AIS SPORTS SUPPLEMENT FRAMEWORK

PROBIOTIC SUPPLEMENTS

It is now well established that acute and chronic exercise perturbs various aspects of an athlete's gastrointestinal tract (e.g., exercise-induced gastrointestinal syndrome;[1]) and immune system function (exercise-associated immune perturbations[2]). Probiotic supplements have been proposed to mitigate some of these perturbations[3].

What does it do?

- Probiotics are live microbial (e.g. bacterial species/strains) food components or supplements that have been proposed to survive oral to colonic transit; and potentially impact function of the gastrointestinal tract, and oral-respiratory mucosal and/or systemic immunity.
- Commercial availability of probiotics in food, fluids, or supplement forms include the following bacterial species/strains:
    - *Lactobacillus* (e.g. *plantarum, acidophilus, rhamnosus, paracasei, bulgaricus, fermentum*)
    - *Bifidobacterium* (e.g. *infantis, longum, animalis lactis, breve*)
    - *Streptococcus* (e.g. *faecium, thermophilus*)
    - *Saccharomyces* (e.g. *cerevisiae, boulardii*)
    - Novel strains: genus *Akkermansia* (e.g. species *muciniphila*), *Clostridium* (e.g. species *leptum*), *Faecalibacterium* (e.g. species *prausnitzii*), *Roseburia*, and *Propionibacterium.*
    - Multi-strain supplements generally include strains from the species *Lactobacillus*, *Bifidobacterium*, and *Streptococcus*
- The interaction between the "gut microbiome" and human biological systems has gained significant research interest and associated translational application. The role of commensal and pathogenic bacteria, and their metabolic by-products such as short chain fatty acids (SCFA) and structural residues (e.g. endotoxins), are increasingly being recognized as contributing to the attenuation or exacerbation of pathophysiologic pathways in numerous clinical conditions (e.g. cardiometabolic, mental health, gastrointestinal disease and disorders, and systemic inflammatory conditions)[4,5]. Therefore theoretically, provisions of bacterial groups that may favourably alter the oral-respiratory and/or gastrointestinal microbiota may provide beneficial health and performance outcomes[4-8].
- The mechanisms by which probiotics might benefit oral-respiratory and/or gastrointestinal tract function of athletes undertaking strenuous training and competition loads include:[4,5,7-14]
    - Upregulation of oral-respiratory anti-microbial agent secretion (i.e., immunoglobulins (IgA), α-amylase, lysozyme, lactoferrin, and defensins).
    - Upregulation of the gastrointestinal-associated lymphoid tissue activity.
    - Increasing the relative abundance of supplemented strain/species of commensal bacteria (e.g., *Bifidobacterium* and *Lactobacillus*), and subsequent potential changes in α-diversity by altering the relative abundance of other commensal bacteria and/or reduction in pathogenic bacteria (e.g. *E.coli, Shigella*) along the gastrointestinal tract. Increased relative abundance of commensal bacterial may increase bacterial fermentation activity leading to enhanced concentrations of luminal and/or plasma SCFA.
    - SCFA may enhance the mucosal lining, enterocyte stability and functional capabilities, antimicrobial protein and immunoglobulin secretions, immune regulation of luminal pathogenic agents including enhanced regulation of local inflammatory responses, and epithelial tight-junction protein stability and regulatory function.
    - Both faecal and plasma SCFA concentrations (and/or aligned bacterial groups) have been linked to protecting gastrointestinal integrity against exertional and exertional-heat stress.
- Research investigating the effects of varied probiotic supplementation on markers **of oral-respiratory mucosal immunity**, from acute exercise bouts to chronic exercise training, are generally limited to reporting reduction in subjective upper-respiratory symptoms (URS), with or without modest changes in mucosal (i.e. enhanced salivary anti-microbial proteins) or systemic biomarker (i.e. reduced cytokine or cellular responses) of oral-respiratory immune status.[15-20]
    - There is no substantial evidence for reduction in pathogen identified oral-respiratory infection/illness or translational impact into performance outcomes.
- Despite consistent reports of the beneficial effects of probiotic supplementation **on gut status of athletes**

in numerous narrative reviews, a recent systematic literature review reported that:

  - Probiotic/synbiotic supplementation increases faecal relative abundance of the supplemented species/strain at rest, but did not alter faecal relative abundance of other commensal bacteria and subsequently α-diversity, and/or faecal SCFA concentrations at rest.
  - Probiotic/synbiotic supplementation did not provide any substantial beneficial effects to markers of EIGS and/or Ex-GIS to acute exercise bouts ranging from 2 h of exertional-heat stress to a long-course triathlon.[3]
  - Synbiotic formulation and outcomes followed probiotic form, as they included insufficient prebiotic dose to warrant any changes to faecal bacterial profile or SCFA concentrations (see prebiotic fact sheet).[3]

- Such outcomes have been further supported by other systematic literature reviews providing no convincing evidence of any substantial beneficial effects resulting from probiotic supplementation in healthy active populations.[21-24]

What does it look like?

- Probiotics can be obtained from both foods and commercial supplements. Foods such as yoghurt and cultured milk products, and fermented drinks such as kombucha and kefir, are a potential choice given synergistic effects between food compounds and probiotic bacterial cultures.
- Single or multi-species/ strain supplements may be purchased in shell-stable (e.g. dried) format for easy transport, or as 'live' products that need to be refrigerated. Additionally, some medical grade probiotic preparations are also available on prescription but are limited to specific clinical diagnosis (e.g. bacterial gastroenteritis).
- The shelf-life of most probiotic products is about 3-6 weeks when kept at 4ºC. The shelf-life of dried supplements is about 12 months, but levels of probiotics may drop significantly over this time[9]. The concentration of bacteria in food products varies substantially and some exploration has indicated that commercially available probiotic products present issues with live bacteria presence and quantity[10,11].

How and when do I use it?

- **Only after manipulation of diet** to facilitate an increase in gut microbiota diversity (e.g. via increase in prebiotic and food-based probiotic sources), should probiotic supplementation be considered (see prebiotic fact sheet).
- Sport and exercise researched doses range from $x10^8$ to $x10^{10}$ CFU (Colony Forming Units)/day and appear to be safely tolerated. Duration of intake in the scientific literature has ranged from 1-16 weeks. However, emphasis is on ongoing consecutive daily consumption in order to theoretically change and maintain the relative abundance of supplemented bacterial species/strain along the oral to colonic tract and/or the gut microbiota commensal bacteria diversity.
  - Research on probiotics and oro-respiratory mucosal immunity points to benefits in reducing incidence and severity of upper-respiratory symptoms[15,19]. Given the reasonable likelihood of athletes experiencing symptoms of potential respiratory illness at some point in a training and competitive season a prophylactic approach before specific periods of heavy training, travel or major competition could be useful[25]. However, prior to probiotic supplementation for upper-respiratory symptom management, it would be advisable for assessment and/or diagnosis of infection vs non-infectious symptomology[26].
  - Athletes taking antibiotics may benefit from taking specific probiotic strains (*Lactobacillus rhamnosus* or *Saccharomyces boulardii* at 5 to 40 billion CFU/day) in order to reduce the risk of antibiotic associated diarrhoea[27].
- Athletes with recurrent history of gastrointestinal symptoms at rest and not around exercise, should avoid using probiotics and should seek assessment and support from a clinical gastroenterologist.
- Athletes with a prior history of gastrointestinal symptoms around or during exercise (e.g. heavy training or competition) should avoid using probiotics, and seek the support of a sports dietitian. Gastrointestinal assessment protocols at rest and during exercise have been developed for athletes and warrant following procedures[28].
- Irrespective of whether the application is targeted or prophylactic, an individual needs to commence daily supplementation for **approximately 14 days beforehand** to allow for colonisation of the specific bacterial species/strain bacteria in the gut.

Prescription

- **What:** In addition to ensuring sufficient prebiotics and probiotic-rich foods, the targeted addition of shelf-stable probiotic supplement strains (capsule / powder form).
- **When:** 14 d before and throughout the period of heavy training, travel and/ or important competition, OR at onset of and throughout the duration of antibiotic use (specifically *Lactobacillus rhamnosus* or *Saccharomyces boulardii).*
- **How much:** x10^8 to x10^{10} CFU/day
- Practitioners are encouraged to check current research regarding specific strains and doses of probiotics for the intended purpose of use due to the dynamic nature of this area.

Are there any concerns or considerations?

- The majority of studies investigating the effects of probiotic (or synbiotic) supplementation within exercise immunology research have reported in subjective URS and transferred these at upper-respiratory tract infection, despite no pathogenic infection/illness generally being explored or identified. One recent study provided an anti-inflammatory spray and observed reductions in URS. This suggest some of the 'so-called' upper respiratory infections are likely to be symptoms from local inflammation origin and not pathogenic infection.[26,29]
- The majority of studies investigating the effects of probiotic (or synbiotic) supplementation within exercise gastroenterology research have generally failed to follow the best practice recommendations.[3,30]
    - Athletes with established diseases/disorders/complications of the gastrointestinal tract, such as coeliac disease, disorders of the gut-brain axis (e.g. irritable bowel syndrome), gastrointestinal inflammatory diseases, and/or history of surgical procedures should avoid taking probiotic supplementation without the guidance of their supportive clinical gastroenterologist and/or sports dietitian.
    - **May cause GI side effects:**
        - On a cautionary note, one acute probiotic study observed greater exercise-associate endotoxemia and cytokinaemia in response to 2 h of exertional-heat stress compared with placebo, likely associated with the increased bacterial load induced by the probiotic intervention before gastrointestinal integrity compromising exertional-heat stress.[1,20] Therefore, such supplementation increases the risk for exercise-induced gastrointestinal symptoms in 'at risk populations'.
        - Some individuals report mild symptoms of stomach rumbles, increased flatulence or changes in the stool during the first week of supplementation as the gut microflora changes to accommodate the newly introduced species. These symptoms may be reduced by a gradual introduction of the probiotic protocol, building up to the recommended dose over a week or two.
    - **Some products may not provide sufficient numbers or types of probiotics.** Issues with dosage, viability of probiotic species/strains, presence of CFUs, lack of industry standardisation, and potential safety issues, are being further investigated by food industries to improve quality control and product quality. However, caution and diligence are still warranted in probiotic consumption choice.
    - **Evidence for benefits of specific strains is still forthcoming.** Research is ongoing regarding the role specific probiotic strains have on health and wellbeing. The quality of research can vary and may not involve the verification of the true probiotic content of supplements used. The role of targeted probiotic strain formulations for specific health concerns is evolving and requires monitoring by practitioners.

Where can I find more information?

Sports Dietitians Australia	**www.sportsdietitians.com.au**
Batch tested products list	https://www.informed-sport.com/ https://hasta.org.au/
Supplement safety information	www.sportintegrity.gov.au/what-we-do/anti-doping/supplements-sport

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Athletes should be aware that the use of supplements may have anti-doping implications. Athletes are reminded that they are responsible for all substances that enter their body under the 'strict liability' rules of the World Anti-Doping Code. We recommend that all athletes consult the advice of Sport Integrity Australia (SIA) regarding contamination issues related to supplements and sports foods. The ASADA Clean Sport mobile app is also a useful resource to help mitigate the risk of inadvertent doping via supplement use by helping to identify supplements that have been independently verified to be free of WADA banned substances. (https://www.sportintegrity.gov.au/what-we-do/supplements-sport)

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