assessment

Given the important role of RMR assessment in both research and clinical arenas of sports medicine, the use of pre-assessment standardization guidelines is critical to reducing error in RMR testing so that the effects of perturbations of energetic status can be more precisely examined. In addition to requiring that the subject be at rest throughout the test [2] (i.e., not expending energy through movement or arousal beyond wakefulness), currently accepted guidelines [13] from the Academy of Nutrition and Dietetics include a 30-min period of pre-assessment supine rest with no movement; abstention from food (≥ 7 h, or ≥ 4 h after a small ≤ 300-kcal snack if necessary), moderate- to vigorous-intensity exercise (12–48 h), and stimulants such as caffeine (≥ 4 h) or nicotine (≥ 140 min); and the maintenance of a quiet, thermoneutral environment during testing [14].

Relevant recommendations for RMR assessment, the strength of recommendations and their underlying evidence, and identified research and gaps presented by the Academy of Nutrition and Dietetics are summarized in Table 1. As acknowledged by the authors [1], the evidence underpinning many of these recommendations is sparse. For instance, the majority of studies informing guidance on the pre-assessment abstention from food did not include a duration of RMR assessment long enough to observe a return to baseline levels after eating, and the recommendations explicitly do not consider the effect of "continuous feedings, macronutrient composition, overfeeding, etc. on RMR" [13]. Only one study was identified by the linked systematic review [1] regarding the impact of resistance exercise on RMR, which

Table 1 Select conclusions from the Academy of Nutrition and Dietetics' Evidence Analysis Library Review of Best Practices for Performing Indirect Calorimetry in Healthy and Non-Critically Ill Adults [1] and 2014 Guideline Recommendations [14]

Question	Recommendation	Conclusion grade[a] and recommendation rating[b]	Identified research and gaps
Fasting period	Individuals should fast for at least 7 h before assessment	Grade II fair; imperative	The majority of studies reviewed did not include a duration of assessment long enough to observe a return to baseline RMR levels after eating. The required duration of the fast may depend upon the amount of energy consumed. Recommendations do not consider the effect of "continuous feedings, macronutrient composition, overfeeding, etc. on RMR."
	If a 7-h fast is not clinically feasible, a small meal (≤ 300 kcal) may be consumed 4 h before assessment	Grade II fair; conditional[c]	
Abstention from resistance exercise	None given	Grade III N/A	One study [15] in untrained older men observed a 3% (57-kcal) increase in RMR at 48 h post-exercise[d]. More research is needed to determine the effects of resistance exercise on subsequent RMR measures in both trained and untrained populations
Abstention from very light-intensity physical activity	A 30-min pre-assessment rest period should be used after the individual engages in very light activity (e.g., getting dressed, driving, or walking < 5 min)	Grade IIII weak; conditional	The single identified study [190] concluded that, after a 300-m walk, recovery to a resting state (< 6% above baseline) occurred within 20 min in 95% of subjects. Future investigations utilizing longer durations of light activity are warranted
Abstention from light- to vigorous-intensity physical activity	Individuals should refrain from physical activity for "a period of time" (e.g., 24–48 h after moderate to vigorous physical activity). Duration, intensity, type, training status, and other factors may influence RMR elevations	Grade V consensus; conditional	No studies examining this question were identified in the evidence analysis. Two studies [16, 17] cited by the guideline suggest that RMR may be elevated for longer after moderate- to high-intensity aerobic (~ 19–48 h) than resistance exercise (up to 24 h)

[a]Strength of evidence for a conclusion is based on the quality, consistency, quantity, clinical impact (importance and magnitude of effect), and generalizability of findings. I: good; II: fair; III: limited; IV: expert opinion only; V: grade not assignable [18]

[b]Recommendations are classified as strong, fair, weak, consensus, or insufficient evidence based upon the balance between potential benefits and harms as well as the strength of underlying evidence. Recommendations are then further categorized as imperative (statements are broadly applicable to the target population) or conditional (statements clearly define a specific situation or population) [13]

[c]Created as its own recommendation in the guideline

[d]This study was included as evidence related to light- to vigorous-intensity physical activity in the guideline. No resistance exercise-specific recommendation was given

reported a 3% (57-kcal) increase at 48 h post-exercise in untrained, older men [15]. While the systematic review identified no studies determining the optimal period of abstention from light- to vigorous-intensity physical activity, two studies [16, 17] cited by the resulting guideline suggest that RMR may be elevated for longer after aerobic (~ 19–48 h) compared with resistance exercise (up to 24 h).

The grading system used by the Academy provides a rating of the strength of evidence as well as of the recommendations stemming from it. Strength of evidence for a conclusion is based on the quality, consistency, quantity, clinical impact (importance and magnitude of effect), and generalizability of findings and ranges from I (good) to V (grade not assignable) [18]. Resulting recommendations are classified as strong, fair, weak, consensus, or insufficient evidence on the basis of the balance between potential benefits and harms as well as the determined strength of evidence [13]. While evidence related to the residual effect of food on RMR was given a quality grade of II (fair), all evidence related to physical activity and exercise received grades ranging from III (limited) to V (not assignable). As a result, only one recommendation —a pre-assessment fast of ≥ 7 h—was given a grade of at least "fair" [14]. Given the state of evidence upon which current recommendations for RMR assessment are based, it is likely that future recommendations may change or be refined as more evidence accumulates.

1.2 Methods and Terms Used

In addition to a general review of the literature, a search of the PubMed database through August 2022 was conducted using combinations of key phrases including "short-term," "long-term," "chronic," and "acute"; "energy restriction," "calorie restriction," "energy surplus," "calorie surplus," "underfeeding," "overfeeding," and "energy availability"; and "resting metabolic rate" and "resting energy expenditure," with the most highly relevant titles and abstracts screened for relevance and the references of relevant works accessed for further consideration. Literature assessing the effect of changes in energy balance or availability on RMR in generally healthy adults, including those with overweight/obesity, were included, with studies assessing RMR in critically ill populations or individuals with chronic disease considered outside the scope of this review. Secondary analyses (i.e., narrative reviews and systematic reviews and meta-analyses) were reviewed and included to provide additional context for findings.

Outcomes reported in cited research as BMR are referenced within this review as RMR, as BMR is assessed in fasted, morning conditions, and thus represents a more conservative estimate of energy requirements at rest. SMR outcomes are generally discussed separately unless specified by study authors that measurements were taken in a fasted state. It should be noted that repeated RMR measurements have been observed to vary 3–5% over 24 h [19], corresponding to ~ 36–85 kcal for RMR values of 1200–1700 kcal/day, assuming the use of contemporary indirect calorimetry techniques. All presented findings should be interpreted in relation not only to the expected variability arising from physiological processes and the technological limitations of RMR assessment but also to the relative age of the indicated research and the degree of standardization used within measurement procedures. For the purposes of interpreting findings within this review, magnitudes of change in RMR ≥ 5% are generally considered beyond the expected day-to-day variability of assessment for most devices used in research since the late twentieth century, though discretion should be used when interpreting findings of older research.

2 Energy Balance and Resting Metabolic Rate

Energy balance (EB) is defined as the overall balance between total metabolizable energy ingested via food and fluid intake versus the total amount of energy expended. The formula for EB is therefore Total Energy Intake − Total Energy Expenditure [20]. Total energy expenditure includes all contributors to the amount of energy expended throughout the day, including RMR, the thermic effect of feeding (TEF, sometimes referred to as diet-induced thermogenesis [DIT]), and energy expended through both non-exercise (non-exercise activity thermogenesis, or NEAT) and exercise activities [22]. In addition to the components of total energy expenditure required during homeostasis, EB also considers any additional energy required for the growth of an organism [20]. EB is considered a dynamic system, and fluctuations in the components of both energy intake and expenditure are considered influential on one another [23, 24].

2.1 The Question of Adaptive Thermogenesis

The change in energy expenditure over and above that predicted by a change in body mass or composition alone is termed adaptive thermogenesis (AT), though no single clear definition or methodology of assessment has yet prevailed in the literature [25–27]. Proposed mechanistic contributors to AT include changes in FFM, sympathetic nervous system, and metabolic pathway activity as well as in hormonal regulators including triiodothyronine, leptin, and insulin [4, 28, 29]. In the context of both energy deficit and surplus, the mere existence of AT remains controversial. For instance, incommensurate decreases in RMR have been observed in response to weight loss by several investigators [30–38] reporting mean adaptive changes ranging

from approximately 60 to 370 kcal/day, though others have reported no changes [39–42]. The debate over whether an adaptive increase in energy expenditure occurs in response to prolonged increased intake is also not new, with discourse and experimental data dating back to the early twentieth century [43]. Differences in the way values are measured and reported in the literature, as well as interindividual differences observed in response to changes in EB, further add to the confusion [44].

While longer-term diet and exercise interventions leading to weight gain or loss are generally associated with changes in RMR, it is unclear how much of a role is played by some additional "adaptive" component versus a simple change in body mass (and, thus, in the amount of energy required to sustain it). Short-term disruptions to EB could also have considerable implications for the assessment of metabolic responses to diet or exercise interventions. For instance, it has been suggested that if individuals either consciously or subconsciously increase their intake above weight maintenance requirements in the period immediately preceding a weight loss intervention, this could artificially inflate baseline RMR values [31, 45]. In fact, the majority of diet and exercise investigations do not appear to utilize a multi-day weight stabilization period leading up to the given intervention to confirm that the subjects were in a state of neutral EB at baseline, though such protocols are not without precedent [41, 46–48]. The following sections will describe the relevant literature related to the effect of both short- (< 14 days) and long-term (≥ 14 days) energy surplus and deficit on resulting RMR values, with particular emphasis on whether these changes are adaptive or simply a function of changes in body mass or composition.

2.2 The Effect of Short-Term Changes in Energy Balance on Resting Metabolic Rate

2.2.1 Responses to Short-Term Energy Surplus

A systematic review by Bray and Bouchard [49] concluded that interventions less than 1 month in duration did not consistently elicit statistically significant increases in RMR. While longer-term overfeeding interventions demonstrated 5–12% increases, these were generally explained by increases in body mass or FFM (Table 2). The consistency of observed changes appears to increase with the duration of overfeeding. In fact, many investigators (though not all [50]) have observed statistically significant RMR increases of up to 90–150 kcal/day within a 9-to-15-day time frame [51–55], often explained as a result of increased body mass or FFM. Some, however, have argued that the observed increases may at least partially be explained by residual TEF lasting up to 9–14 h after the last meal in the context of overfeeding interventions lasting anywhere from 24 h [56] to 14 days [51].

Tellingly, investigators who overfed 16 lean men and women by 1000 kcal/day for8 weeks reported a 5% (88-kcal) increase in RMR by the second week at a corresponding 2% (1.5 kg) increase in body mass, followed by a decrease, rebound, and continued plateau between 79 and 108 kcal above baseline RMR from weeks 5 to 8 [57]. However, the overall change in RMR tracked more closely to changes in body mass and FFM by week 6. These findings indicate that observed short-term increases in RMR may resemble a "metabolic growth spurt"—likely an attempt to dissipate a sudden energy surplus through increased heat production—which is then followed by a settling period in which RMR is linked to small increases in mass. Rather than a prolonged increase in postprandial energy expenditure as the reason for the more immediate observed effects on RMR, the authors suggested alternative hypothesized mechanisms including changes in sympathetic nervous system activity, thyroid hormone, or adipokines such as leptin and ghrelin [57].

2.2.2 Responses to Short-Term Energy Deficit

In individuals with overweight and obesity, periods of energy restriction up to 1 week in duration generally do not appear to affect RMR to a statistically significant degree [58–60], though reported mean changes may be as large as 5% (124 kcal) and more notable decreases may occur shortly thereafter (Table 2). For instance, investigators observed no changes in absolute or body composition-adjusted RMR at 3 days of a very low-energy diet in 31 adults with obesity but reported significant changes in both measures at the point of 5% weight loss, corresponding to a mean duration of 12 days and a 10% (167-kcal) reduction in absolute RMR, approximately half of which was ascribed to AT [60]. In lean subjects, RMR did not significantly change in response to 1 day at a 1100-kcal reduction in intake [56], 4 days of an 800-kcal daily deficit [61], or 1 week at a 1960-kcal daily deficit induced with diet and exercise [62]. However, Müller and colleagues [30] observed an adaptive 72-kcal decrease in RMR after just 3 days of a 50% deficit in eight lean men, though this occurred immediately after 7 days at a 50% energy surplus. Conversely, increases in RMR ranging from 70 up to 193 kcal/day (3–14%) have been observed after just 18–36 h of fasting in non-obese subjects [63–65], suggesting a potentially transient effect of increased cholinergic activity in the first several days of starvation [66].

It has been proposed that different metabolic phenotypes may help explain the differing responses to short-term periods of energy deficit or starvation (Fig. 1). In fact, the observed variability of responses to acute changes in EB was noted in the literature as early as the mid-twentieth century, as discussed by Dauncey [56]. Furthermore, the role of these metabolic phenotypes in mediating responses to changes in EB may be "unmasked" in the context of a

Table 2 Summary of the effects of various states of energy balance, availability, and menstrual function on observed resting metabolic rate values

Factor	Direction	Magnitude	Implications for assessment	Research gaps
1–14 days of positive EB	Interindividual differences may depend on metabolic phenotype, protein balance, or other factors	Likely small to minimal mean change	Residual TEF may affect RMR in the context of very high energy intake (i.e., overfeeding)	Sequential measures of RMR in the 8–24 h after acute overfeeding to help elucidate any impact of prolonged TEF
1–14 days of negative EB	May decrease in some individuals (e.g., obesity-prone, "thrifty" phenotypes) while increasing in others (e.g., lean individuals, "spendthrifts")	Likely small to minimal mean change Acute (~18–36 h) fasting may ↑ RMR by up to 14% in some individuals	As RMR measures may increase with prolonged (≥~18 h) acute fasting in some individuals, taking measures in proximity to a 12-h fast may reduce this effect	Effect of metabolic phenotype, other factors on responses to acute fasting Sequential measures of RMR within first 8–48 h of fasting may elucidate a specific fasting window to reduce error when assuming neutral EB
Positive EB > 14 days	Increased as a function of ↑ body mass/FFM AT not consistently observed and may differ between individual metabolic phenotypes, by diet composition (e.g., protein content), or other factors	Commensurate with ↑ body mass/FFM ~5–12% in interventions lasting 1 month or more, though change in weight and RMR varies widely between individuals	Use of a ≥7 h fast, with a target of ~12 h, before measurement may reduce the potential impact of residual TEF during overfeeding	Impact of methods used to statistically adjust for body composition on observed presence, magnitude, and sources of AT (e.g., types of FFM gained) Effect of metabolic phenotype, diet composition, or other factors on responses to fasted RMR during periods of positive EB (as opposed to SMR, 24 h EE, etc.) Source of EB disruption (↑ EI versus ↓ EE) and energy flux on resulting RMR changes in various populations
Negative EB > 14 days	Decreased as a function of ↓ body mass/FFM AT commonly observed; may "bottom out" beyond a certain level of weight loss or adaptation, and may diminish once EB is restored	Commensurate with ↓ body mass/FFM AT may additionally contribute to ~40–50% + of observed decrease, or ~5–10% of initial values	Monitored weight stabilization period (≥2 weels) at neutral EB after a weight loss intervention may reduce or negate effects of AT on RMR measures ↑ EE achieved through exercise may acutely increase RMR for up to 24–48 h; chronic effects are unclear	Impact of methods used to statistically adjust for body composition on observed presence, magnitude, and sources of AT (e.g., types of FFM lost) Influence of the source of energy deficit (↓ EI versus ↑ EE) and energy flux on RMR in various populations Time course and magnitude of ↑ RMR after various modes of exercise Utility of intermittent periods of ↑/neutral EB in attenuating RMR loss during a long-term energy deficit

Table 2 (continued)

Factor	Direction	Magnitude	Implications for assessment	Research gaps
Chronic low EA	Decreased as a function of ↓ physiological processes (e.g., reproduction)	< 90% of values predicted by commonly used equations (e.g., Harris–Benedict, $Cunningham_{1980}$)	In active populations, RMR assessment within 24–48 h of exercise may artificially inflate values and reduce utility of RMR_{ratio} in screening for low EA Different prediction equations have demonstrated variable sensitivity and may require higher cutoffs than 0.90	Incorporation of organ size in prediction equations to assess RMR_{ratio} Comparison of diagnostic performance across different prediction equations Influence of body composition assessment modality and use of FFM versus lean soft tissue when determining predicted RMR Longitudinal investigations in athletes employing a ≥ 24 h pre-assessment abstention from exercise Utility of RMR_{ratio} to indicate low EA in individuals using hormonal contraceptives
Menstrual status	Commonly decreased in the presence of menstrual disturbances	May decrease linearly in response to ↑ menstrual disturbance severity	Assumption of an ovulatory cycle with regular follicular and/or luteal phase length may not be appropriate, especially in active populations Females with low EA may present with reduced RMR even if asymptomatic for menstrual disturbance, though the time course of menstrual disturbances and RMR changes during low EA is unclear	Assessment of the utility of RMR_{ratio} to screen for subclinical menstrual disturbances in at-risk populations Time course of suppression and/or recovery of RMR in response to changes in EA over time, and in relation to change in menstrual status Use of validated, multi-step methods to confirm menstrual status and cycle phase in research participants Effect of various hormonal contraceptives (e.g., progestin type, dose, potency, route of administration) on short- and long-term changes in RMR Relationship between EB, EI, and cycle phase on resulting RMR measures

AT adaptive thermogenesis, *EA* energy availability, *EB* energy balance, *EE* energy expenditure, *EI* energy intake, *FFM* fat-free mass, *RMR* resting metabolic rate, *TEF* thermic effect of feeding

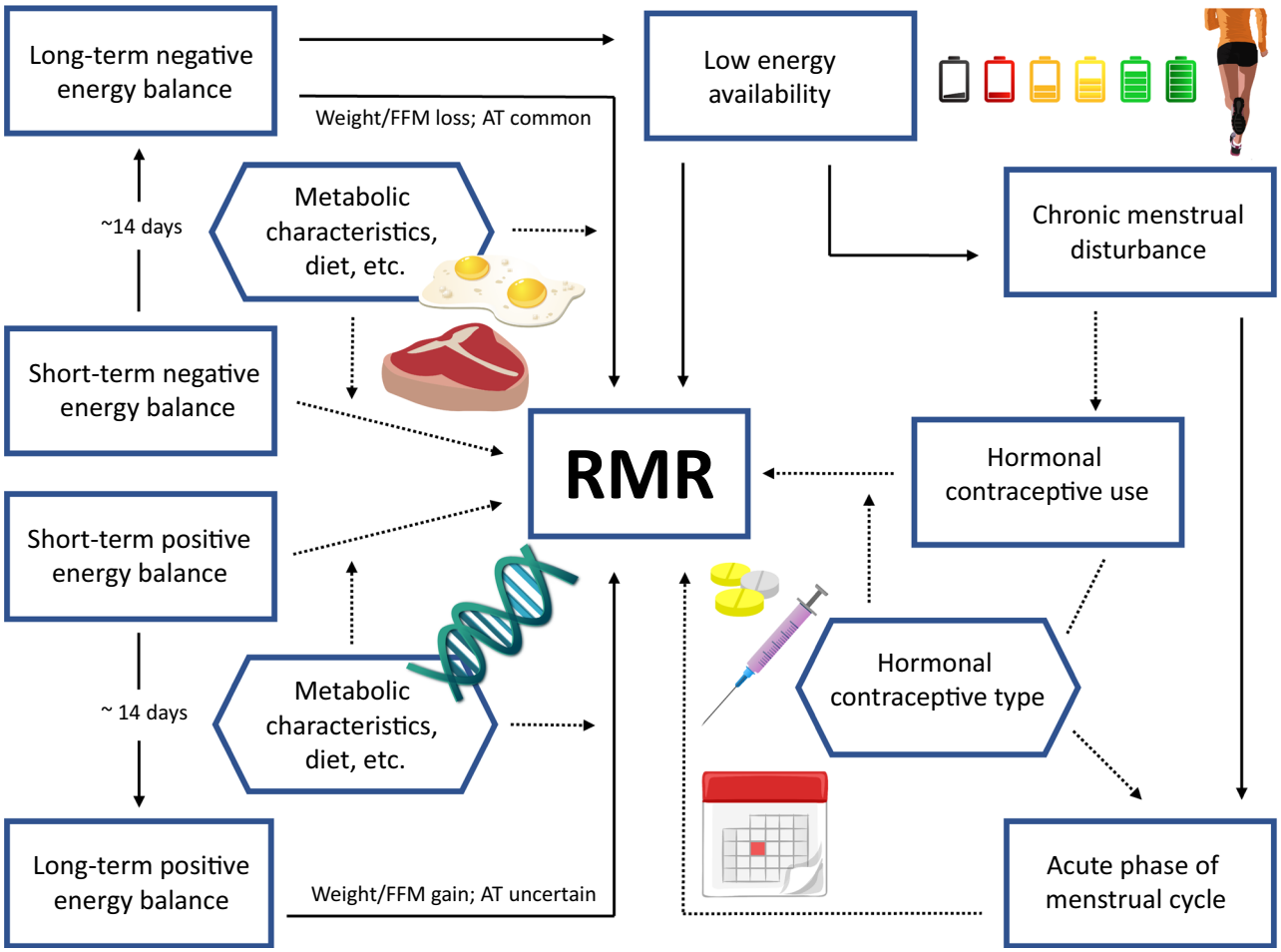

Fig. 1 Potential relationships between varying states of energy balance, availability, menstrual status, and resting metabolic rate. Filled lines denote stronger or more certain relationships. Dashed lines denote weaker or less certain relationships and opportunities for further investigation. *AT* adaptive thermogenesis, *FFM* fat-free mass, *RMR* resting metabolic rate. Created using Microsoft PowerPoint (images from Pixabay)

low- or high-protein diet [67]. When comparing "thrifty" (metabolically efficient and thus predisposed to weight gain) and "spendthrift" (metabolically inefficient and thus weight gain resistant) phenotypes under 24-h neutral EB, fasting, and overfeeding conditions, Hollstein and colleagues [68] found that thrifty types had greater expenditure during neutral EB but demonstrated decreased SMR in response to fasting while spendthrifts demonstrated an increase. These results echoed seminal findings by Weyer et al. [69] comparing responses to fasting among Caucasians and Pima Native Americans. Meanwhile, thrifty types demonstrated smaller increases in adjusted 24-h expenditure in response to overfeeding than spendthrifts, but only in the context of a relatively low- (3%) or high- (30%) protein diet [70].

As these and similarly illuminating investigations [48, 71, 72] did not measure RMR per se, follow-up studies are required to further examine the role of RMR as opposed to non-resting components of energy expenditure as well as the potential influence of macronutrient composition on the individual variability of RMR response to short-term perturbations in EB. These interindividual differences, if present, are likely diminished in the context of mean changes within a metabolically diverse population, further highlighting the need for investigations specifically designed to assess the factors influencing individual responses. While research continues to develop in this area, there is evidence that genetic, congenital, and environmental factors may influence how each individual metabolically responds to changes in EB [67–70, 73]. Though still in its nascency, the application of precision medicine guided by such research may allow practitioners to determine weight loss or weight gain interventions uniquely suited to an individual and their metabolic profile.

2.3 The Effect of Long-Term Changes in Energy Balance on Resting Metabolic Rate

2.3.1 Responses to Long-Term Energy Surplus

In the early twentieth century, individual researchers reported a mysterious mechanism for the dissipation of extra heat during periods of overfeeding that resulted in no observed net change in body mass. This increased thermogenesis in response to increased energy intake was termed "luxuskonsumption" [49] and subsequently refuted by others over the coming decades [43, 53]. More recent reviews have concluded that studies expressing change in RMR in relation to changes in body mass or FFM have generally found no adaptive increases beyond those explained by changes in the non-resting components of total energy expenditure [28, 49], as has been observed in both lean and obese subjects maintaining a body weight 10% higher than baseline values [46] (Table 2).

Metabolic responses to periods of overfeeding longer than 2 weeks in duration appear to vary greatly between individuals [47, 51, 72], perhaps as a result of the variability of changes in body mass [49, 50, 74, 75]. Still, some questions remain as to whether an adaptive component to these changes exists, especially in the context of certain phenotypes or diets. For instance, eight females with constitutional thinness (a form of low body weight in the absence of related physiological or psychiatric pathologies) experienced small but statistically significant increases in both relative (2 kcal/kg FFM/day, or 5.6%) and absolute (49 kcal/day, or 4.3%) RMR measures during a month-long 630-kcal fat overfeeding intervention without a concomitant increase in body mass [76]. However, no such changes were observed in eight normal-weight controls.

Metabolic responses to energy surplus may also depend on the macronutrient composition of the diet (Fig. 1). Investigators comparing three isoenergetic overfeeding diets at a 40% surplus for 8 weeks in non-obese subjects demonstrated that those fed a normal (15%) and high (25%) proportion of energy as protein displayed adaptive increases in RMR while those fed a low (5%)-protein diet did not [77]. More recently, Rodriguez and colleagues [78] observed both absolute and FFM-adjusted increases in RMR among 20 resistance-trained men completing a supervised resistance training program in conjunction with an estimated 11% energy surplus and daily total intake comprising 18% protein. However, whether there may remain some residual effect of high food intake—specifically of protein—on conventionally fasted RMR in the context of overfeeding is a question in need of further investigation, especially as FFM-related differences in protein turnover rates may partially explain variable responses to overfeeding [79].

2.3.2 Responses to Long-Term Energy Deficit

In the context of long-term energy restriction, AT may lead to a decrease of approximately 5–10% from initial RMR values [80] and can contribute to approximately 40–50% or more of the reductions in RMR that are observed in response to weight loss [30–32, 81–83], though the magnitude of the estimate has been shown to vary depending on the methodology used to assess AT [27]. The severity of the reduction has been demonstrated to operate as a function of the magnitude of weight loss in some studies [32, 33, 60]; others cite a relatively weak relationship [28] or propose the existence of a threshold effect, wherein the relationship between body composition and RMR changes with degree of weight loss [84]. Furthermore, whether metabolic adaptations persist once individuals achieve stabilization (and thus, theoretically, neutral EB) at their new set point remains controversial, with some studies in overweight and obese adults demonstrating persistent effects at 32 weeks [37], 44 weeks [33], over 1 year [34], and up to 6 years post-weight loss [85], while others show attenuation of effects at just 10 days [86], 4 weeks [60], 2 months [87], or 1–2 years of follow-up [81]. However, it has been argued that this and other studies demonstrating prolonged metabolic suppression in weight-reduced subjects may not have truly achieved neutral EB in the period immediately preceding RMR measurement [81]. A recent systematic review of studies examining AT in the context of weight loss interventions conducted largely in participants with overweight and obesity [26] reported that a statistically significant degree of adaptation ranging in magnitude from 18 to as high as 504 kcal/day was observed in 21 (88%) of the 24 studies using a diet-only or combined diet-and-exercise approach. Importantly, however, adaptation was generally attenuated in studies that assessed individuals after a period of weight stabilization.

The magnitude of adaptation also appears to vary widely between individuals [88], and differences such as sex, genetics, or baseline metabolic characteristics may play a role [25, 38]. For instance, in an illustrative study by Koehler and colleagues [89], four normal-weight women exposed to a 44% energy deficit using combined diet and exercise demonstrated a decrease in FFM-adjusted RMR, while the other four women did not; however, the latter group had lower baseline values for RMR, leptin, and total triiodothyronine (TT_3), indicating that these individuals may have already reached a metabolically suppressed state and that further time spent in an energy deficit had little effect.

Differences in body composition, and thus the hormonal activity of various tissue compartments, may also explain why some investigators have observed divergent metabolic responses between sexes during energy restriction. Doucet et al. [31] observed that AT persisted through a post-weight loss stabilization period in men while

women metabolically recovered to baseline values. Nymo and colleagues [60] reported the occurrence of AT over 13 weeks of energy restriction in men but not women. In both investigations, an energy deficit-induced change in leptin concentrations was theorized as a contributor, in line with Doucet's [90] previous findings. Namely, as fat mass decreases, so does leptin, and men may therefore begin to experience AT sooner given that they hold less of their total body mass as fat. A decrease in leptin concentrations as a result of fat loss has been called a "starvation signal" that induces energy conservation through multiple pathways, including a decrease in sympathetic nervous system activity [91] and an association between decreases in leptin and adaptive changes in RMR [92] and SMR [93] has been borne out in subsequent weight loss investigations. Future quantitative meta-syntheses may help further elucidate the role of sex in determining metabolic adaptation to weight loss.

Investigations in overweight, obese, or normal-weight, untrained individuals have generally demonstrated no adverse effects on RMR in response to a deficit primarily induced by aerobic [92, 94–99] or resistance training interventions [97], though genetics may modulate individual responses [98]. Compensatory increases in energy intake may partially explain null findings [94]; others, however, have reported opposing results wherein increased intake was associated with metabolic down-regulation [92] or in which spontaneously decreased intake during training did not elicit metabolic adaptation [97]. Conversely, decreases in both absolute and adjusted RMR have been observed in lean rowers and cyclists over 12–28 days of intensified training while energy intake remained constant [100–103]. Additionally, in 23 lean men and women training for a marathon over 40 weeks, a 4.6% decrease in SMR coincided with a 5.5% FFM increase [104]. However, 2 weeks of a 470-kcal daily exercise-induced deficit did not elicit changes in 12 male endurance athletes [105]. Thus, limited evidence suggests that the leanness of an individual may influence whether an exercise-induced energy deficit leads to a notable change in RMR over periods lasting 2 weeks or more. As with the theorized mechanism for between-sex differences, this may be in part due to the relatively small magnitude of weight and fat loss typically achieved by exercise-only interventions. Lean and athletic individuals may simply reach a certain threshold for metabolic adaptation in response to a smaller relative change in mass. Given their higher rates of exercise energy expenditure, investigations examining the relationship between exercise-induced deficits and RMR in active populations should also consider the concept of energy availability.

3 Energy Availability and Resting Metabolic Rate

Energy availability (EA) is the total amount of energy available for basic physiological functions after accounting for energy expended during exercise, with the difference between these values standardized to an individual's FFM [12, 20]. The currently accepted formula for determination of EA is $\frac{(\text{Total Energy Intake [TEI]})-(\text{Exercise Energy Expenditure [EEE]})}{\text{FFM (kg)}}$, expressed in units of kcal·kg^{-1} FFM [20]. Thus, EA is particularly informative for clinicians and researchers working with active and athletic populations, as these individuals expend more energy daily through formal exercise and tend to have more FFM than sedentary populations. Furthermore, energy intake levels that cannot sufficiently sustain one's current exercise energy expenditure in addition to other forms of daily physical activity and basic physiological function may, over time, contribute to negative health consequences outlined within the female athlete triad [7], male athlete triad [8], and RED-S [9] syndromes. While the former two frameworks outline a relationship between disordered eating and its resulting effects on bone and hormonal health, the latter aims to incorporate all individuals under a wider umbrella of potential gastrointestinal, immunological, psychological, and other health consequences, though future research is needed to clearly link these symptoms back to EA [106].

It should be noted that the evolving formulae used to calculate EA [12], in addition to the myriad of methodologies that may be used to calculate both intake and expenditure [6, 9, 20, 107–109], make it difficult to compare EA values across studies. However, the currently proposed zones for EA generally place 45 kcal·kg^{-1} FFM/day as "optimal" with values under 30 kcal·kg^{-1} FFM/day representing "low" EA [20, 110]. These values, however, stem from studies originally conducted in habitually sedentary, able-bodied female participants, and little existing work has assessed their validity in active or athletic individuals despite their frequent application to these groups. Commonly used EA ranges may also not apply equally across all active populations, such as male or wheelchair athletes [12, 20, 108, 111–113]. In addition, seminal studies typically demonstrated effects on hormonal activity after just a few days of participants' exposure to "low" EA. Thus, it is possible that chronic EA levels above the proposed 30 kcal·kg^{-1} FFM/day threshold may still disrupt metabolic and hormonal health if sustained over time [12]. Finally, methods of assessing EA based on dietary and expenditure data are variable, and EA has been shown to vary by as much as 8.5 kcal·kg^{-1} FFM/day among active females with menstrual disturbances depending on which of four methods was used to calculate exercise energy expenditure [107]. Meanwhile, a systematic review found that athletes underestimated energy intake by a mean of

19% compared with their expenditure measured by doubly labeled water [114].

3.1 RMR_{ratio} as an Indicator of Energy Availability

Given the concerns described above, it may be useful to employ other methods that do not require the calculation of these values to screen for potential signs of low EA in free-living individuals. One such possible indicator is RMR_{ratio}, calculated as the quotient of an individual's measured RMR versus that predicted using an equation based on contributing variables such as age, height, body mass, and FFM [5]. Numerous investigations (but not all [107, 115–118]) have observed relationships between RMR_{ratio} and associated markers of EA in active individuals, including 7-day EA [119]; within-day EB [120, 121]; menstrual/estrogen status [119, 120, 122–126]; volumetric bone characteristics [127] and formation markers [122]; alterations in TT_3 concentrations [122, 124, 125, 128, 129]; and in other hormones such as ghrelin, leptin, peptide YY, and insulin-like growth factor-1 [123, 125, 129, 130]. Research in active male populations, though once relatively sparse, is increasing [103, 105, 121, 127, 130–138].

Sustained RMR suppression may explain why individuals at risk for low EA are often observed at a body weight that is not significantly different from their energy-replete counterparts [119, 122, 139]. Over time, EB may readjust back to zero through the mechanism of AT, thus halting further weight loss. Furthermore, individuals with chronically low EA commonly present with symptoms indicating that energy reserves are insufficient for carrying out basic physiological functions such as reproduction [6, 9]. Thus, the low-EA individual has likely only reached neutral EB by way of ceasing physiological processes that otherwise contribute to a higher total energy expenditure [12, 20, 110].

Prediction equations used to compare measured with predicted RMR include those by Cunningham [140, 141] and Harris and Benedict [142] as well as more recent methods such as a dual-energy x-ray absorptiometry (DXA)-derived model using tissue-specific expenditure values [125] within an equation by Hayes [143]. While the reliability of RMR_{ratio} values in exercising, ovulating women has been demonstrated over a 12-month period regardless of which of four equations was used [144], different prediction equations have shown varying diagnostic performance, largely a result of the way they were developed. The Harris–Benedict equation—which was developed in the general population in 1919 [142] and does not incorporate a measure of lean tissue or FFM—was first used to compare predicted with measured RMR in patients with anorexia, finding measured values between 49 and 91% of those predicted [145]. Subsequent research in active females then utilized a cutoff of < 0.90 based on these findings [124].

It is important to note that the terminology used to specify the lean or fat-free component of body mass has evolved since the development of the $Cunningham_{1980}$ equation [140], which specified "lean body mass"—although this was predicted solely from body mass and age rather than measured—versus the 1991 equation [141], which incorporates a measure of FFM. Researchers and clinicians should be aware that, while current-day conceptualizations differentiate lean from FFM largely by the bone mineral component, earlier iterations may vary—for instance, by including essential fat as "lean body mass." In addition, the technology commonly used to assess these components has greatly evolved. Due to the evolution of both the terminology and technologies available for assessing body composition over time, investigators should take care to specify not only the equation(s) used when predicting RMR, but how each component of the equation was defined and the methods with which they were assessed.

Overall, equations incorporating some measure of lean or FFM or developed specifically using reference data from active populations may more accurately predict RMR in athletes (i.e., may provide an estimate closer to the measured value). As a result, a cutoff higher than 0.90 may be warranted when using such equations in order to better identify those with energy deficiency. For instance, in a cohort of 36 female rugby players, the proportion of participants exhibiting measured RMR within $\pm$ 10% of predicted values ranged from 44 to 86% across seven equations, emphasizing the influence of the prediction equation when using RMR_{ratio} to indicate risk of energy deficiency [146]. A comparison of three equations in a mixed-sex cohort of 40 ballet dancers found that the resulting prevalence of $RMR_{ratio} < 0.90$ ranged from 35 to 100% in females and 25% to 80% in males, with the $Cunningham_{1980}$ method (which incorporates a term for lean body mass) deemed the most sensitive (i.e., the most thorough in identifying "true positives," or individuals with other accepted markers of low EA) [131]. Notably, RMR_{ratio} was significantly higher in males using both the $Cunningham_{1980}$ [140] and Harris–Benedict [142] equations. This indicates a potential for sex-based differences in accuracy across equations, which would result in a variable utility of RMR_{ratio} in assessing risk of energy deficiency in males versus females or the need for sex-specific cutoff values unique to each equation. Strock and colleagues [124] also found the $Cunningham_{1980}$ formula to exhibit the highest sensitivity (0.90), but at the risk of low specificity (i.e., the ability to detect true negatives; 0.41) using serum TT_3 as the reference standard in exercising females. Meanwhile, other equations such as the $Cunningham_{1991}$ [141] and DXA-derived method [143] yielded estimates that were closer to the measured RMR values, and thus higher cutoffs were explored. Ultimately, cutoff values of 0.92 and 0.94, respectively, were needed to achieve a sensitivity of 0.80.

Furthermore, the DXA-derived equation demonstrated the strongest relationship with serum TT_3 ($r = 0.453$; $p < 0.001$).

3.2 Relationships Between Menstrual Status, Metabolic Suppression, and Energy Availability

In healthy menstruating individuals of reproductive age, menstruation occurs once about every 25–30 days [147], though the cycle duration appears to decrease slightly with age [148]. The cycle is characterized by a rise and fall of several hormones that control the development and release of an ovarian follicle and the growth of the uterine lining, which is then shed if fertilization does not occur. Generally, the first two weeks comprise the follicular phase during which the follicle is selected, matures, and a mature oocyte is ovulated. This stage is characterized by relatively low baseline concentrations of estrogen at the beginning with a classic estrogen priming peak in the late follicular phase essential for inducing a surge of luteinizing hormone. Luteinizing hormone—which is released in a pulsatile manner from anterior pituitary in response to the pulsatile release of gonadotropin-releasing hormone by the hypothalamus—in turn induces ovulation, or release of the mature oocyte from the follicle. With the formation of a corpus luteum, the luteal phase begins. The luteal phase is characterized by a rise in progesterone, stimulated by luteinizing hormone, and continued synthesesis of estrogen. The eventual decline in estrogen and progesterone in the absence of fertilization triggers the sloughing of the uterine lining (menstruation), and the cycle begins anew [147].

Because this monthly cycle is an energy-dependent process that may be suppressed as a means of energy conservation, dysregulation of the menstrual cycle is a common sign of low EA or energy deficiency which is fundamentally caused by a dysregulation in hypothalamic function [12]. The relationship between EA, metabolic suppression, and menstrual status is further evidenced by disruptions to energy-regulating hormones such as leptin, ghrelin, and TT_3 commonly observed among active individuals with menstrual disturbances [123, 128, 149]. In the early 1990s, a series of investigations began to elucidate the time course of these deleterious adaptations, though focused mainly on non-athletic populations. A seminal study by Loucks and Callister [150] found that, in 46 healthy young women, short-term changes in thyroid hormones induced by periods of low EA were prevented with increases in energy intake regardless of exercise expenditure. A decade later, Loucks and Thuma [151] observed changes in luteinizing hormone pulse frequency and amplitude (indicators of hypothalamic function) after just 5 days at an EA of 20 kcal·kg^{-1} FFM/day in sedentary, regularly menstruating females.

Later work by De Souza and colleagues [129] demonstrated dose–response relationships between the severity of menstrual disturbances and FFM-adjusted RMR as well as hormonal markers including TT_3, ghrelin, and leptin. The severity of energy deficit was also related to the frequency of disturbances occurring over a 3-month weight loss intervention in sedentary, regularly ovulating women [152] and the occurrence of disturbances corresponded to EA within the same month [153]. Additionally, a 3-month reduction in EA from 38 to 28 kcal·kg^{-1} FFM/day was linked to menstrual disturbances such as luteal phase defects, anovulation, and oligomenorrhea in a similar population [154]. However, measured EA may not be sensitive enough to indicate subclinical menstrual disturbances cross-sectionally [155] or prospectively in three-month intervention studies [152–154], further suggesting the potential utility of more readily assessed EA surrogates such as RMR_{ratio}.

Interventions to increase EA have been shown to restore menstrual function in active women [107, 156–158], though a duration greater than 3–4 months may be necessary to achieve this goal [159, 160]. However, the effect of such interventions on RMR deserves further research. A year-long case report involving two active amenorrheic females demonstrated resumption of menses within 23–74 days following 400- and 500-kcal increases in daily intake, respectively, as well as recovery of RMR_{ratio} from 0.81 to 1.01 and from 0.87 to 0.94 [161]. A female wheelchair athlete also demonstrated recovery of RMR_{ratio} in the context of a year-long intervention comprising increases in both intake and expenditure and resulting in a 30% loss of fat mass. Though menses did not resume, this may have been due to the presence of multiple sclerosis, as this condition may independently contribute to amenorrhea [162]. Conversely, while an intervention of 360 additional kcal/day for 6 months restored EB and menstrual function in all eight participants with menstrual disturbances, no impact on RMR was observed [107]. However, this sample had a mean RMR_{ratio} of 1.04 at baseline and reported spending more time exercising per week than nine active eumenorrheic controls—a particularly important point since exercise was not restricted the day before RMR measurement. Findings from a similar study [157] demonstrating no change in RMR are also limited by the normal values that participants displayed at baseline.

4 Implications for Resting Metabolic Rate Assessment: Consideration of Best Practices and Suggestions for Future Research

4.1 RMR Assessment in the Context of Energy Balance

While still a matter of debate, the observed adaptive changes in RMR in response to an energy deficit are generally greater when assessed immediately following an intervention [26, 163]. If investigators wish to reduce the potential impact of

AT on observed RMR values, a post-intervention weight stabilization period of at least 2 weeks may be useful (Table 2). Similarly, while more cost and time intensive, the use of a weight stabilization period immediately preceding an intervention (such as frequent surveillance of body weight and manipulations of energy intake or expenditure if changes exceed an acceptable threshold) will both improve the accuracy of estimated energy needs as well as reduce the potential impact of conscious or subconscious changes to habitual energy intake or expenditure among participants.

Researchers should take care to control for the potential impact of TEF on observed RMR values by measuring after an appropriate period of fasting. The most recent evidence analysis from the Academy of Nutrition and Dietetics on this topic [1] noted that TEF generally remained elevated for up to 5 h after eating across most studies, often without a return to baseline levels, and with only one investigation examining the effects up to 7 h (Table 1). Accordingly, a fasting period of ≥ 7 h prior to RMR assessment was recommended. However, given the lacuna in this research area, it cannot be ruled out that a large influx of food prolonged over the course of several meals or days may elevate thermogenesis beyond this timeframe, especially in light of findings that leaner individuals may demonstrate higher TEF during overfeeding [164]. As such, a longer fasting period of ~ 8–12 h may be warranted, with 12 h representing an appropriate target for research settings. The potential effect of TEF also limits our ability to draw conclusions from both short- [69–71, 164, 165] and long-term [47, 72] overfeeding studies assessing only SMR [166] or 24-h expenditure. Future research examining the time course of fasted RMR in the 8–24 or more hours following short-term overfeeding may shed additional light on this methodological concern (Table 2).

Nunes and colleagues [26] found that investigations of AT in response to weight loss that were of higher methodological quality were less likely to report large or statistically significant results. This finding should be considered in light of the fact that the methodological approaches used to assess AT, such as the determination of the size and composition of bodily tissues and the statistical approach used to normalize for such tissues or estimate predicted RMR, vary widely across studies, which may influence resulting estimates of effect [25, 27, 28, 167]. Adjustments to RMR made with a two-compartment model (that is, adjusting for all FFM as a single unit) may affect the observed magnitude of adaptation compared to models accounting for the anatomical or molecular components of FFM, as each FFM component contributes a different proportion of total RMR. For instance, adjusting for the decrease in RMR based on the change in the mass of the kidneys, heart, and skeletal muscle led to a smaller observed magnitude of adaptation in 32 healthy men during a 21-day energy deficit compared with the two-compartment model of adjustment [168]. However, these assessments were completed using whole-body magnetic resonance imaging, which is likely not feasible in most settings. A recent analysis used a similar approach to effectively question the role of skeletal muscle loss in RMR changes during weight loss [83]. These findings indicate a continued need for rigorous investigations of AT as well as consensus around the ways it should be both defined and assessed.

Future investigations should continue to examine the effect of individual traits such as metabolic phenotype and macronutrient composition on resulting adaptations to both short- and long-term changes in EB. The potentially RMR-sparing effects of exercise-based deficits in overweight, obese, and untrained populations should be considered, though these may not carry over to lean, trained populations. Finally, the utility of intermittent periods of increased EB as a means of attenuating decreases in RMR during a longer-term weight loss intervention deserves further research in both overweight and obese [169–171] and trained populations [172–174].

4.2 Energy Availability, the Menstrual Cycle, and Considerations for RMR Assessment in Athletic Populations

Researchers and practitioners working with active and athletic populations should be aware that measured RMR values that are lower than predicted could indicate the existence of energy deficiency-related health conditions. For researchers in particular, screening participants for related markers of energy deficiency (such as leptin, TT_3, or reproductive markers) may be warranted depending on the aims of the investigation. Additionally, previous research has suggested that the residual effects of exercise may affect RMR for up to 45 h in trained compared to untrained individuals [175]. Thus, attempts to schedule the timing of RMR assessment around athletes' schedules and as consistently far from the test as possible (e.g., the morning after a regular rest day) are worthwhile (Table 2). Notably, at least four investigations showing lack of an association between RMR_{ratio} and measured EA [115, 117, 176] or menstrual status [107] in active populations measured RMR at a minimum of approximately 11–17 h post-exercise.

Similar to the EB literature, research on the influence of EA on RMR has utilized a variety of prediction models. These models range from simple body mass-based equations to those incorporating FFM or its tissue-specific components. While studies utilizing DXA-derived tissue mass values have indicated the presence of AT in active females with menstrual dysfunction [125], future research using magnetic resonance imaging to incorporate organ size will further contribute to our understanding of the true magnitude of metabolic suppression

resulting from low EA. The modality used to assess body composition when determining predicted RMR, as well as whether FFM or lean soft tissue are used in various equations, may also affect resulting RMR_{ratio} estimates [124, 177] and should be further investigated. Longitudinal studies assessing the impact of increased EB over time in metabolically suppressed individuals may help elucidate the time course of RMR recovery in relation to other physiological signs such as restoration of menses and hormone concentrations. Research on the effect of within-day changes in EA/EB [120, 121, 135, 176, 178] and resulting metabolic disturbances should also be further pursued.

The current literature suggests a small but uncertain effect for increased RMR during the luteal phase of the menstrual cycle [179]. Notably, research has indicated both higher energy intake and expenditure [180, 181] during this phase; further, such "high-flux" states have been associated with increased RMR [52, 175, 182–184]. A shared mediating role of beta-adrenergic support may help explain these links [185]. Future investigations should specifically examine cyclic changes in RMR among individuals with menstrual disturbances such as luteal phase defect, especially given their prevalence in active populations [186], and utilize proposed multi-step methods to confirm menstrual cycle phase when feasible [187].

Hormonal contraceptives may mask a lack of naturally occurring menstruation [9], one of the most visible signs of energy deficiency in menstruating individuals. A recent survey of 1020 collegiate female athletes [188] found that over half (59%) of respondents reported either a current or past occurrence of menstrual irregularity. Those athletes who had a history of menstrual irregularity—and thus those who were more at risk for issues related to chronic energy deficiency—were 28% more likely to report current use of hormonal contraception and five times more likely to report that the primary reason for using hormonal contraception was to promote menstrual regularity. Meanwhile, the effect of various contraceptive modalities on RMR is unclear [189], the effect of less systemically active modalities such as intrauterine devices is understudied, and much of the research examining the relationships between EA, menstrual status, and RMR excludes individuals using hormonal contraception. Thus, an examination of the utility of RMR_{ratio} in addition to associated markers of energy deficiency in individuals using different hormonal contraceptive modalities may allow practitioners to provide proper intervention sooner to those who may greatly benefit from it.

5 Conclusion

In response to a change in EB, changes in RMR that are greater than would be expected based on body mass or composition alone have been observed in both lean and overweight or obese individuals, although length of intervention, interindividual differences, and dietary composition may affect observed responses. Hypotheses regarding the interindividual variability commonly observed in metabolic responses to both energy deficit and surplus deserve further investigation. Chronically low EA is common in athletic populations and is linked to observed RMR values below those predicted by commonly used equations. Thus, RMR_{ratio} may be a useful tool for identifying low EA and assessing the impact of therapeutic interventions. The literature related to EB, EA, and related physiological processes such as the menstrual cycle on RMR will benefit from improved methodological rigor, increased precision of measurement, and consensus surrounding the calculation of these complex variables.

Going forward, the assessment of RMR in both research and clinical settings will benefit from (1) utilizing a weight stabilization period (≥ 2 weeks if feasible) before assessing the effect of a longer-term change in energy balance on RMR, (2) measuring RMR as consistently far from a previous bout of moderate- to vigorous-intensity exercise or physical activity as circumstances will allow (preferably ≥ 24 h), and (3) assessing RMR under the condition of a minimum ≥ 7-h fast—preferably ~ 12 h if possible, and with due consideration of very recent changes in energy intake (e.g., short-term overfeeding or fasting). Given the current scarcity of direct evidence underpinning these recommendations, future research is needed to improve the specificity and strength of best practices.

Declarations

Authors' Contributions MRS: conceptualization, writing—original draft; MJD: writing—review and editing; KAS: writing—review and editing; YS: writing—review and editing; GMT: conceptualization, writing—review and editing. All authors read and approved the final version.

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References

1. Fullmer S, Benson-Davies S, Earthman CP, Frankenfield DC, Gradwell E, Lee PS, et al. Evidence analysis library review of best practices for performing indirect calorimetry

in healthy and non-critically ill individuals. J Acad Nutr Diet. 2015;115(9):1417–46.
2. Institute of Medicine. Dietary reference intakes for energy, carbohydrate, fiber, fat, fatty acids, cholesterol, protein, and amino acids (macronutrients). Washington: The National Academies Press; 2005.
3. Mtaweh H, Tuira L, Floh AA, Parshuram CS. Indirect calorimetry: history, technology, and application. Front Pediatr. 2018;6:257.
4. Trexler ET, Smith-Ryan AE, Norton LE. Metabolic adaptation to weight loss: implications for the athlete. J Int Soc Sports Nutr. 2014;11(1):7.
5. Schofield KL, Thorpe H, Sims ST. Resting metabolic rate prediction equations and the validity to assess energy deficiency in the athlete population. Exp Physiol. 2019;104(4):469–75.
6. Logue DM, Madigan SM, Melin A, Delahunt E, Heinen M, Donnell SM, et al. Low energy availability in athletes 2020: an updated narrative review of prevalence, risk, within-day energy balance, knowledge, and impact on sports performance. Nutrients. 2020;12:3.
7. Nattiv A, Loucks AB, Manore MM, Sanborn CF, Sundgot-Borgen J, Warren MP, et al. American College of Sports Medicine position stand. The female athlete triad. Med Sci Sports Exerc. 2007;39(10):1867–82.
8. Wiebe DJ, Storey EP, Orchinik JE, Grady MF, Leddy JJ, Willer BS, et al. The male athlete triad—a consensus statement from the Female and Male Athlete Triad Coalition Part 1: definition and scientific basis. Clin J Sport Med. 2021;31(4):345–53.
9. Mountjoy M, Sundgot-Borgen JK, Burke LM, Ackerman KE, Blauwet C, Constantini N, et al. IOC consensus statement on relative energy deficiency in sport (RED-S): 2018 update. Br J Sports Med. 2018;52(11):687–97.
10. Ravussin E, Lillioja S, Anderson TE, Christin L, Bogardus C. Determinants of 24-hour energy expenditure in man. Methods and results using a respiratory chamber. J Clin Invest. 1986;78(6):1568–78.
11. Muller MJ, Wang Z, Heymsfield SB, Schautz B, Bosy-Westphal A. Advances in the understanding of specific metabolic rates of major organs and tissues in humans. Curr Opin Clin Nutr Metab Care. 2013;16(5):501–8.
12. Areta JL, Taylor HL, Koehler K. Low energy availability: history, definition and evidence of its endocrine, metabolic and physiological effects in prospective studies in females and males. Eur J Appl Physiol. 2021;121(1):1–21.
13. Academy of Nutrition and Dietetics Evidence Analysis Library. Recommendation Ratings. [cited 2022 February 5]; Available from: https://www.andeal.org/recommendation-ratings
14. Academy of Nutrition and Dietetics Evidence Analysis Library. EE: Measuring Resting Metabolic Rate (RMR) in the Health and Non-Critically Ill Guideline. 2014 [cited 2022 February 5]; Available from: https://www.andeal.org/topic.cfm?menu=5299&cat=5217
15. Williamson DL, Kirwan JP. A single bout of concentric resistance exercise increases basal metabolic rate 48 hours after exercise in healthy 59–77-year-old men. J Gerontol A Biol Sci Med Sci. 1997;52(6):M352–5.
16. Hunter GR, Byrne NM, Gower BA, Sirikul B, Hills AP. Increased resting energy expenditure after 40 minutes of aerobic but not resistance exercise. Obesity (Silver Spring). 2006;14(11):2018–25.
17. Jamurtas AZ, Koutedakis Y, Paschalis V, Tofas T, Yfanti C, Tsiokanos A, et al. The effects of a single bout of exercise on resting energy expenditure and respiratory exchange ratio. Eur J Appl Physiol. 2004;92(4–5):393–8.
18. Academy of Nutrition and Dietetics Evidence Analysis Library. Grade Definitions and Chart. [cited 2022 February 5]; Available from: https://www.andeal.org/content.cfm?content_id=11%26auth=1
19. Compher C, Frankenfield D, Keim N, Roth-Yousey L. Best practice methods to apply to measurement of resting metabolic rate in adults: a systematic review. J Am Diet Assoc. 2006;106(6):881–903.
20. Burke LM, Lundy B, Fahrenholtz IL, Melin AK. Pitfalls of conducting and interpreting estimates of energy availability in free-living athletes. Int J Sport Nutr Exerc Metab. 2018;28(4):350–63.
21. Jafari A, Qanie D, Andersen TL, Zhang Y, Chen L, Postert B, et al. Legumain regulates differentiation fate of human bone marrow stromal cells and is altered in postmenopausal osteoporosis. Stem Cell Rep. 2017;8(2):373–86.
22. Maclean PS, Bergouignan A, Cornier MA, Jackman MR. Biology's response to dieting: the impetus for weight regain. Am J Physiol Regul Integr Comp Physiol. 2011;301(3):R581-600.
23. Casanova N, Beaulieu K, Finlayson G, Hopkins M. Metabolic adaptations during negative energy balance and their potential impact on appetite and food intake. Proc Nutr Soc. 2019;78(3):279–89.
24. Piaggi P, Vinales KL, Basolo A, Santini F, Krakoff J. Energy expenditure in the etiology of human obesity: spendthrift and thrifty metabolic phenotypes and energy-sensing mechanisms. J Endocrinol Invest. 2018;41(1):83–9.
25. Muller MJ, Bosy-Westphal A. Adaptive thermogenesis with weight loss in humans. Obesity (Silver Spring). 2013;21(2):218–28.
26. Nunes CL, Casanova N, Francisco R, Bosy-Westphal A, Hopkins M, Sardinha LB, et al. Does adaptive thermogenesis occur after weight loss in adults? A systematic review. Br J Nutr. 2021;25:1–19.
27. Nunes CL, Jesus F, Francisco R, Matias CN, Heo M, Heymsfield SB, et al. Adaptive thermogenesis after moderate weight loss: magnitude and methodological issues. Eur J Nutr. 2021;27:2.
28. Muller MJ, Enderle J, Bosy-Westphal A. Changes in energy expenditure with weight gain and weight loss in humans. Curr Obes Rep. 2016;5(4):413–23.
29. Egan AM, Collins AL. Dynamic changes in energy expenditure in response to underfeeding: a review. Proc Nutr Soc. 2022;81(2):199–212.
30. Muller MJ, Enderle J, Pourhassan M, Braun W, Eggeling B, Lagerpusch M, et al. Metabolic adaptation to caloric restriction and subsequent refeeding: the Minnesota Starvation Experiment revisited. Am J Clin Nutr. 2015;102(4):807–19.
31. Doucet E, St-Pierre S, Almeras N, Despres JP, Bouchard C, Tremblay A. Evidence for the existence of adaptive thermogenesis during weight loss. Br J Nutr. 2001;85(6):715–23.
32. Johannsen DL, Knuth ND, Huizenga R, Rood JC, Ravussin E, Hall KD. Metabolic slowing with massive weight loss despite preservation of fat-free mass. J Clin Endocrinol Metab. 2012;97(7):2489–96.
33. Camps SG, Verhoef SP, Westerterp KR. Weight loss, weight maintenance, and adaptive thermogenesis. Am J Clin Nutr. 2013;97(5):990–4.
34. Rosenbaum M, Hirsch J, Gallagher DA, Leibel RL. Long-term persistence of adaptive thermogenesis in subjects who have maintained a reduced body weight. Am J Clin Nutr. 2008;88(4):906–12.
35. Jimenez Jaime T, Leiva Balich L, Barrera Acevedo G, de la Maza Cave MP, Hirsch Birn S, Henriquez Parada S, et al. Effect of calorie restriction on energy expenditure in overweight and obese adult women. Nutr Hosp. 2015;31(6):2428–36.
36. Martins C, Roekenes J, Hunter GR, Gower BA. Association between ketosis and metabolic adaptation at the level of resting metabolic rate. Clin Nutr. 2021;40(8):4824–9.

37. Nunes CL, Jesus F, Francisco R, Hopkins M, Sardinha LB, Martins P, et al. Effects of a 4-month active weight loss phase followed by weight loss maintenance on adaptive thermogenesis in resting energy expenditure in former elite athletes. Eur J Nutr. 2022;14:2.
38. Martins C, Gower B, Hunter GR. Metabolic adaptation after combined resistance and aerobic exercise training in older women. Obesity (Silver Spring). 2022;30(7):1453–61.
39. Hames KC, Coen PM, King WC, Anthony SJ, Stefanovic-Racic M, Toledo FG, et al. Resting and exercise energy metabolism in weight-reduced adults with severe obesity. Obesity (Silver Spring). 2016;24(6):1290–8.
40. Gomez-Arbelaez D, Crujeiras AB, Castro AI, Martinez-Olmos MA, Canton A, Ordoñez-Mayan L, et al. Resting metabolic rate of obese patients under very low calorie ketogenic diet. Nutr Metab. 2018;15:1.
41. Weinsier RL, Hunter GR, Zuckerman PA, Redden DT, Darnell BE, Larson DE, et al. Energy expenditure and free-living physical activity in black and white women: comparison before and after weight loss. Am J Clin Nutr. 2000;71(5):1138–46.
42. Hintze LJ, Goldfield G, Seguin R, Damphousse A, Riopel A, Doucet E. The rate of weight loss does not affect resting energy expenditure and appetite sensations differently in women living with overweight and obesity. Physiol Behav. 2019;1(199):314–21.
43. Wiley FH, Newburgh LH. The doubtful nature of "Luxuskonsumption." J Clin Invest. 1931;10(4):733–44.
44. Joosen AM, Westerterp KR. Energy expenditure during overfeeding. Nutr Metab (Lond). 2006;12(3):25.
45. Kuchnia A, Huizenga R, Frankenfield D, Matthie JR, Earthman CP. Overstated metabolic adaptation after "the biggest loser" intervention. Obesity (Silver Spring). 2016;24(10):2025.
46. Leibel RL, Rosenbaum M, Hirsch J. Changes in energy expenditure resulting from altered body weight. N Engl J Med. 1995;332(10):621–8.
47. Bray GA, Redman LM, de Jonge L, Covington J, Rood J, Brock C, et al. Effect of protein overfeeding on energy expenditure measured in a metabolic chamber. Am J Clin Nutr. 2015;101(3):496–505.
48. Reinhardt M, Thearle MS, Ibrahim M, Hohenadel MG, Bogardus C, Krakoff J, et al. A human thrifty phenotype associated with less weight loss during caloric restriction. Diabetes. 2015;64(8):2859–67.
49. Bray GA, Bouchard C. The biology of human overfeeding: a systematic review. Obes Rev. 2020;21(9): e13040.
50. Lammert O, Grunnet N, Faber P, Bjornsbo KS, Dich J, Larsen LO, et al. Effects of isoenergetic overfeeding of either carbohydrate or fat in young men. Br J Nutr. 2000;84(2):233–45.
51. Joosen AM, Bakker AH, Westerterp KR. Metabolic efficiency and energy expenditure during short-term overfeeding. Physiol Behav. 2005;85(5):593–7.
52. Goran MI, Calles-Escandon J, Poehlman ET, O'Connell M, Danforth E. Effects of increased energy intake and/or physical activity on energy expenditure in young healthy men. J Appl Physiol. 1994;77(1):366–72.
53. Ravussin E, Schutz Y, Acheson KJ, Dusmet M, Bourquin L, Jequier E. Short-term, mixed-diet overfeeding in man: no evidence for "luxuskonsumption." Am J Physiol. 1985;249(5 Pt 1):E470–7.
54. Jebb SA, Prentice AM, Goldberg GR, Murgatroyd PR, Black AE, Coward WA. Changes in macronutrient balance during over- and underfeeding assessed by 12-d continuous whole-body calorimetry. Am J Clin Nutr. 1996;64(3):259–66.
55. Apfelbaum M, Bostsarron J, Lacatis D. Effect of caloric restriction and excessive caloric intake on energy expenditure. Am J Clin Nutr. 1971;24(12):1405–9.
56. Dauncey MJ. Metabolic effects of altering the 24 h energy intake in man, using direct and indirect calorimetry. Br J Nutr. 1980;43(2):257–69.
57. Harris AM, Jensen MD, Levine JA. Weekly changes in basal metabolic rate with eight weeks of overfeeding. Obesity (Silver Spring). 2006;14(4):690–5.
58. Triffoni-Melo AT, Suen VMM, Resende CMM, Braga CBM, Diez-Garcia RW. Resting energy expenditure adaptation after short-term caloric restriction in morbidly obese women. Rev Nutr. 2015;28(5):505–11.
59. Siervo M, Faber P, Lara J, Gibney ER, Milne E, Ritz P, et al. Imposed rate and extent of weight loss in obese men and adaptive changes in resting and total energy expenditure. Metabolism. 2015;64(8):896–904.
60. Nymo S, Coutinho SR, Torgersen LH, Bomo OJ, Haugvaldstad I, Truby H, et al. Timeline of changes in adaptive physiological responses, at the level of energy expenditure, with progressive weight loss. Br J Nutr. 2018;120(2):141–9.
61. Doucet E, Pomerleau M, Harper ME. Fasting and postprandial total ghrelin remain unchanged after short-term energy restriction. J Clin Endocrinol Metab. 2004;89(4):1727–32.
62. Stubbs RJ, Hughes DA, Johnstone AM, Whybrow S, Horgan GW, King N, et al. Rate and extent of compensatory changes in energy intake and expenditure in response to altered exercise and diet composition in humans. Am J Physiol Regul Integr Comp Physiol. 2004;286(2):R350–8.
63. Zauner C, Schneeweiss B, Kranz A, Madl C, Ratheiser K, Kramer L, et al. Resting energy expenditure in short-term starvation is increased as a result of an increase in serum norepinephrine. Am J Clin Nutr. 2000;71(6):1511–5.
64. Tinsley GM, Givan AH, Graybeal AJ, Villarreal MI, Cross AG. β-Hydroxy β-methylbutyrate free acid alters cortisol responses, but not myofibrillar proteolysis, during a 24-h fast. Br J Nutr. 2018;119(5):517–26.
65. Mansell PI, Fellows IW, Macdonald IA. Enhanced thermogenic response to epinephrine after 48-h starvation in humans. Am J Physiol. 1990;258(1 Pt 2):R87-93.
66. Stratton MT, Albracht-Schulte K, Harty PS, Siedler MR, Rodriguez C, Tinsley GM. Physiological responses to acute fasting: Implications for intermittent fasting programs. Nutr Rev. 2021;2:94.
67. Dulloo AG, Jacquet J. Low-protein overfeeding: a tool to unmask susceptibility to obesity in humans. Int J Obes Relat Metab Disord. 1999;23(11):1118–21.
68. Hollstein T, Basolo A, Ando T, Votruba SB, Walter M, Krakoff J, et al. Recharacterizing the metabolic state of energy balance in thrifty and spendthrift phenotypes. J Clin Endocrinol Metab. 2020;105:5.
69. Weyer C, Vozarova B, Ravussin E, Tataranni PA. Changes in energy metabolism in response to 48 h of overfeeding and fasting in Caucasians and Pima Indians. Int J Obes Relat Metab Disord. 2001;25(5):593–600.
70. Hollstein T, Basolo A, Ando T, Krakoff J, Piaggi P. Reduced adaptive thermogenesis during acute protein-imbalanced overfeeding is a metabolic hallmark of the human thrifty phenotype. Am J Clin Nutr. 2021;114(4):1396–407.
71. Schlogl M, Piaggi P, Pannacciuli N, Bonfiglio SM, Krakoff J, Thearle MS. Energy expenditure responses to fasting and overfeeding identify phenotypes associated with weight change. Diabetes. 2015;64(11):3680–9.
72. Johannsen DL, Marlatt KL, Conley KE, Smith SR, Ravussin E. Metabolic adaptation is not observed after 8 weeks of overfeeding but energy expenditure variability is associated with weight recovery. Am J Clin Nutr. 2019;110(4):805–13.
73. Jorgensen SW, Brons C, Bluck L, Hjort L, Faerch K, Thankamony A, et al. Metabolic response to 36 hours of fasting in young

men born small vs appropriate for gestational age. Diabetologia. 2015;58(1):178–87.
74. Norgan NG, Durnin JV. The effect of 6 weeks of overfeeding on the body weight, body composition, and energy metabolism of young men. Am J Clin Nutr. 1980;33(5):978–88.
75. Bouchard C, Tremblay A, Despres JP, Nadeau A, Lupien PJ, Theriault G, et al. The response to long-term overfeeding in identical twins. N Engl J Med. 1990;322(21):1477–82.
76. Germain N, Galusca B, Caron-Dorval D, Martin JF, Pujos-Guillot E, Boirie Y, et al. Specific appetite, energetic and metabolomics responses to fat overfeeding in resistant-to-bodyweight-gain constitutional thinness. Nutr Diabetes. 2014;14(4): e126.
77. Bray GA, Smith SR, de Jonge L, Xie H, Rood J, Martin CK, et al. Effect of dietary protein content on weight gain, energy expenditure, and body composition during overeating: a randomized controlled trial. JAMA. 2012;307(1):47–55.
78. Rodriguez C, Harty PS, Stratton MT, Siedler MR, Smith RW, Johnson BA, et al. Comparison of indirect calorimetry and common prediction equations for evaluating changes in resting metabolic rate induced by resistance training and a hypercaloric diet. J Strength Cond Res. 2022;36(11):3093–104.
79. Roberts SB, Fuss P, Dallal GE, Atkinson A, Evans WJ, Joseph L, et al. Effects of age on energy expenditure and substrate oxidation during experimental overfeeding in healthy men. J Gerontol A Biol Sci Med Sci. 1996;51(2):B148–57.
80. Westerterp KR. Metabolic adaptations to over- and underfeeding—still a matter of debate? Eur J Clin Nutr. 2013;67(5):443–5.
81. Martins C, Gower BA, Hill JO, Hunter GR. Metabolic adaptation is not a major barrier to weight-loss maintenance. Am J Clin Nutr. 2020;112(3):558–65.
82. Martins C, Roekenes J, Salamati S, Gower BA, Hunter GR. Metabolic adaptation is an illusion, only present when participants are in negative energy balance. Am J Clin Nutr. 2020;112(5):1212–8.
83. Martin A, Fox D, Murphy CA, Hofmann H, Koehler K. Tissue losses and metabolic adaptations both contribute to the reduction in resting metabolic rate following weight loss. Int J Obes (Lond). 2022;46(6):1168–75.
84. Rosenbaum M, Leibel RL. Models of energy homeostasis in response to maintenance of reduced body weight. Obesity (Silver Spring). 2016;24(8):1620–9.
85. Fothergill E, Guo J, Howard L, Kerns JC, Knuth ND, Brychta R, et al. Persistent metabolic adaptation 6 years after "The Biggest Loser" competition. Obesity (Silver Spring). 2016;24(8):1612–9.
86. Weinsier RL, Nagy TR, Hunter GR, Darnell BE, Hensrud DD, Weiss HL. Do adaptive changes in metabolic rate favor weight regain in weight-reduced individuals? An examination of the set-point theory. Am J Clin Nutr. 2000;72(5):1088–94.
87. Amatruda JM, Statt MC, Welle SL. Total and resting energy expenditure in obese women reduced to ideal body weight. J Clin Invest. 1993;92(3):1236–42.
88. Magkos F. On adaptive thermogenesis: just another weight-loss tale? Am J Clin Nutr. 2020;112(5):1157–9.
89. Koehler K, De Souza MJ, Williams NI. Less-than-expected weight loss in normal-weight women undergoing caloric restriction and exercise is accompanied by preservation of fat-free mass and metabolic adaptations. Eur J Clin Nutr. 2017;71(3):365–71.
90. Doucet E, St Pierre S, Almeras N, Mauriege P, Richard D, Tremblay A. Changes in energy expenditure and substrate oxidation resulting from weight loss in obese men and women: is there an important contribution of leptin? J Clin Endocrinol Metab. 2000;85(4):1550–6.
91. Pandit R, Beerens S, Adan RAH. Role of leptin in energy expenditure: the hypothalamic perspective. Am J Physiol Regul Integr Comp Physiol. 2017;312(6):R938–47.
92. Hopkins M, Gibbons C, Caudwell P, Hellstrom PM, Naslund E, King NA, et al. The adaptive metabolic response to exercise-induced weight loss influences both energy expenditure and energy intake. Eur J Clin Nutr. 2014;68(5):581–6.
93. Lecoultre V, Ravussin E, Redman LM. The fall in leptin concentration is a major determinant of the metabolic adaptation induced by caloric restriction independently of the changes in leptin circadian rhythms. J Clin Endocrinol Metab. 2011;96(9):E1512–6.
94. Martin CK, Johnson WD, Myers CA, Apolzan JW, Earnest CP, Thomas DM, et al. Effect of different doses of supervised exercise on food intake, metabolism, and non-exercise physical activity: the E-MECHANIC randomized controlled trial. Am J Clin Nutr. 2019;110(3):583–92.
95. Frey-Hewitt B, Vranizan KM, Dreon DM, Wood PD. The effect of weight loss by dieting or exercise on resting metabolic rate in overweight men. Int J Obes. 1990;14(4):327–34.
96. Tremblay A, Nadeau A, Despres JP, St-Jean L, Theriault G, Bouchard C. Long-term exercise training with constant energy intake. 2: Effect on glucose metabolism and resting energy expenditure. Int J Obes. 1990;14(1):75–84.
97. Broeder CE, Burrhus KA, Svanevik LS, Wilmore JH. The effects of either high-intensity resistance or endurance training on resting metabolic rate. Am J Clin Nutr. 1992;55(4):802–10.
98. Poehlman ET, Tremblay A, Nadeau A, Dussault J, Theriault G, Bouchard C. Heredity and changes in hormones and metabolic rates with short-term training. Am J Physiol. 1986;250(6 Pt 1):E711–7.
99. Bingham SA, Goldberg GR, Coward WA, Prentice AM, Cummings JH. The effect of exercise and improved physical fitness on basal metabolic rate. Br J Nutr. 1989;61(2):155–73.
100. Woods AL, Garvican-Lewis LA, Lundy B, Rice AJ, Thompson KG. New approaches to determine fatigue in elite athletes during intensified training: Resting metabolic rate and pacing profile. PLoS ONE. 2017;12(3): e0173807.
101. Woods AL, Garvican-Lewis LA, Rice A, Thompson KG. 12 days of altitude exposure at 1800 m does not increase resting metabolic rate in elite rowers. Appl Physiol Nutr Metab. 2017;42(6):672–6.
102. Woods AL, Rice AJ, Garvican-Lewis LA, Wallett AM, Lundy B, Rogers MA, et al. The effects of intensified training on resting metabolic rate (RMR), body composition and performance in trained cyclists. PLoS ONE. 2018;13(2): e0191644.
103. Stenqvist TB, Torstveit MK, Faber J, Melin AK. Impact of a 4-week intensified endurance training intervention on markers of relative energy deficiency in sport (RED-S) and performance among well-trained male cyclists. Front Endocrinol (Lausanne). 2020;11: 512365.
104. Westerterp KR, Meijer GA, Schoffelen P, Janssen EM. Body mass, body composition and sleeping metabolic rate before, during and after endurance training. Eur J Appl Physiol Occup Physiol. 1994;69(3):203–8.
105. Jurov I, Keay N, Spudic D, Rauter S. Inducing low energy availability in trained endurance male athletes results in poorer explosive power. Eur J Appl Physiol. 2022;122(2):503–13.
106. De Souza MJ, Strock NCA, Ricker EA, Koltun KJ, Barrack M, Joy E, et al. The path towards progress: a critical review to advance the science of the female and male athlete triad and relative energy deficiency in sport. Sports Med. 2022;52(1):13–23.
107. Guebels CP, Kam LC, Maddalozzo GF, Manore MM. Active women before/after an intervention designed to restore menstrual function: resting metabolic rate and comparison of four methods to quantify energy expenditure and energy availability. Int J Sport Nutr Exerc Metab. 2014;24(1):37–46.
108. Jurov I, Keay N, Hadžic V, Rauter S. A proposal for a standardized approach to inducing low energy availability in athletes. Appl Sci. 2021;11:6679.

109. Dasa MS, Friborg O, Kristoffersen M, Pettersen G, Sundgot-Borgen J, Rosenvinge JH. Accuracy of tracking devices' ability to assess exercise energy expenditure in professional female soccer players: implications for quantifying energy availability. Int J Environ Res Public Health. 2022;19:8.
110. Loucks AB, Kiens B, Wright HH. Energy availability in athletes. J Sports Sci. 2011;29(Suppl 1):S7-15.
111. De Souza MJ, Koltun KJ, Williams NI. The role of energy availability in reproductive function in the female athlete triad and extension of its effects to men: an initial working model of a similar syndrome in male athletes. Sports Med. 2019;49(S2):125–37.
112. Jonvik KL, Vardardottir B, Broad E. How do we assess energy availability and RED-S risk factors in para athletes? Nutrients. 2022;14:5.
113. Jurov I, Keay N, Rauter S. Reducing energy availability in male endurance athletes: a randomized trial with a three-step energy reduction. J Int Soc Sports Nutr. 2022;19(1):179–95.
114. Capling L, Beck KL, Gifford JA, Slater G, Flood VM, O'Connor H. Validity of dietary assessment in athletes: a systematic review. Nutrients. 2017;9:12.
115. Kinoshita N, Uchiyama E, Ishikawa-Takata K, Yamada Y, Okuyama K. Association of energy availability with resting metabolic rates in competitive female teenage runners: a cross-sectional study. J Int Soc Sports Nutr. 2021;18(1):70.
116. Costa PB, Richmond SR, Smith CR, Currier B, Stecker RA, Gieske BT, et al. Physiologic, metabolic, and nutritional attributes of collegiate synchronized swimmers. Int J Sports Physiol Perform. 2019;14(5):658–64.
117. Moss SL, Randell RK, Burgess D, Ridley S, Allison R, et al. Assessment of energy availability and associated risk factors in professional female soccer players. Eur J Sport Sci. 2021;21(6):861–70.
118. Zabriskie HA, Currier BS, Harty PS, Stecker RA, Jagim AR, Kerksick CM. Energy status and body composition across a collegiate women's lacrosse season. Nutrients. 2019;11:2.
119. Melin A, Tornberg AB, Skouby S, Moller SS, Sundgot-Borgen J, Faber J, et al. Energy availability and the female athlete triad in elite endurance athletes. Scand J Med Sci Sports. 2015;25(5):610–22.
120. Fahrenholtz IL, Sjodin A, Benardot D, Tornberg AB, Skouby S, Faber J, et al. Within-day energy deficiency and reproductive function in female endurance athletes. Scand J Med Sci Sports. 2018;28(3):1139–46.
121. Torstveit MK, Fahrenholtz I, Stenqvist TB, Sylta O, Melin A. Within-day energy deficiency and metabolic perturbation in male endurance athletes. Int J Sport Nutr Exerc Metab. 2018;28(4):419–27.
122. De Souza MJ, West SL, Jamal SA, Hawker GA, Gundberg CM, Williams NI. The presence of both an energy deficiency and estrogen deficiency exacerbate alterations of bone metabolism in exercising women. Bone. 2008;43(1):140–8.
123. Scheid JL, Williams NI, West SL, VanHeest JL, De Souza MJ. Elevated PYY is associated with energy deficiency and indices of subclinical disordered eating in exercising women with hypothalamic amenorrhea. Appetite. 2009;52(1):184–92.
124. Strock NCA, Koltun KJ, Southmayd EA, Williams NI, De Souza MJ. Indices of resting metabolic rate accurately reflect energy deficiency in exercising women. Int J Sport Nutr Exerc Metab. 2020;30(1):14–24.
125. Koehler K, Williams NI, Mallinson RJ, Southmayd EA, Allaway HC, De Souza MJ. Low resting metabolic rate in exercise-associated amenorrhea is not due to a reduced proportion of highly active metabolic tissue compartments. Am J Physiol Endocrinol Metab. 2016;311(2):E480–7.
126. Vanheest JL, Rodgers CD, Mahoney CE, De Souza MJ. Ovarian suppression impairs sport performance in junior elite female swimmers. Med Sci Sports Exerc. 2014;46(1):156–66.
127. Chen Z, Sherk VD, Sharma-Ghimire P, Bemben MG, Bemben DA. Site-specific bone differences and energy status in male competitive runners and road cyclists. J Clin Densitom. 2022;25(2):150–9.
128. Gibbs JC, Williams NI, Scheid JL, Toombs RJ, De Souza MJ. The association of a high drive for thinness with energy deficiency and severe menstrual disturbances: confirmation in a large population of exercising women. Int J Sport Nutr Exerc Metab. 2011;21(4):280–90.
129. De Souza MJ, Lee DK, Vanheest JL, Scheid JL, West SL, Williams NI. Severity of energy-related menstrual disturbances increases in proportion to indices of energy conservation in exercising women. Fertil Steril. 2007;88(4):971–5.
130. Lee S, Moto K, Han S, Oh T, Taguchi M. Within-day energy balance and metabolic suppression in male collegiate soccer players. Nutrients. 2021;13:8.
131. Staal S, Sjodin A, Fahrenholtz I, Bonnesen K, Melin AK. Low RMR_{ratio} as a surrogate marker for energy deficiency, the choice of predictive equation vital for correctly identifying male and female ballet dancers at risk. Int J Sport Nutr Exerc Metab. 2018;28(4):412–8.
132. Wilson G, Martin D, Morton JP, Close GL. Male flat jockeys do not display deteriorations in bone density or resting metabolic rate in accordance with race riding experience: implications for RED-S. Int J Sport Nutr Exerc Metab. 2018;28(4):434–9.
133. Taguchi M, Moto K, Lee S, Torii S, Hongu N. Energy intake deficiency promotes bone resorption and energy metabolism suppression in Japanese male endurance runners: a pilot study. Am J Mens Health. 2020;14(1):1557988320905251.
134. Jurov I, Keay N, Hadzic V, Spudic D, Rauter S. Relationship between energy availability, energy conservation and cognitive restraint with performance measures in male endurance athletes. J Int Soc Sports Nutr. 2021;18(1):24.
135. Langan-Evans C, Germaine M, Artukovic M, Oxborough DL, Areta JL, Close GL, et al. The psychological and physiological consequences of low energy availability in a male combat sport athlete. Med Sci Sports Exerc. 2021;53(4):673–83.
136. Moris JM, Olendorff SA, Zajac CM, Fernandez-Del-Valle M, Webb BL, Zuercher JL, et al. Collegiate male athletes exhibit conditions of the male athlete triad. Appl Physiol Nutr Metab. 2022;47(3):328–36.
137. Schofield KL, Thorpe H, Sims ST. Case study: energy availability and endocrine markers in elite male track cyclists. Int J Sports Physiol Perform. 2022;17(2):313–6.
138. Stenqvist TB, Melin AK, Garthe I, Slater G, Paulsen G, Iraki J, et al. Prevalence of Surrogate markers of relative energy deficiency in male Norwegian Olympic-level athletes. Int J Sport Nutr Exerc Metab. 2021;31(6):497–506.
139. Thompson J, Manore MM, Skinner JS. Resting metabolic rate and thermic effect of a meal in low- and adequate-energy intake male endurance athletes. Int J Sport Nutr. 1993;3(2):194–206.
140. Cunningham JJ. A reanalysis of the factors influencing basal metabolic rate in normal adults. Am J Clin Nutr. 1980;33(11):2372–4.
141. Cunningham JJ. Body composition as a determinant of energy expenditure: a synthetic review and a proposed general prediction equation. Am J Clin Nutr. 1991;54(6):963–9.
142. Harris JA, Benedict FG. A biometric study of human basal metabolism. Proc Natl Acad Sci U S A. 1918;4(12):370–3.
143. Hayes M, Chustek M, Wang Z, Gallagher D, Heshka S, Spungen A, et al. DXA: potential for creating a metabolic map of organ-tissue resting energy expenditure components. Obes Res. 2002;10(10):969–77.

144. Strock NCA, Koltun KJ, Mallinson RJ, Williams NI, De Souza MJ. Characterizing the resting metabolic rate ratio in ovulatory exercising women over 12 months. Scand J Med Sci Sports. 2020;30(8):1337–47.
145. Vaisman N, Rossi MF, Goldberg E, Dibden LJ, Wykes LJ, Pencharz PB. Energy expenditure and body composition in patients with anorexia nervosa. J Pediatr. 1988;113(5):919–24.
146. O'Neill J, Walsh CS, McNulty SJ, Gantly HC, Corish ME, Crognale D, et al. Resting metabolic rate in female rugby players: differences in measured versus predicted values. J Strength Cond Res. 2022;36(3):845–50.
147. Reed BG, Carr BR. The normal menstrual cycle and the control of ovulation. In: Feingold KR, Anawalt B, Boyce A, Chrousos G, de Herder WW, Dhatariya K, et al (eds) Endotext. South Dartmouth; 2000.
148. Bull JR, Rowland SP, Scherwitzl EB, Scherwitzl R, Danielsson KG, Harper J. Real-world menstrual cycle characteristics of more than 600,000 menstrual cycles. NPJ Digit Med. 2019;2:83.
149. De Souza MJ, Leidy HJ, O'Donnell E, Lasley B, Williams NI. Fasting ghrelin levels in physically active women: relationship with menstrual disturbances and metabolic hormones. J Clin Endocrinol Metab. 2004;89(7):3536–42.
150. Loucks AB, Callister R. Induction and prevention of low-T3 syndrome in exercising women. Am J Physiol. 1993;264(5 Pt 2):R924–30.
151. Loucks AB, Thuma JR. Luteinizing hormone pulsatility is disrupted at a threshold of energy availability in regularly menstruating women. J Clin Endocrinol Metab. 2003;88(1):297–311.
152. Williams NI, Leidy HJ, Hill BR, Lieberman JL, Legro RS, De Souza MJ. Magnitude of daily energy deficit predicts frequency but not severity of menstrual disturbances associated with exercise and caloric restriction. Am J Physiol Endocrinol Metab. 2015;308(1):E29-39.
153. Lieberman JL, Wagstaff DA, Williams NI. Menstrual disruption with exercise is not linked to an energy availability threshold. Med Sci Sports Exerc. 2018;50(3):551–61.
154. Koltun KJ, De Souza MJ, Scheid JL, Williams NI. Energy availability is associated with luteinizing hormone pulse frequency and induction of luteal phase defects. J Clin Endocrinol Metab. 2020;105:1.
155. Reed JL, De Souza MJ, Mallinson RJ, Scheid JL, Williams NI. Energy availability discriminates clinical menstrual status in exercising women. J Int Soc Sports Nutr. 2015;12:11.
156. De Souza MJ, Mallinson RJ, Strock NCA, Koltun KJ, Olmsted MP, Ricker EA, et al. Randomised controlled trial of the effects of increased energy intake on menstrual recovery in exercising women with menstrual disturbances: the "REFUEL" study. Hum Reprod. 2021;36(8):2285–97.
157. Cialdella-Kam L, Guebels CP, Maddalozzo GF, Manore MM. Dietary intervention restored menses in female athletes with exercise-associated menstrual dysfunction with limited impact on bone and muscle health. Nutrients. 2014;6(8):3018–39.
158. Kopp-Woodroffe SA, Manore MM, Dueck CA, Skinner JS, Matt KS. Energy and nutrient status of amenorrheic athletes participating in a diet and exercise training intervention program. Int J Sport Nutr. 1999;9(1):70–88.
159. Lagowska K, Kapczuk K, Friebe Z, Bajerska J. Effects of dietary intervention in young female athletes with menstrual disorders. J Int Soc Sports Nutr. 2014;11:21.
160. Dueck CA, Matt KS, Manore MM, Skinner JS. Treatment of athletic amenorrhea with a diet and training intervention program. Int J Sport Nutr. 1996;6(1):24–40.
161. Mallinson RJ, Williams NI, Olmsted MP, Scheid JL, Riddle ES, De Souza MJ. A case report of recovery of menstrual function following a nutritional intervention in two exercising women with amenorrhea of varying duration. J Int Soc Sports Nutr. 2013;10:34.
162. Flueck JL, Koehler K. Case study: improving energy status in a wheelchair athlete with suppressed resting energy expenditure. Int J Sports Physiol Perform. 2022;17(7):1151–4.
163. Fogarasi A, Gonzalez K, Dalamaga M, Magkos F. The impact of the rate of weight loss on body composition and metabolism. Curr Obes Rep. 2022;11(2):33–44.
164. Thearle MS, Pannacciulli N, Bonfiglio S, Pacak K, Krakoff J. Extent and determinants of thermogenic responses to 24 hours of fasting, energy balance, and five different overfeeding diets in humans. J Clin Endocrinol Metab. 2013;98(7):2791–9.
165. Schmidt SL, Kealey EH, Horton TJ, Von Kaenel S, Bessesen DH. The effects of short-term overfeeding on energy expenditure and nutrient oxidation in obesity-prone and obesity-resistant individuals. Int J Obes (Lond). 2013;37(9):1192–7.
166. Goldberg GR, Prentice AM, Davies HL, Murgatroyd PR. Overnight and basal metabolic rates in men and women. Eur J Clin Nutr. 1988;42(2):137–44.
167. Dahle JH, Ostendorf DM, Pan Z, MacLean PS, Bessesen DH, Heymsfield SB, et al. Weight and body composition changes affect resting energy expenditure predictive equations during a 12-month weight-loss intervention. Obesity (Silver Spring). 2021;29(10):1596–605.
168. Muller MJ, Heymsfield SB, Bosy-Westphal A. Are metabolic adaptations to weight changes an artefact? Am J Clin Nutr. 2021;114(4):1386–95.
169. Davoodi SH, Ajami M, Ayatollahi SA, Dowlatshahi K, Javedan G, Pazoki-Toroudi HR. Calorie shifting diet versus calorie restriction diet: a comparative clinical trial study. Int J Prev Med. 2014;5(4):447–56.
170. Byrne NM, Sainsbury A, King NA, Hills AP, Wood RE. Intermittent energy restriction improves weight loss efficiency in obese men: the MATADOR study. Int J Obes (Lond). 2018;42(2):129–38.
171. Arguin H, Dionne IJ, Senechal M, Bouchard DR, Carpentier AC, Ardilouze JL, et al. Short- and long-term effects of continuous versus intermittent restrictive diet approaches on body composition and the metabolic profile in overweight and obese postmenopausal women: a pilot study. Menopause. 2012;19(8):870–6.
172. Campbell BI, Aguilar D, Colenso-Semple LM, Hartke K, Fleming AR, Fox CD, et al. Intermittent energy restriction attenuates the loss of fat free mass in resistance trained individuals. A randomized controlled trial. J Funct Morphol Kinesiol. 2020;5:1.
173. Peos JJ, Helms ER, Fournier PA, Ong J, Hall C, Krieger J, et al. Continuous versus intermittent dieting for fat loss and fat-free mass retention in resistance-trained adults: the ICECAP trial. Med Sci Sports Exerc. 2021;53(8):1685–98.
174. Siedler MR, Lewis MH, Trexler ET, Lamadrid P, Waddell BJ, Bishop SF, et al. The effects of intermittent diet breaks during 25% energy restriction on body composition and resting metabolic rate in resistance-trained females: a randomized controlled trial. J Hum Kinet. 2023;86(1):117–32.
175. Bullough RC, Gillette CA, Harris MA, Melby CL. Interaction of acute changes in exercise energy expenditure and energy intake on resting metabolic rate. Am J Clin Nutr. 1995;61(3):473–81.
176. Jurov I, Hadžić V, Rauter S. Markers of energy metabolism affect lactate metabolism and aerobic performance in competitive female cyclists. Appl Sci. 2020;10(21):7563.
177. Sterringer T, Larson-Meyer DE. RMR ratio as a surrogate marker for low energy availability. Curr Nutr Rep. 2022;11(2):263–72.
178. Deutz RC, Benardot D, Martin DE, Cody MM. Relationship between energy deficits and body composition in elite female gymnasts and runners. Med Sci Sports Exerc. 2000;32(3):659–68.

179. Benton MJ, Hutchins AM, Dawes JJ. Effect of menstrual cycle on resting metabolism: a systematic review and meta-analysis. PLoS ONE. 2020;15(7): e0236025.
180. Davidsen L, Vistisen B, Astrup A. Impact of the menstrual cycle on determinants of energy balance: a putative role in weight loss attempts. Int J Obes (Lond). 2007;31(12):1777–85.
181. Pelkman CL, Chow M, Heinbach RA, Rolls BJ. Short-term effects of a progestational contraceptive drug on food intake, resting energy expenditure, and body weight in young women. Am J Clin Nutr. 2001;73(1):19–26.
182. Bell C, Day DS, Jones PP, Christou DD, Petitt DS, Osterberg K, et al. High energy flux mediates the tonically augmented beta-adrenergic support of resting metabolic rate in habitually exercising older adults. J Clin Endocrinol Metab. 2004;89(7):3573–8.
183. Paris HL, Foright RM, Werth KA, Larson LC, Beals JW, Cox-York K, et al. Increasing energy flux to decrease the biological drive toward weight regain after weight loss—a proof-of-concept pilot study. Clin Nutr ESPEN. 2016;11:e12–20.
184. Burke CM, Bullough RC, Melby CL. Resting metabolic rate and postprandial thermogenesis by level of aerobic fitness in young women. Eur J Clin Nutr. 1993;47(8):575–85.
185. Day DS, Gozansky WS, Van Pelt RE, Schwartz RS, Kohrt WM. Sex hormone suppression reduces resting energy expenditure and β-adrenergic support of resting energy expenditure. J Clin Endocrinol Metab. 2005;90(6):3312–7.
186. De Souza MJ, Miller BE, Loucks AB, Luciano AA, Pescatello LS, Campbell CG, et al. High frequency of luteal phase deficiency and anovulation in recreational women runners: blunted elevation in follicle-stimulating hormone observed during luteal-follicular transition. J Clin Endocrinol Metab. 1998;83(12):4220–32.
187. Schaumberg MA, Jenkins DG, Janse de Jonge XAK, Emmerton LM, Skinner TL. Three-step method for menstrual and oral contraceptive cycle verification. J Sci Med Sport. 2017;20(11):965–9.
188. Cheng J, Santiago KA, Abutalib Z, Temme KE, Hulme A, Goolsby MA, et al. Menstrual irregularity, hormonal contraceptive use, and bone stress injuries in collegiate female athletes in the United States. PM R. 2021;13(11):1207–15.
189. Metz L, Isacco L, Redman LM. Effect of oral contraceptives on energy balance in women: a review of current knowledge and potential cellular mechanisms. Metabolism. 2022;126: 154919.
190. Frankenfield DC, Coleman A. Recovery to resting metabolic state after walking. J Am Diet Assoc. 2009;109(11):1914–6.