



Sports Dietitians Australia and Ultra Sports Science Foundation Joint Position Statement: A Practitioner Guide to the Prevention and Management of Exercise-Associated Gastrointestinal Perturbations and Symptoms

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Abstract

It is now well-established that exercise can disturb various aspects of gastrointestinal integrity and function. The pathophysiology of these perturbations, termed “exercise-induced gastrointestinal syndrome (EIGS),” can lead to exercise-associated gastrointestinal symptom (Ex-GIS) inconveniences. EIGS outcomes can impact physical performance and may lead to clinical manifestation warranting medical intervention, as well as systemic responses leading to fatality. Athlete support practitioners seek prevention and management strategies for EIGS and Ex-GIS. This current position statement aimed to critically appraise the role of EIGS and Ex-GIS prevention and management strategies to inform effective evidence-based practice and establish translational application. Intervention strategies with mostly consistent beneficial outcomes include macronutrient (i.e., carbohydrate and protein) intake and euhydration before and during exercise, dietary manipulation of fermentable oligo-, di-, and mono-saccharides and polyols (FODMAP), and gut training or feeding tolerance adjustments for the specific management of Ex-GIS from gastrointestinal functional issues. Strategies that may provide benefit and/or promising outcomes, but warrant further explorations include heat mitigating strategies and certain nutritional supplementation (i.e., prebiotics and phenols). Interventions that have reported negative outcomes included low-carbohydrate high-fat diets, probiotic supplementation, pharmaceutical administration, and feeding intolerances. Owing to individual variability in EIGS and Ex-GIS outcomes, athletes suffering from EIGS and/or support practitioners that guide athletes through managing EIGS, are encouraged to undertake gastrointestinal assessment during exercise to identify underlying causal and exacerbation factor/s, and adopt evidence-based strategies that provide individualized beneficial outcomes. In addition, abstaining from prevention and management strategies that present unclear and/or adverse outcomes is recommended.

1 Background

It is now well established that taking part in exercise (i.e., hobby, fitness, and/or health) and sports activities (i.e., training and/or competition) can disturb various aspects of gastrointestinal integrity and function, leading to signs and symptoms of gastrointestinal abnormality. Early reports of abdominal pain and nausea in response to exercise stress have been documented in scientific literature for a century [1]. However, there is speculation that gastrointestinal complaints by those undertaking competitive sports activities have existed undocumented since the ancient and modern

Olympiad, which takes into account the reported historical perspective of competitive sports across centuries [2] and what is currently known about how exercise stress impacts the gastrointestinal system [3]. Awareness and understanding of “how and why” exercise stress disturbs the gastrointestinal tract, and subsequently promotes gastrointestinal symptoms, only started to develop during the 1980–90s, with landmark exploratory investigations reporting high incidence and severity of gastrointestinal symptoms in endurance-based exercise [4–8]. From a professional practice perspective, gastrointestinal disturbances and associated symptoms in response to exercise are seen as a common outcome in active and athlete populations adhering to training and/or competition schedules, comprising a substantial case load for practitioners (e.g., sports dietitians, sport and

Key Points

Clinical and non-clinical manifestations of exercise-induced gastrointestinal syndrome (EIGS) and subsequent debilitating exercise-associated gastrointestinal symptoms (Ex-GIS) are a common feature of exercise adherence and are exacerbated by various extrinsic and intrinsic factors.

Macronutrient intake during exercise, maintenance of euhydration, dietary manipulations (i.e., FODMAP), and gut training have been shown to provide beneficial outcomes in EIGS and/or Ex-GIS management; while heat mitigating strategies and certain nutritional supplementation (i.e., prebiotics and phenols) have shown promising outcomes, but other dietary manipulations and nutritional supplementation appear less favorable.

Individual athlete assessment, to established main causal factors of EIGS and Ex-GIS, aids tailored and effective prevention or management strategies in translational practice.

exercise nutritionists, and sports medical practitioners) [9, 10]. Indeed, it is evident at a global level that an increasing number of athletes and their support crews (e.g., sport institutes, sport and fitness professionals, coaches, and/or health professionals) are seeking referral for assessment, intervention, and monitoring for such exercise-associated gastrointestinal issues, especially in the endurance and ultra-endurance sports scene [11–14]. In addition, a substantial number of athletes also access local event medical crew support and/or management information, with the aim of seeking prevention or management of their unwanted and potential performance-debilitating exercise-associated gastrointestinal issues [15–17].

Such exercise-induced gastrointestinal disturbances can range from minor to major symptomatic inconvenience that may impact exercise performance; including reduced workload, cessation of exercise, or withdrawal from activity [17–20]. In turn, these symptoms may potentially signal more serious clinical concerns warranting medical attention; which may include, but are not limited to, fecal blood loss and acute colitis, [21–25] gastroparesis with or without ileus, [12, 26–28] sepsis (i.e., endotoxemia and bacteremia) with subsequent systemic inflammatory response and linked to the pathophysiology of heatstroke, [29–33] and/or chronic inflammatory diseases of the gastrointestinal tract in susceptible predisposed individuals [3]. It is therefore not surprising that there has been an exponential growth in exercise gastroenterology research focusing on strategies to prevent or manage (i.e., attenuate

or ameliorate the inevitable) the detrimental effects of exercise on the integrity and function of the gastrointestinal tract. Anecdotal evidence from case reports and referral platforms suggest that practitioners seek expertise in the scientific literature for evidence-based effective and efficient prevention and management strategies to support athletes that present with “exercise-associated gastrointestinal syndrome” (EIGS) and “exercise-associated gastrointestinal symptoms” (Ex-GIS). Therefore, this joint Sports Dietitians Australia (SDA) and Ultra Sports Science Foundation (USSF) position statement will focus on critically appraising the role of EIGS and Ex-GIS prevention and management strategies to provide guidance and recommendations for effective evidence-based practice and establish translational application. A scoping review style approach (i.e., PubMed, SPORTSdiscus, and Ovid Medline) was used to obtain and screen for relevant research studies (i.e., original investigation, field research, and case study, in healthy athlete or active populations) in the respective EIGS and/or Ex-GIS prevention or management strategy assigned to academics, researchers, and/or practitioners with established track records (i.e., research and/or professional practice) in the topic area. Only research papers that provided some level of research methodological competency and/or contributed to the consensus statement discussions were included. Gathered information was used by the author group to establish efficacy in prevention and management of disturbances to gastrointestinal integrity and function, systemic responses, and/or symptoms, with provisions towards a “grade of evidence” established by standardized assessment procedure and group consensus (Sect. 2).

1.1 Exercise-Induced Gastrointestinal Syndrome (EIGS)

The etiology and pathophysiology of EIGS is presented in Fig. 1 [3, 34]. EIGS comprises two primary pathophysiological pathways. The circulatory-gastrointestinal pathway describes the splanchnic hypoperfusion and gastrointestinal ischemia that occurs due to a redistribution of blood flow to skeletal muscle and peripheral circulation, addressing the metabolic and thermoregulatory demands of the exercise [35, 36]. Such typical physiological alterations in response to exercise may result in intestinal epithelial injury and hyperpermeability, as well as local and/or systemic inflammatory effects in response to translocated luminal originating pathogens, including but not limited to whole bacteria and/or bacterial endotoxins [33, 37–40]. The neuroendocrine-gastrointestinal pathway describes the stress response contribution to gastrointestinal integrity and functional disturbances, potentially via

increases in sympathetic activation and stress hormone responses [26–29]. These neuroendocrine stress responses are synonymous with impaired gastrointestinal motility, transit, digestive function, and nutrient absorption [26–28, 41–46]. They are likely associated with negative impacts on the myenteric and/or submucosal plexuses of the enteric nervous system, and/or the independent intestinal smooth muscle activation of interstitial cells of Cajal (i.e., pacemaker cells of the gastrointestinal tract that are coupled with gastrointestinal smooth muscle and epithelial tissue) [47–49]. Two additional pathways have been proposed, but still warrant substantial investigation for clarity in pathophysiological contribution. These include the mechanical strain of exercise (i.e., jarring, jolting, macro- and micro-vibrations, and/or tissue friction) on the splanchnic area and exaggerated metabolic responses to exercise (i.e., increased pH). First, biomechanical abnormalities aligned with mechanical strain on the splanchnic area may impact the circulatory-gastrointestinal and neuroendocrine-gastrointestinal pathways and potentially lead to hypersensitivity of epithelial, connective, and/or surrounding tissues of the gastrointestinal tract [7, 50]. Second, metabolic acidosis associated with high intensity exercise and hypoglycemia associated with prolonged endurance exercise have been identified as culprits in exercise-associated nausea [51–53].

1.2 Exercise-Associated Gastrointestinal Symptoms (Ex-GIS)

One of the predominant outcomes of EIGS, which has been established to affect exercise performance and may provide an indication of something more clinically sinister, is Ex-GIS. Several reviews have reported on the incidence and severity of Ex-GIS predominantly in observational field studies, specifically in endurance and ultra-endurance activities that focus on running and/or cycling modalities in both elite and recreational populations [17, 20, 60–62]. Reported studies applied baseline and/or retrospective post-race gastrointestinal symptoms (GIS) subjective assessment tools of different origins and applications (e.g., established or in-house fabrications, Likert-type or visual analog scale). Considering the difference in methodological approach, it is not surprising that a large variation in symptom incidence and severity is evident. These range from negligible Ex-GIS incidence in a recreational endurance running event, [61] 4% after marathon competition, [20] and $\geq 93\%$ in response to ultra-endurance event participation, [19, 63] with severity ranging from minor inconvenience to severe that warranted event withdrawal. These and other reports provide some indication that longer-duration exercise, especially when conducted in hot ambient conditions, tends to promote higher incidence rates of Ex-GIS [17]. Moreover, longer

duration exercise bouts that require exogenous feeding tend to induce more Ex-GIS incidence despite a lower exercise intensity, which has been linked to individual variation in feeding tolerance [20, 41–43, 64–66]. To improve consistency in Ex-GIS interpretation within exercise gastroenterology research, the use of a standardized exercise-specific validated and reliable GIS assessment tool has been recommended [67, 68].

The type of Ex-GIS reported, in accordance with the ROME criteria for symptom type (i.e., currently ROME IV criteria), [69, 70] can be classified as either gastro-esophageal (i.e., upper-GIS): belching, heartburn (gastroesophageal reflux), upper-abdominal bloating or pain, urge to regurgitate, and/or regurgitation; intestinal (i.e., lower-GIS): flatulence, lower abdominal bloating or pain, urge to defecate, abnormal defecation, and/or fecal blood loss; and/or other symptoms not otherwise specified (i.e., nausea and acute transient abdominal pain—stitch) [68]. Despite mainstream dogma proposing that lower-GIS symptoms (e.g., diarrhea) are more commonly linked to exercise, the scientific literature does not support this notion, with upper-GIS consistently being more commonly reported during and/or immediately after exercise, both in laboratory controlled and field-based experimental models [17, 20, 42, 71–73]. In addition, nausea appears to be a frequently reported symptom in ultra-endurance activities, [19, 20, 63, 74] which is rarely reported in lesser exercise loads or experimental models [20, 44, 61, 65, 72]. Taken together, the available research suggests that the magnitude (i.e., exercise duration, intensity, and environmental factors) of exertional stress and requirement for feeding during the exercise plays a key role in Ex-GIS incidence and severity. The incidence type, severity, time of onset, and when symptoms subside may provide some indication of relationships between Ex-GIS and EIGS pathophysiology (Fig. 1).

1.3 EIGS and Ex-GIS Exacerbation Factors

Several extrinsic and intrinsic factors have now been identified and/or confirmed to exacerbate EIGS and Ex-GIS, ranging from minimal, to modest, to more extensive impact; which has been summarized in Table 1. Consensus impact was assigned on the basis of: (1) the number of research studies (i.e., cross-sectional analysis, exploratory, or intervention laboratory-controlled trials) investigating the impact of the exacerbation factor or factors on gastrointestinal and/or systemic perturbations to exercise; (2) the quality of experimental procedures and control of confounding factors in accordance with exercise gastroenterology research best-practice recommendations checklist [67]; (3) the magnitude of response (i.e., none, to modest, to clinically relevant minimal detectable change) of any identified gastrointestinal and/or systemic perturbations to exercise [33]. Assigned magnitude of impact on EIGS and/or Ex-GIS may include:

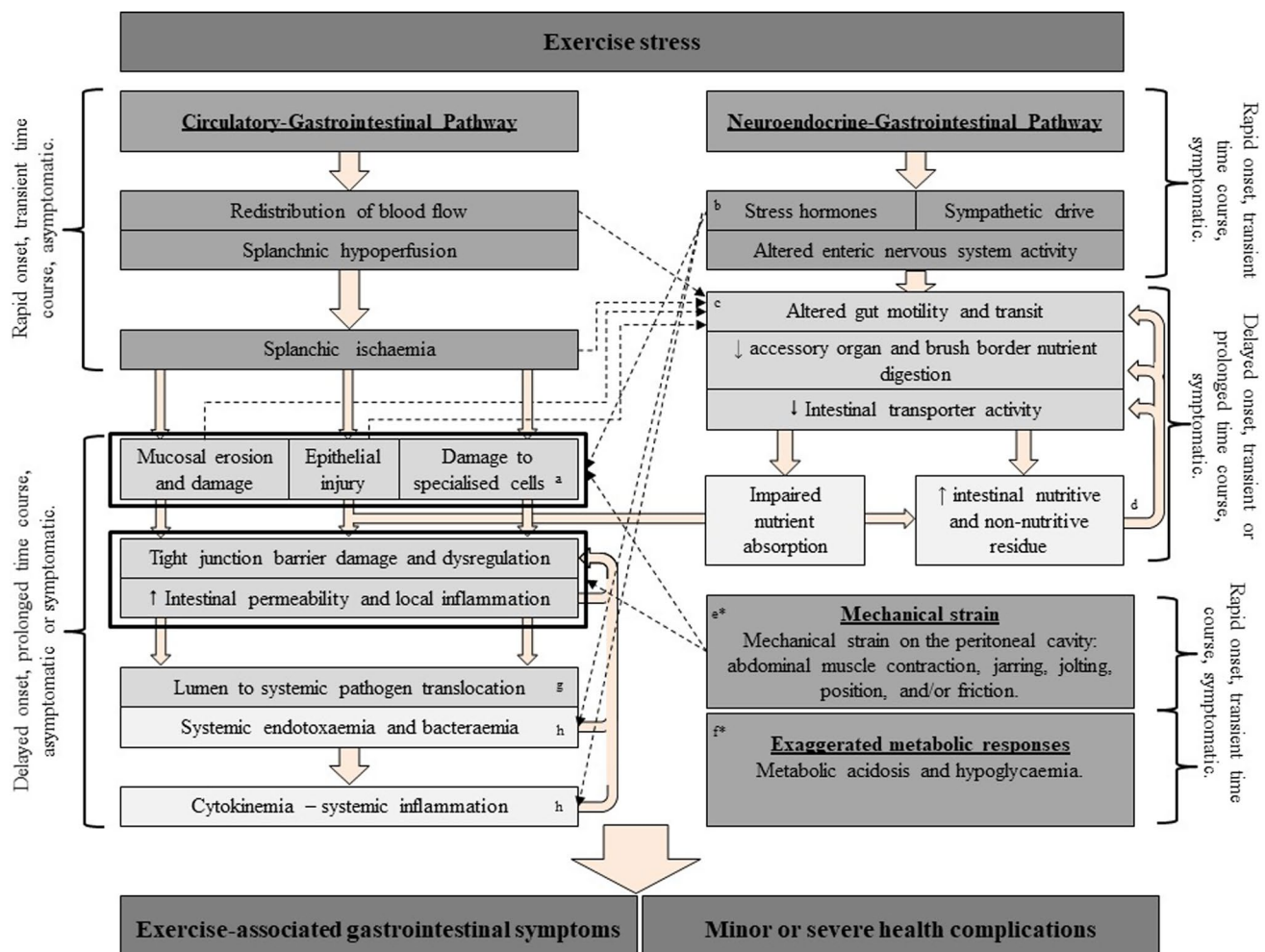


Fig. 1 Updated schematic description of exercise-induced gastrointestinal syndrome (EIGS) and links to exercise-associated gastrointestinal symptoms (Ex-GIS). Text boxes: Darkest grey, instigation and final outcome; dark grey, primary causal mechanisms; medium grey, secondary outcomes to the causal mechanisms; light grey, subsequent follow-on outcomes in response to the secondary outcomes. Beige arrows indicate EIGS pathway flow and direction, and black arrows indicate intra-EIGS linkage. ^aSpecialized antimicrobial protein-secreting (i.e., Paneth cells) and mucus-producing (goblet cells) cells aid in preventing intestinal-originating pathogenic microorganisms entering systemic circulation. ^bIncrease in neuroendocrine activation and suppressed submucosal and myenteric plexuses may result in epithelial cell loss and subsequent perturbed epithelial tight junctions [49, 54]. ^cSplanchnic hypoperfusion and subsequent intestinal ischemia and injury (including mucosal erosion) may result in direct (e.g., enteric nervous system and/or enteroendocrine cell) or indirect (e.g., braking mechanisms) alterations to gastrointestinal motility [27–29, 37, 55]. ^dGastrointestinal brake mechanisms: nutritive and non-nutritive residue along the small intestine, including the terminal ileum, results in neural and enteroendocrine negative feedback to gastric activity [44, 55–58]. ^eAggressive acute or low-grade, prolonged mechanical strain is proposed to contribute to disturbances

to epithelial integrity (i.e., epithelial cell injury and tight junction dysregulation) and subsequent “knock-on” effects for gastrointestinal functional responses [50]. ^fMetabolic acidosis associated with high intensity exercise and hypoglycemia associated with prolonged endurance exercise may prompt Ex-GIS [51–53]. ^gLumen originating to circulatory translocation of pathogenic agents may include, but is not limited to: whole bacteria, bacterial endotoxins (e.g., lipopolysaccharide, lipid A, flagella, and/or peptidoglycan), exocrine originated digestive enzymes, and/or food protein allergens [38]. ^hBacteria and bacterial endotoxin MAMPs and stress induced DAMPs are proposed to contribute toward the magnitude of systemic immune responses (e.g., systemic inflammatory profile) [59]. ^{*}Primary role in EIGS pathophysiology still warrants substantial exploration and investigation. EIGS, exercise-induced gastrointestinal syndrome; GIS, gastrointestinal symptoms; MAMPs, microorganism molecular patterns; DAMPs, danger-associated molecular patterns. Adapted with permission from “Systematic review: exercise-induced gastrointestinal syndrome- implication for health and disease,” by R.J.S. Costa, R.M.J. Snipe, C. Kitic, and P. Gibson, 2017, *Alimentary Pharmacology and Therapeutics*, 46(3), pp. 246–265. Copyright 2017 by John Wiley & Sons Ltd. [3]

unknown (?), minimal (+), moderate (++) , and extensive (+++). These factors and their potential magnitude of impact need to be considered when assessing the potential

effectiveness of proposed prevention or management strategies for EIGS and Ex-GIS, and using such strategies for individual athlete therapeutic intervention. This is important,

as these constitute potential confounding factors for exercise-associated disturbances to gastrointestinal integrity and function and systemic immune responses [12, 75].

2 Methodological Considerations in Exercise Gastroenterology Research and Translational Practice

In the last decade, there has been exponential growth in EIGS and Ex-GIS prevention and management strategy research in response to potential performance and health implications. It has, however, been highlighted that a large proportion of EIGS and Ex-GIS prevention and management strategy intervention studies contain substantial limitations in experimental methodologies to a degree that may influence data outcomes and interpretations in professional practice [67]. Areas of identified methodological concern include, but are not limited to: the clear selection and screening of participants; the justification of exercise protocols (e.g., intensity, duration, and modality); ambient temperature control and/or application of sufficient heat stress; dietary control and nutritional provision before and during exercise; regulation and monitoring of hydration status; the justification of EIGS measurement variables (e.g., intestinal epithelial tissue integrity and pathogenic translocation biomarkers, systemic inflammatory response biomarkers, and/or gastrointestinal functional responses) and application of a suite of such markers; and the choice of Ex-GIS assessment tool employed. In addition, the consideration for other identified outcome and interpretation impacting factors have been acknowledged, such as power calculations to support sample size; data presentation (i.e., baseline values, absolute and relative change); inclusion of broad heterogeneous populations (e.g., biological sex, age, fitness status, and/or modality participation); and/or inclusion of confirmed erroneous measurement variables and analytical techniques. It has been argued that “such limitations increase the risk of misrepresenting research outcomes, which can have significant translational implications for practitioners, with outcomes ranging from ineffective interventions to the risk of fatality” [67]. In the context of the current review, the experimental design checklist, as presented in Costa et al. (2022), was followed to ascertain the experimental quality and subsequent justification for inclusion in assessing the level of evidence for overall therapeutic strategy efficacy in the prevention and management of EIGS and Ex-GIS. Table 2 provides details of categories and types of disturbance to gastrointestinal integrity and function, and systemic responses, commonly reported in the published literature. In addition, it provides a level of evidence based on best practice recommendations in exercise gastroenterology research. Research that predominantly meets best-practice recommendations in

exercise gastroenterology research may be assigned “Grade I” or “Grade II” level of evidence, while research that does not predominantly meet best-practice criteria is limited to “Grade III” evidence.

3 EIGS and Ex-GIS Prevention and Management Strategies

To assess the impact of researched interventions on the prevention and management of the various primary causal mechanisms, pathophysiological pathways, secondary outcomes, performance and/or clinical manifestation, Table 2 provides a general overview of exercise-associated gastrointestinal disturbance categories and outcomes. Table 3 presents a summary of evidence of efficacy. The level of evidence used, after screening for best practice experimental quality, [67] is also described in Table 2 and was adapted from levels of evidence presented in Thomas et al. [107]. Areas of coverage include macronutrient intake before and during exercise, dietary interventions, nutritional supplement interventions, hydration status, heat stress mitigating strategies, gut training and tolerance to feeding during exercise (supplementary file 1) in specific relation to Ex-GIS. Other prevention and management strategies (i.e., physical applications and pharmaceutical interventions) and considerations (i.e., recovery nutrition) explored are presented in the supplementary materials (supplementary file 2).

4 Macronutrients and Derivatives

A variety of macronutrients or their derivatives, which are consumed for a short- (< 24 h) or long-term ($\geq$ 24 h) period before and/or during an exertional or exertional-heat stress model, have been studied for their efficacy in the prevention and management of EIGS. These include carbohydrate, protein, certain singular amino acids (i.e., glutamine, cysteine, arginine, and/or L-citrulline), and amino acid mixture formulations. Such nutritional intervention approaches appear to target splanchnic perfusion dynamics via villi microvascular regulation, epithelial cell metabolism and/or stability, and/or epithelial tissue tight-junction stability [37, 108–112].

4.1 Carbohydrate

Carbohydrate ingestion during prolonged exercise is common practice, and its effects on EIGS and Ex-GIS are therefore of interest. Carbohydrate ingestion immediately before or during exercise may attenuate disturbances to gastrointestinal integrity associated with EIGS through postprandial hyperemia [108, 112]. Carbohydrate ingestion during exercise also aids the maintenance of blood glucose that

Table 1 Summarized overview of extrinsic and intrinsic exacerbation factors of exercise-induced gastrointestinal syndrome (EIGS) and exercise-associated gastrointestinal symptoms (Ex-GIS). Critical explanation includes impact on markers of gastrointestinal integ-

ity and function, systemic responses, symptomology, and degree of exposure required to instigate perturbation to minimal detectable change [33]

Factors	Impact	Description	References
Extrinsic factors			
Exercise duration	+++	- Increasing exercise duration, irrespective of intensity, results in increased EIGS integrity and systemic response biomarkers and Ex-GIS, likely attributed to splanchnic hypoperfusion and subsequent gastrointestinal ischemia - Exercise stress per se impairs gastrointestinal function without any duration impact (i.e., 1–3 h of exercise comparison), likely attributed to sympathetic drive and stress hormone responses, with or without splanchnic hypoperfusion effects - Considerable perturbations occur with ≥ 2 h exercise duration compared with < 2 h, but appears to plateau ≥ 2 h thereafter - Substantial Ex-GIS, with episodes of medical management, in prolonged endurance and ultra-endurance events. However, the full impact of ultra-endurance exercise activities on EIGS integrity/systemic and functional outcomes is still unknown and warrants further exploration	[17, 26, 28, 71, 76]
Exercise intensity	++	- Increasing exercise intensity (e.g., continuous $\geq 70\%$ $\text{VO}_{2\text{max}}$ or HIIT or resistance exercise of ≤ 2 h) results in modest increases in EIGS integrity and systemic response biomarkers, functional responses, and Ex-GIS	[33, 40, 77–80]
Exercise modality	+	- Field exploratory studies suggest running-based activities prompt greater gastrointestinal disturbance and Ex-GIS compared with swimming and cycling (i.e., with or without inclusion in triathlon events) modalities, proposed to be linked with the addition of mechanical strain on the splanchnic area - Controlled laboratory studies have not provided substantial evidence to suggest exercise modality differences (i.e., running vs. cycling) for markers of EIGS and Ex-GIS - Impact of other exercise activities with respective body positioning and mechanical strain (e.g., swimming, canoeing and kayaking, motor and/or winter sports) on EIGS markers and Ex-GIS is warranting exploration	[7, 20, 81]

Table 1 (continued)

Factors	Impact	Description	References
Environmental conditions	+++	- Exercising in hot ambient conditions (e.g., $\sim 35^{\circ}\text{C}$), irrespective of relative humidity, results in increases in EIGS integrity and systemic response biomarkers, and Ex-GIS. Correlation and regression analysis have confirmed a positive association and prediction between maximal and Δ core body temperature with pathophysiological markers of EIGS. Core body temperature values of $\geq 39.5^{\circ}\text{C}$ or $\Delta \geq 2.5^{\circ}\text{C}$ indicative of clinical significance^a, but values of $\geq 39.0^{\circ}\text{C}$ or $\Delta \geq 2.0^{\circ}\text{C}$ are reported above minimal detectable change and of clinical relevance - Exercise stress per se impairs gastrointestinal function without any substantial additional heat stress impact - Other thermoregulatory modifiers that may influence maximal (e.g., $\geq 39^{\circ}\text{C}$) or magnitude of change ($\geq 2^{\circ}\text{C}$) in core body temperature (e.g., clothing, wind speed, water temperature, hydration status, heat acclimation/acclimatization and/or individual thermoregulatory responses (i.e., heat tolerance) may result in increases in EIGS integrity and systemic response biomarkers, and Ex-GIS	[27, 33, 72, 82, 83]
Topographical elevation*	+	- Some evidence suggested that altitude (e.g., > 2500 m ASL) at which exercise is performed may increase disturbances to gastrointestinal integrity and function, and subsequently exacerbate Ex-GIS. However, further and repeatable exploration of the impact of altitude on EIGS integrity and functional markers is warranted	[11, 84–86]
Time of day exercise is performed (circadian variation)	++	- Nocturnal exercise prompts greater disturbance to gastrointestinal function responses and subsequent Ex-GIS compared with diurnal exercise - No effect of nocturnal versus diurnal exercise on EIGS integrity and systemic biomarkers	[26]
External pharmaceutical administration	+++	- Nonsteroidal anti-inflammatory drugs (NSAIDs) are considered gastrointestinal irritants, impacting stomach gastric secretions, bicarbonate release in the duodenum, and/or erosion of the mucosal lining along the gastrointestinal tract - The administration of NSAIDs prior to exercise can markedly increase gastrointestinal integrity perturbations, impair functional responses, and/or exacerbate Ex-GIS	[87–92]
Intrinsic factors			
Biological sex*	+	- Differences in gastrointestinal integrity and function, systemic responses, and Ex-GIS between male and female participants in exercise gastroenterology research have been observed. Outcomes have not been consistent, with both biological sexes reporting varied markers of EIGS and Ex-GIS dependent on the experimental model. Any differences have also been low to modest in nature - It is proposed that female athletes present greater EIGS and Ex-GIS than male athletes owing to the menstrual cycle. However, clear and consistent evidence with substantial magnitude to support this plausibility is still warranted	[42, 93–95]

Table 1 (continued)

Factors	Impact	Description	References
Age*	+	- Some speculation has suggested that the developing gastrointestinal tract and immune system of youth athletes (≤ 18 years) may result in greater EIGS marker responses and Ex-GIS compared with well-trained and exercise-experienced adults. However, current evidence suggests any age-related differences are modest in nature - Despite active older adults (≥ 40 years) presenting differences in gut bacterial composition (i.e., fecal profile) compared with younger active adults (≤ 30 years), only modest differences have been reported in EIGS integrity and/or systemic biomarkers, and Ex-GIS, between these two age populations - The full extent of exertional or exertional-heat stress on EIGS integrity/systemic and functional outcomes and Ex-GIS in developing youth athletes and older masters athletes is still unknown and warrants exploration	[93, 96–98]
Fitness status	+	- Higher-trained individuals, and individuals with the ability to cope with greater exertional or exertional-heat stress loads (i.e., duration, intensity, and heat), are at lower risk of EIGS compared with lower-trained individuals at the same absolute load. However, the ability to cope inevitably exposes higher-trained individuals to these higher exertional or exertional-heat stress loads and subsequently poses greater relative EIGS and Ex-GIS risk - Higher-trained individuals have a greater ability to cope with feeding and/or drinking during exercise (i.e., greater feeding tolerance) and the same absolute intake (i.e., volume, concentration, type, and/or texture); therefore, they present lower risk of Ex-GIS. However, the ability to better cope with feeding during exercise inevitably pushes higher trained individuals to attempt greater feeding volumes, and subsequently poses greater relative Ex-GIS risk	[15, 16, 20, 65, 66, 99]
Gastrointestinal and/or circulating microbial and/or short chain fatty acid composition*	+	- The bacterial composition of the gastrointestinal tract (i.e., commensal versus pathogenic bacteria), and subsequent levels of short chain fatty acids (SCFAs; e.g., acetate, butyrate, and/or propionate) in the lumen and/or circulation may impact the magnitude to which gastrointestinal integrity and systemic responses are perturbed, and Ex-GIS are instigated, in response to exertional or exertional-heat stress	[29, 33, 93]

Table 1 (continued)

Factors	Impact	Description	References
Individual characteristics*	+++	- The feeding tolerance to food and/or fluid intake volume (e.g., mL/h), concentration (e.g., 6% versus > 10% carbohydrate solution), type (e.g., macronutrient profile and/or singular versus multiple transportable carbohydrates), and texture (e.g., solid versus liquid) may increase the risk of EIGS and Ex-GIS (Supplementary file 1) - Individuals presenting gastrointestinal structural or function diseases or disorders may be predisposed to greater incidence and severity of EIGS and Ex-GIS - Individuals with recurrent Ex-GIS with or without etiological and/or pathophysiological confirmation and/or clinical diagnosis are likely to present more incidence and severity of EIGS and Ex-GIS	[12, 41–43, 64, 66, 100, 101]
Psychological state*	?	- It has been proposed that a pre-exercise state of anxiety is linked to Ex-GIS on the basis of field exploratory observations and/or survey/questionnaire research designs. Such experimental approaches lack the rigors of laboratory and confounder-control experimental protocols, as previously described in pre-exercise mental prompts and physiological response to exercise [102]. To date, only one study has explored the role of pre-exercise anxiety state using a sport anxiety questionnaire of EIGS integrity, systemic, and/or functional markers, and subsequent Ex-GIS, using controlled experimental procedures [106]. Somatic trait anxiety scores were not correlated with Ex-GIS in both exercise trial occasions (i.e., pre- and post- intervention)	[103–105]

Impact on magnitude of response in EIGS markers and Ex-GIS include: unknown: ?; minimal: +; modest: ++; extensive: +++; and further research warranted since current literature provides only extrapolation of study outcomes and speculation: *. Comments and impact outcomes are a general representation of reference literature. The high variability in intra- and inter-individual responses in EIGS markers and Ex-GIS in response to exertional and exertional-heat stress models, and feeding tolerance (i.e., volume, concentration, type, and texture) intake during exercise, is acknowledged. ^aClinical significance: above established minimal detectable change, and/or aligned with impacting exercise output, severe Ex-GIS, and/or warranting medical management. The role of dietary intake and hydration status as potential intrinsic exacerbation factors is covered in Sects. 5 and 7, respectively

ASL, above sea level; EIGS, exercise-induced gastrointestinal syndrome; Ex-GIS, exercise-associated gastrointestinal symptoms; h, hours; HIIT, high intensity interval training; NSAIDs, non-steroidal anti-inflammatory drugs; SCFA, short chain fatty acids; VO_{2max} , maximal oxygen uptake

attenuates stress hormone responses and potential rises in systemic inflammatory cytokines; [73] thus, it may play a role in mitigating EIGS. On the contrary, excessive carbohydrate ingestion and the type of carbohydrate ingested during exercise may adversely affect the function of the gastrointestinal tract (e.g., delayed gastric emptying and/or malabsorption) and lead to Ex-GIS, subsequently impacting exercise performance (Sect. 9 and supplementary file 1).

The majority of research to date suggests that carbohydrate ingestion before and/or during exercise can minimize or prevent perturbations to gastrointestinal integrity [73, 114–116]. For example, carbohydrate doses of 15.0–22.5 g every 15–30 min (20–90 g/h) during cycling or running

exercise of 1–2 h duration, with or without heat exposure (32–35 °C and 27–70% relative humidity (RH)), has attenuated the rise in plasma intestinal fatty acid binding protein (I-FABP; a surrogate biomarker indicative of intestinal epithelial cell injury) concentration and small intestine permeability (i.e., via dual-sugars test for lactulose to rhamnose (L:R) ratio) compared with ingestion of water alone [73, 114–117]. Two studies did not observe a reduction in I-FABP with carbohydrate intake of 27 g/h during 60 min running (70% VO_{2max} , 30 °C) and 108 g/h during 3 h cycling [118, 119]. However, these studies failed to show any substantial increase in I-FABP compared with the control, suggesting that the lack of effect may be due to insufficient

Table 2 Categories of exercise-associated gastrointestinal disturbance (A) and level of evidence for establishing efficacy of exercise-induced gastrointestinal syndrome (EIGS) and exercise-associated gastrointestinal symptoms (Ex-GIS) prevention and management strategies (B)

A. Disturbance category		Disturbance type	
Gastrointestinal epithelial integrity		Intestinal epithelial tissue injury, tight-junction protein injury, gastrointestinal permeability, systemic endotoxemia and/or bacteremia	
Gastrointestinal function		Gastric emptying, intestinal transit, nutrient absorption, smooth muscle myoelectrical activity, and/or malabsorption of feeding challenge	
Systemic responses		Leukocyte trafficking, systemic inflammatory cytokine responses, immune functional response to endotoxemia and/or bacteremia	
Gastrointestinal signs and symptoms		Gut comfort, total-GIS symptoms, upper-GIS symptoms, lower-GIS symptoms, nausea, regurgitation or projectile vomiting with or without blood loss, abnormal defecation with or without blood loss	
Feeding tolerance		Taste and/or flavor fatigue, interest in food/drink, tolerance in food/drink, appetite, and thirst, with or without GIS impact	
B. Grades of evidence*		Description exemplar	Practical application
Good	Grade I	SLR, RCT, and/or original investigation with predominantly repeatable and consistent outcomes**	Yes
Fair	Grade II	RCT and/or original investigation**; however, limited to single or minimal studies	Yes
Limited	Grade III	RCT and/or original investigation, with limited, conflicting or unclear outcomes, with or without single or minimal studies	Yes—with caution and justification
Not fully supported or refutable	Grade IV	Original investigation with or without questionable, conflicting, inconsistent outcomes, and/or unclear in nature (i.e., methodologies and results including data analysis and interpretation)	Not warranted and justified, or application with caution and justification
No clear evidence	Grade V	Field observational data, or individual case-study and case-series approaches	Not warranted or justified
No clear evidence		Not assignable—no evidence to support or refutable conclusions	Not warranted or justified

* Adapted from Thomas et al. [107]. ** Predominately based on experimental procedure best practice recommendation checklist from Costa et al. [67]. Further discussion within each specific section when experimental protocols do not adhere to proposed best practice guidance. GIS, gastrointestinal symptoms; RCT, randomized control trial; SLR, systematic literature review

Table 3 Summary of the efficacy of proposed exercise-induced gastrointestinal syndrome (EIGS) and exercise-associated gastrointestinal symptoms (Ex-GIS) prevention and management strategies taking into account: (1) experimental procedures following best practice recommendation, and (2) magnitude of impact in reducing EIGS assessment markers and Ex-GIS

Intervention	Integrity	Function	Systemic	Ex-GIS	Grade of evidence	EIGS/Ex-GIS potential prevention and management strategy	Key comments
Macronutrients (Before and/or during)							
Carbohydrate	✓	? ^a	✓	N and X ^a	I	Yes/Yes	Ex-GIS: volume and type dependent
Glutamine	N and ?	?	N	N	III	No/No	Unclear due to inconsistent research outcomes and research methodological issues in some studies**
Arginine	N	?	N	X	III	No/Yes	Avoid intake to ↓ Ex-GIS
Citrulline	✓	?	N	?	II	Yes/No	Benefit possibly aligned with nutrient presence
Amino acid combinations	✓	?	✓	N	II	Yes/Yes	Dependent on specific formulations
Whole protein	✓	?	✓	X	II	Yes/Yes	Ex-GIS: volume and tolerance dependent
Dietary interventions (short- and/or long-term)							
Gluten-free diet	N	?	N	N	III	No/No	Gluten free diets inadvertently reduce FODMAP load
Low FODMAP diet	X	✓	N	✓	I	No/Yes	↑ EIGS pathophysiology, but ↓ Ex-GIS severity. ↓ malabsorption risk from a functional perspective
High FODMAP diet	✓	X	N	X	I	Yes/No	↓ EIGS pathophysiology, but ↑ Ex-GIS severity. ↑ malabsorption risk from a functional perspective
LCHF	X	?	X	?	II	No/No	Dietary lipid intake and digestion/absorption are synonymous with luminal pathogenic translocation
LEA (short-term)	N	?	N	N	III	No/No	Longer periods of LEA leading to REDs diagnosis may result in EIGS and/or Ex-GIS
Low fiber/residue diet	?	?	?	✓	IV	No/Yes	Only field observational data and case study approach evidence available. No controlled experimental trial data available
Nutritional supplements (short- and/or long-term)							
Antioxidant—Ascorbic acid	✓	?	?	?	V	No/No	Research methodologies not aligned with best practice recommendations**
- Tocopherol	N	?	?	✓	IV	No/No	Research methodologies not aligned with best practice recommendations**
- Capsaicin	?	?	N	X	III	No/No	Supplementation resulted in greater Ex-GIS incidence
Biotics- Prebiotics	✓	N	N	N	II	Yes/No	Also refer to FODMAP research, considering the prebiotic properties of FODMAP
- Probiotics	N	?	N	N	I	No/No	Proposed outcomes from SLR
- Synbiotics	N	?	N	N	I	No/No	Proposed outcomes from SLR
Bovine colostrum	N	?	N	?	II-III	No/No	Unclear due to inconsistent research outcomes and research methodological issues in some studies**
Curcumin	✓	?	✓	?	III	Yes/No	Further research using more methodologically robust studies is required to establish clinical or practice relevance**
Anthocyanins	✓	?	N	?	III	Yes/No	Only modest attenuation observed in intestinal epithelial injury, with no effects on pathogenic translocation observed
Nitrate	N	?	N	N	III	No/No	Further research using more methodologically robust studies are required to establish clinical or practice relevance**

Table 3 (continued)

Intervention	Integrity	Function	Systemic	Ex-GIS	Grade of evidence	EIGS/Ex-GIS potential prevention and management strategy	Key comments
Hydration strategies							
Pre-exercise euhydration	✓	✓	?	✓ and X ^a	II	Yes/Yes	Start exercise euhydrated, but without fluid overload that may overburden gastric tolerance
During exercise euhydration	✓	✓	N	N and X ^a	II	Yes/Yes	Maintain euhydration, but without fluid overload that may overburden gastric tolerance
Heat mitigating strategies							
Heat acclimation	N	?	N	N	III	Yes/Yes ^b	Positive impact on core body temperature evidence; but further research with longer exposure is warranted to thoroughly assess impact on EIGS
Internal pre- and per-cooling	N	?	N	N	III	Yes/Yes ^b	Positive impact on core body temperature evidence; but further research on pre- and/or per-cooling, with or without external cooling strategies, is warranted to thoroughly assess impact on EIGS
External pre- and per-cooling	?	?	✓	?	III	Yes/Yes ^b	Positive impact on core body temperature evidence; but further research on pre- and/or per-cooling, with or without internal cooling strategies, is warranted to thoroughly assess impact on EIGS
Gut training							
Repetitive feeding challenge	N	✓	?	✓	I	No/Yes	Magnitude of effect dependent on repetitive challenge exposure (i.e., quantity, quality, and duration), and individual responsiveness
Noncaloric sweeteners	?	?	?	N	III	No/No	Only one study that used sucralose pre-exercise, and Ex-GIS was a secondary variable of focus
Fluid tolerance training	?	?	?	✓	III	No/Yes	Only one study that used sweat rate matched fluid challenge versus ad libitum (within comfort), and Ex-GIS was a secondary variable of focus
Other strategies							
Pharmaceutical administration							
- Antiemetics	?	?	?	N	V	No/No	One serotonin 5-HT ₃ receptor antagonist field-based study, with no confounder control, and only assessed nausea and vomiting
- Antacids	✓	?	?	✓	IV	No/No	H ₂ receptor antagonists and proton-pump inhibitor field-based studies with no confounder control, and only assessed nausea, vomiting, and/or fecal blood presence
Physical maneuvers	?	?	?	✓	IV	No/No	Only one study that focused on reducing Ex-GIS intensity with proposed physiological maneuver
- Abdominal muscle contraction,							
- Modified breathing,							
- Abdominal belt tightening							
Compression socks	✓	?	?	?	IV	No/No	Only one study that applied a parallel intervention experimental design in a field race, with no adequate confounder control
Feeding tolerance***							
Intake volume	-	-	-	X	I	-/Yes	↑ volume ↑ the risk of Ex-GIS
Carbohydrate concentration	-	-	-	X	I	-/Yes	↑ carbohydrate intake concentration ↑ the risk of Ex-GIS

Table 3 (continued)

Intervention	Integrity	Function	Systemic	Ex-GIS	Grade of evidence	EIGS/Ex-GIS potential prevention and management strategy	Key comments
Carbohydrate dose and frequency	-	-	-	X	III	-/Yes	↑ carbohydrate intake dose and ↓ frequency increases the risk of Ex-GIS
Intake texture form	-	-	-	X	I	-/Yes	Ex-GIS risk ↑ from liquid to solid form
Carbohydrate type							
- Fructose	-	-	-	X	II	-/Yes	↑ fructose intake ↑ risk of Ex-GIS
- Glucose molecular weight	-	-	-	N	II	-/No	↑ in molecular weight of carbohydrate type does not generally and substantially ↑ the risk of Ex-GIS
- Isomaltulose	-	-	-	X	IV	-/No	↑ Ex-GIS with singular isomaltulose use
- Multiple transportable carbohydrates	-	-	-	N	III	-/No	Contradictory findings, methodological issues, and questionable result interpretation in research that has explored Ex-GIS on the impact of multiple transportable carbohydrate blends versus singular carbohydrate on Ex-GIS. Onset of Ex-GIS appears to depend on individual tolerance and linked to malabsorption (i.e., namely fructose)
- Modified starch	-	-	-	X	III	-/Yes	Use of modified starch carbohydrate ↑ risk of Ex-GIS
- Hydrogel	-	-	-	N	I	-/No	Use of hydrogel carbohydrate products pre- and/or during exercise does not lower the incidence or severity of Ex-GIS
Caffeine inclusion	-	-	-	N	I	-/No	Caffeine, with or without carbohydrate pre- and/or during exercise, in modest doses does not exacerbate Ex-GIS compared with water and carbohydrate alone
Coconut water	-	-	-	N	III	-/No	Coconut water during exercise does not exacerbate Ex-GIS compared with water
Dairy (containing lactose)	-	-	-	N	III	-/No	Dairy intake pre-exercise does not exacerbate Ex-GIS compared with a carbohydrate control comparator

✓: beneficial effect reported in research; X: detrimental effect reported in research; N: no effect reported in research; ? : unclear (due to conflicting outcomes, no study and/or warrants further exploration); NA: not applicable; ↑: increase; ↓: decrease (note, symbol does not provide indication of the magnitude of beneficial to detrimental effect). EIGS: exercise-induced gastrointestinal syndrome; Ex-GIS: exercise-associated gastrointestinal symptoms; FODMAP: fermentable oligo-, di-, and mono-saccharides and polyols; LCHF: low-carbohydrate high-fat diet; LEA: low energy availability. ^aVolume- and type-dependent, ^btargeted at lowering peak and relative change in core body temperature [83] **based on experimental procedure best-practice recommendation checklist from Costa et al. [67] and ***based on experimental procedures for confounding factors and assessment tool quality for Ex-GIS

thermophysiological impact rather than carbohydrate ingestion [67]. Moreover, another study that showed a reduction in I-FABP with carbohydrate intake compared with water failed to observe differences in splanchnic perfusion (i.e., gap between gastric and arterial $p\text{CO}_2$) by gastric tonometry [115], potentially owing to the lack of sensitivity of this method to detect difference in perfusion at the level of the intestinal villi. In the aforementioned studies, there has been no difference observed in markers of endotoxemia (i.e., lipopolysaccharide (LPS) and lipopolysaccharide binding protein (LBP)). However, Snipe et al. [73] observed an increased endogenous endotoxin core antibody (EndoCAB IgM) concentration with carbohydrate ingestion and depressed concentrations with water. This suggests potential activation of EndoCAB, which is associated with systemic appearance of pathogenic agents, was overused in the water trial, but not on the carbohydrate trial, irrespective of the post-exercise LPS concentration (i.e., via limulus amoebocyte lysate gram-negative bacterial endotoxin determination). Only one study has explored systemic inflammatory responses in conjunction with other EIGS markers with carbohydrate intake and found attenuation of interleukin (IL)-6 compared with water intake, but no differences in the exertional-heat stress induced increases in proinflammatory (i.e., tumor necrosis factor alpha (TNF α) and IL-1 β) or anti-inflammatory (i.e., IL-10 and IL-1ra) cytokines between the carbohydrate and water control trials [73]. Together, the current research shows good evidence that ingestion of moderate (20–60 g/h) and/or high (> 60 g/h) amounts of carbohydrates during exercise is an effective strategy to attenuate disturbances to gastrointestinal integrity and systemic responses. However, carbohydrate ingestion tolerance will dictate intake impact on gastrointestinal functional responses and Ex-GIS incidence and severity (Sect. 9 and supplementary file 1).

Grade of Evidence: I

4.2 Glutamine

The ingestion of protein (i.e., containing a variety of amino acids) and/or specific amino acids (and derivatives) may play a role in preventing EIGS through the provision of energy substrate to intestinal epithelial cells, regulation of intestinal barrier structure and function, and intestinal immune function [120]. The most well-researched singular amino acid to date for EIGS prevention or management is glutamine, on the basis of its provision as a primary fuel source for epithelial enterocytes [121]. Several studies have demonstrated that acute (0.25–0.9 g/kg fat-free mass (FFM) consumed 2 h before exercise) and prolonged (0.9 g/kgFFM/day

for 7 days and 3 g L-glutamine with 0.69 g L-cysteine for 5 days) glutamine supplementation attenuated the modest rise in exercise-associated small intestine permeability in response to 60 min running at 65–75% $\text{VO}_{2\text{max}}$ in 25–30 °C and 12–60% RH [122–125]. However, the studies failed to show any beneficial effects on luminal to systemic pathogenic translocation (e.g., bacterial endotoxin) and systemic inflammatory cytokine responses (e.g., TNF α). A dose response study demonstrated small reductions in plasma I-FABP concentration with higher (0.5 and 0.9 g/kgFFM), but not lower (0.25 g/kgFFM), acute glutamine supplementation compared with a non-nutritive placebo [122]. These findings contrast with other studies that have observed small, but significant reductions, in plasma I-FABP concentrations pre-exercise on the second day of exercise in the heat with low glutamine doses provided 1 h before exercise (0.15 g/kgBM) and post-exercise with prolonged (3 g/day L-glutamine with 0.69 g/day L-cysteine for 5 days) supplementation [123, 126]. It should be noted that values present in all studies for gastrointestinal integrity disturbance through the experimental procedure timeline were minor and of little clinical relevance [33, 67]. In contrast, several recent studies have shown no benefit to EIGS prevention and management with glutamine ingested before exercise. For example, 0.9 g/kgFFM L-glutamine ingested 60 min before a 20 km cycling time trial (~33 min) in 35 °C and 51% RH did not attenuate the post-exercise modest rise in plasma I-FABP, IL-6, or TNF α concentrations, and responses were not different to the non-nutritive placebo [127]. Similarly, ingestion of 0.3 g/kgFFM L-glutamine 60 min before 80 min treadmill walking at 6 km/h with 6% gradient in 35 °C and 30% RH and run to exhaustion (~22 min) at lactate threshold speed in 40 °C and 40% RH did not substantially attenuate disturbances to gastrointestinal integrity [128, 129]. Methodological limitations have been raised in these studies, questioning the results validity into real-world practice [67]. The majority of studies have not reported Ex-GIS with L-glutamine ingestion [122, 127–129]. However, a dose–response study showed increased Ex-GIS with glutamine ingestion at 0.9 compared with 0.6 and 0.3 g/kgFFM, which were more pronounced during the 2 h following ingestion [130]. Overall, there are conflicting findings on the effect of glutamine on EIGS, with any beneficial effects reported linked to magnitude of response being small and of no clinical relevance.

Grade of Evidence: III

4.3 Arginine and Citrulline

L-arginine and L-citrulline (i.e., L-arginine precursor) may enhance nitric oxide production at the intestinal villi

microvascular compartment, with a proposed subsequent enhancement in splanchnic perfusion that would support the maintenance of gastrointestinal epithelial integrity during exercise [131, 132]. Laboratory-controlled research with L-arginine and EIGS outcomes is lacking. However, ingestion of 30 g/day L-arginine for 14-days before a marathon did not have any effect on small intestine permeability, fecal occult bleeding, or Ex-GIS compared with equivalent supplementation with glycine [132]. Although, it should be noted that small intestine permeability, assessed by urinary dual-sugar (i.e., lactulose and mannitol) probe was not significantly elevated post-marathon compared with pre-race. Whilst this study did not observe differences in Ex-GIS, a review of arginine side effects suggests that GIS, particularly diarrhea, may occur with L-arginine intake with single doses of > 9 g or daily doses of > 30 g/day [133]. Indeed, a small increase in Ex-GIS (i.e., nausea and fullness) with the addition of L-arginine to a carbohydrate electrolyte solution has been observed during prolonged (2.5 h) submaximal (50% peak power) cycling exercise [134].

L-citrulline may enhance L-arginine-derived nitric oxide production, as the ingestion of 10 g of L-citrulline 30 min before 60 min cycling at 70% maximum workload has been shown to modestly attenuate splanchnic hypoperfusion and attenuate the rise in plasma I-FABP concentration, but with no effect on gastric or small intestine permeability [131]. It is also noteworthy to report the attenuated hypoperfusion and epithelial injury on L-citrulline supplement intervention increased to similar values as placebo immediately post-exercise. Therefore, it is not clear whether the acute attenuation during exercise was due to mechanistic effects of the L-citrulline or simply just having nutrients (e.g., amino acid derivative) along the gastrointestinal tract, as per the mechanistic alignment with carbohydrate feeding before and during exercise (Sect. 4.1).

Grade of Evidence: II to III

4.4 Amino Acid Combinations

In response to the lack of clarity on the impact of singular amino acids or derivatives on biomarkers representative of EIGS, recent studies have investigated the impact of amino acid combinations on EIGS biomarkers. First, collagen peptides (10 g/day for 7 days and 45 min pre-exercise) did not influence a cluster of intestinal epithelial integrity biomarkers and inflammatory cytokines compared with a placebo in response to 70 min running at 70–90% $\text{VO}_{2\text{max}}$ in 22 °C [135]. The application of a multiple amino acid (i.e., 4.5–6.4 g/L: valine, aspartic acid, serine, threonine, and tyrosine, with or without isoleucine) beverage intervention for 7 days, immediately pre-exercise, and during 2 h running at 60% $\text{VO}_{2\text{max}}$ in ~35 °C attenuated intestinal epithelial

cell injury, perturbations to bacterial and endotoxin profiles, and systemic inflammatory responses, but not circulatory bacterial DNA presence and/or alterations to systemic bacterial profile compared with the water control trial [136, 137]. Furthermore, the amino acid content within the beverage provisions did not substantially exacerbate Ex-GIS incidence and severity in response to the exertional-heat stress compared with water. It was reported that these beneficial effects may be due to the 7-day supplementation period promoting amino acid delivery before the stress exposure, subsequently improving the robustness and stability of the intestinal enterocyte cell membrane and/or tight-junction structure and function [108, 111, 112, 120, 138]. Additionally, intake during exercise may have supported villi microvascular perfusion via the nitric oxide pathway [109].

Grade of Evidence: II

4.5 Whole Protein

The ingestion of whole protein, which is more commonly consumed in foods during prolonged steady state exercise (e.g., ultra-endurance) [15, 16], has also been previously investigated for the prevention and management of EIGS. Whey protein hydrolysate (i.e., 14.8 g protein/serve) consumed before and every 20 min during 2 h running at 60% $\text{VO}_{2\text{max}}$ in 35 °C and 27% RH attenuated plasma I-FABP concentration and small intestine permeability, and subsequently resulted in a more beneficial bacterial endotoxin profile, although these differences in plasma endotoxin concentration were not significant [73, 117]. It was speculated that these beneficial outcomes were potentially due to increased heat shock protein expression and/or stabilization of tight-junction protein complexes. While whole protein may be beneficial to EIGS outcomes linked to the circulatory–gastrointestinal pathway, such high intakes increased Ex-GIS compared with ad libitum water [73], which has feeding tolerance and performance implications [17, 42]. Although large doses of protein during exercise may induce and/or exacerbate Ex-GIS, smaller doses (i.e., 3 g every 15 min) co-ingested with glucose appear to be tolerable [139]. However, the impact of lower protein doses during exercise on EIGS markers still warrants investigation.

Grade of Evidence: II

5 Dietary Components and/or Interventions

5.1 Gluten-Free

Adherence to a gluten-free diet is prevalent amongst non-celiac athletes, with the primary reason of self-diagnosis of

gluten sensitivity symptom (i.e., gastrointestinal origin) or non-symptom related benefits (i.e., improves overall health and/or ergogenic effect) [140]. A gluten-free diet restricts gluten, a storage form composite of gliadins and glutenins commonly found in wheat, rye, barley, and triticale. Unlike celiac disease, at present there is no established clinical diagnostic biomarker (i.e., allergic or autoimmune response) for non-celiac gluten sensitivity [141, 142]. Nevertheless, non-celiac athletes have reported symptomatic improvements at resting and during exercise after implementing a gluten-free diet. Such symptomatic improvements may be due to the subsequent adjunct reduction of fermentable oligo-, di-, and mono-saccharides and polyols (FODMAPs), specifically fructans and galactooligosaccharides [143–146]. Other possible reasons are a change in dietary habits per se. For example, Lis et al. [140] reported that athletes increased their fruit, vegetable, and gluten-free wholegrain consumption when they switched to a gluten-free diet. To date, there is only one study that investigated the effects of a gluten-free diet versus a gluten-containing diet in non-celiac athletes on markers of EIGS and Ex-GIS. Non-celiac competitive cyclists found no overall effect of 7 days gluten-free versus gluten-containing diet on intestinal epithelial injury, systemic inflammatory cytokines, and Ex-GIS in response to an exertional stress experimental model [147]. At present, there is no evidence supporting a gluten-free diet in non-celiac athletes in the prevention and management of EIGS and Ex-GIS.

Grade of Evidence: III

5.2 Fermentable Oligo-, Di-, and Mono-Saccharides and Polyols (FODMAP)

A low FODMAP diet is a well-recognized dietary intervention for managing diseases of gut–brain interaction (DGBI), namely irritable bowel syndrome (IBS)) [148–151]. Athletes who experience Ex-GIS often report similar symptom types as those with IBS; and commonly include flatulence, lower abdominal bloating and pain, and urge to defecate [3]. Many athletes often implement a low FODMAP diet pre-exercise as an effective strategy to reduce Ex-GIS [10, 11, 13, 152]. FODMAPs are rapidly fermentable short-chain carbohydrates, which are synonymous with increases in intestinal luminal gas, water, and metabolic by-products (e.g., short-chain fatty acids (SCFA)) [153, 154]. Collectively these biological changes result in luminal distension leading to lower-GIS symptoms in individuals with heightened visceral sensitivity [155]. Conversely, a low FODMAP diet is reported to reduce microbial diversity and total bacterial abundance [149], which may be counter productive to EIGS

management. This is postulated to be due to diminished luminal content, fermentation, and SCFA production [29, 33]. Therefore, it is plausible that a lowered dietary intake of FODMAPs may support the management of Ex-GIS, but may negatively influence the pathophysiology of EIGS in susceptible athletes.

Owing to the increased energy requirements of athletes, the typical FODMAP dietary intake can be up to 81 g/day [144] compared with a typical westernized (i.e., Australian) diet of 24 g/day [153]. When adopting a low FODMAP diet (i.e., < 8 g/day of FODMAP), for either 6 days [11, 13, 152] or a short-term (i.e., 24–48 h) dietary intervention (i.e., ≤ 5 g/day) before exercise, [82, 156] a reduction in Ex-GIS severity before, during, and after exercise has been reported in response to exertional experimental models. Of interest, a 24-h low FODMAP diet before a substantial exposure to exertional-heat stress (i.e., 2 h running at 60% $\dot{V}O_{2\max}$ in ~35 °C) showed greater intestinal injury along with a trend for a greater magnitude of bacterial endotoxin translocation, but did not impact systemic inflammatory responses compared with a high FODMAP diet. It has been proposed that the potential EIGS protective effects of a high FODMAP diet align with those mechanisms described with carbohydrate feeding before and during exercise in Sect. 4.1. In addition, they align with the increased SCFA concentrations observed in plasma and feces after high FODMAP diet adherence [28]. As discussed, there is evidence supporting the role of a short-term (i.e., 24–48 h) low FODMAP diet before exercise in reducing the severity of Ex-GIS, and there is also some evidence for a high FODMAP diet attenuating EIGS pathophysiology in athletes undertaking prolonged endurance-type exercise. Therefore, if implementing a short-term low FODMAP diet for the management of Ex-GIS severity, consideration must be given to other possible protective dietary influences on EIGS pathophysiology; namely, carbohydrate loading and/or carbohydrate feeding during exercise within tolerance levels.

Grade of Evidence: I

5.3 Low Carbohydrate High Fat (Ketogenic Targeted Diets)

Maximizing fat as a substrate for endurance exercise, via a ketogenic low-carbohydrate high-fat (LCHF) diet, originated in the early 1980s and has since been thoroughly investigated, primarily in respect to fuel kinetics and exercise performance [157]. For athletes undertaking prolonged endurance-based exercise, it is theorized that a LCHF diet may facilitate extended durations of exercise performance without the need for frequent ingestion of carbohydrate-based

fuels, which seems a positive outcome in respect to lowering the gastrointestinal burden during exercise, and subsequently favoring the abolishment of Ex-GIS. However, there is currently a scarcity of research focusing on gastrointestinal responses to the application of LCHF dietary interventions. Although enhancing the ability for endogenous fat oxidation at the expense of not having to or limiting the need for exogenous carbohydrate intake during exercise seems promising, several concerning aspects can be raised. Following dietary lipid consumption, such as a high-fat meal, circulating bacterial endotoxins (i.e., LPS) concentrations have been observed to increase in human experimental models [158], linking high-fat diets with increased bacterial endotoxin entry from the intestinal lumen into systemic circulation. In addition, an increased circulating concentration of I-FABP is also commonly reported in diets aimed at increasing lipid intake and oxidation [159]. Although I-FABP is indicative of intestinal epithelial cell damage, its levels are generally proportionally linked to the rate of cellular fatty-acid metabolism [160].

In an athletic population, an increase in plasma I-FABP concentration was observed following an acute 6 days LCHF diet (i.e., <50 g/day carbohydrate, energy availability = 40 kcal/kgFFM/day) at rest and in response to prolonged strenuous exercise (i.e., 25 km race walk) in elite race walkers compared with a high-carbohydrate diet (i.e., 65% carbohydrate, energy availability = 40 kcal/kgFFM/day) [161]. In addition, the proposed compromised epithelial barrier before and during exercise was further supported by increased concentrations of soluble CD14 (sCD14) and lipopolysaccharide binding protein (LBP), both surrogate biomarkers indicative of luminal to systemic bacterial endotoxin translocation, in the LCHF group versus the high carbohydrate group. This likely influenced systemic inflammatory responses [162]. Despite evidence of increased injury and compromise to the intestinal epithelial barrier in athletes following a LCHF diet, incidence of Ex-GIS was observed, but did not significantly differ compared with the high carbohydrate diet. It is important to highlight that the higher FODMAP content of the high carbohydrate diet may have inadvertently exacerbated Ex-GIS incidence and severity via malabsorption and bacterial fermentation (as per Sect. 5.2), and subsequently masked potential effects of LCHF on Ex-GIS via the observed intestinal epithelial perturbations. In addition, from a professional practice perspective, following 32 weeks on a LCHF diet, a world-class long-distance triathlete experienced the worst-ever performance outcomes following half-ironman and ironman competitions. He experienced negative subjective well-being, and his usual gastrointestinal disturbances were not alleviated [14]. On the basis of the current evidence to date, LCHF dietary interventions

do not support the prevention or management of EIGS and Ex-GIS.

Grade of Evidence: II

5.4 Low Energy Availability

It is well-established that in medical conditions associated with acute or chronic periods of compromised nutritional intake (e.g., anorexia nervosa), gastrointestinal derangement and subsequent symptoms (e.g., gastro-esophageal and/or intestinal symptoms associated with disturbances to gastric motility, gastric emptying, and intestinal transit) are common manifestations [163, 164]. More recently, the exploration of athletes adhering to unmatched dietary and training regimes, synonymous with low energy intake, and/or high training and competition energy outputs has led to the greater knowledge and understanding of low energy availability (LEA), and the development of relative energy deficiency in sport (REDs) and its clinical consequences [165]. Clinical cases and exploratory research have revealed the multisystem impact of chronic LEA, including gastrointestinal disturbances and symptomatic outcomes potentially based on underlying neuroendocrine (e.g., altered and abnormal stress hormone responses) pathophysiology [166]. On the basis of these reports, it is plausible that individuals in a state of LEA and/or presenting diagnostic criteria for REDs may be more prone to EIGS and Ex-GIS as a result of the perturbed neuroendocrine–gastrointestinal pathway.

To date, only one study has investigated the effects of a short-term (i.e., 6 days) LEA intervention on gastrointestinal integrity biomarkers and Ex-GIS in elite race walkers [161]. Acute LEA (i.e., 65% carbohydrate, energy availability = 15 kcal/kgFFM/day) did not result in differing intestinal epithelial injury, bacterial endotoxin profile perturbations, or Ex-GIS compared with a high carbohydrate (i.e., 65% carbohydrate, energy availability = 40 kcal/kgFFM/day) diet over the dietary intervention period, in response to a 25 km race walk in temperate ambient conditions. Food and fluid were provided to mimic a race feeding regimen during exercise. It is possible that the short duration intervention may have resulted in these null effects, as longer-term LEA (i.e., timeline that impacts lean body mass and resting metabolic rate) results in more pronounced perturbations to physiological systems [165]. In addition, the provision of any carbohydrate dose during exercise may have also contributed to the lack of group differences [64, 73, 113–115]. Therefore, at this stage, it may be suggested that short-term LEA does not exacerbate EIGS or Ex-GIS; however, it is unknown if chronic LEA,

leading to REDs, impacts how an individual gastrointestinal tract responds to exercise stress.

Grade of Evidence: III

5.5 Low Fiber (and/or Residue)

It is well recognized that manipulating (i.e., increasing, reducing, or altering type) the fiber (e.g., insoluble: lignin and cellulose; and soluble: arabinoxylan, beta-glucan, guar gum, inulin, and psyllium) and/or other residues (e.g., resistant starches such as amylose) of dietary intake plays a key role in symptomatic management of DGBI (e.g., gastrointestinal functional disorders—IBS) and inflammatory diseases of the gastrointestinal tract (e.g., inflammatory bowel conditions such as Crohn's diseases and ulcerative colitis) [167–172]. Considering the neuroendocrine–gastrointestinal and circulatory–gastrointestinal pathways of EIGS presents similar pathophysiological manifestations as these disease states, respectively; it seems logical that manipulating the intake of dietary residues (i.e., insoluble and soluble fibers, and resistant starches) before exercise may influence EIGS and subsequent Ex-GIS outcomes. From a theoretical perspective, the consumption of dietary residues before and during exercise may promote both increased gastric and intestinal content that may lead to a direct (i.e., *in situ* content) or an indirect (i.e., gas production and water translocation aligned with bacterial fermentation of soluble fibers and resistant starches) increase in luminal pressure leading to intestinal hypersensitivity, local dysmotility, and/or ileal brake mechanisms, contributing to Ex-GIS [43, 55, 57, 58]. Nevertheless, considering the fermentable capacity of soluble fibers and resistant starches by commensal bacteria along the gastrointestinal lumen, effects may mimic those reported in research of dietary FODMAP content (see Sect. 5.2) and/or prebiotic supplementation (see Sect. 6.2) on EIGS and Ex-GIS outcomes, whether it be exacerbating Ex-GIS severity and/or providing a beneficial effect on gastrointestinal integrity.

To date, only one retrospective field-based observational study has reported on the relationship between dietary fiber intake and Ex-GIS occurrence during competition in endurance athletes (i.e., long-course triathlon) [6]. The results were limited to those triathletes that presented with “intestinal cramps” also consumed fiber-rich foods in the pre-event meal. Despite these limited observational field research findings, it is surprising that a recent experimental survey ($n = 277$) found that endurance athletes (15.2%) self-reported following a low fiber diet in the management of Ex-GIS, which was the highest reported management strategy [9, 10]. In addition, the cohort reported lowering dietary fiber intake leading into competition was the most successful strategy in their perceived reduction in

Ex-GIS. Current sports nutrition recommendations caution athletes to be wary of high-fiber foods prior to competition owing to the possibility of increasing the risk of developing Ex-GIS [173]. It is unclear where such therapeutic information and adherence is coming from, but speculation may possibly lie with unquestioned social acceptance stemming from clinical research in DGBI (i.e., functional diseases/disorders of the gastrointestinal tract) management [167, 168, 170, 171] and/or broad-spectrum sports nutrition recommendations. Nevertheless, low-residue intake, using low-fiber and elemental-based dietary components, formed part of EIGS and Ex-GIS management in a recent case series on endurance and ultra-endurance athletes experiencing severe Ex-GIS [12]. Outcomes from the individually tailored therapeutic interventions suggested including low-fiber and residue foods and beverages within the dietary regime of certain case athletes reduced Ex-GIS incidence and severity in subsequent competitive events, leading to these athletes reporting performance improvements (e.g., event completions and victories). It is worth highlighting that other therapeutic-focused interventions formed part of the overall management plan within the case series (e.g., gut training, low FODMAP diet, measured and planned carbohydrate intake during exercise, and euhydration without fluid overload, among others), and likely also contributed to the positive outcomes. Owing to anecdotal evidence in professional practice, it is speculated that adherence to low-fiber and/or residue diets may lower the predisposition to Ex-GIS [11]. However, considering that there is no experimental evidence on this topic, well-conducted randomized controlled trials are needed to provide full insight into the impact of dietary fiber on EIGS and Ex-GIS outcomes.

Grade of Evidence: IV

6 Dietary and Nutritional Supplements

Various dietary and nutritional supplements have been explored in the context of attempting to ameliorate the pathophysiological pathways of EIGS, namely the circulatory–gastrointestinal pathway (i.e., intestinal epithelial cell and tight-junction injury and/or dysfunction, lumen to circulation pathogenic translocation, and systemic immune responses), and subsequently Ex-GIS. These include proposed antioxidants (i.e., ascorbic acid, tocopherol, and capsaicin); biotics (i.e., pre-, pro-, and syn-biotics), bovine colostrum, curcumin, anthocyanin, and nitrate.

6.1 Antioxidants

Oxidative stress may contribute to the exacerbation of exercise-associated intestinal epithelial injury and subsequent local inflammatory responses [174, 175]. As such, the increased activity of intestinal epithelium reactive oxygen species, during exercise and/or in the recovery period after exercise (i.e., splanchnic reperfusion), may facilitate epithelial cell injury and tight-junction protein rupture or dysfunction, leading to enhanced translocation of pathogenic agents into systemic circulation [3, 37, 138]. It has, therefore, been proposed that supplementing with nutrients that present antioxidative or anti-inflammatory properties before exercise may ameliorate the associated gastrointestinal disturbances. To date, supplements containing antioxidative or anti-inflammatory properties, including ascorbic acid, tocopherol, and capsaicin have been investigated.

Using a test–retest model, an acute dose of L-ascorbic acid (1000 mg) 2 h before an incremental cycling test to exhaustion reduced circulating gram-negative endotoxin concentration compared with a control trial 8 weeks prior [176]. Given the lack of crossover, no placebo control, and extensive time between trials, it is unclear if the modestly reduced post-exercise endotoxin levels are directly related to acute ascorbic acid ingestion. Another investigation determined the impact of 2 weeks tocopherol or soy lecithin placebo supplementation on intestinal permeability, fecal blood loss, and GIS following a marathon [177]. There was no significant change in intestinal permeability with tocopherol supplementation in response to the marathon. Additionally, no significant difference in heme-positive fecal samples was observed (tocopherol: 10% versus placebo: 20%). While abdominal cramping and pain were significantly reduced with tocopherol supplementation, heme-positive fecal samples were unrelated to Ex-GIS.

It has also been proposed that an intervention involving the administration of an antioxidant rich compound, capsaicin, may be effective in preventing and/or managing gastrointestinal epithelial injury [178]. Capsaicin is a proposed antioxidant and anti-inflammatory compound found within hot peppers and has been shown to increase blood perfusion in the gastrointestinal epithelium, albeit within animal models [178]. Thus, an increase in blood perfusion from capsaicin consumption has been hypothesized to ameliorate gastrointestinal epithelial injury in humans. A randomized control trial undertaken to assess the effect of capsaicin supplementation on sprinting performance and IL-6 response implemented an intervention where participants received 25.8 mg of capsaicin immediately prior to performing 15×30 m sprints at 35 s intervals at maximum effort [179]. It was determined that participants experienced increased Ex-GIS with supplementation; however, IL-6 response was unchanged pre- to post-exercise [179]. Taken together, and

considering the limited studies in the area that do not meet the minimal best practice recommendations, [2] there is no clear evidence to suggest a period of antioxidant supplementation before an exercise bout prevents or can be used to manage EIGS and/or Ex-GIS.

Grade of Evidence: III to V

6.2 Biotics (Pre-, Pro-, and Syn-biotics)

It is a common belief among athletes and athlete support practitioners that a period of biotic supplementation, in the form of prebiotics (i.e., non-digestible material that can be fermented by bacteria in the lower gastrointestinal tract), probiotics (i.e., live bacteria which survives transit to colonize the lower gastrointestinal tract), or a combination referred to as synbiotics, will confer some beneficial effects to the gastrointestinal tract, particularly in response to exercise, when the gastrointestinal tract is compromised [180]. The mechanisms by which biotics may infer a beneficial effect on EIGS are associated with increasing the relative abundance of commensal bacterial along the gastrointestinal tract. This β -change may subsequently increase bacterial fermentation activity, leading to enhanced concentrations of luminal and/or plasma SCFA (e.g., acetate, butyrate, and propionate) [148, 181–183], newly termed post-biotics. Both fecal and plasma SCFA concentrations have been linked to protecting gastrointestinal integrity against exertional and exertional-heat stress [29, 33, 93]; although direct mechanistic explanation warrant further exploration and clarification.

A recent systematic literature review was undertaken to provide clarity on the impact of short or long-term biotic (i.e., pre-, pro-, syn-biotic) supplementation on markers of EIGS and Ex-GIS in response to exertional or exertional-heat stress [180]. However, no study that investigated the impact of prebiotic supplementation on EIGS and Ex-GIS was identified within the SLR. Recently, an 8-week prebiotic supplementation intervention (i.e., 16 g/day of a fructooligosaccharides, galactooligosaccharides, resistant starch, and dietary fiber formulation) prior to a 3 h exertional-heat stress experimental protocol resulted in a noticeable reduction in intestinal epithelial injury and luminal to systemic bacterial endotoxin translocation. However, it had no impact on attenuating systemic inflammatory response and did not influence gastrointestinal functional responses [184]. Additionally, the prebiotic supplementation did not further exacerbate Ex-GIS severity compared with the non-prebiotic-containing and low FODMAP placebo. It is important to note that the observed beneficial outcomes on ameliorating intestinal epithelial injury and bacterial endotoxin translocation with prebiotic supplementation were modest in nature, and overall exertional-heat stress associated gastrointestinal integrity perturbation were lower than previously reported

[67]. This is likely attributed to the attenuating effects of carbohydrate feeding, as described in Sect. 4.1, which was provided in the first 2 h of the protocol.

Within the systematic literature review, probiotic and synbiotic supplementation interventions included single or multiple species/strains: *B. animalis*, *B. bifidum*, *B. breve*, *B. lactis*, *B. longum*, *B. subtilis*, *E. faecium*, *L. acidophilus*, *L. brevis*, *L. casei*, *L. fermentum*, *L. helveticus*, *L. lactis*, *L. paracasei*, *L. plantarum*, *L. rhamnosus*, *L. salivarius*, and/or *S. thermophilus*, with or without fructooligosaccharides (55.8 mg/dose) or inulin (2.3 g/dose). Bacterial doses ranged between $\times 10^8$ to $\times 10^{11}$ colony forming units, with supplementation period ranging from 7 days to 3 months. Exercise protocols varied from an incremental cycling test to exhaustion, to an ultra-endurance triathlon event, as well as a military training protocol. Probiotic or synbiotic supplementation did not present any substantial beneficial effect compared with placebo or control on surrogate markers of intestinal epithelial injury. Inconsistent outcomes were observed with assessment markers of intestinal permeability with probiotic or synbiotic supplementation; with higher, lower, and no difference in outcomes between supplementation and placebo were reported. Of note, the reported beneficial effects of synbiotic supplementation on intestinal permeability was as a result of using the erroneous zonulin biomarker to quantify permeability [185–188]. No probiotic or synbiotic supplementation intervention reduced markers of exercise-associated endotoxemia compared with the study's respective placebo or control. However, one intervention (seven days *L. casei*) reported a substantial increase in gram-negative bacterial endotoxin plasma concentration in response to 2 h steady-state treadmill running (60% $\text{VO}_{2\text{max}}$) in hot ambient conditions (34.0 °C, 32% RH) compared with a modest reduction in the placebo group [189]. The increased endotoxemia was speculated to be associated with a greater bacterial luminal load as a result of the 7 days *L. casei* supplementation dose (i.e., more bacterial endotoxin in the lumen available to translocate across the exercise-associated compromised epithelial barrier). There was no consistency in the impact of probiotic or synbiotic supplementation on systemic inflammatory responses, with no substantial differences reported in included studies. Regarding Ex-GIS, four out of the five studies within the SLR presented data indicative of no effect on Ex-GIS incidents and/or severity. One study reported lower Ex-GIS severity in the probiotic supplement group (i.e., 4 weeks, > 25 billion CFU/day from *L. acidophilus* CUL60, *L. acidophilus* CUL21, *B. bifidum* CUL20, *B. animalis* subsp. *Lactis* CUL34) in response to a simulated marathon. However, at closer inspection of the data and considering the methodological issues, it can be argued that the placebo group outperformed the probiotic

supplementation group in regards to incidence of Ex-GIS and GIS in recovery from exercise. No study to date has assessed the impact of biotics on markers of gastrointestinal function. It was not surprising that no substantial differences were observed for EIGS markers, considering probiotic and synbiotic supplementation did not result in any changes in fecal bacterial composition (i.e., α -diversity and/or relative abundance), with only the supplemented strain or species showing increases in relative abundance. These increases, however, did not translate into increases in SCFA. The SLR concluded that probiotic supplementation with the strain or species studied does not substantially influence intestinal injury and permeability, subsequent systemic endotoxin or inflammatory cytokine responses, or GIS in response to exercise. As reported in the risk of bias assessment, many studies lacked adequate exertional and/or heat stress, or appropriate spectrum of biomarkers, to make definitive conclusions. Synbiotic supplementation appears to closely resemble the effects of probiotic, rather than prebiotic supplements, owing to the generally very small quantity of prebiotic ingredients included within the study intervention formulation.

Grade of Evidence: I to II

6.3 Bovine Colostrum

Bovine colostrum has been proposed to support the gastrointestinal system via promotion of villus development and mucosal thickness throughout the gastrointestinal tract [190]. As reported in animal experimental models, evidence suggests that bovine colostrum protects against intestinal hyperpermeability associated with non-steroidal anti-inflammatory drugs (NSAIDs) or hyperthermia [191, 192]. It is therefore plausible that bovine colostrum supplementation may contribute towards a management strategy for EIGS. Several randomized controlled trials have investigated the effect of acute and prolonged bovine colostrum supplementation on markers of EIGS, with conflicting findings reported in regards to intestinal epithelial injury and permeability outcomes in response to exercise. A wide variety of exertional stress protocols have been used, ranging from 20 min running at high intensity (up to 80% $\text{VO}_{2\text{max}}$) to 1.5 h combined cycling and running, and within diverse environmental conditions (i.e., ambient temperature ranging from 22 to 40 °C) [193–200]. Supplementation protocols included ingestion of bovine colostrum for 14 days at 20 g/day with or without zinc carnosine, [193–196] 8 weeks at 60 g/day, [199] and 7 days at 1.7 g/kgBM, [198] before the respective exercise protocol. The proposed protective effects of bovine colostrum were assessed via urinary L:R ratio for intestinal permeability, plasma I-FABP concentrations pre- to

post-exercise, and exercise-induced systemic inflammatory response (i.e., cytokine profile). Research outcomes appear inconsistent, with some studies reporting modest positive effect with 14 days of supplementation at 20 g/day supplementation on mitigating L/R and/or the rise in I-FABP from pre- to post-exercise, compared with placebo [193–196]. However, other studies, using more substantial exercise models with or without the addition of heat exposure (e.g., 1.5 h cycling and running and 45 min exercise in 40 °C) demonstrated no beneficial effects of supplementation on markers of intestinal permeability or systemic inflammatory response [197–200]. Previous arguments in support of bovine colostrum in protecting the gastrointestinal tract (i.e., intestinal epithelial injury and permeability) in response to exercise are acknowledged [201]. However, several supplement intervention studies, with closer adherence to best practice recommendations for research methodologies, [67] have shown no beneficial outcomes compared with respective placebo or control [197–200]. In addition, a systematic literature review with meta-analysis that included exploration of measures related to EIGS (i.e., circulating immunoglobulins and leukocytes) reported none to fairly low impact of bovine colostrum supplementation intervention on these biomarkers [202]. Taken together, the current evidence suggests there is no strong and consistent evidence to recommend acute or prolonged supplementation with bovine colostrum to attenuate disturbances to the gastrointestinal integrity and/or systemic inflammatory responses associated with EIGS.

Grade of Evidence: II–III

6.4 Curcumin

Curcumin, the primary compound found in turmeric, is of interest owing to its anti-inflammatory properties and proposed function in strengthening intestinal endothelial tight junctions, demonstrated both *in vitro* and *in vivo* [203–205]. It also appears to attenuate proinflammatory LPS signaling pathways, moderating disturbance to gastrointestinal epithelial lining and resulting in reduced bacterial translocation. This potentially reduces systemic inflammatory responses [204, 205]. To date, only one study has investigated the potential role of curcumin in moderating markers synonymous with EIGS. It was observed that participants who supplemented with 500 mg/day of curcumin for 3 days had a significantly smaller increase in plasma I-FABP (absolute difference ~366 pg/mL) and IL-1ra (absolute difference ~8 pg/mL) after 60 min of moderate-intensity running in 37 °C ambient temperature compared with those who

supplemented with placebo [206]. Unfortunately limitations, including insufficient exercise stress to induce substantial elevations in relevant biomarkers, confirmed by a rise in I-FABP under the minimal detectable change (MDC), [33] make it challenging to conclude if differences were of clinical and practical relevance. Therefore, more methodologically robust studies are required to unveil the preventative or mitigating potential of curcumin supplementation on EIGS. Given that limited research is available, it is currently not recommended as a first-line action for athlete application as a strategy for reducing EIGS.

Grade of Evidence: III

6.5 Anthocyanins

Anthocyanin, a bioactive flavonoid polyphenol, has been proposed to attenuate nuclear factor-kappa B (NF- κ B)-mediated inflammatory responses, including targeted effects on protecting gastrointestinal barrier integrity in human experimental models [207–210]. Moreover, ingestion (240 mg) of blackcurrant extract that contains a substantial anthocyanin dose (e.g., cyanidin-3-O-glucoside, cyanidin-3-O-rutinoside, delphinidin-3-O-glucoside, and delphinidin-3-O-rutinoside), [211] before exertional stress (i.e., 30 min rowing at 80% $\text{VO}_{2\text{max}}$), was reported to mitigate oxidative stress (e.g., plasma carbonyls), and inhibit LPS-stimulated cytokine secretion (i.e., TNF α and IL-6) and NF- κ B activation, compared with placebo [212]. It is therefore plausible that such supplementation before exercise may provide some attenuating effects on markers respective of exercise-associated gastrointestinal integrity perturbations. A recent study investigated the effects of 7 days of anthocyanin-rich blackcurrant extract administration (600 mg/day) on gastrointestinal integrity markers in response to exertional-heat stress (i.e., 60 min running at 70% $\text{VO}_{2\text{max}}$ in 34 °C and 40% RH ambient conditions) [213]. Although, the supplementation intervention led to a significant reduction in intestinal epithelial injury (i.e., plasma I-FABP concentration) after exertional-heat stress compared with placebo, no differences were observed for small intestinal permeability (i.e., 4 h urinary L/R ratio), bacterial endotoxin translocation (i.e., sCD14 and LBP), or an array of systemic inflammatory responses biomarkers (i.e., IL-6, IL-10, and IL-1ra). Similar to other nutrition supplement studies attempting to manage exercise-associated perturbation to gastrointestinal integrity, it is important to note that the indication of overall intestinal epithelial injury, bacterial endotoxin translocation, and inflammatory cytokine biomarker values, in both the anthocyanin and placebo trials, were modest in nature. In addition,

they were under the MDC previously proposed to warrant practical and clinical significance; which was likely associated with the modest exertional-heat stress model adopted [33, 67]. Taken together, it appears that the positive effect of acute intake of anthocyanin on in vitro pathogen challenge and inflammatory responses are not supported by a more prolonged supplementation period and its impact on in vivo biomarkers within human trials. In view of the current limited research available and the need for more robust experimental designs (e.g., more prolonged exertional-heat stress models to test supplementation hypothesis and adequate confounder control), it is currently not recommended as a first-line action for athlete application as a strategy for reducing EIGS.

Grade of Evidence: III

6.6 Nitrate

Gastrointestinal perfusion is dependent on macro- and micro-vascular activity throughout the splanchnic vasculature network, in which nitric oxide is a key regulator, inducing vasodilation [109, 214]. It can be proposed that increasing local availability of nitric oxide through nitrate supplementation may play a role in preventing and/or attenuating exercise-associated splanchnic hypoperfusion, and subsequent local ischemia. To date, only one study has investigated the effects of a nitrate-containing beverage (800 mg) on markers of splanchnic perfusion and ischemia, epithelial integrity, and Ex-GIS compared with carbohydrate (20 g sucrose) and water trials, in response to 60 min cycling at 70% $W_{\max}$ [115]. Participants were provided with a supplement dose 15 min pre-exercise and half-way through a 60 min cycle at 70% $W_{\max}$. Despite a clear increase in plasma nitrate and nitrite, supplementation did not improve splanchnic perfusion, epithelial ischemic injury, or bacterial endotoxin translocation. Compared with water, nitrate supplementation resulted in a 50% increase in intestinal epithelial injury (i.e., plasma I-FABP concentration), whereas sucrose ameliorated intestinal epithelial injury. The percentage change in plasma I-FABP concentration pre- to post-exercise with a nitrate (299%) beverage was considerably larger compared with sucrose (179%). Ex-GIS were similar between groups. It appears that nitrate supplementation does not dampen, and may even exacerbate, intestinal epithelial injury during moderate duration exercise (≤ 1 h) when compared with water. However, it is important to note that the exercise model used within this study was insufficient to warrant substantial gastrointestinal perturbations and associated Ex-GIS of any relevance, [33] and thus no ideal experimental design has been undertaken to appropriately test nitrate supplement intervention in regard to EIGS mitigation or exacerbation [67].

Grade of Evidence: III

7 Hydration

The ingestion of water, via an array of fluid types, during prolonged exercise (e.g., ≥ 1 h), especially when performed in hot (≥ 35 °C) ambient conditions, is important to maintain euhydration and avoid adverse physiological consequences of hypohydration, which may lead to exercise performance decrements [101, 215]. Current water replacement guidance for sport and exercise modalities are substantially affected by fluid shifts (e.g., endurance and ultra-endurance), and they suggest fluid intake should be individually tailored using either ad libitum or planned fluid intake strategy to avoid adverse consequences associated with both hypohydration and overhydration (i.e., exercise-associated hyponatremia) [101, 173, 216, 217]. Considering the naturally large intra- and inter-individual variation in sweat rates in response to exercise, there is a potential risk for both under- and overhydration to impact the gastrointestinal tract leading to GIS [218–220]. For example, fluid intake above individual gastric tolerance levels will increase intragastric pressure, causing gastric distension and contributing to the development of upper-GIS symptoms (e.g., upper abdominal bloating and/or pain, belching, urge to regurgitate or regurgitation) [41–43]. In contrast, hypohydration may exacerbate EIGS through reductions in plasma volume that enhance splanchnic hypoperfusion and increases in sympathetic drive that may suppress gastrointestinal functional responses [41]. Thus, the maintenance of euhydration in response to exercise would seem a plausible strategy to prevent or ameliorate EIGS and Ex-GIS.

7.1 Pre-Exercise Hydration

Commencing exercise at 3.0% body mass loss via pre-exercise sauna exposure slowed gastric emptying during 90 min cycling at 70% $W_{\max}$ compared with starting exercise euhydrated [221]. Orocecal transit time (OCTT) and post-exercise small intestine permeability were similar between pre-exercise euhydration and hypohydration where fluid was ingested during exercise, although prior hypohydration resulted in greater Ex-GIS (i.e., nausea and upper abdominal pain) [221]. Moreover, pre-exercise hypohydration induced by limiting fluid intake to 0.5 L/day prior to 1 h cycling at 70% $W_{\max}$, with no fluid intake during exercise, resulted in modestly higher intestinal epithelial injury (i.e., I-FABP: + 300 pg/mL, no statistical analysis presented) compared with pre-exercise euhydration achieved by habitual fluid intake [222]. On the basis of these findings, and considering the difficulties in consuming large volumes of fluid during certain exercise activities [173, 216, 217], it is

recommended that individuals commence exercise activities in the euhydrated state. However, caution is warranted, as excessive pre-exercise fluid ingestion in the attempt to obtain euhydration may promote Ex-GIS, likely associated with increased gastrointestinal load. For example, fluid ingestion (1134 mL) immediately pre-exercise significantly increased the severity of exercise-related transient abdominal pain during the first 5 min of running compared with no fluid ingestion [223]. In addition, although the impact of hyperhydration status on markers of EIGS and Ex-GIS is unknown and warrants exploration, some of the strategies used to promote hyperhydration (e.g., glycerol supplementation and sodium intake) have been reported to instigate GIS (supplementary file 2) [224].

Grade of Evidence: II

7.2 Hydration During Exercise

In a recent study, an increase in post-exercise plasma I-FABP concentration was accompanied by varying magnitudes of increased systemic inflammatory cytokines with fluid restriction during 2 h running at 70% $\text{VO}_{2\text{max}}$ ($3.1 \pm 0.7\%$ body mass loss and $P_{\text{Osmol}} > 300$ mOsmol/kg) in temperate conditions when compared with programmed fluid ingestion rates that maintained euhydration ($0.6 \pm 0.6\%$ body mass loss and $P_{\text{Osmol}} < 300$ mOsmol/kg) [41]. Hypohydration resulted in higher incidence and severity (82% and 240 mean summative accumulation during exercise, respectively) of total Ex-GIS compared with euhydration (64% and 176 mean summative accumulation during exercise, respectively). However, it is important to highlight that no significant difference was observed between the hypohydration and euhydration trials for Ex-GIS variables (i.e., trend at $p=0.058$ and $p=0.068$ for lower-GIS and lower abdominal pain, respectively). This can possibly be attributed to the large individual variation common to GIS reporting and/or that participant numbers were underpowered for such a subjective variable. Moreover, a separate study focused on ad libitum water intake during exercise (i.e., 2 h running at 60% $\text{VO}_{2\text{max}}$ in temperate ambient conditions) to maintain euhydration. Although Ex-GIS incidence was similar (70%), symptom severity was much lower (58 mean summative accumulation during exercise), possibly suggesting that fluid intake behavior may impact Ex-GIS outcomes (i.e., forceful intake via programming versus ad libitum intake within comfort) [71]. Nevertheless, carbohydrate malabsorption, as determined by breath H_2 , of the high-mixed carbohydrate meal given 2 h before exercise was pronounced with hypohydration, but not with euhydration; this likely explains the trend towards greater lower-GIS in the hypohydration trial compared with euhydration trial [41].

In another study, 1 h running at 70% $\text{VO}_{2\text{max}}$ without fluid provisions significantly increased intestinal permeability compared with pre-exercise values; this was not significantly dampened by the provision of a carbohydrate beverage or a no-carbohydrate placebo beverage [225]. However, exercise-induced body mass loss was only 1.5%, likely linked to the modest exertional stress model used, which is not indicative of exercise-associated dehydration. Fluid provision during exercise resulted in greater feelings of fullness, but other GIS types were not affected. The optimal timing and volume of fluid provisions during exercise to reduce EIGS and Ex-GIS remains to be determined, but it is likely to be individualized [12]. Additionally, the effectiveness of fluid provision to reduce perturbations to gastrointestinal integrity may be dependent upon exercise duration or the extent of exercise-induced hypohydration. Considering hypohydration and excessive fluid intakes may contribute to EIGS and/or Ex-GIS, individuals should aim to establish a balance between individual tolerance levels to fluid intake during exercise and adequate fluid intake during prolonged exercise (> 1 h) to aid the maintenance of euhydration throughout.

Grade of Evidence: II

8 Heat-Mitigating Strategies

The rise in core body temperature during exercise as a result of skeletal muscle function and metabolism, exacerbated further by hot and/or humid conditions, is directly positively correlated with increased perturbations to gastrointestinal integrity, systemic responses, and Ex-GIS [83]. A recent meta-data analysis from $n=132$ exertional and exertional-heat stress trials suggested that maximal core body temperature accounted for 16.4%, 24.9%, 42.4%, and 12.4% of the predictive variance in the magnitude of epithelial injury, systemic endotoxemia and inflammatory response, and total-GIS, respectively [83]. Moreover, core body temperatures of ≥ 39.5 °C consistently elicit intestinal epithelial injury, bacterial endotoxin translocation, systemic inflammatory responses, and Ex-GIS over minimal detectable change synonymous with clinical relevance [33, 83]. Heat mitigation strategies, such as heat acclimation/acclimatization, pre- (before exercise) and per- (during exercise) cooling, using internal (e.g., cold beverages or ice slurry) and external strategies (e.g., ice-vest, cold water immersion, or cooling showers), and fluid ingestion (covered in the hydration section) may attenuate the rise in core body temperature during exercise in the heat and therefore may minimize EIGS and Ex-GIS [226].

8.1 Heat Acclimation/Acclimatization

Heat acclimation/acclimatization (e.g., prolonged and repeated exposure to heat stress) appears to be an effective extrinsic heat mitigation strategy [226]. However, research to date is not supportive of its efficacy at mitigating EIGS. Intestine permeability was not different in response to a 45 min run at 50% $\dot{V}O_{2\max}$ in 46 °C (20% RH) following 7-day (100 min exertional-heat stress) heat acclimation [227]. Permeability was not increased from rest and was measured by lactulose ingestion and excretion only, therefore making it difficult to interpret small intestine permeability outcomes. This study, however, showed a reduction in IL-6 and IL-10 cytokines that coincided with reduced thermoregulatory and cardiovascular strain. Further studies have also demonstrated that 5–10 days of heat acclimation (i.e., running in 41.4 °C, until a +2 °C core body temperature increase and 60 min cycling at 50% $\dot{V}O_{2\text{peak}}$ in 35 °C and 50% RH or 40 °C and 25% RH) have been insufficient at attenuating I-FABP, gastric emptying rate, LPS, or the cytokine profile in response to heat stress or hypoxic ($F_{iO_2}=0.14$, 40 min cycle at 50% $\dot{V}O_{2\text{peak}}$) exercise [228–230]. Considering the proposed benefits of heat acclimation/acclimatization at attenuating cardiovascular and thermoregulatory strain during exercise in the heat [226], further research with heat acclimation regimens of more prolonged exposure (e.g., > 10 days) and sufficient adaptive stimulus (e.g., ≥ 90 min/exposure) are required to elucidate if this is an effective strategy for attenuating EIGS and Ex-GIS.

Grade of Evidence: III

8.2 Internal Cooling

Internal cooling methods include the ingestion of cold fluids or ice slurry before (pre-cooling) and/or during (per-cooling) exercise. Internal cooling can lower pre-exercise core body temperature (e.g., when ingested prior to exercise) and create a heat sink that enables greater heat storage capacity, and subsequently, improved exercise performance in the heat [226]. Therefore, internal cooling methods may attenuate EIGS through directly lowering peak core body temperature and/or delaying the rise in core body temperature during exercise and heat stress load [83] with respect to exercise intensity and duration, ambient conditions of exercise adherence, and other thermoregulatory modifiers (e.g., air flow, clothing, and/or equipment). Internal per-cooling research has shown a suppressed rise in core body temperature (mean reduction of 0.3–0.4 °C) with water bolus ingestion with 0 °C and 7 °C water temperature compared with 22 °C water temperature given every 15 min during 2 h running at 60% $\dot{V}O_{2\max}$ in 35 °C (25% RH). This resulted in modestly attenuated I-FABP and lower incidence (i.e., 67% versus 83%) and

severity (i.e., 129 versus 235 summative accumulation) of upper-GIS symptoms; however, they did not reach statistical significance (i.e., trend at $p=0.066$ and $p=0.087$), respectively [231]. Additionally, no difference in cytokine profile was reported. These modest benefits with lower drink temperatures on intestinal injury and/or Ex-GIS (i.e., incidence and severity) are likely attributed to the modest suppressed rise in core body temperature; it can be speculated that it could potentially have been more beneficial if greater difference in core body temperature were observed [71, 83]. Further research has shown that ingestion of 617 g of a sports drink ice slurry during the cycle leg of a simulated Olympic distance triathlon in 32–34 °C (20–30% RH) attenuated intragastric body temperature and was well-tolerated, but no other markers of EIGS were reported [232]. One recent study reported no difference in markers representative of disturbed gastrointestinal integrity (i.e., I-FABP and LPS) with the frequent (i.e., pre-exercise and every 15 min) provisions of a carbohydrate–electrolyte ice slurry and respective carbohydrate–electrolyte beverage at ambient temperature during 45 min running at 60% $\dot{V}O_{2\text{peak}}$ that was followed by a second run until volitional exhaustion at 70% $\dot{V}O_{2\text{peak}}$ [233]. The research protocol of this study provided carbohydrates during exercise, which is aligned with attenuating exercise-associated disturbances to gastrointestinal integrity, as previously discussed in Sect. 4.1. Therefore, it is not surprising that no intervention outcomes were observed, since the study overall negated its primary research focus owing to this erroneous protocol oversight (i.e., carbohydrate provisions before and during exercise) in assessing the impact of internal per-cooling on markers of gastrointestinal integrity [67]. To date, internal cooling with cold water and ice slurry during exercise appears to be well-tolerated and contributes to suppressing the rise in core body temperature, which has positive associations and can predict the magnitude of EIGS and Ex-GIS [83]. Indeed, additional research using more robust experimental designs and control, ensuring that greater difference in core temperatures are achieved, and employing a wide array of EIGS markers is warranted.

Grade of Evidence: III

8.3 External Cooling

External cooling methods consist of the application of a cold medium such as ice vests/packs, cold towels, or cold-water immersion. These methods can reduce pre-exercise core body temperature and increase the core to skin temperature gradient [226]. Similarly to internal cooling, external cooling strategies may attenuate EIGS through directly lowering peak core body temperature and/or delaying the rise in core body temperature during exercise and heat stress load. Research on the gastrointestinal responses to

external cooling methods is limited to systemic inflammatory cytokine responses, with one pre-cooling study demonstrating a small attenuation of IL-6 and IL-10 responses with 60 min cold water (20 °C) immersion before 90 min of running at 65% $\dot{V}O_{2\max}$ in 32 °C (47% RH) [234]. While another study demonstrated no difference in IL-6 with application of an ice vest and cold towel before 30-min intermittent sprint exercise in the heat [235]. Further exploration into external pre- and per-cooling methods in isolation and in combination with internal cooling methods is warranted and may provide a more thorough insight into how cooling strategies may directly or indirectly impact markers of gastrointestinal integrity or function, systemic responses, and subsequent Ex-GIS. In addition, despite extensive research into the impact of cold (i.e., ≤ 0 °C) exposure, with and without exercise, on many physiological variables [236–239], the direct impact of external extreme cold stimulus and/or states of hypothermia on the gastrointestinal tract is still relatively unknown and warrants exploration.

Grade of Evidence: III

9 Gut Training

The idea of a highly adaptable gastrointestinal tract was first proposed in the 1990s [240]. Training the gut through constant exposure to nutrition around exercise is proposed to improve its function and thus an individual's tolerance to feeding during exercise, subsequently reducing the risk of Ex-GIS [241]. With the first few proof-of-concept studies in athletes only published in recent years, gut training remains an understudied topic.

9.1 Repetitive Feeding Challenge

The various approaches to gut training target the gastrointestinal tract's adaptive potential that may occur with this strategy, and its relevance in managing EIGS and/or Ex-GIS have been explored through a SLR [241]. First, increasing the stomach's capacity and tolerance to larger gastric content could reduce the sensation of fullness. The ability for gastric adaptation to food intake volume is observed anecdotally or in non-exercise settings (e.g., competitive speed eating contests and eating disorders) [242–244]. Gut comfort and/or Ex-GIS improved among runners through daily repetitive ingestion of nutrients (90 g/h 2:1 glucose:fructose 10% w/v) and a high fat supplement (33 g fat, 9 g protein, and 9 g CHO per hour) during exercise for 1–2 weeks [42, 43, 106], and repeated ingestion of sweat rate-matched fluids [245].

Second, it is proposed that gut training can increase gastric emptying. Despite the existing evidence on nutrient-specific changes in gastric emptying in non-athletic human populations [246–248], this has yet to be proven within an exercise model. Third, a higher carbohydrate intake both during exercise and/or overall daily intake can increase intestinal absorptive capacity. Preliminary evidence in animal models showed nutrient-specific upregulation of intestinal transport proteins through taste-transduction pathways (e.g., type 1 taste G protein-coupled receptors (GPCRs), α -gustducin) [249–251].

Additionally, the increase in nutrient absorption, gastric emptying, and gastrointestinal motility may also be improved through the inhibition of the ileal break mechanism [55, 252, 253]. This is only indirectly supported by existing gut-training studies looking at breath H_2 concentrations, [42, 43, 65] and carbohydrate availability and oxidation [42, 254]. Specifically, carbohydrate malabsorption to a 90 g/h 2:1 glucose:fructose gut-challenge was reduced after gut training (i.e., 2 weeks of daily repeated feeding-challenge), but not on matched placebo [42, 43]. These findings were speculated to be caused by improved intestinal carbohydrate absorption, as supported by higher blood glucose concentration during exercise post-gut training, but not on matched placebo. This increased carbohydrate availability seen in Costa et al., [42] was not observed by increasing daily dietary carbohydrate intake for 28 days [254]. Moreover, carbohydrate malabsorption was not observed to any substantial relevant level (i.e., breath H_2 : 5 ppm before gut training and 4 ppm post-gut training) in response to a formulated 87 g/h glucose feeding challenge during exercise [106, 255]. This suggests that fructose may be the prime culprit in the malabsorption observed in the initial trial of Costa et al. [42], irrespective of co-ingestion with glucose, and subsequent improved fructose absorption in the post-gut training trial (also see supplementary file 1, carbohydrate type). From a professional practical perspective, such outcomes have been observed in athlete support intervention (i.e., case study). In these, higher carbohydrate doses with the inclusion of fructose (25 g) result in greater carbohydrate malabsorption (10 ppm breath H_2) versus lower total carbohydrate and fructose (12.5 g) dose (6 ppm breath H_2) [64]. Lastly, the impact of a repetitive feeding challenge on intestinal epithelial integrity (i.e., plasma I-FABP concentration) has been explored, but no effects have been observed. There was a substantial amount of individual variation within studies for intestinal epithelial integrity markers, likely associated with differences in nutrient (e.g., carbohydrate) content and processing along the gastrointestinal tract during the experimental procedures [42, 65], as discussed in Sect. 4.1.

PREVENTION OR MANAGEMENT OF EIGS AND EX-GIS

A. Essential prerequisite for professional practice:

- Updated knowledge and understanding of aetiology, pathophysiology, and exacerbation factors.
- Updated assessment methods and technique skill development and competency.

↓
**Theoretical education package.
Practical training and competency review**
↓

Bi. Gut assessment during exercise:

- Prior clinical assessment and/or investigation to dismiss inflammatory diseases of the gastrointestinal tract and disorders of gut-brain interaction (a.k.a., functional gastrointestinal disorders).
- Stage 1: Standard feeding challenge during exercise- feeding tolerance, gastrointestinal integrity and functional issues, and exacerbation factor investigation (Table 1)^a.
- Stage 2^b: Specific assessment: gastrointestinal integrity and/or functional markers, and/or systemic response markers.
- Stage 3^b: Additional specific assessment: gastrointestinal integrity and/or functional markers, and/or systemic response markers.
- Additional specialist referral, if required.

^a Medical clearance- After confirmation and in the absence of gastrointestinal integrity and/or functional diseases/disorders, and other medical conditions that may affect gastrointestinal status.
^b If required, and based on data outcomes from Stage 1.

Individually tailored intervention:

- Dietary adjustments.
- Training and competition (i.e., exercise) adjustments.
- Heat mitigating strategies.
- Hydration.
- Pre, during, and post exercise food and fluid intake.
- Intrinsic and extrinsic exacerbation factor management.

Bii.

Generalised broad approach

First line action:

- Start exercise euhydrated and maintain euhydration throughout (within individual tolerance).^{**}
- Identify and apply individual feeding tolerance to carbohydrate intake during exercise (e.g., feeding challenge assessment or 1 g/kgBM/h).[#]
- Carbohydrate and/or protein immediately before and frequently throughout exercise (within individual tolerance).^{**}
- Gut training protocol (foods and/or fluids).[#]
- Cooling strategies aimed to limit substantial rises in core body temperatures (e.g., $\geq 39.5^{\circ}\text{C}$).^{*}
- 24 to 48 h high carbohydrate low FODMAP diet.[#]
- Avoidance of non-steroidal anti-inflammatory agents.^{*}

Adjustment strategies:

- Nutritional supplementation strategies (i.e., mixed amino acid formulation, citrulline, prebiotics, curcumin, and anthocyanins).^{*c}
- Feeding tolerance adjustment considerations: intake volume, nutrient concentration, dose and frequency, intake texture form, and carbohydrate type.[#]

^c Considering the substantial beneficial impact of pre- and during-exercise carbohydrate and/or protein intake (within tolerance) on exercise-associated perturbations to gastrointestinal integrity and systemic responses, and ease of application, the proposed nutritional supplementation strategies are of no additional benefit and are obsolete in nature.

^{*} Targeted at gastrointestinal integrity, and subsequent systemic responses, with links to delayed and prolonged upper and lower Ex-GIS.

[#] Targeted at gastrointestinal functional responses, with links to rapid onset and transient or prolonged upper and lower Ex-GIS.

C. Strategies to avoid, unlikely to be beneficial, or have no impact:

- Hyperhydration intervention strategies including glycerol and sodium.
- Dietary modification and adherence: gluten-free, low carbohydrate high fat (ketogenic), and short-term low energy availability.
- Nutritional supplement interventions (i.e., glutamine, arginine, antioxidants, probiotics, synbiotics, bovine colostrum, and nitrate).
- Pharmaceutical administration including antiemetics and antacids.
- Gut training protocol using non-caloric sweeteners.
- Application of physical manoeuvres.
- Use of compression socks.
- Feeding tolerance adjustment considerations that increase risk of Ex-GIS: fructose tolerance, glucose molecular weight, and modified starch.
- Feeding tolerance adjustment considerations that have no effect: multiple transportable carbohydrates, hydrogel, caffeine inclusion, coconut water, and dairy.
- Despite limited empirical evidence, it has frequently been reported by ultra-endurance athletes that consuming high fibre food leading into and during single- and multi-stage events results in an increased lower-abdominal discomfort, flatulence, urge to defecate, defaecation, and abnormal stools (e.g., loose and watery stools, and diarrhoea). In such cases, high fibrous foods and fluids should be avoided and an alternative adopted.

◀**Fig. 2** Schematic flow illustration of the professional practice guidance for the prevention or management of exercise-induced gastrointestinal syndrome (EIGS) and aligned exercise-associated gastrointestinal symptoms (Ex-GIS) [12, 67, 75]

Overall, the potential adaptations to gastrointestinal accommodation, motility, and absorption could lead to less Ex-GIS and better tolerance of nutrition during exercise, and subsequent enhanced exercise performance outcomes, as previously observed [42, 43]. To date, there is some evidence to support repetitive gut-challenge protocols in the prevention and management of EIGS and Ex-GIS [12, 241]. However, it appears to mainly benefit carbohydrate malabsorption and associated Ex-GIS, with more advanced gastrointestinal functional measures still warranting investigation and no impact on gastrointestinal integrity evident.

It is also important to highlight that intermittent fasting is now a common practice in the sporting community with the aim of modifying body composition without performance decrements [256]. Considering the potential physiological and biochemical adaptations associated with gut training are at the expense of substantial and constant nutrient provisions, it is unknown whether such fasting practices and subsequent reductions in nutrient exposure are counterproductive in regard to gastrointestinal functional responses, Ex-GIS, and their performance implications. Nevertheless, from a gastrointestinal and professional practice perspective, it appears that overall carbohydrate intake tolerance in the general active population equates to a liquid form at ≤ 1.0 g/kgBM/h in 6–10% w/v with a simple glucose formulation [42, 54, 66, 73, 117]. Greater carbohydrate volumes and concentrations and/or altered forms (e.g., other and/or multiple carbohydrate forms, semisolid to solid textures, and/or inclusion of other substances such as caffeine) appear to be at the discretion of individual tolerance and/or gut training to improve formulation specific tolerance (see supplementary file 1).

Grade of Evidence: I

9.2 Non-caloric Sweeteners

Similar to the mechanisms proposed for repetitive feeding challenge, consumption of non-caloric sweeteners may play a role in enhancing intestinal glucose uptake through the upregulation of active (i.e., SGLT1) and passive (GLUT5) transporters at the enterocyte apical surface, with or without upregulating GLUT2 at the basolateral surface, although this has primarily been observed in animal models [250, 257]. As such, enhancing glucose absorption and reducing the overall nutrient residue along the gastrointestinal tract may be linked to reducing Ex-GIS. Only one study to date has investigated the effects of sucralose supplementation (1 mM every

15 min for 2 h) prior to 2 h cycling at 48% $\text{VO}_{2\text{peak}}$ [258]. No difference in overall Ex-GIS was observed in response to a carbohydrate challenge (1.2 g/kg/h maltodextrin) during exercise between the sucralose and control trials. While the exercise stress was insufficient to warrant any substantial gastrointestinal disturbance [67], it is important to note that GIS were only measured post-exercise retrospectively.

Grade of Evidence: III

9.3 Fluid Tolerance Training

Considering the plasticity of the stomach chamber to volume, repeated exposures to ingesting large fluid volumes (e.g. > 800 mL/h) may effectively improve stomach emptying rate and subsequent comfort. Ingesting a 4% w/v carbohydrate–electrolyte beverage every 10 min during running to match sweat losses (830 mL/h) increased stomach fullness from 2 (2.0: comfortable) to 2.3 (3: moderately uncomfortable), when compared with ingesting the beverage ad libitum (338 mL/h) [245]. A total of five repeated trials (every 7–11 days) of 90 min running at 65% $\text{VO}_{2\text{max}}$ with volumes to match sweat loss significantly improved stomach comfort. Gastric emptying assessed on the first and fifth run remained unchanged, indicating that the improvement may be related to sensory factors and tolerance (e.g., desensitization) in coping with increased intragastric pressure.

Grade of Evidence: III

10 Translation to Practice

Considering that intervention research shows large individual variation in assessment markers synonymous with EIGS and factors exacerbating Ex-GIS in athletes [3, 67, 259], there is no one standard approach and therapeutic intervention for EIGS and Ex-GIS prevention or management. This means practitioners should be cautioned against providing generalized prevention and management strategies of EIGS and EX-GIS, as each individual athlete case is different and unique. To determine the most effective strategy in prevention and management, an individualized assessment to establish the underlying causes and exacerbators of EIGS and Ex-GIS is of vital importance. Supplementary file 3 covers practical aspects of the management of EIGS and Ex-GIS in sports and exercise clinical practice, elite sports performance, and field based competitive events. Context acknowledges and highlights individualization in the prevention and management pathway [12, 75], as well as other underlying factors from an individual athlete perspective and sports-specific training or competition aspects, which may promote exacerbation of EIGS and subsequent

Ex-GIS. These can include predisposition, established diseases/disorders, or other underlying health influencing behaviors that may alter gastrointestinal integrity and/or functional response to exercise [165]. It can include training or competition aspects relating to pathogen exposure and contamination (i.e., environmental, population contact, and/or equipment cross-contamination) that may induce acute or chronic gastrointestinal-associated illness or infection [260].

11 Summary

From historical to more recent evidence, it is now established that exercise stress causes an array of asymptomatic and symptomatic gastrointestinal integrity and functional disturbances, which may lead to health-impacting systemic responses and outcomes. Furthermore, such gastrointestinal disturbances are linked with rapid onset or delayed, and acute or prolonged, gastrointestinal symptoms, which have profound performance-impairment implications (i.e., reduced workload, cessation of exercise, or withdrawal from activity). From a professional practice perspective, it is therefore not surprising that athletes and athlete support practitioners are exploring effective ways to prevent and manage exercise-associated gastrointestinal perturbations and aligned symptoms. On the basis of the current available evidence from exercise gastroenterology research that generally meets a minimum level of quality of methodologies for best-practice experimental design, Table 3 presents a summary of prevention and management strategies and their impact on parameters of EIGS and Ex-GIS. On the basis of the efficacy of presented strategies, Fig. 2 presents a professional practice guidance schematic in the prevention and management of EIGS and Ex-GIS.

In short, the first-line actions consist of: (i) preparing the gastrointestinal tract for exercise; (ii) limiting gastrointestinal integrity, functional perturbation, and systemic responses during exercise; and (iii) restoring gastrointestinal patency post-exercise to support recovery nutrition. First-line actions also include avoiding factors and strategies reported to exacerbate or have no impact on EIGS and Ex-GIS. For those athletes experiencing recurrent Ex-GIS episodes, second-line action include undertaking a gastrointestinal assessment during exercise, as described in supplementary file 3 entitled Translation to practice: Assessment and intervention procedures for clinical practice—Supporting the individual athlete. This process would take into consideration individualized data and findings from testing procedures into EIGS and Ex-GIS causal factors and align with relevant prevention and management strategies that have proven effective in research settings. Adopting and adhering to such assessment and intervention procedures requires a multidisciplinary approach.

Therefore, understanding one's scope of practice and appropriate local and/or external referral pathways is a fundamental part of competent and effective practice. In addition, it is recommended that professional practitioners supporting athletes with gastrointestinal issues undertake ongoing education and training to gain or update knowledge and understanding of how the gastrointestinal tract responds to exercise, thus enabling the provisions of effective and competent practice.

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Conflicts of Interest Costa, Gaskell, and Snipe have contributed to the development of exercise gastroenterology educational material previously presented on the Future Learn online learning platform, targeting health and exercise professionals, as part of Monash University continued professional development educational packages. Costa is currently responsible for the delivery and management of educational resources in the training of sport and exercise professionals supporting athletes with gastrointestinal issues within national sport institutes and professional sports clubs. Costa is the lead of the Monash University Exercise & Nutrition Clinic that offers specialized gastrointestinal assessment services to athletes with clinical justification. Costa and Scheer are members of the USSF scientific committee. Costa is a member of the SDA education committee. Costa, Gaskell, Henningsen, Jeacocke, Martinez, Scrivin, Snipe, and Young are members of SDA. RC was the chief investigator of two EIGS prevention or management strategy research projects that received funding from commercial industry collaborators [136, 184]. All funding and conflicts of interest regarding these original studies are fully disclosed in the original publication. All other authors have no other conflict of interest to declare.

Availability of Data and Materials Data and materials presented within this review can be made available by contacting the corresponding author, at reasonable request.

Ethics Approval Not applicable.

Author Contributions Authors contributions, which included exploration of the topic area literature using a scoping review approach, critical evaluation of referenced studies' methodological application against best-practice checklist (Costa et al., 2022), level of evidence proposal, practical application, and/or initial text draft of section, are as follows and based on track record (research and practice) in the specific topic: background, R.C.; exercise-induced gastrointestinal syndrome (EIGS), R.C.; exercise-associated gastrointestinal symptoms (Ex-GIS), R.Sc.; EIGS and Ex-GIS exacerbation factors, R.C.; methodological considerations, R.C.; macronutrients and equivalents, R.Sn. and R.C.; dietary strategies, S.G., R.Sc., A.W., and R.C.; nutritional supplements, K.H., P.Y., and R.C.; hydration, R.C.; heat mitigating strategies, R.Sn.; gut training, I.M.; feeding tolerance (supplementary file 1), R.C.; other considerations (supplementary file 2), A.M. and R.C.; and translational application (supplementary file 3), S.G., N.J., and V.S. R.C. compiled

sections and levels of evidence. All authors reviewed and approved the compiled sections and grade of evidence. All authors read and approved the final version.

Informed Consent Not applicable.

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