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Title: Limits of Ultra: Towards an interdisciplinary understanding of ultra-endurance running performance

Running head: Limits of Ultra

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Abstract

Ultra-endurance running (UER) poses extreme mental and physical challenges that present many barriers to completion, let alone performance. Despite these challenges, participation in UER events continues to increase. With the relative paucity of research into UER training and racing compared with traditional endurance running distance (e.g., marathon), it follows that there are sizable improvements still to be made in UER if the limitations of the sport are sufficiently understood. The purpose of this review is to summarise our current understanding of the major limitations in UER. We begin with an evolutionary perspective that provides the critical background for understanding how our capacities, abilities, and limitations have come to be. Although we show that humans display evolutionary adaptations that may bestow an advantage for covering large distances on a daily basis, these often far exceed the levels of our ancestors, which exposes relative limitations. From that framework, we explore the physiological and psychological systems required for running UER events. In each system, the factors that limit performance are highlighted and some guidance for practitioners and future research are shared. Examined systems include thermoregulation, oxygen delivery and utilisation, running economy and biomechanics, fatigue, the digestive system, nutritional and psychological strategies. We show that minimising the cost of running, damage to lower limb tissue, and muscle fatigability may become crucial in UER events. Maintaining a sustainable core body temperature is critical to performance, and an even pacing strategy, strategic heat acclimation and individually calculated hydration all contribute to sustained performance. Gastrointestinal issues affect almost every UER participant and can be due to a variety of factors. We present nutritional strategies for different event lengths and types, such as personalised and evidence-based approaches for varying types of carbohydrate, protein, and fat intake in fluid or solid form, and how to avoid flavour fatigue. Psychology plays a vital role in UER performance, and we highlight the need to be able to cope with complex situations, and that specific long and short-term goal setting improves performance. Fatigue in UER is multi-factorial, both physical and mental, and the perceived effort or level of fatigue have a major impact on the ability to continue at a given pace. Understanding the complex interplay of these limitations will help prepare UER competitors for the different scenarios they are likely to face. Therefore, this review takes an interdisciplinary approach to synthesising and illuminating limitations in UER performance to assist practitioners and scientists in making informed decisions in practice and applicable research.

Keywords

Ultra-endurance running; ultra-running; evolution; thermoregulation; psychology; gastrointestinal function; fatigue; applied practice

Key points

- Humans display evolutionary adaptations that may confer an advantage for moving long distances daily. Modern ultra-endurance runners engage in exercise that exceeds the levels of physical activity that formed the evolutionary pressures of our ancestors, which exposes relative weaknesses and limitations.
- Successful ultra-endurance running training and performance requires appreciation of, and attention to, multiple factors that include thermoregulation, oxygen utilisation and exercise economy, digestion, supporting nutrition, and fatigue.
- Ultra-endurance runners are typically intrinsically motivated, possess greater pain tolerance than non-runners and adopt multi-faceted adaptive strategies to mitigate fatigue and maintain or improve performance.
- Targeting the factors that limit performance in training and during races may lead to improved outcomes.

1. Introduction

Ultra-endurance running (UER) events are defined by distance or time and are running events that are longer than a traditional marathon (42.195 km) or exceeding 6 hours, although the most common distances are in the range of 50 – 160 km (50km being the most popular), and some are thousands of kilometres [1-3]. Unlike standardised running and walking races, UER events last many hours or days, and may incorporate topographical or environmental challenges such as traversing mountain ranges or enduring extreme heat or altitude [3]. Whereas there are no comprehensive databases of all UER results, the Deutsche Ultramarathon Vereinigung (DUV) is the largest database on UER events and show that there were fewer than 20 ultramarathons each year from 1798 until 1969. Since then, the number has risen to peak at 7465 events worldwide in 2019, just prior to the pandemic which meant such events did not run. From 2005 - 2019 the number of UER events held and athlete finishes has increased exponentially from fewer than 1,000 events with 89597 finishes (73920 men, 15677 women) in 2005 to more than 7,000 events with 682156 finishes (528579 men, 153577 women) in 2019 [4]. Numbers have not quite returned to those levels but were over 7,000 in 2022. Participation by unique individuals has followed a similar trend with 16585 persons participating in UER events in 1980 to 432,000 in 2019, again prior to the pandemic. In 2022, it was 338,064 persons. There has been a huge change in the ratio of men to women over the years. In 1980, there were 22.2 men for every woman participating in ultramarathons, and that declined to just 3.4 men for every woman participant in 2019 [4] . These findings are consistent with trends reported for specific races or geographic regions [2, 5-7]. It is

reasonable to hypothesise that there are sizeable gains in UER performance still to be made in light of the increasing participation in UER events and the paucity of experimental studies on UER events [8] relative to the marathon where sizeable gains have been made through deeper understanding of the underlying physiology limiting performance [9-11]. Increased participation will arguably lead to more available data which can be analysed to help understand the many limiting factors to UER performance and can also lead to more focused experimental studies. A more nuanced integrated understanding of the capacity and influence of relevant systems and their limitations may facilitate the advancement of UER performance (see Table 1, 2, 3 and 4).

---Insert Table 1 around here---

Researchers to date have employed a wide range of research designs, encompassing large scale assessments of race participants, deeper investigations of single or small groups of athletes, and synthesised these data into performance frameworks to identify variables that predict UER performance (see Table 1, 2 and 3) [12-19]. For example, peak UER performance times are achieved by older populations at the age of 35-45 years for both genders, and the age of best performance increases with increasing race duration or distance [1]. Training volume and type to maximise UER performance have been examined before [14-17], and describing in detail the ideal training methods for the vast range of UER events goes beyond the scope of this article. As a result, we decided to focus on the numerous remaining factors that limit UER performance and will not specifically address training type or volume. Likewise, a comparison of male and female participants in UER events has been completed, concluding that "The literature indicates that while females exhibit numerous phenotypes that would be expected to confer an advantage in ultra-endurance competition (e.g., greater fatigue resistance, greater substrate efficiency, and lower energetic demands), they also exhibit several characteristics that unequivocally impinge on performance (e.g., lower O_2-carrying capacity, increased prevalence of gastrointestinal (GI) distress, and sex-hormone effects on cellular function/injury risk)" [20]. Therefore, we will not specifically address sex-differences but instead refer the interested reader to that publication.

---Insert Table 2 around here---

Given the duration and complexity of UER, prior analyses have shown that the physiological, biomechanical, and psychological predictors of performance are not easily extrapolated from traditional endurance running distance (i.e., 5km to marathon) and may be more susceptible to adverse events leading to poor performances or participant withdrawal (Table 2). For example, at the two most famous UER events, the Ultra-Trail du Mont-Blanc (UTMB) and the Western States Endurance Run (WSER), 34% of entrants either did not finish (DNF) or were over the time limit in 2021 [4]. Therefore, an interdisciplinary exploration of UER was performed to review the limits of:

- The evolutionary adaptations that underlie human capacity for ultra-endurance running.
- Critical physiological systems responsible for successful ultra-endurance running performance and how these systems are adapted for and respond to ultra-endurance running exercise.
- Psychological characteristics of successful ultra-endurance running athletes.

---Insert Table 3 around here---

2. Evolutionary framing of human endurance

Relative to other apes, humans are unusual in our bipedal locomotion, capacity for muscular endurance rather than strength [21], high body fat percentage [22-24], high metabolic rate supported by high-cost, high-reward foraging [25], and the ability to regulate heat via near-naked skin with a profusion of eccrine sweat glands [26, 27]. Hypotheses concerning the purposes of and extent to which early humans engaged in endurance running are contentious and difficult to test [28, 29], but this evolutionary history has clearly endowed us with an unusual ability to run long distances. An evolutionary perspective also informs our understanding of what factors limit UER performance.

Our capacity to thermoregulate via sweating - which evolved to facilitate longer travel distances over the African savannah, probably for food acquisition [30] - enables the sustained metabolic heat dissipation required during UER , but also demands an enormous water intake and predisposes ultra-endurance runners to dehydration. Our ancestors faced this problem too: a persistence hunt by *Homo erectus*, in whose fossil remains we see the hallmarks of an efficient endurance runner [28], would have been limited to ~5.5 hours without drinking due to onset of life-threatening dehydration [31]. Ultra-endurance runner Ann Trason's characterization of UER events as "an eating and drinking competition" highlights what may be the ultimate limit for human endurance: energy intake and fluid maintenance. Humans evolved in a food-scarce environment and our bodies are thus endowed with austere energy saving mechanisms [32]. This explains the "use it or lose it" nature of exercise abilities. Phenotypic responses to physical activity - the training adaptations that endurance athletes seek, including production of more red blood cells, capillaries and mitochondria - are energetically costly and are only produced and maintained to match capacity to demand [33], requiring athletes to train extensively to maximise their potential in UER . Indeed, this phenotypic plasticity, in addition to innate running ability, may have been the biggest target of selection. Periodic low energy availability in our evolutionary past also explains our higher body fat relative to other apes (which may provide a coincidental energetic buffer during UER), and reductions in basal/non-activity energy expenditures in response to increased physical activity [34]. This metabolic compensation occurs *during* weeks-long

UER events, effectively reallocating energy to locomotor performance [35], and because energy extraction from food is thought to set an upper limit on total energy expenditure over long durations [35], this response may constitute an important performance enhancing adaptation during extreme duration events; one that does not bear upon performance in shorter distances.

Evolution has endowed humans with a phenotype uniquely suited to long-distance locomotion, especially running mixed with walking, as required by many UER events. However, an evolutionary perspective should temper the popular narrative of humans as "born to run", and we should not view UER as the ultimate expression of our evolved physical nature, nor ultra-endurance runners as proxies for our ancestors, for several reasons. First, the human body has also evolved for other physical activities including digging, throwing, using tools, gestation and giving birth, and its morphology and physiology reflect these compromises [33]. Second, UER is a decidedly modern activity. The high running volumes maintained by modern ultra-endurance runners in training provide a more specific and robust stimulus for phenotypic adaptation to running than early humans likely had, supported by an essentially unlimited food supply and reduced immune expenditure as compared with modern hunter-gatherer and subsistence populations who ostensibly better represent the lifestyle of pre-industrial humans [36, 37]. UER competitions challenge our evolved endurance capacities to degrees that our ancestors likely rarely faced. UER competitors run much farther, and elite ultra-endurance runners run much faster, than what is observed in modern recorded persistence hunts- a hypothesized use of endurance running in early humans in which hunters track and run large prey into hyperthermia [28]. Third, UER is "W.E.I.R.D", as it is practised predominantly by individuals in Western, Educated, Industrialised, Rich Democracies (WEIRD), and thus is not representative of the breadth of contemporary human biological and cultural diversity [36]. Therefore, while endurance running is not novel, UER is.

3. Oxygen delivery, utilisation, and management

There is a ceiling above which the energetic costs of running cannot be met by oxidative phosphorylation at the whole-body level, called critical velocity (CV; [38]). CV occurs at ~90% maximal oxygen uptake ($\dot{V}O_2max$) in well-trained runners, with elite marathon runners capable of sustaining >94% of CV (>85% of $\dot{V}O_2max$ [39]). As the event distance increases to UER competitions, the average work rate decreases: 65-70% $\dot{V}O_2max$ for 60km [40], 51% $\dot{V}O_2max$ for 12h [41], 66.5% $\dot{V}O_2max$ for 80km [42], 67% $\dot{V}O_2max$ for 84km [43], and 40% $\dot{V}O_2max$ for 24h and above [44]. It is important to appreciate that all of these studies were done in non-elite runners, on a treadmill [41-43], or in a flat, urban setting [40], and it is probable that decreases in work rate would be less pronounced in elite runners participating in UER events. At these relatively low intensities, the energetic costs of

running are unlikely to exceed the capacity for oxygen supply, delivery, and utilisation. However, maximum steady-state dynamics, relevant fatigue processes, and even substrate utilisation can still conspire to place significant demands on oxidative metabolism that may limit performance.

Below CV, oxygen consumption stabilises. Above CV, oxygen consumption rises until athlete reaches $\dot{V}O_2$max (in 3-30 minutes) and cannot continue. Critical power (CP; the cycling correlate of running's critical velocity) declines significantly beyond 2 hrs of cycling at ~65% $\dot{V}O_2$max [45], and if also applicable to running, then UER performance may ultimately be limited by the athlete's starting CV and the rate of its decline relative to the race duration (see Fig.1). As such, maximal oxidative capacity may become a primary limiting factor as it defines the upper limit of all work rates that are sustainable. Moreover, UER events often include altitude (e.g. UTMB, Hardrock), where the maximum sustainable work rate is further limited by reduced oxygen pressures [46].

---- Insert Figure 1 around here ----

These work rates can be quantified as the cost of running (Cr). It has long been appreciated that the Cr, expressed as either the oxygen consumption (in $ml.kg^{-1}.min^{-1}$ or $ml.kg^{-1}.km^{-1}$) or the energy use ($kcal.kg^{-1}.min^{-1}$ or $J.kg^{-1}.min^{-1}$), is fundamental to performance in long distance running [10, 47, 48] because it defines the relative amount of sustainable capacity that is utilised at any given moment. We will use Cr to refer to either expression of the cost of running (i.e., by oxygen consumption or by energy use) but there may be important differences between the two expressions to be explored in future studies.

For low work rates (e.g., below the first lactate threshold, LT1), the Cr is relatively constant and sustainable without contributing to fatigue [49, 50]. At higher work rates, there is an additional and delayed cost (called the slow component of oxygen uptake kinetics) that increases the energetic demands of locomotion after 2-3 minutes into the change in work rate [51-53]. Because trail and hilly races inherently produce continually varying work rate demands, oxygen uptake kinetics and the slow component make the energetics of such UER events very difficult to ascertain [54]; an 'average' value is unlikely to inform understanding of the limitations under these conditions because the work rate is cycling between moderate and heavy (and perhaps severe) domains with different fatigue processes at play among them [55]. Work rates in the heavy domain (above LT1 but below CV) are sustainable for hours in a quasi-steady state where oxidative metabolism may become limiting. Thus, oxygen consumption is a proxy for the underlying fatigue process [56], even at the intensities required for some UER events.

For the reasons stated above, the rate of oxygen consumption at a given running speed, called running economy (RE), garnered interest decades ago [10, 47, 48]. In the marathon, RE is a critical factor in performance [9, 10]. However, RE did not correlate with performance in 50-, 80-, or 160-km trail races [14]. Even when RE was assessed at a 12% incline to approximate race conditions, it did not correlate with performance in mountain trail races at distances of 40-, 55-, 101-, 145-, or 170-km [18]. A systematic review of performance indicators in trail running found a low correlation (r=-0.31) between RE and performance; even body fat % was a better predictor (r=0.55 [57]).

In the studies cited above, RE is measured at one (or maybe two) inclines on a flat surface (e.g., treadmill). It's important to appreciate, however, that RE varies under different conditions (e.g., uphill, flat, downhill, rocks, roots) [58]. It would be a monumental undertaking to align moment-by-moment race conditions (e.g., grade) with running economies that are quantified under all those conditions. But, to confidently determine the extent to which RE limits performance under real-world conditions in trail and mountain races, such a study would have to be performed. The costs of running in the context of biomechanics over UER distances will be further explored in the next section.

Interestingly, the time constant of oxygen uptake kinetics was a good predictor of marathon performance [9]; the time constant measures the rate at which aerobic metabolism adjusts to rapid changes in work rate. Decades ago, Whipp et al. [59] made a case for this time constant as a marker of endurance capacity which they described as a 'stamen of stamina'. It remains unknown if the time constant of oxygen uptake kinetics predicts performance in UER events where terrain conditions, and thus work rate, vary continuously. It's a logical hypothesis that the time constant should play an even bigger role under such constantly varying, sinusoid-like conditions of trail and mountain UER events than in the relatively stable demands of most marathons, and this is a very easy measurement to make for most exercise science researchers.

The relative amount of energy derived from fat increases with exercise duration [60], which has been confirmed during simulated and real-world UER events [40, 49, 61, 62]. Fat yields less caloric value per litre of oxygen consumed than carbohydrate (4.73 vs 5.05 kcal/L). At low relative work rates, the additional oxygen cost of fat reliance may go unnoticed, but late in a race when oxygen cost is increasing and CV is decreasing, this inefficiency may become more relevant to performance. But, largely due to gastrointestinal (GI) limitations, ultra-endurance runners are typically unable to consume sufficient carbohydrate to prevent glycogen depletion [63] and can accrue significant energy deficits during events [64, 65], meaning that in many cases there will be an inevitable shift to a greater reliance on fat oxidation. Carbohydrate ingestion can mitigate the decline in the athlete's maximum sustainable aerobic capacity [66] and enhance endurance performance [67], but the increased frequency and severity of GI problems (particularly nausea and vomiting) that occur in the latter portions of single-stage UER events

[68] can make consuming high amounts of exogenous carbohydrates difficult, if not impossible, for some athletes.

The oxygen cost of running at any point during an UER event will depend on the complex interplay among the topology and geography of the course along with the athlete's fitness, work rate relative to their prevailing aerobic limits, accumulated time in the race, food digested, substrate utilisation, and shifts in underlying physiological capacities throughout the race (Table 3 and 4).

4. The costs of running and biomechanics at ultra-endurance running event distances

Strategies to lower the Cr improve performance in traditional running events, yet minimising damage to lower limb tissue and muscular fatigability may become more crucial in UER events, even at the expense of small increases in the Cr [69]. A good example in trail UER is using poles, which reduces the load on lower limb tissue [70], but requires carrying an additional (moderate) weight and use of energy-consuming upper body musculature. In practice, runners must consider this compromise between Cr and fatigue/endurance when choosing their equipment (poles vs no poles, minimalist vs traditional shoes), or technique (foot strike, step frequency) when running UER events.

Most studies show a deterioration of Cr in a fatigued state, including after an UER event [e.g., [49]], but an improved Cr (7-14%) has also been observed after UER events [71]. This is surprising considering the factors that should lead to a deterioration of Cr (e.g., higher ventilation, higher motor unit recruitment due to muscle fatigability, alteration of muscle efficiency, changes in running patterns). Although the underlying mechanisms explaining a better Cr in a fatigued state are unclear, it is possible that UER induces positive adaptations in the neural control of movement [72]. Methodological issues (lack of control group or familiarisation) may also explain this unexpected result [72]. A direct examination of this issue has been recently performed [50] and confirmed that the change in Cr was significant for short (< 60 km) but not long (>100 km) trail running races. The slope at which Cr is measured may partially explain these findings. Cr has been measured during uphill, level, and downhill running in different investigations conducted in UER events, but most 'classic' studies traditionally measured Cr only during level running. Because many UER events include a wide range of slopes (e.g., trail and mountain events), the Cr in all three conditions (including several levels of slope for uphill and downhill) may be required to fully appreciate the demands and adjustments within a single event. For example, the deterioration of Cr with fatigue induced by UER events were correlated when measured during level and uphill running, yet the changes in Cr showed a tendency to be greater in level compared to uphill running [50].

Running patterns depend on several parameters (see Fig.2), some of them specific to UER events, that influence biomechanics and the Cr. An obvious example is the low intensity at which an UER event is run relative to the marathon, which lowers repetitive impact forces that must be tolerated for hours, if not days. As previously mentioned, another characteristic of many UER events compared to most traditional races (5 km to marathon distance) is the slope, as they are often performed in mountainous terrain (e.g., UTMB®, Hard Rock 100), or even on road with large portions of uphill and downhill (e.g., Comrades marathon). Graded running leads to specific running patterns including changes in foot strike pattern and ground reaction forces, modification of joint kinematics and kinetics, and impact shock [for a review, see [72]]. It also leads to distinct neuromuscular activation compared to level running, this activation being dependent on the lower limb muscles considered. Moving from stretch-shortening cycles to alternating between mostly concentric (uphill) and mostly eccentric (downhill) may also affect fatigue; although, it has been suggested that the degree of alterations in neuromuscular function depend on the duration of the UER event rather than the positive and negative elevation [73]. It has been shown that the fatigue accrued when performing an UER event alters running patterns, in particular it leads to an increased step frequency while decreasing flight time (i.e. increasing duty cycle) as well as reducing vertical oscillation of the centre of mass and increasing stiffness (e.g., [74, 75]). Although these running pattern changes may potentially be compensatory strategies for decrements in propulsive capacity, they are believed to be protective from mechanical stress. Indeed, because fatigue characterised by metabolic rather than mechanical stress does not lead to altered running patterns [75], these modifications to running mechanics are hypothesised to decrease the impact experienced at each step, potentially reducing pain and muscle damage during running (see Fig.2). Runners must anticipate the consequences of running patterns by trying to minimise muscle damage, particularly for long (>100 km) UER events. This can be done throughout (i) training [both resistance training and running downhill [76] to optimise the repeated-bout effect], (ii) appropriate choice of equipment and technique (see above) and (iii) conservative pacing, especially in the first downhills (Table 3 and 4).

---- Insert Figure 2 around here ----

5. Thermoregulation and Hydration

Humans have evolved a thermal profile that reflects our tropical origin [77-79] and a thermoregulatory system that can outlast the thermo-physiological capabilities of its prey when hunting [80], or scavenging [28]. The stochastic nature of UER appeals to our evolutionary thermoregulatory origins as hunter-gatherers/scavengers and allows for behavioural (thermo) regulatory changes (e.g., drinking patterns, pace changes, adding/removing clothing, minimising radiation, and maximising convection; some of which can be manipulated to improve performance). Due to its relatively long duration, UER requires lower average exercise intensities, which generate less internal heat that may be dispersed across the diurnal range of thermal conditions [81], compared with shorter events such as the marathon.

Nevertheless, optimal pacing during both marathon and UER is likely to be important as recent evidence suggests that more experienced marathon runners (i.e., those finishing in the top 10) adopt a more conservative pace relative to their personal best in hot conditions and perform better consequently (Table 1 and 2) [82]. The scope for significant pacing errors and catastrophe (e.g., injury and withdrawal) during the longer UER events is greater owing to a larger number of variables that can influence performance. Hence, conservative pacing is advised to maximise the chances of event completion.

Nevertheless, ultra-endurance runners are less likely to be limited by sustained critically-high core body temperature, even in a tropical environment, although transient increases may be seen [83]. Maintaining hydration status to facilitate extended sub-maximal thermoregulatory sweating to offset moderate thermal loads may be a useful strategy to complement other techniques (e.g., icing). Potential hydration options during UER events range from highly structured fluid consumption plans (e.g., targeting a specific hourly rate) to simply relying on thirst. Historically, athletes in all endurance events should avoid water deficits exceeding ~2% body mass loss to sustain athletic performance [84, 85], but more recently, recommendations to rely on thirst have become more common, in part to minimise the risk of fluid overconsumption and exercise-associated hyponatremia [86]. Various research supports the notion that drinking with the goal to fully prevent body mass losses is not advisable in UER races. For example, data from the 161.3 km WSER indicate that the fastest runners tolerated body mass losses of ~3.5-4.0% [83], a relationship that is also reported to exist in faster marathoners [87]. Also in competitors in the WSER, Valentino et al. [88] found no correlation between 3% body mass losses and raised deep body temperatures despite hot (39°C), dry (38.2 ± 16.0% relative humidity) conditions for part of the race. Yet a 4% body mass loss has been associated with an increased risk of developing hyperthermia [89], so this threshold might represent a maximal tolerable threshold for body mass loss. Should exercise-induced hyperthermia develop, slowing or ceasing exercise may be necessary followed by administering post-exercise cooling techniques [90]. If hyperthermia develops into heat stroke, cool or cold-water immersion may be necessary to reduce deep body temperature to safe levels [91, 92].

Some of these observations could partly be explained by the fact that body mass losses from non-fluid sources are expected to be higher during many UER events. Indeed, due to the large total energy expenditures that occur during UER events, body mass changes are less accurate as a surrogate for water balance [93]. For example, running a marathon may produce 0.89% of body mass loss from non-sweat sources, whereas running a 100-km event may lead to a 2% reduction in mass from non-sweat sources [93]. Further, the intake of foods and the loss of mass from faeces complicates the use of body mass change as a marker for hydration during UER events. Due to these reasons, using thirst to guide drinking is likely to be the simplest strategy and the one that best minimizes the risk of overdrinking [86], with highly structured fluid consumption plans that don’t account for sweat rate are associated

with potentially developing hyponatraemia [94]. Still, controlled experimental data directly comparing drink-to-thirst to structured hydration strategies are largely non-existent for UER competitions, meaning that definitive answers on the optimal approach remain elusive. If an ultra-endurance runner does decide to use a structured approach to hydrating, they should attempt to determine their projected sweat rate and avoid consuming fluids in excess of that rate.

Heat acclimation (or acclimatisation; HA) is one means of extending the limits of thermoregulatory capacity [95]. This form of preparation is recommended for athletes entering events where there is a significant thermal load [96, 97]. HA requires serial exposures to the heat (i.e., a minimum of 5-consecutive days; e.g. [98]), typically while exercising, that are sufficient to sustain core body above 38.5°C and skin temperature to a level that challenges sudomotor and vasomotor thermoeffector responses [95], i.e., sweating and vasodilation. HA culminates in expanded plasma volume, improved sweating efficiency (higher rate and more dilute sweat), improved cardiovascular stability, lowered core body and skin temperatures for a given work rate and thermal load (Table 3) [99]. It also leads to increased self-belief, lower perceived exertion, and lower anxiety [100]. Moreover, even in cooler conditions there are suggestions that HA, due to increases in plasma volume and associated cardiac output, can increase $\dot{V}O_2max$, lactate threshold, and running economy [101], thereby extending the limits to UER performance through non-thermal mechanisms even when there is an absence of significant thermal load during an UER race. There have also been suggestions that permissive dehydration enhances short-term HA alone [102], but this is equivocal [103] and very recent data from non-acclimated resting participants suggest that cutaneous vasomotor and central cardiac responses are mediated by thermal but not (de)hydration responses [104].

Collectively, the thermoregulatory limits to UER in warm or cool conditions probably reside with the capability to maintain thermoregulatory sweating and cardiovascular stability, via adequate fluid intake to sustain exercise intensity; especially under high solar radiative load typically found at the high altitudes of UER events; albeit occurring in a minority of races. Risk of GI distress is also increased in the heat (see below; [97]). HA may improve all these factors. Importantly, psychological skills training has been found to enhance beliefs in being able to run in the heat, and therefore, should be encouraged during HA [100]. Less is known about UER in cold conditions, although protecting the extremities from risk of freezing by generating sufficient heat alongside appropriate clothing strategies to offset cooling while minimising sweating, may be sufficient to sustain performance [105].

Practical recommendations for athletes and coaches include: adopt a conservative initial pace to maximise chances of event completion particularly if inexperienced, remain aware of the sensations of heat and how they often contribute to higher perceived effort, maintain hydration status and core temperature to preserve plasma volume and cardiovascular stability to sustain cardiac output, and

consider heat acclimation to maximise adaptation of thermal and hydration responses particularly for performance in the heat (Table 2).

6. Digestion, the gut, and gastrointestinal distress

Ultra-endurance runners experience some of the highest rates of GI disturbances during competition of any endurance athlete populations. For example, in a study of 272 participants from the WSER, 96% reported experiencing some type of GI symptom during the race [106]. Although the relatively benign symptoms of belching and flatulence were the two most prevalent complaints, more troublesome symptoms like nausea, bloating, and stomach cramps/pain were reported by 60.3%, 48.7%, and 31.9% of respondents, respectively [106]. Moreover, 43.9% of race finishers indicated the perception that GI symptoms affected their performance, with nausea being the most commonly reported symptom. In another analysis of WSER competitors, nausea and/or vomiting was the leading reason for race withdrawal [68]. Studies from other races confirm that GI distress is prevalent during UER [107-109], although the severity varies with exercise duration (increased severity with longer duration), environmental conditions (more common in heat), nutritional intake (type and volume), and competitive experience (fewer issues with more experience; Table 1 and 4) [110, 111].

Nausea deserves special consideration among the GI issues that ultra-endurance runners face given its prevalence and propensity to impact performance and in-race energy intake. One factor contributing to nausea during UER is a reduction in splanchnic blood flow. Blood flow changes to the gut depend on exercise intensity and duration, but in some cases (e.g., during prolonged exercise in the heat), reductions of up to 80% may occur [110]. Reduced blood flow and oxygen delivery to the intestinal mucosa can enhance GI permeability and thereby increase bacterial endotoxin translocation into the circulation, which has been linked to nausea in ultra-endurance runners (Table 4) [107, 112].

Of note, nausea prevalence can increase over three-fold from the first quarter to the latter half of a 100-mile race, indicating that distance is an important nausea risk factor in single-stage UER events [106]. Some of the physiological mechanisms underpinning the increased nausea could include elevated blood concentrations of catecholamines, glucagon, arginine vasopressin, and cytokines. These substances can induce nausea via activation of the chemoreceptor trigger zone and vomiting centre in the brain [111]. Exercising in the heat is associated with higher blood concentrations of these substances [113-115], which may, in part, explain the greater incidence of nausea with heat stress. Indeed, Snipe *et al.* [116] demonstrated that during 2 hours of running at 60% $\dot{V}O_2max$, nausea prevalence increased from 10% in 22°C conditions to 40% in 35°C conditions. It is worth pointing out that exercising in a hypohydrated state - which is more likely in warmer conditions - can exacerbate nausea [117].

Strategies for lessening the risk of nausea during UER include heat acclimatisation, use of pre-exercise and during-exercise cooling strategies, avoiding excessive hypohydration, and being mindful not to over hydrate [111, 118]. In addition, foods and nutrients that delay gastric emptying (e.g., fat, fibre, solid protein, hypertonic sports drinks) should be avoided in large quantities during competition. Runners planning to consume exogenous carbohydrate at high rates (≥50-60 g/h) should choose sources containing a mix of glucose and fructose to optimise absorptive capacity [119], and repeatedly expose the gut to these high intakes during training sessions in the weeks leading up to competition (see Fig. 3) [120]. Although carbohydrate ingestion as high as 90-120 g/h has been reported amongst runners in some studies [121, 122], these aggressive intakes are not achievable by all athletes, primarily due to GI intolerance. Achieving a high per-hour intake (60-120 g/h) is most important for elite competitors, given that they oxidise carbohydrate faster than amateurs [123]. In addition, these aggressive intakes are primarily applicable in shorter UER events (3-12 h) that are characterised by carbohydrate oxidation rates exceeding 90 g/h [63, 123, 124]. Intakes of greater than 60 g/h may be unnecessary for many runners during longer events (>12 h), owing to their lower average relative intensity [49, 125], though experimental data on the matter are sparse.

Runners who experience elevated pre-competition anxiety appear prone to developing nausea while racing [126]. Currently unconfirmed with experimental evidence in athletes, psychological interventions such as deep breathing and mindfulness are low risk strategies that could, in theory, reduce nausea and other GI symptoms [126]. In addition, runners who suffer from anxiety-related GI issues may need to modify their pre- and during-exercise fuelling strategies to avoid exacerbating their symptoms.

In sum, GI problems are a major concern for ultra-endurance runners and can impair performance in moderate-to-severe cases (Table 3 and 4). To some extent, ultra-endurance runners may need to accept that a degree of GI disturbance is likely in many races given the extreme demands of the sport. Because there are numerous potential causes of GI symptoms (nutritional, environmental, psychological, etc.), many cases turn out to be multifactorial in nature. As such, athletes and practitioners should consider tracking GI symptoms in conjunction with monitoring potentially causative factors in order to identify the strategies that work best for them. Validated rating scales for assessing GI symptoms have been published previously [127, 128]. Although near-complete or partial resolution of GI issues may occur by tracking and addressing suspected underlying triggers, consulting a medical professional with expertise in GI function may be warranted, especially when symptoms are persistent and/or severe.

---- Insert Figure 3 around here ----

7. Nutritional strategies

Nutrition and hydration strategies employed by ultra-endurance runners may help to mitigate the performance limiting factors explored elsewhere in this review. Although the rate of energy expenditure is not as high as that in the marathon and shorter events, total energy expenditures can be extremely high during UER due to their duration, and may be exacerbated by environmental factors (e.g., climate, topography etc.). Therefore, strategies that are palatable, easily implemented, and well-tolerated are likely ergogenic by directly improving relative energy intake, while minimising GI side-effects.

Elevated rates of carbohydrate ingestion (e.g. >60g/h) may be relevant for elite ultra-endurance runners engaging in single-stage races of relatively short duration (e.g., up to 6h), but they may be unnecessarily high for longer events given the submaximal nature of those endeavours and the reported variability in athletes' abilities to tolerate food intake during events [109, 129].

The extrapolation of these values from lab-based studies (primarily in cyclists [130, 131]) further highlights the need for a personalised and well-trialled approach to UER nutrition. Individualised and well-practised nutrition strategies likely present the best countermeasure against GI distress and perhaps fatigue. Intakes up to 120g/h of carbohydrate have occasionally been reported during UER [122, 132], though 60g/h represents a more realistic target that can be readily attained via real foods, sports nutrition products or a combination of the two. Ginger, for example, has been used prophylactically to combat GI symptoms by enhancing GI integrity, and act as an analgesic during UER activity, although evidence is preliminary [129, 133].

Chronic high-fat diets markedly increase fat oxidation and negatively impact Cr compared to high-carbohydrate diets during prolonged submaximal exercise [124, 134, 135]. On the other hand, endogenous carbohydrate stores are limited in comparison to endogenous fat stores, which has led some to suggest that implementing strategies that maximise fat adaptation could be of benefit for UER athletes [124, 135, 136], especially where exogenous sources of carbohydrate are not readily available or have the potential to induce GI distress. By extension, maximising fat oxidation could, in theory, lower the demand for in-race carbohydrate intake and, in turn, the risk of subsequent GI issues. Unfortunately, controlled experimental research on chronic high-fat vs. high-carbohydrate diets for UER performance is rather limited due to logistical difficulties of carrying out such work. At present, evidence supporting chronic high-fat diets to improve prolonged exercise performance (>2-3 h) is lacking [134]. If an ultra-endurance runner does choose to undertake a high-fat diet, undertaking a transient 2-3-day period of elevated carbohydrate intake prior to races is hypothesised to help maintain elevated fat oxidation rates while maximising endogenous carbohydrate stores [137]; but underpinning mechanisms and response

variability require further examination [137, 138]. Regardless of the diet chosen, responses will inevitably vary among athletes.

Flavour fatigability also presents a relevant challenge to ultra-endurance runners [139]. With emerging evidence on the ergogenic potential of tastes [140], athletes and practitioners should consider how taste may be strategically applied to complement macronutrient composition and energy intake. Flavour fatigability likely occurs following over-stimulation of taste receptors, either through using a repetitive nutrition strategy, circadian variability, or a cumulative response to repeated feeding during exercise. Efforts to combat flavour fatigue may explain the reported trend towards an increased fat consumption in the latter part of some races; indeed, significantly greater percent (16.5 ± 2.6% vs. 11.1 ± 5.0%; p = 0.03) and absolute (0.06 ± 0.3 vs. 0.03 ± 0.01 $g.kg^{-1}.hr^{-1}$; p = 0.01) fat intakes differentiated runners with and without GI distress during a 161km race [141], although it should be noted that this sample size was affected by participant attrition of 53% i.e. 47% race completion. Nutritional 'form' is also an emerging consideration, with hydrogels of particular interest following the Nike Breaking2 and Ineos 1:59 Challenge marathon projects [142]. Hydrogels reportedly facilitate a greater rate of exogenous carbohydrate oxidation (≤180g/h; [143]) than standard beverages or gels, potentially sparing endogenous carbohydrates. However, their effects upon GI symptoms and running performance over traditional running event durations are equivocal [143-145], suggesting further investigation is required to support athlete testimonials and to better understand the potential role of hydrogels, if any, in single-stage UER .

The practicalities of a nutrition strategy should be carefully planned and rehearsed as this builds confidence in feeling prepared. These include food carriage and disposal, whether an athlete has access to food-stations or must be self-supported for the race duration, and by extension care provided by support crews. For practitioners, feeding presents a valuable opportunity to interact with athletes and assess the progression (time course, severity) of performance limiting factors such as temperature, hydration status, rating of perceived exertion (RPE), and motivation (e.g., [19]) in real time. If event duration is sufficient, or timing relevant, the circadian effects of appetite [146, 147] may also warrant consideration, with feeding strategies altered accordingly.

While a comprehensive review of all nutritional factors that contribute to UER performance is beyond the scope of this review, there are a few others worth briefly discussing. Iron deficiency is common in runners (particularly females), although research on ultra-endurance runners is more limited. In one investigation of 2019 WSER participants, 0 of 19 women had ferritin concentrations indicating clear iron deficiency (<10 ng/mL), but 63% had concentrations that might be considered suboptimal for endurance performance (<35 ng/mL). Notably, 50% of the women reported taking iron supplements [148]. Practitioners should keep in mind that ferritin levels often increase for 1-2 weeks following UER

574 races, which could mask a true iron deficiency [149, 150]. Vitamin D deficiency may also negatively
575 impact an ultra-endurance runner's performance and health, as vitamin D plays a role in regulating
576 muscle function, muscle repair/remodelling, bone remodelling, and immune function [151]. While
577 studies of vitamin D deficiency (usually defined by low 25[OH]D) among ultra-runners are sparse, the
578 aforementioned investigation of 2019 WSER participants found that 11 of 19 women had 25(OH)D
579 levels in the insufficiency/deficiency range [148]. Both iron and vitamin D deficiencies are possible
580 manifestations of undereating and relative energy deficiency [152, 153]. Investigations into the
581 prevalence of RED-S (relative energy deficiency in sport) among ultra-endurance runners are limited,
582 but among a sample of WSER participants, 61% of women and 29% of men were deemed moderate
583 risk, while ~6% of both men and women were high risk based on the Triad Cumulative Risk Assessment
584 [148].
585

586 ## 8. Psychological factors and effects
587

588 The following sections explore commonalities in the psychology of UER participants (motivation and
589 traits), the psychological effects of UER participation and how fatigue may manifest over the course of
590 an UER event. A recent systematic review showed the opportunity to achieve personal goals, and a
591 drive to explore physical and mental limits were important to participants [154]. Fatigue is
592 predominantly considered from a psychological standpoint, i.e., the symptom of fatigue is self-reported
593 [155]. Of course, physiological systems will also exhibit declines in performance (performance
594 fatigability) at different rates over the course of an UER event. The longer the event, the greater the
595 possibility of more extreme responses, but this may be tempered somewhat by the obligate reduction in
596 exercise intensity. However, there is a lack of controlled studies that investigate differences among
597 distances.
598

599 ### *8.1 Motivation, traits, and effects of ultra-endurance running participation*
600

601 There is evidently an interplay between physiological and psychological factors limiting performance.
602 However, the decision to stop by default is a psychological factor [156]. Knowledge of influential
603 psychological factors is useful for practitioners. Knowledge of factors that could be trained and
604 malleable are especially important. Evidence suggests that UER athletes do not show a consistent set
605 of stable personality traits. However, ultra-endurance runners may be higher in task orientation than
606 ego orientation [157], and personality traits such as reliance are clearly desirable [154]. However, these
607 stable personality traits have greater influence in how an athlete interprets their environment rather than
608 a direct effect.
609

Evidence suggests that ultra-endurance runners are predominantly intrinsically motivated. The most important motivating factor appears to be the opportunity to achieve personal goals [158-160], with health- and self-esteem-related reasons also significant (Table 1). It should be noted that the level of athlete ability is likely to influence the goal setting process and that elite athletes with goals of attaining a finish position can lead to intense anxiety. The goal of obtaining a certain finish position is partly influenced by one's own performance, but it is also influenced by the performance of others and how others perform is not under your control. It is more advantageous to focus on factors under your control that will influence performance and anxiety can negatively influence concentration, leading to making poor decisions. Recent research has argued that overcoming boredom is important for UER athletes, and that managing the mind so that it is engaged should be part of mental preparation [161].

The perceptual nature of fatigue experienced by ultra-endurance runners is captured eloquently in qualitative studies, where ultra-endurance runners describe experiencing a strong drive to explore their physical and mental limits and feel an intense sense of achievement after finishing a race [162]. They report using a range of psychological strategies to cope with the demands of UER, including goal-setting strategies, attentional focus strategies, positive self-talk, challenging negative thoughts, visualisation, and seeking support from other runners and support teams [162, 163]. These strategies can be learned via self-help information or via formal consultation with a sport psychologist, and therefore, are inherently trainable [164].

Researchers have also investigated the psychological characteristics of ultra-endurance runners and whether they possess any traits that contribute to their ability to tolerate the pain and discomfort and other stressors that they experience during races. Ultra-endurance runners were more psychologically resilient than non-runners and more mentally tough than a norm group consisting of athletes from multiple sports [154, 165]. However, it is not known if these differences emerge as a result of UER experience. So, there is a possibility that UER can help to develop mental toughness [165-167]. Practitioners should consider building self-efficacy towards displaying mental toughness and managing pain and fatigue via progressive training. Research should tease out the direction of relationships between personality characteristics to be resilient and tough in difficult situations and the influence of such traits on learning.

Psychological variables that have been found to predict performance in races include mental toughness, self-efficacy, task-oriented goals and inhibitory control skills [168-170]. There is also evidence that ultra-endurance runners respond to pain differently than others. Specifically, they appear to have higher pain tolerance and lower pain-related anxiety compared with non-runners [154, 171]. They are also more likely to utilise adaptive pain-coping strategies than maladaptive ones [172].

The psychological effects of running an UER event are wide-reaching. Mood effects of UER include increased fatigue and decreased vigour and tension [173, 174], which are contextualised further below. It has been hypothesised that the ability to manage such mood changes is an important determinant of UER performance [175]. Moreover, these effects may persist for several weeks after a race [176]. There is evidence that both trait emotional intelligence and mental toughness are associated with smaller mood fluctuations during UER events [175, 177, 178]. UER may also negatively impact cognitive function, although the evidence is currently inconclusive [154, 169]. Importantly, longer UER events often involve sleep deprivation so that the effects of these races on mood and cognition are likely due to a combination of prolonged exercise and sleep deprivation [179]. When seen collectively, it suggests that psychological and sleep strategies [180] for the anticipated challenges should form a vital part of deliberate preparation. Awareness of mood and emotions and how they respond to changes in physiological status becomes relevant. Athletes should appreciate that mood repair in an UER event could require suppression of feelings until there is an opportunity to change behaviour or re-appraise conditions.

8.2 Perceived and Performance Fatigability

It is widely assumed that fatigue limits UER performance [156, 167], but most studies describe the development of fatigue during UER (fatigue as a dependent variable) rather than investigate its effect on UER performance (fatigue as an independent variable). Furthermore, fatigue is generally used as an umbrella term that confusingly refers to a variety of physiological and psychological phenomena, each with different mechanisms that may require different countermeasures. With these limitations in mind, we review various factors that contribute to fatigue and their potential impact on UER performance.

Perceived fatigability has been defined as changes in the sensations that regulate the integrity of the performer [155]. The most important of such changes is the increase in perceived effort necessary to sustain the pace required to achieve the desired competitive outcomes (perceived fatigability). An increase in perception of effort during UER has been measured using the RPE scale [181]. However, there are no experimental studies investigating the role of perception of effort independently limiting UER performance. Various theoretical models and studies of endurance performance suggest that the perception of effort associated with a certain pace is likely to affect the decisions to change pace, or slow down [182], or withdraw [183] from UER events.

Also contributing to perceived fatigability, ultra-endurance runners often report an increase in the feelings of fatigue and a decrease in the feelings of vigour, measured at rest after UER competitions (Table 4) [154]. The mechanisms of this are poorly understood but mood changes are likely to reflect mental as well as physical factors [178]. Indeed, an increase in the feelings of fatigue and a decrease in

684 the feelings of vigour have been measured after prolonged cognitive exertion [184], and successful
685 ultra-endurance runners have demonstrated superior cognitive functioning than their slower
686 counterparts [169]. Because of the duration and high cognitive, motivational, and emotional demands
687 of UER competitions [154, 167] it is likely an increase in perception of effort can limit UER
688 performance [184].
689
690 Performance fatigability is the decline in an objective measure of performance over a discreet period
691 [155]. The better-understood factor contributing to performance fatigability is the fatigability of the
692 neuromuscular system, defined as the reduction in muscle strength or power induced by exercise [156,
693 185], which can be measured at both the locomotor muscles and the respiratory muscles. A significant
694 reduction in the capacity of locomotor muscles has been measured in humans after simulated or real
695 UER competitions [41, 186]. Studies investigating the loss of maximal voluntary isometric knee
696 extensor force after running exercise suggest that losses can reach 35-40% when exercise duration is
697 over 20 hours [41]. It is worth noting, however, that the locomotor muscle force required for endurance
698 exercise is quite low even at an intensity corresponding to 100% $\dot{V}O_2$max [187]. Therefore, it is highly
699 unlikely that impairments in locomotor muscle function directly limit the pace chosen by the athlete
700 and, thus, their UER event performance [41]. However, it was recently shown that muscle pain reduces
701 exercise performance [188], which may be a significant factor in UER events. Similarly, although
702 significant reductions in respiratory muscle capacity develops during UER events [189], UER
703 performance is unlikely to be limited solely by reducing the oxygen delivery to the locomotor muscles,
704 or by inhibiting their recruitment via reflex pathways [190], to the point that locomotor muscles are no
705 longer able to produce the submaximal forces required during UER events. However, impaired function
706 of both locomotor muscles [191] and respiratory muscles [190] increase perception of effort during
707 endurance exercise because a higher central command is required to maintain the required output [192].
708 Therefore, both locomotor and respiratory muscles may indirectly limit UER performance via their
709 negative effects on perception of effort.
710
711 Cardiovascular factors may also contribute significantly to performance fatigability during UER events.
712 For example, a transient reduction in left ventricular function induced by prolonged exercise in
713 otherwise healthy people has been reported[193] . Unlike declines in muscle function, which are caused
714 by well-defined central and peripheral alterations [194], the mechanisms resulting in declining cardiac
715 function and their relevance for UER performance are poorly understood.
716
717 ---Insert Table 4 around here---
718
719 9. **Limitations and suggestions for further research**
720

A recurring theme running through this article is the absence of controlled experimental studies. There are clear practical reasons why this is the case, including recruiting suitable motivated participants. However, practical reasons could be overcome if key stakeholders in running support the research - for example, running events and / or running media. An example, data collected at the Marathon of Britain [178] was done in conjunction with race organisers, However, researchers need to experimentally investigate the effects of various factors (e.g., fatigue, training, nutritional interventions etc.) on UER performance. Randomised trials in the field are possible but the statistical power is very low because of the obligatory post-test-only design and the high variance in performance. In the laboratory, it is possible to identify how variables change with greater accuracy, but a limitation of laboratory tests of UER performance is that athletes are less likely to perform to exhaustion with the same intensity. A possible solution to this issue would be to assess runners performing in a treadmill competition [41, 49, 65, 125, 175] , or extrapolate from fixed workload results based upon established (linear) relationships between variables e.g. RPE and time. Researchers need to develop persuasive arguments to develop a research design where there are appropriate ecologically representative factors, but where there is sufficient control to identify variables that should cause changes in performance. As indicated in the psychology section of this article, investigating how changes in physiological capacity to cope with the demands of UER influence perceived ability to cope warrants investigation and it requires a detailed study that assesses perceptions of performance, and attributions of the causes of change along with physiological data.

Although controlled studies in controlled settings (e.g., a laboratory) can provide the opportunity for better isolating specific variables to test hypotheses rigorously, the conclusions of such studies may not carry over well to real-world scenarios. For example, studying running economy on inclines and declines is convenient on a laboratory treadmill where the precise grade and time-at-grade can be controlled. But those findings may be less applicable to undulating trail grades where the surface is full of rocks and a runner's technical abilities to move smoothly over such terrain with precise foot placement can have a larger impact on economy than laboratory-manipulated factors. Thus, it is important to be very careful that the laboratory is used for not only the control afforded but that the conditions will also provide useful results for real-world conditions. Specific physiological questions about factors involved in endurance running may be answered in the laboratory without being relevant to real-world conditions if researchers are not very careful about the questions asked and methodologies employed. To that end, many factors contribute to performance in UER that cannot reasonably be controlled or reproduced in a laboratory. Moreover, there is a severe limitation in laboratory experiments by virtue of the small sample sizes and short durations of study, as noted above. With online databases providing large datasets to lend statistical power sufficient to overcome variables beyond control, coupled with appropriate statistical tools to analyze such data, it may be possible to conduct retrospective, real-world natural experiments (and perhaps even experiments of nature) as have

been elegantly argued for by Joyner and colleagues in other domains of medicine, physiology, and exercise science [195, 196]. An online and freely accessible database like the Doubly Labelled Water Database (dlwdatabase.org) or Meta-analysis of Skeletal Muscle Response to Exercise (metamex.serve.scilifelab.se) would be an invaluable tool for researchers interested in conducting natural experiments. Athletes could connect their training- and race-tracking devices (e.g., GPS watches, power devices, heart rate monitors) much like they do to the proprietary analysis tools of the manufacturers (such as COROS Training Hub and Garmin Connect) or other platforms (such as Strava, Training Peaks, and Final Surge) along with other data they would be willing to provide (e.g., date of birth, sex, gender, height, weight, ethnicity, etc.).

10. **Conclusion**

Successful UER event performance requires a nuanced interplay between, and understanding of, the limits of athletically pertinent systems. Therefore, an interdisciplinary appraisal and prioritisation of performance limiting factors should be performed by athletes seeking to improve their UER performance (see Table 2 and 3, and Fig.3 for overview). While homo sapiens evolved to tolerate running long distances, humans are not optimally designed for such efforts. Furthermore, optimized strategies for the management of environmental, logistical, and gastrointestinal/nutritional challenges by athletes and their supporting practitioners are often required for successful completion and performance in races. As event duration increases, athletes and practitioners must focus on attenuating the progression of performance-limiting symptoms (e.g., GI distress, energy intake, dehydration, etc.). Performance can be further improved with appropriate monitoring, pacing and psychological strategies to combat fatigue. While running fitness and psychological capacities are required for all endurance running distances, the limits of UER event performance differ appreciably from those of traditional running distances, especially as the distances and durations increase. Enhancements in UER performance will likely come from advancements in managing the deterioration of the systems outlined in this review.

Author contributions

In line with the publisher's guidance for authorship, all authors have made substantial contributions to the conception or design of the work; (Nicolas Berger and Shawn Bearden) have drafted the work and revised it critically for important intellectual content; (all authors) have approved the version to be published; and (all authors) agree to be accountable for the parts of the work he or she has done, and are able to identify which co-authors are responsible for specific other parts of the work. In addition, all authors have confidence in the integrity of the contributions of their co-authors, as per ICMJE guidance (all authors).

Conflict of interest

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Tables (and captions)

Table 1. Physiological and psychological factors that impact and predict performance in an ultra-endurance running event

● Age; older athletes perform better (35-45 years peak performance)
● Maximal oxygen uptake; high $\dot{V}O_2$max improves performance
● Lactate threshold; high lactate threshold allows faster relative pace
● Running economy; lower relative O_2 cost improves performance
● Experience; more experienced runners perform better
● Gender; male athletes generally outperform female athletes
● Competitive level; previous performance at high level predicts better outcome
● Pacing ability awareness; even pacing strategy and pacing according to conditions improves performance
● Injury incidence & illness history; previous injury and/or illness can reduce performance
● Mental strength; ability to cope with complex situations increases performance
● Physical strength; strong musculoskeletal system improves performance
● Long-term goals; setting long-term achievable goals improves performance
● Short-term goals: setting specific achievable goals for the event improves performance
● Gastro-intestinal training status; training the gut improves performance
● Heat tolerance; ability to cope with hot environments improves performance

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Table 2. Factors that impact and predict performance during an ultra-endurance running event

● Environmental conditions – heat, cold, altitude
● Appropriate clothing and equipment choice for conditions (cold and wet vs hot)
● Kit choices, e.g., weight penalty vs benefits of using poles to decrease muscular damage
● Running pattern changes to reduce pain and muscle damage
● Carried or supplied foods not agreeing with the athlete
● Hydration and fuelling plan (liquid vs. solid; sports foods/fluids vs. real foods) not being tested in similar environmental and terrain conditions as event
● Accessibility of fluids/fuel - (carried vs. aid stations vs. both)
● Awareness that ingestion of food post event and in race conditions is often difficult due to GI distress.
● Taking alternative (fluid) formats to ensure some recovery, particularly important in multi-stage events.
● Knowledge on race stations for nutrition available, carrying items that are not available.
● Crew education, interaction and placement
● Self-awareness of body condition (in relation to hydration, sleep-deprivation, pace etc.)
● Underfoot conditions (track, road, trail, sand, ice, snow)
● Level of resilience
● Being prepared for potential scenarios that may arise
● Coping with fatigue, pain and discomfort

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Table 3. Factors that impact and predict performance when preparing for an ultra-endurance running event

● Physiological, biomechanical and psychological demands of event and individual athlete gap analysis to these demands
● Prioritised and targeted individual athlete interventions to enhance training and performance outcomes
● Optimised interventions, such as carbohydrate intake rates, sweat rates and gastro-intestinal impact
● Previous training loads - over the last years and especially over the last months before event
● Using the appropriate terrain to mimic target race profile (e.g., hilly vs. flat - net uphill vs. downhill etc) to train biomechanical / neuromuscular adjustments
● Having an appreciation for environmental challenges (e.g., altitude, terrain, temperature (hot vs. cold vs. wet, remoteness)
● Using appropriate evidence based environmental adaptation prior to event (e.g., altitude acclimation, heat adaptations etc.)

Table 4. Factors that change over the time-course of an ultra-endurance running event

● Heart rate ↑ without ↑ work rate
● Biomechanics: ↑step frequency with ↓ flight time.

● Cost of running ↑
● O_2 cost of exercise ↑
● Fat oxidation ↑
● Physical fatigability ↑
● Mental fatigability ↑
● Damage to lower limb tissue ↑
● Muscular fatigability ↑
● Locomotor muscle fatigability ↑
● Respiratory muscle fatigability ↑
● Cardiac fatigability ↑
● Core body temperature ↑
● Nausea ↑
● Gastro-intestinal discomfort ↑
● Pain ↑
● Perception of effort ↑
● Motivation ↑ and ↓ throughout
● Critical Velocity ↓
● Ability to digest exogenous carbohydrates ↓
● Carbohydrate oxidation ↓
● Hydration status ↓
● Maximal voluntary muscle strength ↓
● Neuromuscular function ↓
● Cognitive function ↓
● Feelings of vigour ↓
● Pace ↓
● Reaction time ↓
● Decision making ability ↓

Figure Legends

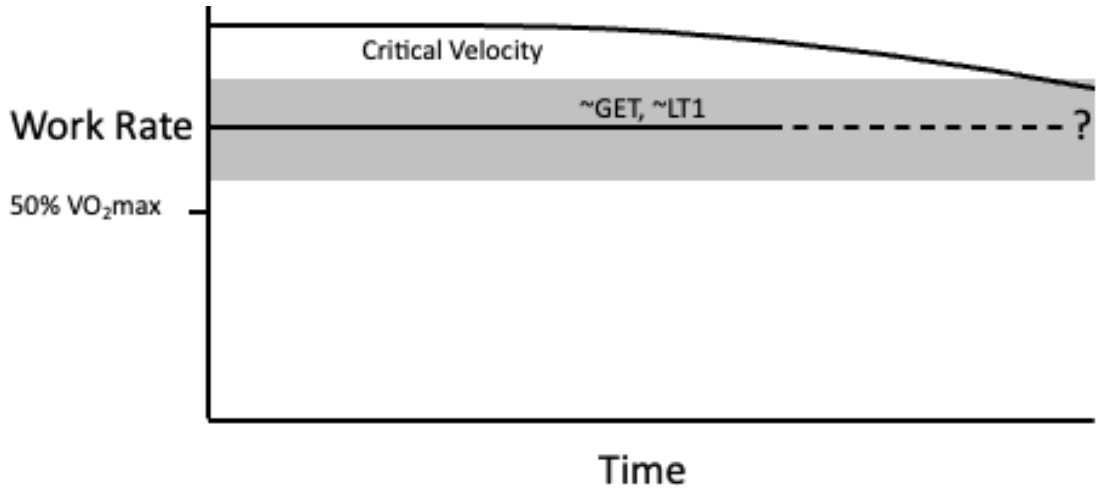

Figure 1. Illustration of fluctuation in work rate for ultra-endurance running events. Grey box = work rate for most ultra-endurance running events for elite athletes, including variable output within the event. Declining critical velocity (CV) may encroach or enter the range of work rates that were comfortably sustainable in the early hours of a race. Whether the metabolic underpinnings, and therefore the sustainability, of work rate at the gas exchange threshold (GET) or first lactate threshold (LT1) change as with CV is unknown. Work rates above CV will result in attainment of $\dot{V}O_2max$ (severe domain) or produce fatigue before it is obtained (extreme domain) [197].

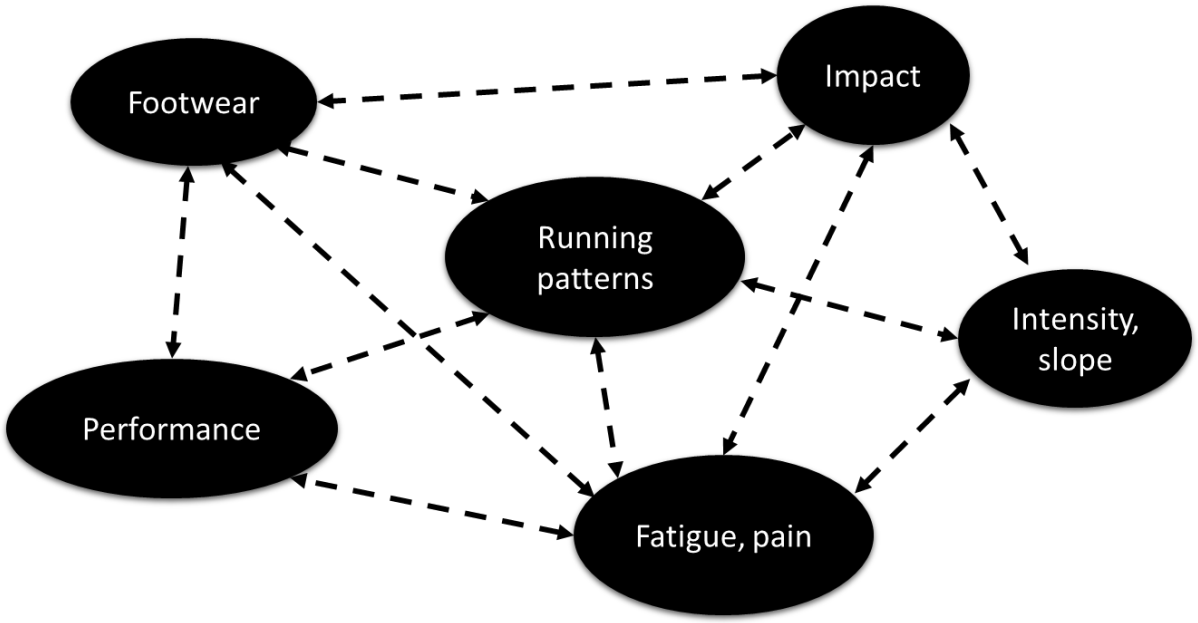

Figure 2. Main parameters influencing running biomechanics in ultra-endurance running events (adapted from M Giandolini's PhD thesis).

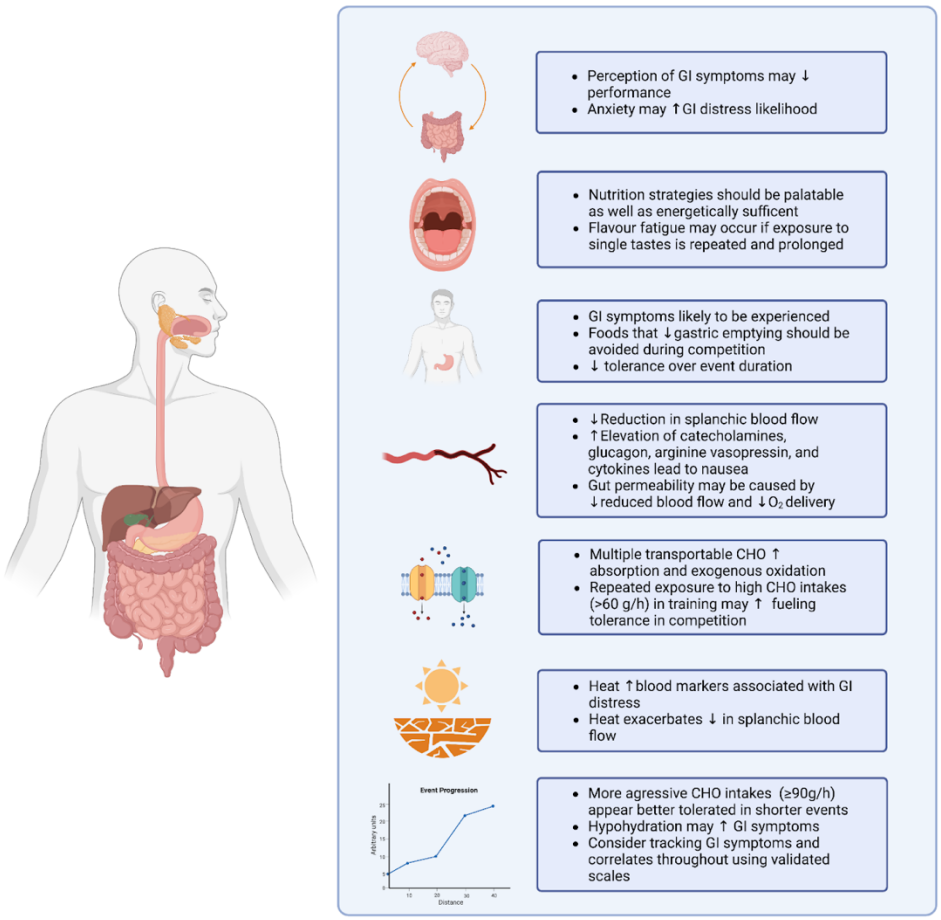

Figure 3. Gastro-intestinal (GI) symptoms and their causes, with potential solutions to minimise disturbance. Current best nutritional strategies to help alleviate GI distress.