# DSTG Human Biotechnologies Program: Trajectory

# **Papers**

The following Ergogenic Aids Trajectory Paper forms one part of a series of 7 documents:

- Preamble
- Brain-Immunology Trajectory Paper
- Microbiome Trajectory Paper
- Epi- and Genetic-Manipulation Trajectory Paper
- Ergogenic Aids Trajectory Paper
- Real-Time Biometrics Trajectory Paper
- Addendum compiled by the Chair of Human Biotechnologies program, Professor Mark Hutchinson

Although each Trajectory Paper may be treated as a standalone document, it is highly recommended to read the preamble first. Importantly, the preamble contains relevant background on basic physiological concepts that span across the Trajectory Papers. This format streamlined the Trajectory Papers to focus on the current state of knowledge as it related to their respective fields and prevented repetition of concepts. The preamble also highlights the interrelated nature of the Trajectory Papers which can be visually conceptualised in a flow diagram. Hyperlinks are prevalent throughout the documents to assist the reader in locating relevant information across all of the documents. The preamble includes cliff notes on various topics related to physiological concepts explored throughout the Trajectory Papers and may be useful for readers depending on their expertise. Throughout each Trajectory Paper hyperlinks refer the reader back to the preamble to access basic physiological concepts.

# 5. DSTG Trajectory Paper Series: Ergogenic Aids

#### Authors

Professor Paul E. Rolan<sup>1</sup>, Dr Juliana E. Bajic<sup>1,2</sup> & Professor Mark R. Hutchinson<sup>1,2</sup>

1. School of Medicine, University of Adelaide, Adelaide, SA 5005, Australia

2. ARC Centre of Excellence for Nanoscale Biophotonics, University of Adelaide, Adelaide, SA 5005, Australia

# 5.1. State-of-the-Art Review of Ergogenic Aids: Current Status and Limitations

### 5.1.1. General Background

The environments and scenarios encountered by military personnel are some of the most physically and mentally challenging ones in which human beings are regularly required to operate. Military action can require personnel to rapidly be placed under physically and mentally demanding environments whilst maintaining the highest possible levels of performance leading to competitive advantage and enhanced survival. Whilst it is noted that the physiological and psychological stressors of athletes in competitive sports is distinct to the general population, these stressors can not be asymmetrically compared with Warfighters. Regardless of this matter, data obtained from athletes and in some cases civilian populations offer military researchers with valuable sources.

This paper summarises the current state of knowledge on ergogenic aids and explores opportunities and activities with a suggested timescale for the adaptation or development of medical and related technologies that will provide competitive advantage to military personnel. Additionally, a framework for the safe application of such technologies will be included. The technologies discussed in this paper include pharmaceuticals and devices which enhance, but do not replace, physiological function. Pharmaceuticals have generally been developed to treat illness or replace deficiencies to restore physiology to the normal state, homeostasis. Already, some pharmaceuticals developed to treat illness have been shown to have military application, e.g. stimulant use to enhance military flight crew performance [1]. However, the differentiation between restoring to normal physiology (homeostasis; relief of disease) and the enhancement of normal physiology to give competitive military advantage requires a different evidence-base and regulatory and application framework. Although pharmacological effects demonstrated in the relief of disease might be useful for generating hypotheses as to potential performance enhancement, a specific research program directed at military performance enhancement will be necessary to obtain optimal results.

### 5.1.1.1. Defining Ergogenic Aids

*Ergogenic aids* are mechanical, nutritional, pharmacological, physiological and psychological tools used by an individual to strategically advantage themselves through the enhancement of their physical or psychological performance and/or recovery capabilities [2]. For the purposes of this paper, the term *ergogenic aids* will include pharmaceuticals and biotechnology products alone or in combination with devices/wearables, together or in sequence, to optimise Warfighter performance and resilience. Given the increasingly specialised nature of many Warfighter roles, it is likely that optimum use of ergogenic aids will not be on a universal all-personnel basis but will be targeted to address the following questions:

- What is the desired enhancement?
- For which personnel is this enhancement most valuable?
- What is the time course over which this enhancement is to take place is it be be sustained or to be turned on and off in a situation-specific manner? Interventions with intense effects may not be suitable for sustained use hence the temporal aspects of such interventions need to be optimised.
- How are the risk of undesired effects to be mitigated?

# 5.1.2. Current State of Knowledge on Ergogenic aids in Civilian/Athlete Populations

### 5.1.2.1. Key Findings from Meta-Analyses Search on Ergogenic Aids

A pubmed meta-analyses search on ergogenic aids (post 2010) to provide a foundation of the current literature consensus resulted in 18 studies. One of the studies examined personal and psychosocial predictors associated with doping use in physical activity settings [3]. This study based variables on the theory of planned behaviour and we believe this was outside the scope of the current paper as it failed to relate the findings to performance outcomes, rather focused on the psychosocial and personal aspects associated with doping intentions. Another study investigated the global lifetime prevalence of anabolic-androgenic steroid (AAS) use and identified that the prevalence rate of use for men was higher than women, 6.4% over 1.6%, respectively [4]. Again, as this study focused on the epidemiology of AAS use rather than evaluating performance measures and accordingly was not included in the current paper. Similarly, a risk assessment conducted on the safety of oral BA supplementation was not included in the current paper as it failed to report on performance outcomes, yet it found that BA does not adversely affect those who consume it [5]. The remaining studies examined the effects of a range of ergogenic aids on performance outcomes which included physiological strategies, such as ischemic preconditioning, inspiratory muscle training, precooling with cold water immersion and ice ingestion, dietary supplementation, such as caffeine, carbohydrate,  $\beta$ alanine (BA), citrulline, creatine, ginkgo biloba, sodium bicarbonate and anabolic-androgenic steroids. The studies are summarised in Table 1 and a brief summary of the key findings are presented here.

### 5.1.2.1.1. Ischemic Preconditioning

Ischemic preconditioning has minimal to non-significant effects on performance when considering the fitness level of the individual [6]. Importantly, this study identified inconsistences in the statistical analyses and interpretation of the studies included in their analysis, advising a revision and refinement on the evaluation and interpretation of IPC on performance for future studies.

### 5.1.2.1.2. Dietary/Nutritional Supplements

Caffeine, sodium bicarbonate, BA, citrulline and carbohydrates were reported as generally having the most significant effects on various performance measures [5, 7-12]. However, it should be noted that caffeine appears to have a superior effect on improving the performance of rowers when compared to other dietary supplemental ergogenic aids, such as BA and sodium bicarbonate [12]. Caffeine taken in combination with carbohydrates was observed to have a small, yet significant effect on endurance performance compared to carbohydrate alone [13]. Sodium bicarbonate has an overall moderate effect size for its ergogenic potential but appeared to be more effective in recreation groups compared to trained participants [8]. Although BA was reported to improve exercise performance outcomes compared to placebo, improvements were evident in exercise capacity rather than performance and were not observed in exercise lasting <60s [7]. The acute effects of citrulline supplementation on high intensity strength and power training was identified to be somewhat beneficial to performance outcomes but with a small effect size of 0.20 [11]. Creatine appears to have beneficial effects on anaerobic performance tests in soccer players, yet no effect was evident on aerobic performance [14]. Ginkgo biloba was reported to have no ascertainable positive effect on various targeted cognitive functions in healthy individuals despite previous reports of cognitive improvement [15].

### 5.1.2.1.3 Anablolic-Androgenic Steroid (AAS) Therapy

Amongst athletes, competitive advantage has been (illegally) sought by using AAS which enhance muscle strength and endurance. These agents have shown that improvements in muscle strength and endurance can be achieved but not safely, with the transparency and completeness of adverse events reporting is lacking [16, 17]. There are a host of adverse events associated with AAS use, especially cardiovascular risks and psychopathologies, resulting in these agents being unsuitable for military use. However, recent pharmacological research has shown that selective androgen receptor modulators (SARMs) [18] may be able to produce some of the benefit on improving muscle function, without the adverse effects of full agonist anabolic steroids [17, 19-21].

### 5.1.2.1.4. Inspiratory muscle training (IMT)

IMT with linear workload devices (IMT-linear) improves sports performance across a range of modalities through improving maximal inspiratory pressure [22]. IMT-linear had no influence on maximal expiratory pressure and cardiopulmonary function markers in these athletes which suggests

that IMT-linear is a useful tool at improving inspiratory muscle strength and the sports performance of athletes.

### 5.1.2.1.5. Precooling Strategies

Precooling with cold water immersion (CWI) in hot environments improves a range of endurance performance measures, such as time-to-exhaustion and various psychophysiological parameters (e.g. lowering peak core temperature, whole body sweat response, etc.) [23]. Cold water immersion is more effective in improving performance measures than ice ingestion prior to exercise in hot conditions.

### 5.1.2.1.6. Hyperoxia Training

Hyperoxia training has been used as a long-term training stimulus or a recovery intervention due to its ability to increase tissue oxygen availability. Though it has been suggested to have ergogenic potential, it remains unclear as to whether this training form is effective in enhancing exercise performance or recovery. A recent survey of the literature of 51 studies on the topic identified that definitive conclusions were difficult to draw due to small sample sizes and a wide disparity in experimental protocols explored [24]. Nonetheless, they reported that exercise training and recovery in combination with hyperoxia training trended towards having a large and small ergogenic effect, respectively. Mallette *et al.* (2018) further explained that acute exercise performance was increased with hyperoxia training with improvements in the fraction of inspired oxygen (FiO2)  $\geq$  0.30 appearing to be beneficial for performance; elevated FiO2 was correlated to greater performance improvement in a range of exercises and muscle function tests. The effects reported in this meta-analysis discussed here warrants further exploration of hyperoxia training on enhancing performance.

Reference	Participants	Exercise	Ergogenic aid	Performance
		protocol		outcomes
Turnes <i>et al</i> .	Male rowing	2000 metre	Different	Caffeine showed
2019 [12]	athletes	rowing race	preconditioning	greatest
			strategies;	improvement
			caffeine, sodium	followed by sodium
			bicarbionate, β-	bicarbonate & BA.
			alanine (BA),	Heat acclimation,
			heat	rehydration, and
			acclimatisation,	creatine resulted in

Table 1. A summary of meta-analyses examining the effects of various ergogenic aids onperformance post 2010

			rehydration,	small to moderate
			creatine	enhancements
Marocolo <i>et al.</i> 2019 [6]	A wide array of healthy and active men and women from college to middle aged adults who are either on sports teams or active, play recreational games or are highly trained sports athletes.	Various forms: cycling, swimming, running, jumping/sprints, rowing, team sports, anaerobic cycling, resistance training, isokinetic, fatiguing, YOYO intermittent, drop jumps, leg extension and hand grip.	Ischemic preconditioning (IPC)	IPC has minimal to non-significant effects on performance when considering the fitness level of the individual and advised a revision and refinement on the evaluation and interpretation of IPC on performance for future studies.
Trexler, <i>et al</i> . 2019 [11]	Healthy men and women	High intensity strength and power performance measures.	Citrulline	Citrulline supplementation significantly benefited performance measures compared with placebo (p = 0.036) with a small effect size of 0.20.
Mielgo-Ayuso, et al. 2019 [14]	Healthy male athletes	Soccer	Creatine	Creatine did not improve aerobic performance tests or phosphagen metabolism performance tests (strength, single jump, single sprint, and agility tests). It did, however, show beneficial effects on anaerobic performance tests in soccer players at a specific dose.
Karsten <i>, et al.</i> 2018 [22]	Healthy young athletes, male dominated but some studies included women	A range of sports including swimming and wheel-chair sports	Inspiratory muscle training (IMT) with linear workload devices (IMT-linear)	IMT-linear improves sports performance via improving maximal inspiratory pressure, no effect

				on maximal
				expiratory pressure
				and cardiopulmonary
				function.
Choo, et al.	Healthy adults	Endurance	Precooling with	CWI is more
2018 [23]		performance	cold water	effective from both
			immersion (CWI)	ergogenic and
			or ice ingestion	thermoregulatory
				perspectives,
				compared to ice
				ingestion as a
				precooling
				treatment prior to exercise in the heat.
Mallette <i>et al</i> .	Healthy adults	A wide variety of	Hyperoxia	Exercise training
2018 [24]		exercise and	training	and recovery
[]		dynamic muscle		supplemented with
		activity tests		hyperoxia training
				has a beneficial
				effect on various
				exercise and muscle
				activity
Andrews <i>et al</i> .	Healthy adults	Various physical	Anabolic-	performance tests. Healthy exercising
2018 [16]		Various physical exercises	androgenic	adults who use AAS
2010 [10]		CACICISES	steroid use	underwent small
				absolute increases
				in muscle strength
				and moderate
				increases in lean
				mass. Adverse
				event data was
				missing in some studies, yet
				increased low
				density lipoprotein,
				decreased high
				density lipoprotein,
				irritability, and acne
				were reported by
D Y de la YU		Table 1	Carlada I. I.	some studies.
Pöchmüller <i>et</i>	Healthy male athletes	Trained cyclists	Carbohydrate	Significant
al. 2016 [9]	athletes		(СНО)	ergogenic benefit of CHO
				supplementation
				especially in
				concentration
				range of 6-8% when

				exercising longer
Hobson <i>, et al.</i> 2012 [7]	Healthy males and females of all ages from students to elite athletes	Cycling, running, isokinetic force production, strength and muscular endurance and rowing.	B-alanine (BA) supplementation, different doses	than 90min. BA improved exercise measure outcomes compared to placebo; improvement evident in exercise capacity rather than performance. No benefit of BA on exercise lasting <60 s, yet exercise lasting >60 s was significantly improved.
Peart <i>, et al.</i> 2012 [8]	Healthy men and women	Differing levels of activity from moderate to trained athletes.	Sodium bicarbonate	An overall moderate effect size was observed for its ergogenic potential but appeared to be more effective in recreation groups compared to trained participants.
Temesi <i>, et al.</i> 2011 [10]	Healthy men and women >16 years	Endurance time trials or exercise to exhaustion with varying exercises	СНО	CHO supplementation of between 30-80g/h enhances endurance exercise performance in adults.
Conger <i>, et al.</i> 2011 [13]	Healthy men and women	Endurance exercise performance task	CHO + caffeine	CHO+CAF ingestion provides a significant but small effect on improving endurance performance compared with CHO alone.

From the evidence presented above, some of the dietary supplementary ergogenic aids with performance enhancing outcomes may be readily incorporated into the diet of modern military members, such as caffeine, CHO, sodium bicarbonate, BA and citrulline. Additionally, IMT-linear strategies may have beneficial performance enhancing outcomes for military members, unlike ischemic preconditioning. However, the whole body cold water immersion strategy may prove unfeasible before or during deployment. It is unclear from the studies in this meta-analyses of the long term benefits of CWI prior to training in the heat. For example, would the implementation of repeated CWI practices in training improve the overall performance outcomes of military members during deployment and without access to cold water? Further, as technology develops it may be reasonable to assume that future ergogenic aids could facilitate the thermoregulatory capacity of military members to mimic CWI benefits through the use of appropriate smart textiles, biosensors and air/cooling filtration systems. For example, clothing that uses space as the heat sink is being developed at MIT which is inherently cooling [25]. As discussed in the **s47** Trajectory Paper, the engineering of thermoregulatory biosensors are well underway.

### 5.1.2.2. Key Findings from a Systematic Review Search on Ergogenic Aids

### 5.1.2.2.1. Caffeine

Caffeine is a useful ergogenic aid when taken moderately (3-6mg/kg) for endurance performance when slight improvements and small margins have significant implications for athletes [26]. This finding was measured by time trial performance and 46 studies were utilised to conduct a metaanalysis with improvements observed in overall mean power output and time trial to completion. Seven of the studies included in this review reported lower or slower time trial to completion and power output performance measures. Caffeine ingestion resulted in a significant ergogenic effect on the maximal muscle strength of upper body and muscle power, but improvements were not noticeable in lower body strength [27]. Supplementation with 3-6 mg/kg of caffeine increases the glycolytic contribution to energy metabolism during the execution of real or simulated combats, as indicated by elevated blood lactate concentrations [28]. This review also found that caffeine intake improved levels of strength, power and upper arm muscular endurance. Another study reported that the ergogenic effect of acute caffeine intake on anaerobic performance may be higher in men than in women as performance measures with respect to a placebo were higher in men than women athletes despite the same dose of caffeine being administered [29].

### 5.1.2.2.2. Sodium Bicarbonate

A recent systematic review on the effects of sodium bicarbonate on athletes divided their studies according to exercise duration;  $\leq$ 4 mins or >4 mins [30]. Sodium bicarbonate supplementation enhanced performance in 11 of 20 studies, whilst 6 of 15 studies with an exercise duration of >4 mins reported performance enhancing effects. The remaining included studies (total of 18/35) reported diverse results and this led to the researchers concluding that, supplementing the diet with sodium bicarbonate may enhance performance according to duration of exercise, but to which extent, remains unclear due to the inconsistencies in the remaining studies. It is important to note here that the systematic review aforementioned reported on a range of exercise tasks performed by athletes and on different dose regimes of sodium bicarbonate. These limitations can be avoided in future studies by examining the same (or very similar) exercise tasks, such as running, and dose regimes.

Runners may benefit from ingestion of sodium bicarbonate to improve middle distance performance [31]. Caffeine and carbohydrates were also reported to have similar enhancing effects on athletic running performance across multiple distances. Of the 23 studies reported, it was concluded that the most effective supplemental ergogenic aids for running distances between 400 m to 40 km were sodium bicarbonate (4 studies), sodium citrate (6 studies), caffeine (7 studies), and carbohydrate (6 studies). Research on the additive potential of combining such supplementary ergogenic aids is lacking, warranting exploration of this gap in the literature.

### 5.1.2.2.3. β-Hydroxy-β-Methylbutyrate Free Acid (HMB-FA)

HMB-FA supplementation was reported to have several performance enhancing benefits when taking in conjunction with resistance training [32]. This compound is a free acid which is suggested to accelerate skeletal muscle regenerative capacity following high-intensity exercise and attenuate markers of skeletal muscle damage. Additional performance improvements have been reported by its ability to augment acute immune and endocrine responses and enhance training-induced muscle mass and strength. Whilst this study only included a small number of articles (9), the evidence indicated that HMB-FA supplementation may also improve markers of aerobic fitness when combined with highintensity interval training. More studies are needed to expand on the limited amount of literature on the performance enhancing effects of this compound.

#### 5.1.2.2.4. Ginger

Like HMB-FA, only a modest number of studies have reported on the analgesic and ergogenic effect of ginger; the most recent systematic review on this topic was published in 2015 [33]. Ginger modestly reduces muscle pain stemming from eccentric resistance exercise and prolonged running, particularly if taken for a minimum of 5 days. When assessing the ergogenic effect of ginger, no discernible effects on body composition, metabolic rate, oxygen consumption, isometric force generation, or perceived exertion were observed. However, ginger may accelerate the recovery of maximal strength after eccentric resistance exercise, reducing the cardiorespiratory exercise-induced inflammatory response. The major limitations of the findings to the systematic review here related to the use of untrained individuals, insufficient reporting on adverse events, and no direct comparisons with nonsteroidal anti-inflammatory drug ingestion.

### 5.1.2.2.5. Herbal Extract Tribulus Terrestris (TT)

There is a belief across many athletic and bodybuilder audiences, which has been fuelled by marketing claims, that TT can enhance testosterone concentrations. Accordingly, a systematic review was conducted to assess this claim in animals and healthy humans [34]. The animal studies included in this review reported a significant increase in serum testosterone levels after TT administration. This effect was also noted in humans but only when TT was included as part of a combined supplement administration. Evidence from this review published in 2014, suggested that TT is ineffective for increasing testosterone levels in humans, thus marketing claims are unsubstantiated. The nitric oxide release effect of TT may offer a plausible explanation for the observed physiological responses to TT supplementation, independent of the testosterone level.

### 5.1.2.2.6. Cocoa Flavanols (CFs)

Due to the anti-inflammatory and anti-oxidant capacity of CF, it was suggested that CF may improve vascular function and potentially enhance exercise performance and recovery. A review of the literature published in 2018 identified that CF intake had little to no effect on exercise performance in a range of studies with untrained-overweight, untrained-healthy and trained individuals [35]. Regardless, several improvements were reported relating to vascular function, reductions in exercise-induced oxidative stress, and alterations in fat and carbohydrate utilization during exercise. Whilst there is clear evidence that CF improves numerous aspects related to exercise and recovery, the lack

of findings on the direct effects on performance warrants further investigation of the synergistic effects of chronic CF intake with exercise training.

#### 5.1.2.2.7. β-alanine (BA)

BA was reported to have positive effects on perceived performance exertion and biochemical parameters related to muscle fatigue [36]. The study mentioned here indicated that less evidence was found for an improvement in performance, similar to the meta-analysis conclusion mentioned above which found that BA improved exercise capacity rather than performance [7]. BA was also reported to decrease the feeling of fatigue and exhaustion, whilst increasing power output and working capacity related to exercise and athletic performance [37]. Body composition and carnosine content was also suggested to improve with BA supplementation. Conclusions made on the perceived positive effects on performance, including the reduced feelings of fatigue and exhaustion with BA supplementation warrant further exploration of this compound.

#### 5.1.2.2.8. Betaine supplementation

A systematic review on the effects of betaine on muscle strength and power, found 7 studies that fitted the inclusion criteria [38]. They concluded that there was an insufficient number of studies conducted to evaluate the effectiveness of betaine on enhancing performance with only 2 reporting improvements, again warranting further studies.

#### 5.1.2.2.9. Nicotine (smokeless)

There is a limited base of studies evaluating the effects of smokeless nicotine on exercise performance and physiological responses, yet some indicate that some endurance based performance parameters have been improved with use [39]. Substantial evidence indicates several beneficial physiological outcomes, anaerobic parameters were generally unaffected except one study that showed improvements in leg extensor torque.

#### 5.1.2.2.10. Whey Protein Supplements (WPS)

WPS enhances muscle performance and recovery via its effects on amino acids, creatinine kinase and myoglobin [40]. The overall quality of clinical evidence on WPS and its effects on performance was

deemed valid and reliable from a comprehensive survey of the literature published in 2019 [41]. The findings from this review supported the efficacy and safety of WPS on athletes' sports performance and recovery, validating its use a superior ergogenic aid when compared with L-alanine, bovine colostrum, carbohydrate, casein, leucine, maltodextrin, rice, protein, caffeine and placebos.

### 5.1.2.2.11. Transcranial Direct Current Stimulation (tDCS)

A systematic review published in 2019 identified that tDCS has beneficial effects on muscle strength (18 studies with 66.7% showing improvements in parameters assessed) with no adverse events reported [42]. The majority of the studies included were published post 2013. Isometric and dynamic contractions were evaluated. 10 studies examined strength alterations in regards to muscular endurance and/or muscular strength (50% revealed improvements of parameters assessed) and cycling was the only form of exercise reported. Endurance results were inconsistent amongst the literature so much work is needed in this area. Critically, this identifies a gap in available data of the potential effects of tDCS on upper body endurance. This is of particular interest to military as Warfighters on the frontline are expected to bear the heavy weight of weapons during battle, sometimes holding them pointed for unknown/long periods. Central fatigue can be improved through the use of tDCS on the primary motor cortex region due to its role in motor execution [43], thus stimulation of this region should be evaluated in military populations for its potential performance and endurance enhancing properties.

### 5.1.2.2.12. Respiratory Muscle Training (RMT)

RMT is an effective ergogenic aid, enhancing several modalities of exercise performance, such as running, cycling, swimming and rowing and a recent review of the literature (post 2013) was conducted [44]. The positive physiological mechanisms associated with the performance enhancing RMT effects are proposed to include diaphragm hypertrophy, muscle fiber-type switching, improved neural control of the respiratory muscles, increased respiratory muscle economy, attenuation of the respiratory muscle metaboreflex, and reductions in perceived breathlessness and exertion [see review for references; 44]. More recently, unequivocal evidence suggests that new strategies (i.e. functional RMT) may have an additive effect on performance under RMT conditions. These additive effects further improve various performance-related physiological mechanisms, such as, changes in ventilatory efficiency, oxygen delivery, cytokine release, motor recruitment patterns, and respiratory muscle fatigue resistance.

#### 5.1.2.2.13. Red ginseng

There is a limited amount of studies on the effects of red ginseng on performance. A systematic review reported on 14 clinical trials and concluded that the lack of performance improvements in the clinical trials contradicted the positive performance-enhancing effects of the compound reported in animals studies, yet some antioxidant effects were reported [45]. Inconsistencies in methodological approaches and pitfalls, such as, insufficient power, preparation of compound, lack of reporting randomisation methods, etc. could partially explain the mixed results.

#### 5.1.2.2.14. Pseudoephedrine

The ergogenic effect of pseudoephedrine is dose-dependent and is effective at supra-therapeutic thresholds [46]. The side-effects associated with pseudoepherdrine use outweigh the potential ergogenic benefit. However, it is plausible that future drug developments remove the negative side-effects associated with pseudoephedrine use, though this will take time and the benefit may also be affected.

#### 5.1.2.2.15. Phototherapy

Phototherapy administered before resistance exercise consistently has been found to provide ergogenic and prophylactic benefits to skeletal muscle [47]. When administered to skeletal muscle immediately before resistance exercise, phototherapy can enhance contractile function, prevent exercise-induced cell damage and improve post exercise recovery of strength and function. Limitations on the logistics of using phototherapy immediately prior to exercise to enhance Warfighter muscle strength make this approach unfeasible for battlefield incorporation. The long-term positive ergogenic effects of phototherapy have not been fully elucidated and warrant exploration as an ergogenic aid to reduce fatigue-related performance effects.

#### 5.1.2.2.16. Compression stockings (CS)

A small number of studies (3 out of 21) have reported that wearing CS below the knee improves exercise/physical activity performance [48]. However, the findings from the systematic review identified that several of these studies demonstrated that CS use benefits various muscle function

indicators and improves perceptions on muscle soreness during recovery. CS use also points towards other potential physiological benefits, such as, lowering blood lactate levels and fibrinolytic activity, higher oxygen saturation in recovery. These acute measures observed during recovery periods should be further investigated to determine whether the beneficial effects persist and improve athletic performance in the longer term.

### 5.1.2.2.17. Occlusal Splint Therapy (OST)

There are reports of a limited interaction between the use of OST and improving muscle strength or performance, with a recent systematic review (12 studies) concluding that there was no general agreement as to whether occlusal splints were effective ergogenic aids [49]. Despite this, a positive relationship between OST and enhanced isometric muscle strength in upper body exercise was confirmed in several studies. Conversely, for isokinetic muscle contractions, as well as for tasks involving muscle power, the existent research revealed significant methodological inconsistencies. Training status and selected muscle contraction type appear to be important factors in determining the effects of OST on muscle strength and performance.

### 5.1.2.2.18. Platelet-based applications

Autologous platelet-rich plasma applications are permitted in competitive sports by the World Anti-Doping Agency (WADA) due to the lack of apparent evidence in their ergogenic effect, though they acknowledge its potential therapeutic effects. Despite this, accumulating research has shed light on the role of platelet-derived growth factors in wound healing, skeletal myogenesis, muscle stem cell function and tissue regeneration. Scully and Matsakas (2019) provided an extensive review on novel evidence suggesting that platelet-derived growth factors influence muscle, tendon, ligament, protein synthesis/degradation, vascularization, energy utilization and improve regenerative capacity across a wide range of experimental settings [50]. Whilst the ergogenic potential of platelet-derived growth factors remains elusive in relation to sports performance, the robust evidence presented in the aforementioned review demonstrates that platelet-based applications improve myoblast proliferation, early inflammatory response, myogenic regulatory factors, regeneration time and muscle fiber hypertrophy with a decrease in pain, claudication score, oxidative stress and time-to recovery. Further, platelet-derived growth factors have demonstrated improvements in skeletal muscle by encouraging muscle regeneration [51] making this cell-based application potentially autologous and allogeneic in manner/nature. The studies outlined in the review indicate that whilst some cell-based platelet applications may play an important role in improving recovery and injury processes, little is known of their effects on uninjured muscles. Regardless of future studies clarifying whether cell-based platelet applications have a positive effect on uninjured muscle, the known therapeutic benefits warrant further exploration for military purposes to improve recovery times, reducing the delays associated with returning to duties post-muscle/tendon injury.

#### 5.1.2.2.19. Exoskeletons

There is a substantial mechanical bionics component to the ergogenic aids definition with the engineering of robotics and prostheses capable of benefiting users with sensory feedback (e.g. replacing a lost hand with a prosthetic hand) [52]. To date, these remarkable prosthetics and exoskeletons have been developed to fix a problem (i.e. a lost limb/hand, heart malfunction, cochlear implant) as opposed to enhance or improve something that is functioning normally. In doing so, exoskeletons have been instrumental in assisting some individuals to reach independence in their daily activities, particularly in upper and lower limb rehabilitation [53]. Emerging evidence suggests robotic exoskeletons as rehabilitation tools to ameliorate a range neurodegenerative and trauma related disorders, such as stroke, cerebral palsy or spinal cord injuries [54-56]. Consequently, the brain-computer interface has been presented as an exciting avenue in the development of tools that not only provide ambulation for paraplegic patients through controlling robotic exoskeletons, but also restore vision in people with acquired blindness; detect and control epileptic seizures; and improve control of movement disorders and memory enhancement [57]. Undoubtedly, the potential therapeutic modalities associated with exoskeletons/robotic devices will continue to expand as technologies and our pathophysiological understanding progresses.

The utilisation of exoskeletons and robotic technologies for human performance enhancement is an inevitable area of investigation warranted for military exploitation when gaining advantage is optimal. However, their use in enhancing human performance (when it is otherwise healthy) amongst civilian populations raises several ethical considerations. Recently, several safety concerns have also been raised which question their use in current clinical practice [58, 59]. There is no doubt on the rehabilitative capacity of exoskeletons and robotics devices for the future, yet little data exists on the potential for using this technology in an ergogenic capacity. That being said, this also opens up new avenues for exploration, especially for military. Potential military applications include accelerating the

rate of fitness, improving either strength or endurance when there is a need to deploy personnel with inadequate time to achieve such results with physical training alone.

### 5.1.2.3. Recreational and Ergogenic Substance Use

A wide variety of substance classes are used recreationally, for the self-treatment of various disorders or for performance enhancement. A comprehensive review recently published by McDuff *et al.* (2019) [60] compared the prevalence and patterns of substance use, misuse and use disorders in elite athletes with those of non-athletes. In doing so, they provided detailed demographic and sport variations in reasons for use, risk factors and performance effects for each main substance class. Their findings confirmed that **a**lcohol, cannabis, tobacco (nicotine) and prescribed opioids and stimulants were the most commonly used substances in elite athletes, but the rate of use was generally lower than in non-athletes. Contrastingly, the use/misuse rates for binge drinking alcohol, tobacco use, non-prescription opioids and anabolic-androgenic steroids were higher among elite athletes compared to non-athletes, particularly in power and collision sports. Cannabis/cannabinoids use has replaced nicotine as the second most commonly used substance.

# 5.1.2.4. Evidence Lacking to Support the Performance Enhancing Effects of the WADA List of Prohibited Substance Classes

WADA currently lists 23 substance classes that are prohibited for athletes [61]. A recent review of the listed substances highlighted that only five of the substance classes were evidenced to have any therapeutic or performance enhancing properties and these included anabolic agents,  $\beta$ 2-agonists, stimulants, glucocorticoids and  $\beta$ -blockers [62]. Growth hormone was somewhat supported by a limited evidence base in untrained individuals. The observed effects were mostly related to strength or sprint performance (and accuracy for  $\beta$ -blockers). Yet, despite traditional beliefs based on early evidence, there were no studies that showed a beneficially effect on endurance performance. A lack of well-designed studies were evident in 11 of the studies presented and the remaining 6 classes failed to report positive effects [62]. Their conclusions highlight that convincing evidence for performance enhancement using compounds on the WADA prohibited list is lacking. Furthermore, there are currently no Cochrane reviews on ergogenic aids which importantly identifies a gap in the literature and may also partially explain the underlying lack of quality studies on which to base a Cochrane review.

# 5.1.2.5. Current State of Knowledge on Ergogenic aids for Cognitive Enhancement in the Army

Whilst the military have invested in cognitive enhancement research and development for over a century, little progress has been made. As mentioned in other Trajectory Papers in this series, the risks and safety issues associated with this area make advancement challenging. Nonetheless, several novel approaches have been investigated and include pharmaceutical, dietary, neuroscientific, instructional, technological, and sleep-related enhancement strategies. A recent exploration on these approaches focused on the positive cognitive effects of targeting neural mechanisms and processes directly responsible for enhanced task performance, which included tDCS, augmented reality (AR), and targeted skills training [63]. Brunyè et al. (2020) objectively reviewed various safe, reliable and robust strategies and technologies that would assist military personnel in achieving dominance via enhanced skill acquisition, vigilance and threat detection, situation awareness, decision-making, teamwork and emotional control [63]. Additional approaches discussed in this review are: approaches targeting nthorder mechanisms and processes that relatively indirectly affect perception, cognition, and/or emotion and include nutritional and dietary intervention, resilience, cognitive and teamwork training, peripheral nerve stimulation, and sleep modification. Brunyè et al. (2020) provide a detailed overview of forward-looking research objectives currently being pursued by the US Army. In addition, they provide an overview of some of the ethical, regulatory, methodological, technological, doctrinal, and reliability challenges facing cognitive enhancement research.

The effectiveness and safety of pharmacological and biotechnological products for cognitive enhancement are constantly under scrutiny, with justified reason. Accordingly, the Australian Army commissioned a systematic review in 2015 which assessed this evidence as it related to personnel [64]. A meta-analyses could not be performed due to the heterogeneity of findings. A total of 22 studies were included examining 16 pharmacological compounds exclusively in the Army population. An alarming 3 studies were published post 2010 which highlights a lack of quality research in the area and advancement in the field. Interventions were limited to pharmacological products in the form of drugs, supplements, nutraceuticals or functional foods. Biologicals or biopharmaceutical engineered products, such as NMDA (NR2B) expression, oxygen (O2) enhancers (such as blood doping and erythropoietin (EPO)), and manufactured growth factors. Cell therapies included tissue engineering that could be used to produce various growth factors for use as performance enhancers. Caffeine, levothyroxine and prazosin provided cognitive improvements compared to placebos. Ko *et al.* (2017)

concluded that their findings should be interpreted with considerable caution due to the mixed performance findings reported and the lack of adverse event reporting.



s47

The rationale for each of these objectives with some examples of potential technologies are described below.

### 5.2.1. Improving Physical Strength and Endurance

Our society is becoming increasingly sedentary such that physical fitness of military and reserve personnel may be suboptimal. However, such personnel may be required to be rapidly deployed in scenarios where high levels of fitness are required to carry heavy equipment, travel long distances on foot and where physical fatigue and poor endurance may be limitations in combat performance. Amongst athletes, competitive advantage has been (illegally) sought by using anabolic steroids which enhance muscle strength and endurance. These agents have shown that the objective of improving muscle strength and endurance can be achieved but not safely, with a multitude of adverse events, especially cardiovascular risks and psychological impairments, making these agents unsuitable for military use. However, recent pharmacological research has shown that selective androgen receptor modulators (SARMs) [18] may be able to produce some of the benefit on improving muscle function without the adverse effects of full agonist anabolic steroids [17, 19-21]. No SARM is yet marketed and we have not been able to find any publications on their application to improving normal muscle strength. Potential clinical applications of SARMs have included amelioration of disease-related muscle loss. Potential military applications of SARMs include accelerating the rate of fitness on deployment of personnel where there is inadequate time to do this by physical training alone.

Improving muscle and bone strength may also be achievable by growth factor technologies. Although there are existing biotechnology agents to strengthen bone [e.g. denosumab], and hence which might be useful in increasing the resilience of military personnel, there are no such growth factor medical technologies for improving muscle bulk and function. This could be a productive area of research.

Given differences in baseline levels of fitness and performance between individuals, because of genetic or environmental variability, a "one-size-fits-all" approach may not produce optimal results. There are now many commercially available fitness / performance monitors which could be adapted so that interventions can be appropriately targeted, and perhaps more importantly, monitored, to ensure that the desired performance enhancements are being achieved in the desired timescale. If not, it may be necessary to intervene to, for example, change dose or duration of the intervention or to add an additional agent or switch to an alternative agent.

# 5.2.2. Improving Psychological Function: Attention, Alertness, Wakefulness and Reaction Time

Mental fatigue is a major problem impairing military performance [1]. Improvements in psychological function is the area in which there is the most evidence of military research and indeed the only drug specifically recommended for military application is Modafinil to enhance alertness of aviation crew [65]. Modafinil has replaced amphetamines previously used for this purpose. Modafinil was initially developed for the management of narcolepsy but has consistently demonstrated improvements in attention and performance. However, whether Modafinil is the ideal drug or whether analogues could produce superior outcomes should be researched. Additionally, there is considerable use of nootropics (piracetam and analogues) to improve study and exam performance in university students [66] suggesting that these agents might also enhance performance in the military scenario, alone or in combination with other treatments such as Modafinil. Such hypotheses warrant further exploration for translatable application.

In addition to pharmacological agents, there is military interest in electrical neuromodulation to enhance performance. The technique most studied is transcranial direct current stimulation (references) [67]. Conceivably such technology could be built into a helmet making it easily deployed in the field. Suitable simulation paradigms, frequency of use, and the personnel and scenarios in which most benefit can be demonstrated need exploration. Possible synergy with pharmacological agents could be explored.

s47

s47

# 5.2.4. Accelerating and Increasing Adaptation to Challenging Physical Environments

Warfare can take place anywhere, not necessarily in the environment to which the personnel has adapted. High altitude, resulting in tissue hypoxia is clearly performance-limiting. Agents which alter haemoglobin-oxygen binding characteristics could rapidly improve tissue oxygen delivery at altitude, having positive effects on Warfighter performance. Regarding challenging ambient temperature environments, conflict in the future could take place in extreme environments, such as the Arctic and Antarctic, the latter an area of particular interest to Australia. Prevention of hypothermia generally relies on specialised garments which add to the already challenging physical burden on the Warfighter and can impede mobility. Even modest levels of hypothermia impair muscle function [74]. Pharmacological agents which assist in thermogenesis, e.g. adrenergic  $\beta$ 3-stimulants or other agents [75] could uncouple oxidative phosphorylation and help maintain body temperature to avoid hypothermia-related decreases in muscle performance. This angle of investigation is warranted for military use.

s47

s47

# 5.2.7. Challenges in Determining the Optimal Approaches to be undertaken for the Desired Enhancement Effects

Some of the difficulties in developing ergogenic aids for military relate can be related to the lack of understanding researchers' have in the enhancement needs of the modern Warfighter. Gaining knowledge from soldiers and leaders is an essential way to advance this understanding and the next step will be to amalgamate the convergent science approaches that co-develop real-world applications and solutions. This will only be achieved via a needs-based approach and appropriate prioritisation of needs. Thus, the following framework is presented below.

### 5.3. The Development Framework

### 5.3.1. Developing a Robust Clinical Trial System Specific for Military

It is essential that real-world benefit of a potential new medical technology is adequately assessed before deployment. Although initial studies can use laboratory measures, such as endurance, muscle strength and vigilance tests, relying on such surrogates alone can be misleading. For example, caffeine has been shown to improve alertness but decreases firearm accuracy, presumably due to tremor [76, 77]. Hence the overall benefit may not be positive. Thus, there is a need for a robust clinical trial system within the military to determine the efficacy and safety agents specific for this population and not in a civilian/patient setting. It is envisioned that following successful laboratory testing, medical research personnel would be deployed with military personnel on exercises to assess real-world efficacy. Novel performance-measuring interventions may be developed and used. It is therefore recommended to develop a suitable framework for conducting safe clinical military trials with appropriate ethics and governance systems in place.

### 5.3.1.1. Safety

Military personnel receiving medical technology have a right to be ensured that technologies are being administered correctly, to the right people, with the right safeguards. Appropriate monitoring for adverse effects needs to be undertaken, if not mandated. As pointed to earlier, a recent review commissioned by the Australian Army alarmingly identified that safety outcomes, such as those relating to adverse events or addiction, were rarely reported [64]. For medicines and medical devices, there is a well-established regulatory agency in Australia, the Therapeutic Goods Administration (TGA). The TGA review of the evidence of safety and efficacy for a new medicine is a lengthy process (years). Efficacy claims must be based on a therapeutic effect. Such a framework is not suitable for the

approval of military ergogenic aids due to the lack of experience in risk assessment and benefit in the combat situation, as well as the lengthy timescale for review. In order to accelerate the benefit that new technologies/ergogenic aids may provide, it is suggested that a specific body charged with the assessment of the evidence base is created. Further, this body will include provisions of safety standards that are developed to oversee the deployment of new medical technologies in the military.

### 5.3.1.2. Ethical Considerations

A suitable framework for conducting clinical trials and suitable ethics and governance system needs to be in place specifically for the military. Given the national security nature of the information on the use of ergogenic aids in military personnel, the usual Human Research Ethics Committees (HRECs) may not be appropriate for reviewing proposals for such investigations. Additionally the specific risk-benefit situation with regard to military use will be likely to be outside the range of experience of usual HRECs. For example, a drug may have a significant adverse event potential but its lack of its effect could result in sufficient military disadvantage to put the recipient at increased risk of fatality from lack of effect. Further bioethical concerns specific to military bioenhancement relate not only to the paramount safety of the individual, but carries over to effects on civilian life and the fairness associated with voluntary or mandated use of bioenhancements [78]. It is for these reasons that suggestions for a committee with the specific expertise and training to make such judgements should be developed. Such a committee is likely to have representation from military medical staff, as well as from security cleared individuals with broad experience in clinical trials across a range of therapeutic areas and scenarios.

### 5.3.1.3. Commercial Issues for Consideration

Drug development is usually an expensive process. The military should consider partnership with local and possibly international pharmaceutical companies on specific development projects. This could use existing drug development capability efficiently and synergy with Australian companies would be positively seen by Federal government. It also may be seen as ideal from a national security point of view. It is possible that pharmaceutical companies may be willing to take on the risk and cost of development in the presence of an agreement to purchase medicines that meet prespecified criteria. It is also possible that a successful project could be licensed to our Allies to provide a return on investment here.

### 5.3.1.4. Why Australia?

Why should a relatively small country like Australia invest in such a program? Some of our allies have vastly larger resources to address the proposals in this trajectory document. Our advantages are the following:

- Australia is only one of two countries in the developed world (the other being The Netherlands) which does not require regulatory review for clinical trials. This means faster and leaner (i.e. less costly) drug development, which combined with the novel regulatory process proposed gives us advantage;
- Due to this less regulated environment, Australia has developed a culture of innovative clinical pharmacology and proof-of-concept clinical development with appropriate skills, expertise and resources base;
- A less bureaucratic environment leading to more flexible and innovative use of our intellectual resources; and
- A modest size population requiring us to obtain the optimal performance of our limited pool of military personnel.

# 5.4. Recommended Research Targets

The project will have the following aims and objectives that align with near, mid and long term trajectories:

## 5.4.1.a. Recommended Research Targets for the Near (<3y) Timeframe

### 5.4.1.a.1. Aim 1: Identification of Objectives/Traits

In this context, an objective is defined as a pharmacological or technological effect likely to lead to performance enhancement in the military. Objectives might, for example include increased muscle strength, more restful sleep, increased psychological or cognitive endurance, immune resilience measures. The identification of objectives will be achieved through 3 processes:

- 1. Survey of the literature (both military and civilian) and potentially liaison with other allied medical military bodies who are working in this area (2),
- 2. Interviews with relevant military and medical personnel, and
- 3. "Needs-finding" observational studies in the field to identify unmet needs.

Regarding the latter point, although some of the likely therapeutic objectives, such as increased physical and mental endurance are appropriate to be pursued, it may be that there are symptoms or problems encountered by military personnel that have not yet been specifically articulated, i.e. there may be unmet needs. One efficient way to elicit these it is to have trained researchers accompany military personnel in exercises observing performance and interviewing personnel to understand the barriers they have to peak performance. This "immersion in the environment" approach has been found to be highly productive for medical innovation and medical technologies in the healthcare setting. An example of this program is SPARK which has been internationally adapted from its origins at Stanford University. It is likely to be productive in the military setting. A different perspective is obtained by researchers in this manner (by observing end-users) than that would be obtained from management.

This initial objective scanning would be completed without filtering or prioritisation to avoid early discarding of worthwhile but potentially difficult objectives.

### 5.4.1.a.2. Aim 2: Determining Objective Priorities

For each objective, the following question-based approach will be used:

- What is the anticipated benefit?
- What is the strength of the current scientific and medical evidence for this intervention having the desired effect? Importantly, is there any evidence of this intervention in military application?
- How could it be measured in the laboratory and how would its effects be assessed in the field?
- What is the scientific likelihood of achieving the desired effect?
- Are there technical barriers in the development and implementation of the intervention?
- What would be the approximate time and cost for development and validation?

Following on from this, project staff would need to meet with military personnel to sort objectives and a 3 x 3 matrix of low, medium and high impact, including a low medium and high anticipated technical difficulty. This will assist in the selection process to identify the priority of objectives for the next phase of the framework.

# 5.4.1.a.3. Aim 3: Assessing the Pharmacological and Physiological Actions Likely to Achieve the Objective

For objectives likely to be of medium-high impact and medium-high technical success, the literature will be examined and expert opinion will be sought to determine which pharmacological actions are likely to achieve the objective.

# 5.4.1.b. Proposed Operational Plan to Align with Research Target Aims 1 and 2 (<3y timeframe)

### 5.4.1.b.1. Objective 1: Development of a Core Team

- Establishment of core team with the following skills and expertise is essential:
  - Medicinal chemistry and drug discovery,
  - o Clinical pharmacology, drug development and clinical trials,
  - Project management, and
  - Research assistants to go on exercises with military personnel to observe staff in action to assist with identification of unmet needs.

# 5.4.1.b.2. Objective 2: The Proposed Expert Panel Met with Appropriate Military Staff to Discuss the Steps of the Proposed Project

# 5.4.1.b.3. Objective 3: Assessment of the Pharmacological/Physiological Actions of the Desired Objective(s)

For objectives likely to be of medium to high impact and medium to high technical success, the literature will be examined and expert opinion will be sought to determine which pharmacological actions are likely to achieve the objective.

## 5.4.2. Recommended Research Targets for the Mid (<6y) Timeframe

### 5.4.2.1. Aim 4: Pharmacological or Technological Candidate Selection

The development of entirely novel drugs is a lengthy and expensive process. However, the repurposing of existing drugs, i.e. one approved for another purpose being examined for efficacy in another indication, can be relatively rapid and inexpensive in comparisons, as the basic pharmacology and safety have already been demonstrated. This has also been explored in other papers presented in this Trajectory Paper Series, such as the Brain-Immunology paper.

Initially, existing drugs for which the principal pharmacological action is likely to be of military advantage (e.g. nootropics; agents affecting haemoglobin-oxygen characteristics) would be evaluated for their evidence of efficacy for the indication. However, there are many drugs with which clinical benefit may be obtained quite separately from the initial primary pharmacology. Subsequently, a repurposing approach could be used for drugs were the primary indication it is not aligned with the pharmacological action sought for military use. Some examples of successful repurposing are listed below (Table 1.).

Drug	Initial indication	Repurposed indication
Sildenafil	Heart failure	Erectile dysfunction
Bupropion	Depression	Smoking cessation
Ketamine	General anaesthesia	Depression
Thalidomide	Sedation nausea	Cancer

Table 1. Drugs successful	ly repurposed.
---------------------------	----------------

The successful repurposing of many drugs have often arisen by chance observation by patients or physicians (e.g. Viagra). Relying on such serendipity is not the most efficient way of progressing this program. There are now advances in Al-guided drug candidate selection approaches where large libraries of existing drugs could be screened, initially *in silico* for the desired action, to increase speed and efficiency of the discovery program. Alternatively, for the pursuit of new chemical entities, once a target pharmacological profile has been established, one mechanism of finding candidate agents would be to invite submissions from academia through a competitive bidding process.

### 5.4.2.2. Aim 5: Preclinical and Clinical Development Plans

Once promising co-candidates have been identified, the pathway to utilisation including proof of concept milestones will be drafted. A Target Product Profile [79] approach is recommended, as is best practice in medical drug development. The profile produces a document summarising the benefits, indications, cautions and risks and would be completed by the expert panel. A preclinical and clinical development plan with time and cost estimates will be drafted. Key decision point milestones, again with time and cost estimates, will be included in the plan to assist with project prioritisation, budgeting and go/no-point decisions. Cost estimates will be obtained from contract research organisations who would then bid to undertake the work.

### 5.4.2.3. Aim 6: An Appropriate HREC

Australia has an excellent system of institutional affiliated HRECs, as well as independent fee-forservice committees. It is ideal to keep any HREC at arm's length from the sponsor hence, if an existing independent committee has the skills and knowledge to review proposed clinical development projects this will be satisfactory. However, it may be necessary to establish a specific independent ethics committee for the review of military clinical research projects given the specialised pharmacology, health science (versus disease), safety and ethical considerations, as well as the nature of consent and confidentiality in this environment.

### 5.4.3. Recommended Research Targets for the Long (>10y) Timeframe

### 5.4.3.1. Aim 7: Execution of Development Plans

Although as mentioned above, contract research organisations and academic units could undertake development work, it is essential that the sponsor, i.e. the military has a specialised team with experience of drug development and working with such organisations to manage, monitor and troubleshoot the execution of such plans and contracts.

### 5.4.3.2. Aim 8: Approval and implementation

As mentioned earlier, it is likely that a separate approval process will be necessary. Once new agents are ready for utilisation, planning for safe and effective implementation is required. This will ensure the effective development and dissemination of appropriate information sheets, both for the end user as well as their supervising military medical personnel. Guidance on management of adverse effects should be included.

### 5.4.3.3. Aim 9: Monitoring and review

As is the case for conventional pharmaceuticals, safety and efficacy in the community may be different from that observed in clinical trials. Hence, a post-implementation review and monitoring process needs to be established in case any modification of utilisation or safety information is required.

## Summary

Ergogenic aids have the potential to improve military personnel performance and survivability. The key components of this proposal to develop a suite of ergogenic aids are as follows:

- A comprehensive needs-finding approach from interviewing military personnel as well as observation of personnel in the field by project staff;
- o Prioritisation of projects for further development based on impact and feasibility;
- Liaising with other military medical groups in allied nations to ensure that work is not being unnecessarily repeated;
- The initial approach for new ergogenic aids will focus on drug repurposing;
- Subsequent phases of development for ergogenic aids may include new drug development and new biotechnology products;
- Parallel development of biosensors / wearables to ensure optimal performance of the agents in the field and to monitor for adverse effects;
- A dedicated research ethics evaluation framework suitable for military use needs to be established;
- The development of a suitable regulatory environment for ergogenic aids needs to be developed; and
- A system for monitoring the safety and well-being of the personnel who have received ergogenic aids needs to be in place.

### Glossary and explanation of terms

#### Drug development

The processes of drug discovery; preclinical and clinical development; manufacturing process development; regulatory approval and clinical utilisation.

#### Preclinical development

Studies to be conducted in laboratory and / or in animals before studies in humans. Generally consisting of pharmacology, metabolism, toxicology and pharmacokinetics.

#### **Clinical Development**

Clinical trials in humans prior to product registration.

#### **Target Product Profile**

A tool used in drug development as an overview of the indications, target population, dosage and administration, desired effects and undesired effects.

#### Drug repurposing

The process of developing an already registered drug for another indication.

#### **Drug registration**

The process of developing an already registered drug for another indication.

#### Drug candidate

A drug with potential as a therapeutic substance.

## References

- 1. Gore, R.K., T.S. Webb, and E.D. Hermes, *Fatigue and stimulant use in military fighter aircrew during combat operations.* Aviat Space Environ Med, 2010. **81**(8): p. 719-27.
- 2. Thein, L.A., J.M. Thein, and G.L. Landry, *Ergogenic aids*. Phys Ther, 1995. **75**(5): p. 426-39.
- 3. Ntoumanis, N., *et al.*, *Personal and psychosocial predictors of doping use in physical activity settings: a meta-analysis.* Sports Med, 2014. **44**(11): p. 1603-24.
- 4. Sagoe, D., et al., The global epidemiology of anabolic-androgenic steroid use: a metaanalysis and meta-regression analysis. Ann Epidemiol, 2014. **24**(5): p. 383-98.
- 5. Dolan, E., et al., A Systematic Risk Assessment and Meta-Analysis on the Use of Oral *B-Alanine Supplementation*. Adv Nutr, 2019. **10**(3): p. 452-463.
- 6. Marocolo, M., et al., Ischemic preconditioning and exercise performance: shedding light through smallest worthwhile change. Eur J Appl Physiol, 2019. **119**(10): p. 2123-2149.
- 7. Hobson, R.M., *et al.*, *Effects of β-alanine supplementation on exercise performance: a meta-analysis.* Amino Acids, 2012. **43**(1): p. 25-37.
- 8. Peart, D.J., J.C. Siegler, and R.V. Vince, *Practical recommendations for coaches and athletes: a meta-analysis of sodium bicarbonate use for athletic performance.* J Strength Cond Res, 2012. **26**(7): p. 1975-83.
- 9. Pöchmüller, M., et al., A systematic review and meta-analysis of carbohydrate benefits associated with randomized controlled competition-based performance trials. J Int Soc Sports Nutr, 2016. **13**: p. 27.
- 10. Temesi, J., *et al.*, *Carbohydrate ingestion during endurance exercise improves performance in adults.* J Nutr, 2011. **141**(5): p. 890-7.
- 11. Trexler, E.T., et al., Acute Effects of Citrulline Supplementation on High-Intensity Strength and Power Performance: A Systematic Review and Meta-Analysis. Sports Med, 2019. **49**(5): p. 707-718.
- 12. Turnes, T., et al., The Impact of Preconditioning Strategies Designed to Improve 2000m Rowing Ergometer Performance in Trained Rowers: A Systematic Review and Meta-Analysis. Int J Sports Physiol Perform, 2019. **14**(7): p. 871-879.
- 13. Conger, S.A., *et al.*, *Does caffeine added to carbohydrate provide additional ergogenic benefit for endurance?* Int J Sport Nutr Exerc Metab, 2011. **21**(1): p. 71-84.
- 14. Mielgo-Ayuso, J., et al., Effects of Creatine Supplementation on Athletic Performance in Soccer Players: A Systematic Review and Meta-Analysis. Nutrients, 2019. **11**(4).
- 15. Laws, K.R., H. Sweetnam, and T.K. Kondel, *Is Ginkgo biloba a cognitive enhancer in healthy individuals? A meta-analysis.* Hum Psychopharmacol, 2012. **27**(6): p. 527-33.
- Andrews, M.A., et al., Physical Effects of Anabolic-androgenic Steroids in Healthy Exercising Adults: A Systematic Review and Meta-analysis. Curr Sports Med Rep, 2018. 17(7): p. 232-241.
- 17. Piacentino, D., *et al.*, *Anabolic-androgenic steroid use and psychopathology in athletes. A systematic review.* Curr Neuropharmacol, 2015. **13**(1): p. 101-21.
- 18. Bhasin, S. and R. Jasuja, *Selective androgen receptor modulators as function promoting therapies.* Curr Opin Clin Nutr Metab Care, 2009. **12**(3): p. 232-40.

- 19. Chang, S., et al., Anabolic Androgenic Steroid Abuse: The Effects on Thrombosis Risk, Coagulation, and Fibrinolysis. Semin Thromb Hemost, 2018. **44**(8): p. 734-746.
- 20. Kanayama, G., M.J. Kaufman, and H.G. Pope, Jr., *Public health impact of androgens*. Curr Opin Endocrinol Diabetes Obes, 2018. **25**(3): p. 218-223.
- 21. Solimini, R., *et al.*, *Hepatotoxicity associated with illicit use of anabolic androgenic steroids in doping.* Eur Rev Med Pharmacol Sci, 2017. **21**(1 Suppl): p. 7-16.
- 22. Karsten, M., et al., The effects of inspiratory muscle training with linear workload devices on the sports performance and cardiopulmonary function of athletes: A systematic review and meta-analysis. Phys Ther Sport, 2018. **34**: p. 92-104.
- 23. Choo, H.C., et al., Ergogenic effects of precooling with cold water immersion and ice ingestion: A meta-analysis. Eur J Sport Sci, 2018. **18**(2): p. 170-181.
- Mallette, M.M., D.G. Stewart, and S.S. Cheung, *The Effects of Hyperoxia on Sea-Level Exercise Performance, Training, and Recovery: A Meta-Analysis.* Sports Med, 2018. 48(1): p. 153-175.
- 25. Hsu, P.-C., *et al.*, *Radiative human body cooling by nanoporous polyethylene textile*. Science (New York, N.Y.), 2016. **353**(6303): p. 1019.
- 26. Southward, K., K.J. Rutherfurd-Markwick, and A. Ali, *The Effect of Acute Caffeine Ingestion on Endurance Performance: A Systematic Review and Meta-Analysis.* Sports Med, 2018. **48**(8): p. 1913-1928.
- 27. Grgic, J., et al., Effects of caffeine intake on muscle strength and power: a systematic review and meta-analysis. J Int Soc Sports Nutr, 2018. **15**: p. 11.
- 28. López-González, L.M., *et al., Acute caffeine supplementation in combat sports: a systematic review.* J Int Soc Sports Nutr, 2018. **15**(1): p. 60.
- 29. Mielgo-Ayuso, J., et al., Effect of Caffeine Supplementation on Sports Performance Based on Differences Between Sexes: A Systematic Review. Nutrients, 2019. **11**(10).
- 30. Hadzic, M., M.L. Eckstein, and M. Schugardt, *The Impact of Sodium Bicarbonate on Performance in Response to Exercise Duration in Athletes: A Systematic Review.* J Sports Sci Med, 2019. **18**(2): p. 271-281.
- 31. Schubert, M.M. and T.A. Astorino, *A systematic review of the efficacy of ergogenic aids for improving running performance*. J Strength Cond Res, 2013. **27**(6): p. 1699-707.
- 32. Silva, V.R., *et al.*, *β*-hydroxy-*β*-methylbutyrate free acid supplementation may improve recovery and muscle adaptations after resistance training: a systematic review. Nutr Res, 2017. **45**: p. 1-9.
- 33. Wilson, P.B., *Ginger (Zingiber officinale) as an Analgesic and Ergogenic Aid in Sport: A Systemic Review.* J Strength Cond Res, 2015. **29**(10): p. 2980-95.
- 34. Qureshi, A., D.P. Naughton, and A. Petroczi, *A systematic review on the herbal extract Tribulus terrestris and the roots of its putative aphrodisiac and performance enhancing effect.* J Diet Suppl, 2014. **11**(1): p. 64-79.
- 35. Decroix, L., *et al.*, *Cocoa Flavanol Supplementation and Exercise: A Systematic Review.* Sports Med, 2018. **48**(4): p. 867-892.
- 36. Berti Zanella, P., F. Donner Alves, and C. Guerini de Souza, *Effects of beta-alanine supplementation on performance and muscle fatigue in athletes and non-athletes of different sports: a systematic review.* J Sports Med Phys Fitness, 2017. **57**(9): p. 1132-1141.

- 37. Quesnele, J.J., *et al.*, *The effects of beta-alanine supplementation on performance: a systematic review of the literature.* Int J Sport Nutr Exerc Metab, 2014. **24**(1): p. 14-27.
- 38. Ismaeel, A., *Effects of Betaine Supplementation on Muscle Strength and Power: A Systematic Review.* J Strength Cond Res, 2017. **31**(8): p. 2338-2346.
- 39. Johnston, R., K. Doma, and M. Crowe, *Nicotine effects on exercise performance and physiological responses in nicotine-naïve individuals: a systematic review.* Clin Physiol Funct Imaging, 2018. **38**(4): p. 527-538.
- 40. Lam, F.C., et al., Effectiveness of whey protein supplements on the serum levels of amino acid, creatinine kinase and myoglobin of athletes: a systematic review and meta-analysis. Syst Rev, 2019. **8**(1): p. 130.
- 41. Lam, F.C., et al., Efficacy and Safety of Whey Protein Supplements on Vital Sign and Physical Performance Among Athletes: A Network Meta-Analysis. Front Pharmacol, 2019. **10**: p. 317.
- 42. Machado, S., et al., Is tDCS an Adjunct Ergogenic Resource for Improving Muscular Strength and Endurance Performance? A Systematic Review. Front Psychol, 2019. **10**: p. 1127.
- 43. Taylor, J.L., *et al.*, *Neural Contributions to Muscle Fatigue: From the Brain to the Muscle and Back Again.* Medicine and science in sports and exercise, 2016. **48**(11): p. 2294.
- 44. Shei, R.J., *Recent Advancements in Our Understanding of the Ergogenic Effect of Respiratory Muscle Training in Healthy Humans: A Systematic Review.* J Strength Cond Res, 2018. **32**(9): p. 2665-2676.
- 45. Lee, N.H., H.C. Jung, and S. Lee, *Red Ginseng as an Ergogenic Aid: A Systematic Review of Clinical Trials.* J Exerc Nutrition Biochem, 2016. **20**(4): p. 13-19.
- 46. Trinh, K.V., J. Kim, and A. Ritsma, *Effect of pseudoephedrine in sport: a systematic review.* BMJ Open Sport Exerc Med, 2015. **1**(1): p. e000066.
- 47. Borsa, P.A., K.A. Larkin, and J.M. True, *Does phototherapy enhance skeletal muscle contractile function and postexercise recovery? A systematic review.* J Athl Train, 2013.
  48(1): p. 57-67.
- 48. Mota, G.R., et al., Effects of Wearing Compression Stockings on Exercise Performance and Associated Indicators: A Systematic Review. Open Access J Sports Med, 2020. **11**: p. 29-42.
- 49. Dias, A., et al., A systematic review on the effects of occlusal splint therapy on muscle strength. Cranio, 2020. **38**(3): p. 187-195.
- 50. Scully, D. and A. Matsakas, *Current Insights into the Potential Misuse of Platelet-based Applications for Doping in Sports.* Int J Sports Med, 2019. **40**(7): p. 427-433.
- 51. Scully, D., et al., Platelet releasate promotes skeletal myogenesis by increasing muscle stem cell commitment to differentiation and accelerates muscle regeneration following acute injury. Acta Physiologica, 2019. **225**(3): p. n/a-n/a.
- 52. Raspopovic, S., et al., Restoring natural sensory feedback in real-time bidirectional hand prostheses. Sci Transl Med, 2014. **6**(222): p. 222ra19.
- 53. Molteni, F., *et al., Exoskeleton and End-Effector Robots for Upper and Lower Limbs Rehabilitation: Narrative Review.* Pm r, 2018. **10**(9 Suppl 2): p. S174-s188.
- 54. Hayes, S.C., et al., The effects of robot assisted gait training on temporal-spatial characteristics of people with spinal cord injuries: A systematic review. J Spinal Cord Med, 2018. **41**(5): p. 529-543.

- 55. Reyes, F., C. Niedzwecki, and D. Gaebler-Spira, *Technological Advancements in Cerebral Palsy Rehabilitation*. Phys Med Rehabil Clin N Am, 2020. **31**(1): p. 117-129.
- 56. Weber, L.M. and J. Stein, *The use of robots in stroke rehabilitation: A narrative review.* NeuroRehabilitation, 2018. **43**(1): p. 99-110.
- 57. Rosenfeld, J.V. and Y.T. Wong, *Neurobionics and the brain-computer interface: current applications and future horizons.* Med J Aust, 2017. **206**(8): p. 363-368.
- 58. Dijkers, M.P., *et al.*, *Systematic Reviews of Clinical Benefits of Exoskeleton Use for Gait and Mobility in Neurologic Disorders: A Tertiary Study.* Arch Phys Med Rehabil, 2019.
- 59. Gorgey, A.S., *Robotic exoskeletons: The current pros and cons.* World J Orthop, 2018. **9**(9): p. 112-119.
- 60. McDuff, D., et al., Recreational and ergogenic substance use and substance use disorders in elite athletes: a narrative review. Br J Sports Med, 2019. **53**(12): p. 754-760.
- 61. Agency, T.W.A.-D., *Standard prohibited list 2018*, W.A.-D. Agency, Editor. 2018: Montreal.
- 62. Heuberger, J. and A.F. Cohen, *Review of WADA Prohibited Substances: Limited Evidence for Performance-Enhancing Effects.* Sports Med, 2019. **49**(4): p. 525-539.
- 63. Brunyé, T.T., et al., A Review of US Army Research Contributing to Cognitive Enhancement in Military Contexts. Journal of Cognitive Enhancement, 2020.
- 64. Ko, H., *et al.*, *A systematic review of performance-enhancing pharmacologicals and biotechnologies in the Army*. J R Army Med Corps, 2018. **164**(3): p. 197-206.
- 65. Friedl, K.E., U.S. Army Research on Pharmacological Enhancement of Soldier Performance: Stimulants, Anabolic Hormones, and Blood Doping. J Strength Cond Res, 2015. **29 Suppl 11**: p. S71-6.
- 66. Carton, L., *et al.*, *Pharmaceutical cognitive doping in students: A chimeric way to geta-head?* Therapie, 2018. **73**(4): p. 331-339.
- 67. Wiegand, A., et al., Improvement of cognitive control and stabilization of affect by prefrontal transcranial direct current stimulation (tDCS). Sci Rep. 2019. **9**(1): p. 6797. s47

74. Ferretti, G., Cold and muscle performance. Int J Sports Med, 1992. 13 Suppl 1: p. S1857.

<sup>75.</sup> Astrup, A., *et al.*, *Pharmacology of thermogenic drugs*. Am J Clin Nutr, 1992. **55**(1 Suppl): p. 246s-248s.

- 76. Nygaard, H., et al., Effect of caffeine ingestion on competitive rifle shooting performance. PLoS One, 2019. **14**(10): p. e0224596.
- 77. Research, I.o.M.U.C.o.M.N., Food Components to Enhance Performance: An Evaluation of Potential Performance-Enhancing Food Components for Operational Rations. Effects of Caffeine on Cognitive Performance, Mood and Alertness in Sleep-Deprived Humans, ed. B.M. Marriott. Vol. 20. 1994, Washington (DC): National Academies Press (US).
- 78. Mehlman, M., *Bioethics of military performance enhancement*. J R Army Med Corps, 2019. **165**(4): p. 226-231.
- 79. Narayanan, R., C.C. Coss, and J.T. Dalton, *Development of selective androgen receptor modulators (SARMs)*. Mol Cell Endocrinol, 2018. **465**: p. 134-142.

s47



Defence FOI 386/22/23 Document 2

RESEARCH



# The Influence of Training on New Army Recruits' Energy and Macronutrient Intakes and Performance: A Systematic Literature Review



Bradley A. Baker, MDietSt, APD, AccSD\*; Matthew B. Cooke, PhD; Regina Belski, PhD, AdvAPD, AdvSD, RNutr\*; Julia E. Carins, PhD

#### **ARTICLE INFORMATION**

Article history: Submitted 19 December 2019 Accepted 4 June 2020 Available online 19 August 2020

Keywords:

Military Diet and nutrition Exercise Physical functional performance

2212 2672/Copyright © 2020 by the Academy of Nutrition and Dietetics. https://doi.org/10.1016/j.jand.2020.06.004

\*Certified in Australia.

#### ABSTRACT

**Background** New army recruits undertake initial training to develop their skillset and physical and mental preparedness for military service. Recruits experience a range of stressors both physical and psychological, often at extremes, and in combination. These stressors place recruits at risk of suboptimal energy and macronutrient intakes, which may negatively influence their performance.

**Objective** The objectives of this systematic literature review are to examine, against the Military Recommended Dietary Intakes (MRDIs), the energy, carbohydrate, protein, and fat intakes of army recruits and trainees undertaking initial training internationally, and identify any associated influence on their performance.

**Design** A systematic literature review was conducted in accordance with the preferred reporting items for systematic reviews and meta analyses guidelines. Information sources were searched from their inception until May 2019.

**Main outcome measures** Outcome data included dietary intakes of energy, carbohy drate, protein, and fat before, during, and/or after army initial training, as well as measures of physical fitness and performance. A custom tool was used to assess the quality of included studies.

**Results** The results of 14 studies were synthesized. Six were conducted in the United States and four in each of Australia and Israel. Average energy intake represented 69% to 120% of the MRDIs before training commencement, 69% to 106% of the MRDIs in the early weeks of training and 56% to 77% of the MRDIs in the later weeks of training. Average carbohydrate and protein intakes represented 49% to 121% and 64% to 143% of the MRDIs, respectively, across the various time points. Three studies measured physical fitness and/or performance outcomes, with one showing a significant improvement in push up performance when extra protein was provided.

**Conclusions** The novel findings of this systematic literature review are that army re cruits, internationally, are likely to be underconsuming energy for extended periods of their initial training, with greater deficits in carbohydrate intake compared with other macronutrients. Only a handful of studies investigated the subsequent influents on performance, with no definitive conclusions drawn in most instances. Further research is needed to understand the influence of suboptimal dietary intake on military relevant performance indicators to help better inform key stakeholders when devising nutrition guidance and strategies for army recruits in the future.

J Acad Nutr Diet. 2020;120(10):1687 1705.

The Continuing Professional Education (CPE) quiz for this article is available for free to Academy members through the MyCDRGo app (available for iOS and Android devices) and through www.jandonline.org (click on "CPE" in the menu and then "Academy Journal CPE Articles"). Log in with your Academy of Nutrition and Dietetics or Commission on Dietetic Registration username and password, click "Journal Article Quiz" on the next page, then click the "Additional Journal CPE quizzes" button to view a list of available quizzes. Non members may take CPE quizzes by sending a request to journal@ eatright.org. There is a fee of \$45 per quiz (includes quiz and copy of article) for non member Journal CPE. CPE quizzes are valid for 1 year after the issue date in which the articles are published.

RMY RECRUITS UNDERTAKE INITIAL TRAINING TO develop their skillset and physical and mental preparedness for military service. Initial training for new army members, other than those commissioned for officer training, commences with basic training (BT), or basic combat training (BCT) as it is commonly referred to in the United States. Regardless of the country, BT and BCT are physically and psychologically demanding,<sup>1</sup> and are followed by further training that is specific to each army occupation (eg, infantry, artillery, and engineering). Although the physical fitness of enlisted recruits can vary, all enlistees will experience increased physical workload as well as elevated

### RESEARCH

psychological and environmental stressors throughout their initial training—which typically lasts between 4 and 7 months depending on the nation.<sup>2,3</sup> In addition, recruits' eating habits and food environment will change due to the intensive training schedules and rigid timing of meals as well as environments in which they train (eg, field training).

Individual studies published during the past 15 years suggest that energy and macronutrient intakes of army recruits may be insufficient.4-8 Recently, a US study found that without nutritional supplementation, the average energy balance of recruits was -595 kcal/day, with most recruits consuming insufficient carbohydrate compared with recommended levels.<sup>4</sup> Suboptimal energy and carbohydrate intakes in the medium- to long-term can lead to low energy availability, possibly reduced training quality and performance, and increased risk of illness and injury.<sup>6,9,10</sup> A recent metaanalysis found that the duration and magnitude of energy deficit and associated changes in body mass were predictive of declines in performance in soldiers engaged in training activities after the completion of initial training; with smaller decrements in performance indicative of smaller accumulative daily negative energy balances. Although the authors acknowledged that motivation and injury could also be contributing factors, both were not included in the analysis.<sup>11</sup> Indeed, reports of higher incidences of stress fractures have been observed in army recruits consuming lower intakes of carbohydrate, as well as calcium and vitamin D, while in energy deficit.<sup>6</sup> Taken together, it is evident that both new recruits and soldiers may experience periods of energy deficit during their training, with possible influence on their performance. Although militaries in countries such as Australia and United States have set recommended dietary intakes for periods of heavy physical activity such as initial training,<sup>8,12</sup> very few studies report dietary intakes in relation to military-specific dietary recommendations.13 Consequently, the frequency, magnitude, and duration of inadequate energy and macronutrient intakes among new recruits undertaking initial training internationally is unclear. It is also unclear whether patterns in particular dietary inadequacies are more readily observed and in that case, whether these are shown to influence measures of performance (eg, in their routine physical fitness tests).

Therefore, the objectives of this systematic literature review are to compare and contrast reported energy, carbohydrate, protein, and fat intakes of army recruits undertaking initial training internationally, compare reported intakes to military-specific recommended dietary intakes to determine how common inadequate intakes are among individual studies, determine the magnitude and duration of any dietary inadequacies during initial military training, and identify any associated influences on performance measures. Areas of future research for advancing understanding in this area will also be discussed.

#### METHODS

In accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement, the protocol of this systematic review was prospectively registered with the PROSPERO international prospective register of systematic reviews (CRD42019128328; http://www.crd.york.ac.uk/ PROSPERO/display\_record.php?ID\_CRD42019128328).

#### RESEARCH SNAPSHOT

Research Question: What are the energy, carbohydrate, protein, and fat intakes of army recruits and trainees undertaking initial training internationally, how do these compare with the military recommended dietary intakes, and are there any associated influence on their performance?

Key Findings: Army recruits undertaking initial training are likely to underconsume energy compared with the recommended intake, with greater deficits in carbohydrate intake compared with other macronutrients. Only three of 14 studies concurrently measured physical fitness and/or performance outcomes, which highlights a major gap in this area. Further research focusing on accurate measures of dietary intakes, strategies to improve intakes, and relationships with military-relevant performance indicators is needed.

#### Eligibility Criteria

Eligibility criteria are shown in Table 1 in the participants/ population, intervention or exposure, comparator/control, outcome, and study type) format. Eligible studies were those that report the energy and macronutrient intakes of new army recruits during their initial training (ie, recruits and trainees and excluding officers).

#### Information Sources and Search Strategy

The following eight databases were searched from their inception to May 2019: Scopus, Proquest Central, SPORTDiscus, Cumulative Index of Nursing and Allied Health Literature Complete, Web of Science Core Collection, PubMed, National Technical Reports Library, and the Defense Technical Information Center. Searches were limited to records published in the English language, and the fields searched were title, abstract, and keyword in all databases except the National Technical Reports Library (which was searched in the title field). The following search terms were devised from medical subject headings: background reading, and piloting and refining the search strategy: military OR army OR conscript\* OR combat OR "national guard" OR "basic training" AND train\* OR recruit<sup>\*</sup> AND food OR energy OR diet<sup>\*</sup> OR nutri<sup>\*</sup> OR macronutrient\* OR micronutrient\*. All sources were searched using this combination of search terms except for the Defense Technical Information Center, in which simplified terms were used and the search was limited to the first 10 pages of results sorted by relevance. The reference lists of included studies were screened for potentially relevant articles and in addition; all included studies underwent forward citation searches in Google Scholar and Web of Science Core Collection. Finally, forward and backward author searches were conducted in Web of Science Core Collection.

## Study Selection, Data Collection Process, and Data Items

The methods for study selection, data collection, and data items have been described in our PROSPERO protocol. In addition, where a study reported collecting dietary intakes, but did not report all required outcomes (ie, mean energy, carbohydrate, protein, and fat intakes) a lead or

Inclusion criteria **Exclusion criteria** Participants/population Army recruits and trainees who are undertaking Studies involving civilians or defence members other than army enlistees initial training, such as basic training and occupation-specific training Intervention or exposure Army initial/recruit training such as the Australian Officer training Army Recruit Training Course, the Australian Army Infantry Initial Employment Training, and the US Army Initial Entry Training Comparator/control NA<sup>a</sup> NA Outcome Studies that report the total energy, carbohydrate, Studies that do not report participants' protein, and fat intake of participants during total energy intake and/or their intake training of all three macronutrients Study type Original peer-reviewed studies and grey literature Literature reviews and nonempirical (eg, government reports, theses, and conference research proceedings) of any study design

**Table 1.** Inclusion and exclusion criteria for a systematic literature review investigating the influence of training on new army recruits' dietary intakes of energy and macronutrients and performance

<sup>a</sup>NA=not applicable.

corresponding author was contacted to request the data. In the case that a response was not received after 2 months, the study was excluded.

#### Data Synthesis

Energy intake (EI) data reported in megajoule was converted to kilocalories as required using the International System of Units guidelines Where mean daily intakes of carbohydrate, protein, and/or fat are reported as a percentage of total EI or in energy values, the data were converted into grams using conversion rates of 4 kcal/g, 4 kcal/g, and 9 kcal/g for carbohydrate, protein, and fat, respectively. Intakes of energy, carbohydrate, and protein during recruit training are reported in relation to the lower end of the Australian activity category (AC) 3 Military Recommended Dietary Intakes (MRDIs) for adult males and females, which are the criteria for assessing the adequacy of energy and macronutrient intakes within groups.<sup>12</sup> The AC 3 MRDIs for energy, carbohydrate and protein are 3,824 kcal (16 MJ), 540 to 590 g, and 122 to 169 g, respectively, for males and 2749 kcal (11.5 MJ), 388 to 424 g, and 88 to 122 g, respectively, for females. The AC 3 energy values correspond to the US Military Dietary Reference Intakes for heavy activity, which are 3,700 kcal for males and 2,700 kcal for females.<sup>8</sup> The AC 1 MRDIs were used to assess the adequacy of recruits' dietary intakes before the commencement of their military training. For energy, carbohydrate, and protein, these are 2,868 kcal (12 MJ), 375 to 413 g and 106 to 141 g, respectively, for adult males and 2,032 kcal (8.5 MJ), 266 to 292 g, 75 to 100 g, respectively, for adult females. The AC 1 energy values correspond to the US Military Dietary Reference Intakes for light activity, which are 3,000 kcal for males and 2,100 kcal for females.<sup>8</sup> For studies that reported mean dietary intakes for both males and females combined, weighted mean MRDIs were calculated using the proportion of males and females in each study group.

#### RESULTS

#### **Study Selection**

Database searches retrieved 5,613 records (1,664 from Scopus, 986 from Proquest Central, 445 from SPORTDiscus, 369 from Cumulative Index of Nursing and Allied Health Literature Complete, 1,116 from Web of Science Core Collection, 80 from PubMed, 23 from the National Technical Reports Library, and 100 from the Defense Technical Information Center). A further 1,002 records were retrieved from other sources, including citation searches, forward and backward author searches, and screening of reference lists for potentially relevant records. The publication dates of studies screened as eligible spanned  $\sim$  100 years, from 1919 to 2018, and whereas earlier studies offer a historical perspective, there are limitations in how generalizable their findings are to modern-day army recruit training. Consequently only studies published from 1988 onward were included. The Figure provides an overview of record attrition.

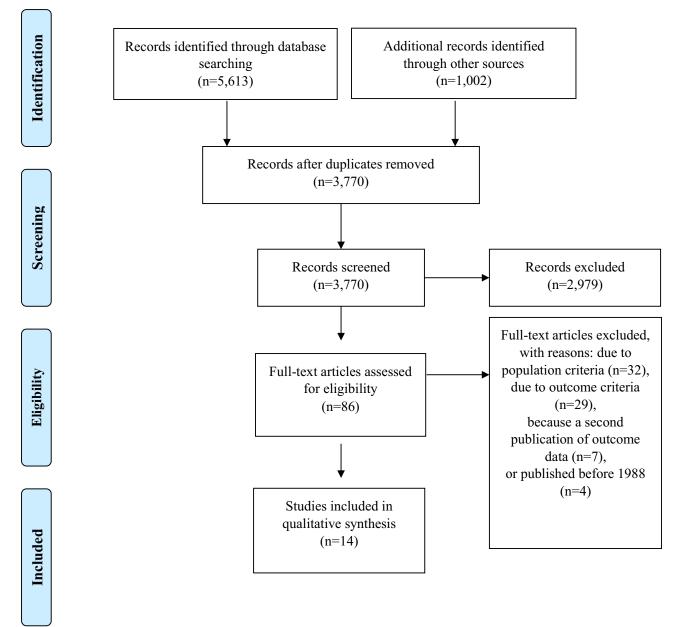
#### **Study Characteristics**

Included studies were published between 1988 and 2018, with six conducted in the United States, <sup>4,5,14-17</sup> and four in each of Australia<sup>2,3,18-20</sup> and Israel.<sup>6,7,21,22</sup> A range of study designs was used—with 10 of the 14 included employing a before-after design.<sup>2,4,6,7,15-17,19-21</sup> Table 2 lists the study design and characteristics of included studies.

#### **Risk of Bias in Individual Studies**

A custom quality assessment tool (Table 3) was constructed to assess the risk of bias of included studies (Table 4). Questions one to nine were sourced from the National Heart, Lung, and Blood Institute's quality assessment tool for before—after studies with no control group,<sup>23</sup> question 10 was custom, and questions 11 and 12 were sourced from Academy of Nutrition and Dietetics quality checklist,<sup>24</sup> as described in our PROSPERO protocol.

### RESEARCH



**Figure.** Inclusion and exclusion criteria for a systematic literature review investigating the influence of training on new army recruits' dietary intakes of energy and macronutrients and performance.

#### Synthesis of Results

Outcomes from individual studies are presented in Tables 5 and 6. The target population was army recruits and trainees undergoing initial training, and within included studies participants ranged from elite combat recruits (eg, those progressing toward a career in special forces)<sup>6</sup> to recruits with differing prospective career paths following BT (eg, infantry, artillery, and engineering).<sup>2,19</sup> Varying methods of dietary intake and physical performance assessment were employed, with the most popular being food frequency questionnaires (FFQs) and predetermined distance runs (eg, 2.4 km), and maximum push-ups and sit ups, respectively.<sup>2,5-7,14,15,18,21,22</sup> Two studies investigated the effects of other supplementation in the form of whey protein and carbohydrate,<sup>5</sup> and calcium and vitamin D (vs placebo).<sup>14</sup> Three of the 14 included studies reported physical fitness and/or performance outcomes, and their results were also included in the present review.<sup>2,5,22</sup> One other included study conducted measures of physical fitness and performance; however, on a different group of participants to the dietary intake measures, and consequently these results were not included.<sup>16</sup>

#### Energy and Macronutrient Intakes before Training Commencement

Seven studies investigated dietary intakes of recruits immediately before commencement of their army training—all of these studies utilized FFQs to assess dietary intake over the 

 Table 2. Key characteristics of studies included in a systematic literature review investigating the influence of training on new army recruits' dietary intakes of energy and macronutrients and performance

Reference (year of publication)	Country	Study design	Study group and sex	Participants age (mean±standard deviation)	Details of intervention	Dietary intake assessment method
Gaffney-Stomberg and colleagues <sup>14</sup> (2014)	United States	RCT <sup>a</sup>	Placebo Male (n=56) Female (n=29) Ca <sup>b</sup> + Vit D <sup>c</sup> supp <sup>d</sup> Male (n=49) Female (n=34)	Placebo: 21.4±3.7 y Ca + Vit D supp: 21.4±3.8 y	Participants in both groups were instructed to consume 2 bars/ d for 9 wk (containing 130-140 kcal, 23-25 g CHO <sup>e</sup> , 5 g fat, and 1-2 g PRO <sup>f</sup> ). The Ca + Vit D supp group received bars supplemented with 1,032 mg Ca + 546 IU Vit D	FFQ <sup>9</sup> capturing previous 3 mo intake, completed under supervision of registered dietitians upon commencement of BCT <sup>h</sup> and at the end of BCT (Week 9)
Moran and colleagues <sup>6</sup> (2012)	Israel	BAS <sup>i</sup>	All male NSF <sup>j</sup> (n=74) SF <sup>k</sup> (n=12)	NR <sup>I</sup>	NA <sup>m</sup>	FFQ capturing previous 6 months' intake upon commencement of BT <sup>n</sup> , and a FFQ capturing previous 4 mo intake at the end of 4-mo BT. These were completed with the assistance of a dietitian
McAdam and colleagues <sup>4</sup> (2018a)	United States	BAS	All male (n=85)	19±2 y	NA	Food logs that were meal- specific to dining facility where participants dined. These were conducted after each meal on 3 nonconsecutive days during the first week of IET <sup>o</sup>
Margolis and colleagues <sup>15</sup> (2012)	United States	BAS	Male (n=85) Female (n=67)	Male: 23±5 y Female: 23±6 y	ΝΑ	Semiquantitative FFQ at Week 0 (ie, pre-BCT) and Week 9 of BCT

RESEARCH

RESEARCH

**Table 2.** Key characteristics of studies included in a systematic literature review investigating the influence of training on new army recruits' dietary intakes of energy and macronutrients and performance (*continued*)

Reference (year of publication)	Country	Study design	Study group and sex	Participants age (mean±standard deviation)	Details of intervention	Dietary intake assessment method
McAdam and colleagues <sup>5</sup> (2018b)	United States	Non-RCT	All male (n=55) WP <sup>p</sup> supp (n=27) CHO supp (n=28)	WP supp: 19±1 y CHO supp: 19±1 y	Twice daily supplementation of WP (containing 293 kcal: 38.6 g PRO, 19.0 g CHO, 7.5 g fat, 20.1 g essential amino acids, 9.5 g BCAs <sup>q</sup> ) or CHO (containing 291 kcal: 0.5 g PRO, 63.4 g CHO, 3.9 g fat, and 0.1 g, and 0.0 g essential and BCAs)	Meal-specific food logs after each meal on 3 nonconsecutive days during Weeks 1 and 9 of IET
Booth and Coad <sup>18</sup> (2001)	Australia	CSS <sup>r</sup>	Male (n=91) Female (n=16)	Age range=17-36 y	NA	Semiquantitative FFQ on Day 1 of BT
Herzman-Harari and colleagues <sup>21</sup> (2013)	Israel	BAS	All female Pre-BT (n=44) BT Month 2 (n=43) BT Month 4 (n=38)	18.8±0.1 y	A 2-mo intervention based on the theory of planned behavior and a social cognitive approach. It involved 15 sessions, posters, and handouts	FFQ developed for the Israeli population that included a food atlas and measurement aids
Israeli and colleagues <sup>22</sup> (2008)	lsrael	CSS	Male (n=78) Female (n=220)	Male: $19.3 \pm 1.1 \text{ y}$ Female: $19.1 \pm 0.6 \text{ y}$	NA	FFQ developed for the Israeli population
King and colleagues <sup>16</sup> (1994)	United States	BAS	All female (n=49)	21.2±3.4 y	NA	In the dining facility, a visual estimator recorded all foods on each participant's plate before and after eating on 7 of 7 days. The estimator used a diet recall to estimate types and amounts of foods and beverages consumed between meals

(continued on next page)

**Table 2.** Key characteristics of studies included in a systematic literature review investigating the influence of training on new army recruits' dietary intakes of energy and macronutrients and performance (*continued*)

Reference (year of publication)	Country	Study design	Study group and sex	Participants age (mean±standard deviation)	Details of intervention	Dietary intake assessment method
Rose and colleagues <sup>17</sup> (1988)	United States	BAS	Male (n=41) Female (n=40)	Male: 19±NR y Female: 20±NR y	NA	Observers recorded foods on each participant's plate before and after eating in the dining facility and in the field. Dietary interviews were conducted to assess food intake outside of the dining facility
Etzion-Daniel and colleagues <sup>7</sup> (2008)	Israel	BAS	Male (n=28) Female (n=83)	Age range=18-19 y	NA	FFQ validated for the Israeli population
Skiller and colleagues <sup>3</sup> (2005)	Australia	BAS	Males (n=38) Females (n=5)	Male: 22.0±NR y Female: 29.5±NR y	NA	FFQ capturing previous 12 mo completed on commencement of BT. During Week 5 of BT, participants completed a food diary at the time of each meal and snack for 3 d
Morrissey <sup>19</sup> (1988)	Australia	BAS	Sex NR Two platoons (n=NR)	NR	NA	Weighing and recording of all foods offered in the mess, and subsequent weighing of all waste from both the mess and diners' plates for 7 of 7 days
Forbes-Ewan and colleagues <sup>20</sup> (2008)	Australia	BAS	Male (n=9)	20±NR y	NA	Food diaries were used over the 2 d before Infantry IET commencement. During Weeks 1 and 6, weighing of plates/hot boxes before and after each meal, including estimation of the weights of each food on plates using
						(continued on next page)

(continued on next page)

RESEARCH

RESEARCH

Table 2. Key characteristics of studies included in a systematic literature review investigating the influence of training on new army recruits' dietary intakes of energy and macronutrients and performance (continued)

Reference (year of publication)	Country	Study design	Study group and sex	Participants age (mean±standard deviation)	Details of intervention	Dietary intake assessment method
						mean weights of servings. During field training during Week 10, all eaten and uneaten combat ration food wrappers were collected. Participants were asked to report all foods eaten outside of the mess

**Table 3.** Custom quality assessment tool used to assess the risk of bias in studies included in a systematic literature review investigating the influence of training on new army recruits' dietary intakes of energy and macronutrients and performance

Criterion	Question
1	Was the study question or objective clearly stated?
2	Were eligibility/selection criteria for the study population pre-specified and clearly described?
3	Were the participants in the study representative of those who would be eligible for the test/service/intervention in the general or clinical population of interest?
4	Was the sample size sufficiently large to provide confidence in the findings?
5	Was the test/service/intervention/exposure clearly described and delivered consistently across the study population?
6	Were the outcome measures pre-specified, clearly defined, valid, reliable, and assessed consistently across all study participants?
7	Were the people assessing the outcomes blinded to the participants' exposures/interventions?
8	Was the loss to follow-up after baseline 20% or less? Were those lost to follow-up accounted for in the analysis?
9	If the intervention was conducted at a group level (eg, a whole hospital or a community) did the statistical analysis take into account the use of individual-level data to determine effects at the group level?
10	Did the statistical methods examine changes in outcome measures from before to after the intervention? Were statistical tests done that provided <i>P</i> values for the pre- to postchanges where applicable? Were effect sizes and/or confidence intervals reported where applicable?
11	Were study groups comparable?
12	Are conclusions supported by results with biases and limitations taken into consideration?

preceding periods of 3 to 12 months.<sup>2,6,7,14,15,18,21</sup> The precommencement El of study groups—some of which included both men and women—averaged between 2,242 and 2,916 kcal/day, representing 69% to 120% of the AC 1 MRDIs.<sup>2,6,7,14,15,18,21</sup> Average precommencement carbohydrate and protein intakes among both male and female recruits represented 64% to 121% and 74% to 129% of the AC 1 MRDIs, respectively. From the 7 studies, almost all (11 out of 12) groups monitored consumed carbohydrate intakes at the lower end of the MRDI.<sup>2,6,7,14,15,18,21</sup> Protein intakes were close to or above the recommended level in nearly all (10 of the 12) study groups, representing 90% to 129% of the MRDI.<sup>2,6,7,14,15,18,21</sup> Finally, average precommencement fat intakes contributed to ~30% to 37% of total Els among both males and females.<sup>2,6,7,14,15,18,21</sup>

## Energy and Macronutrient Intakes Measured during the Early Weeks of BT and BCT

Six studies examined the energy and macronutrient intakes of recruits during the early weeks (ie, Weeks 1 to 3) of their army training.<sup>4,5,16,17,19,22</sup> The mean Els for males ranged from 2,644 kcal/day (69% of the AC 3 MRDI),<sup>4</sup> to 4,070 kcal/day (106% of the MRDI).<sup>19</sup> Most male study groups (five of the six) had Els representing 69% to 84% of the AC 3 MRDI,<sup>4,5,17,22</sup> with the higher El (106% of the MRDI) arising from a study that employed a more robust method for measuring dietary intake—weighing and recording all foods on recruits' plates before and after each meal in the army dining facility.<sup>19</sup> Although few studies measured energy expenditure (EE), one study by McAdam and colleagues<sup>4</sup> reported an average EE of 3,238 kcal/day throughout Weeks 2 and 3 of initial training. When participants' EE was compared with their average EI measured during Week 1 of their initial training (2,643 kcal/day), it indicated an average energy deficit of ~595 kcal/day. The only other study to estimate EE during the early weeks of BT found EE to be 4,039 kcal/day, which was similar to the reported EI of 4,070 kcal/day in the same study, indicating energy balance on average.<sup>19</sup> In female study cohorts, mean EIs ranged between 77% and 94% of the AC 3 energy MRDI (2,210 to 2,592 kcal/day), with higher mean EIs among women undertaking US Army BT and BCT (90% to 94% of the MRDI) compared with females undertaking BT in Israel (77% of the MRDI).<sup>16,17,22</sup>

Carbohydrate intakes also varied widely during the early weeks of BT, representing 62% to 93% of the MRDI for males, with the majority of studies (six of the seven) reporting intakes ranging between 62% and 76% of the MRDI.<sup>4,5,17,19,22</sup> The study reporting an average carbohydrate intake representing 93% of the MRDI also reported the highest EI.<sup>19</sup> In females, carbohydrate intakes represented 76% to 94% of the MRDI, with the highest intake reported in US recruits. Compared with carbohydrate intakes, males' protein intakes were closer to meeting the recommended intake, representing 87% to 117% of the MRDI.<sup>4,5,17,19,22</sup> Females' protein intakes were generally closer to recommended intakes at 93% to 109% of the MRDI across all studies.<sup>16,17,22</sup> Males' and females' fat intakes contributed from 30% to 37% and 30% to 34% of their total EIs, respectively.<sup>4,5,16,17,19,22</sup>

#### Energy and Macronutrient Intakes Measured During Early and Later Weeks of BT and BCT

Collectively, seven studies undertaken in the United States, Israel, and Australia measured dietary intakes during the later weeks of either BT or BCT, in addition to measuring either **Table 4.** The risks of bias in studies included in a systematic literature review investigating the influence of training on new army recruits' dietary intakes of energy and macronutrients and performance, for each criteria in a custom quality assessment tool (shown in Table 3)

	Criteria											
Reference (year of publication)	1	2	3	4	5	6	7	8	9	10	11	12
Gaffney-Stomberg and colleagues <sup>14</sup> (2014)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes
Moran and colleagues <sup>6</sup> (2012)	Yes	Yes	Yes	Yes	Yes	Yes	NA <sup>a</sup>	CD <sup>b</sup>	Yes	Yes	Yes	Yes
McAdam and colleagues <sup>4</sup> (2018a)	Yes	Yes	Yes	Yes	Yes	CD	NA	CD	Yes	NA	NA	Yes
Margolis and colleagues <sup>15</sup> (2012)	Yes	Yes	Yes	Yes	Yes	Yes	NA	CD	Yes	Yes	NA	Yes
McAdam and colleagues <sup>5</sup> (2018b)	Yes	Yes	Yes	Yes	Yes	CD	Yes	CD	Yes	Yes	Yes	Yes
Booth and Coad <sup>18</sup> (2001)	Yes	Yes	Yes	Yes	Yes	Yes	NA	Yes	Yes	NA	NA	Yes
Herzman-Harari and colleagues <sup>21</sup> (2013)	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	NA	Yes
Israeli and colleagues <sup>22</sup> (2008)	Yes	Yes	Yes	Yes	Yes	Yes	NA	Yes	Yes	NA	Yes	Yes
King and colleagues <sup>16</sup> (1994)	Yes	Yes	Yes	Yes	Yes	Yes	NA	CD	Yes	NA	NA	Yes
Rose and colleagues <sup>17</sup> (1988)	Yes	Yes	Yes	Yes	Yes	Yes	NA	Yes	Yes	NA	NA	Yes
Etzion-Daniel and colleagues <sup>7</sup> (2008)	Yes	Yes	Yes	Yes	Yes	Yes	NA	Yes	Yes	Yes	NA	Yes
Skiller and colleagues <sup>3</sup> (2005)	Yes	Yes	Yes	Yes	Yes	CD	NA	No	Yes	Yes	NA	Yes
Morrissey <sup>19</sup> (1988)	Yes	Yes	Yes	CD	Yes	CD	NA	CD	CD	NA	NA	CD
Forbes-Ewan and colleagues <sup>20</sup> (2008)	Yes	Yes	Yes	Yes	Yes	Yes	NA	No	Yes	No <sup>c</sup>	NA	Yes

<sup>a</sup>NA=not applicable.

<sup>b</sup>CD=cannot determine.

<sup>c</sup>Outcome data wer requested from the authors.

precommencement dietary intakes,<sup>2,6,7,14,15,21</sup> or intakes during the early weeks of training.<sup>5</sup> When compared with precommencement and earlier training weeks, the mean EIs (not including EI from supplementation provided as part of the study protocol) among both males and females in the later weeks of BT and BCT (ie, after 5 to 17 weeks' of BT or BCT) represented either similar or lower proportions of the MRDIs: 56% to 77% (2,117 to 2,930 kcal).<sup>2,5-7,14,15,21</sup> During the later weeks of BT and BCT, carbohydrate intakes ranged from 49% to 68% of the MRDI across both males and females in the various countries.<sup>2,5-7,14,15,21</sup> Daily protein intakes ranged more widely than carbohydrate intakes, from 64% to 118% of the MRDI, with intakes closer to meeting the MRDIs compared with carbohydrate intakes in most instances.<sup>2,5-7,14,15,21</sup> Protein intakes assessed during US Army BCT were found to represent 64% to 77% of the MRDI among both males and females,<sup>14,15</sup> 93% to 102% of the MRDI in males undertaking BT in the United States,<sup>5</sup> 93% to 108% of the MRDI in males undertaking BT in the Israeli Defense Force,<sup>6,7,22</sup> 71% to 93% of the MRDI in females undertaking BT in the Israeli Defense Force,<sup>7,21,22</sup> and 118% of the MRDI in one study involving males and females undertaking BT in Australia.<sup>2</sup> Fat intakes differed across the studies, from  $\sim 30\%$  to 39% of total El across both males and females in the various countries.<sup>2,5-</sup> <sup>7,14,15,21</sup> Among both males and females, fat intakes above the

All final Among both males and females, fat intakes above the AC 3 recommended range (23% to 33% total energy from fat) were reported in five of the 11 study groups.<sup>2,15</sup>

#### **Dietary Intakes and Performance**

Only three studies reported physical fitness and/or performance outcomes.<sup>2,5,22</sup> One of these, by McAdam and

colleagues,<sup>5</sup> investigated the effectiveness of carbohydrate or protein supplementation in enhancing various measures of fitness and performance. The results are shown in Table 6, with a significant improvement in push up performance in the group receiving protein supplements. The other two studies did not statistically analyze the influence of dietary intakes on measures of fitness or performance.<sup>2,22</sup>

#### DISCUSSION

The major findings of this systematic review suggest that army recruits undertaking initial training are unlikely to be meeting the recommended EIs, with greater intake deficits in carbohydrate compared with other macronutrients. Few studies concurrently measured physical fitness and/or performance outcomes, which highlights a major gap and an area for future research.

#### El and EE of New Recruits Beginning Their Training: Does Their Intake Meet the Demands of Training?

Before commencement, reported average Els represented 69% to 120% of the AC 1 energy MRDI.<sup>2,6,7,14,15,18,21</sup> Half of the study groups reported intakes <90% of the MRDI, whereas the other half reported intakes ≥90% of the MRDI. This suggests that many new recruits are already below the MRDI before training commencement; to meet the increased energy requirements of military training (ie, AC 3 MRDI), a substantial increase from previous Els may be required.<sup>12</sup> Among the studies that reported Els in the early weeks of training, levels of intake as proportions of the AC 3 energy MRDIs varied widely.<sup>4,5,16,17,19,22</sup> Daily Els were 2,644 to 40,70

**Table 5.** Energy expenditures and energy and macronutrient intakes (kilocalories per day and grams per day) of army recruits in relation to the Military Recommended Dietary Intakes (MDRIs) from studies included in a systematic literature review investigating the influence of training on new army recruits' dietary intakes of energy and macronutrients and performance<sup>a</sup>

Reference (year of publication)	Study groups	Time point(s) of dietary intake assessment (sex)	Energy expend-iture (kcal/d)	Energy intake (kcal/d) (%MRDI)	Carbohydrate intake (g/d) (%MRDI)	Protein intake (g/d) (%MRDI)	Fat intake (g/d) (%total energy)
Gaffney-Stomberg and colleagues <sup>14</sup> (2014)	Placebo	Pre-BCT <sup>e</sup> over 3 mo (M <sup>f</sup> +F <sup>g</sup> ) End (Week 9) BCT (M+F)	NM <sup>h</sup> NM	2,242±961 (85) <sup>i</sup> 2,121±697 (60)	272±118 (78) <sup>i</sup> 246±95 (49)	88±40 (90) <sup>i</sup> 73±29 (64)	89±42 (37) 71±28 (30)
	Ca <sup>b</sup> +Vit D <sup>c</sup> supp <sup>d</sup>	Pre-BCT over 3 mo (M+F) End (Week 9) BCT (M+F)	NM NM	2,289±976 (91) <sup>i</sup> 2,261±680 (67)	266±112 (81) <sup>i</sup> 276±99 (58)	90±44 (97) <sup>i</sup> 77±26 (71)	95±44 (37) 75±27 (30)
Moran and colleagues <sup>6</sup> (2012)	WSF <sup>j</sup>	Pre-BT <sup>I</sup> over 6 mo (M) End (Month 4) BT (M)	NM NM	2,824±1,086 (98) <sup>i</sup> 2,587±974 (68)	369±165 (98) <sup>i</sup> 335±178 (62)	128.6±62.8 (121) <sup>i</sup> 114.0±42.4 (93)	100.3±40.5 (32) 89.7±31.5 (31)
	SF <sup>k</sup>	Pre-BT over 6 mo (M) End (Month 4) BT (M)	NM NM	2,325±974 (81) <sup>i</sup> 2,447±879 (64)	272±104 (73) <sup>i</sup> 285±129 (53)	111.7±43.1 (105) <sup>i</sup> 131.7±48.3 (108)	84.5±14.8 (35) 108.0±35.0 (34)
McAdam and colleagues <sup>4</sup> (2018a)	NA <sup>m</sup>	IET <sup>n</sup> Week 1 (M)	3,238±457°	2,644±639 (69)	352 (65)	114 (93)	89 (30)
Margolis and colleagues <sup>15</sup> (2012)	NA	Pre-BCT (M) Pre-BCT (F)	NM NM	1,975±909 (69) <sup>i</sup> 1,824±1,014 (89) <sup>i</sup>	240±124 (64) <sup>i</sup> 222±125 (83) <sup>i</sup>	78±36 (74) <sup>i</sup> 69±38 (92) <sup>i</sup>	77±37 (35) 73±46 (36)
		End (Week 9) BCT (M) End (Week 9) BCT (F)	NM NM	2,216±777 (58) 1,789±613 (65)	286±101 (53) 240±84 (62)	87±33 (71) 68±23 (77)	85±35 (35) 66±26 (33)
McAdam and colleagues <sup>5</sup> (2018b)	WP <sup>p</sup> supp CHO <sup>q</sup> supp	IET Week 1 — Pre-I <sup>r</sup> DF <sup>s</sup> (M) IET Week 1 — Pre-I DF (M)	NM NM	2,825±611 (74) 2,624±740 (69)	371±84 (69) 349±95 (65)	122±25 (100) 112±32 (92)	98±27 (31) 90±31 (31)
	WP supp CHO supp	IET Week 9 — Post-I <sup>t</sup> DF (M) IET Week 9 — Post-I DF (M)	NM NM	2,930±681 (77) 2,766±542 (73)	392±97 (73) 368±85 (68)	124±29 (102) 113±21 (93)	100±30.9 (31) 98±23.2 (32)
	WP supp	IET Week 9 – Post-I DF+supp (M)	NM	3,516±681 (92)	430±97 (80)	201±29 (165)	98±23.2 (32) 115±31 (30)
	CHO supp	IET Week 9 — Post-I DF+supp (M)	NM	3,348±542 (88)	495±85 (92)	114±21 (93)	106±23 (29)

**Table 5.** Energy expenditures and energy and macronutrient intakes (kilocalories per day and grams per day) of army recruits in relation to the Military Recommended Dietary Intakes (MDRIs) from studies included in a systematic literature review investigating the influence of training on new army recruits' dietary intakes of energy and macronutrients and performance<sup>a</sup> (*continued*)

Reference (year of publication)	Study groups	Time point(s) of dietary intake assessment (sex)	Energy expend-iture (kcal/d)	Energy intake (kcal/d) (%MRDI)	Carbohydrate intake (g/d) (%MRDI)	Protein intake (g/d) (%MRDI)	Fat intake (g/d) (%total energy)
Booth and Coad <sup>18</sup> (2001)	NA	Pre-BT (M) Pre-BT (F)	NM	2,868±717 (100) <sup>i</sup> 2,438±717 (120) <sup>i</sup>	321±105 (86) <sup>i</sup> 289±82 (109) <sup>i</sup>	127±34 (120) <sup>i</sup> 107±29 (143) <sup>i</sup>	116±33 (36) 93±50 (34)
Herzman-Harari and colleagues <sup>21</sup> (2013)	NA	Pre-BT (F) BT Month 2 — Pre-I (F) End BT (Month 4) — Post-I (F)	NM NM NM	2,380±112 <sup>u</sup> (118) <sup>i</sup> 1,694±126 <sup>u</sup> (59) 1,916±119 <sup>u</sup> (67)	323±17 <sup>u</sup> (121) <sup>i</sup> 218±19 <sup>u</sup> (56) 257±20 <sup>u</sup> (66)	97±5 <sup>u</sup> (129) <sup>i</sup> 62±5 <sup>u</sup> (71) 76±5 <sup>u</sup> (86)	79±4 (30) 65±5 (35) 66±4 (31)
lsraeli and colleagues <sup>22</sup> (2008)	NA	BT Week 1 (M) BT Week 1 (F)	NM NM	2,656±1,068 (69) 2,210±946 (77)	333±143 (62) 295±140 (76)	106±47 (87) 82±38 (93)	98±41 (33) 81±37 (33)
King and colleagues <sup>16</sup> (1994)	NA	BCT Week 2 (F)	NM	2,592±500 (94)	365±69 (94)	82.1±18.3 (93)	94±25 (33)
Rose and colleagues <sup>17</sup> (1988)	NA	BT Weeks 1—3 (M) BT Weeks 1—3 (F)	NM NM	3,199±736 (84) 2,467±560 (90)	410±97 (76) 318±74 (82)	125±33 (103) 96±22 (109)	121±41 (34) 94±34 (34)
Etzion-Daniel and colleagues <sup>7</sup> (2008)	NA	Pre-BT (M) End (Month 4) BT (M) Pre-BT (F) End (Month 4) BT (F)	NM NM NM NM	2,368±723 (83) <sup>i</sup> 2,117±546 (56) 1,993±736 (98) <sup>i</sup> 1,697±574 (62)	310±94 <sup>v</sup> (83) <sup>i</sup> 305±87 <sup>v</sup> (56) 263±97 <sup>v</sup> (99) <sup>i</sup> 265±95 <sup>v</sup> (68)	$87\pm 33^{\vee} (82)^{i}$ $90\pm 28^{\vee} (74)$ $73\pm 37^{\vee} (97)^{i}$ $70\pm 25^{\vee} (80)$	$89\pm 30^{\vee}$ (34) $86\pm 30^{\vee}$ (37) $75\pm 31^{\vee}$ (34) $75\pm 31^{\vee}$ (39)
Skiller and colleagues <sup>3</sup> (2005)	NA	Pre-BT over 12 mo (M+F) BT Week 5 (M+F)	M: 4,111 <sup>w</sup> F: 3,059 <sup>w</sup>	2,916±1,028 (105) 2,486±454 (67)	280±91 (77) 273±66 (52)	140±60 (102) 105±20 (118)	133 (38) <sup>×</sup> 105.3±21 (35)
Morrissey <sup>19</sup> (1988)	Groups 1 and 2 Group 1	BT Week 1 (NR) BT Week 1 (NR)	NM 4,039 <sup>w</sup>	4,070 (106) NA	500 <sup>y</sup> (93) NA	143 <sup>y</sup> (117) NA	167 <sup>y</sup> (37) NA

(continued on next page)

**Table 5.** Energy expenditures and energy and macronutrient intakes (kilocalories per day and grams per day) of army recruits in relation to the Military Recommended Dietary Intakes (MDRIs) from studies included in a systematic literature review investigating the influence of training on new army recruits' dietary intakes of energy and macronutrients and performance<sup>a</sup> (*continued*)

Reference (year of publication)	Study groups	Time point(s) of dietary intake assessment (sex)	Energy expend-iture (kcal/d)	Energy intake (kcal/d) (%MRDI)	Carbohydrate intake (g/d) (%MRDI)	Protein intake (g/d) (%MRDI)	Fat intake (g/d) (%total energy)
Forbes-Ewan and colleagues <sup>20</sup> (2008)	NA	Pre Inf IEmT <sup>z</sup> over 2 d (M) Inf IEmT Week 1 (M) Inf IEmT Week 6 (M) End (Week 10) Inf IEmT (M)	NM 4,087 <sup>w</sup> 4,326 <sup>w</sup> 5,951 <sup>w</sup>	3,919 (103) 3,967±813 (104) 2,772±478 (73) 3,561±980 (78) <sup>aa</sup>	382 (71) 480±108 (89) 281±60 (52) 374±107 (56) <sup>aa</sup>	147 (120) 141±15 (116) 150±30 (123) 144±22 (107) <sup>aa</sup>	139 (32) 159±42 (36) 110±31 (36) 157±57 (40)

<sup>a</sup>Energy and macronutrient values are mean±standard deviation unless specified otherwise, and intakes are reported in relation to the MRDIs as an approximate percent.

Energy and macronuclient values are mean instandard deviation unless specified otherwise, and intakes are report
<sup>b</sup> Ca=Calcium.
<sup>c</sup> Vit D=Vitamin D 3.
<sup>d</sup> supp=supplement.
<sup>e</sup> BCT=basic combat training.
<sup>f</sup> M=males.
<sup>g</sup> F=females.
<sup>h</sup> NM=not measured.
<sup>i</sup> Energy and macronutrient intakes are in relation to the activity category 1 MRDIs.
<sup>j</sup> WSF=without stress fracture.
<sup>k</sup> SF=stress fracture in the tibia or femur.
BT=basic training.
<sup>m</sup> NA=not applicable.
<sup>n</sup> IET=initial entry training.
$^\circ$ Energy expenditure measured by wearable actigraphs during Weeks 2 and 3 of initial employment training.
PWP=whey protein.
<sup>q</sup> CHO=carbohydrate.
'Pre I=pre intervention.
<sup>s</sup> DF=dining facility dietary intakes.
<sup>t</sup> post I=postintervention.
<sup>u</sup> DF+supp=dining facility and supplement dietary intakes.
<sup>v</sup> Intakes in grams per day were calculated from reported intakes in kilocalories per day.
<sup>w</sup> Measured by the factorial method.
*Author provided additional data.
<sup>y</sup> Approximate intakes in grams per day were calculated from intakes reported as a percent of total energy.

<sup>z</sup>Inf IEmT=Infantry Initial Employment Training.

<sup>aa</sup>Dietary intakes are reported in relation to the activity category 4 MRDIs.

JOURNAL OF THE ACADEMY OF NUTRITION AND DIETETICS

1699

**Table 6.** Results of army recruits' physical fitness and/or performance assessments from studies included in a systematic literature review investigating army recruits' dietary intakes of energy and macronutrients and performance

Author (year of publication)	Study groups	Time point(s) of assessment (sex)	Aerobic fitness/ performance (units) <sup>a</sup>	Anaerobic fitness/performance (units) <sup>a</sup>	Significant improvement regarding dietary intake or intervention?
McAdam and colleagues <sup>4</sup> (2018a)	WP <sup>b</sup> supp <sup>c</sup> CHO <sup>j</sup> supp WP supp CHO supp	IET <sup>d</sup> Week 2 post-l <sup>e</sup> (M <sup>f</sup> ) IET Week 2 post-l (M) IET Week 8 post-l (M) IET Week 8 post-l (M)	<ul> <li>2-mile run time NR<sup>9</sup></li> <li>2-mile run time NR</li> <li>14:41±1:9 2-mile run time (minutes:seconds)</li> <li>14:32±1:11 2-mile run time (minutes:seconds)</li> </ul>	50.4±14.3 sit-ups (maximum number) 51.8±13.3 sit-ups (maximum number) 59.7±11.0 sit-ups (maximum number) 53±12 push-ups (maximum number) 60.7±9.2 sit-ups (maximum number) 46±9 push-ups (maximum number)	2-mile run — no <sup>h</sup> Sit-ups — no <sup>i</sup> Push ups — yes <sup>k</sup>
Israeli and colleagues <sup>22</sup> (2008)	NA	BT <sup>m</sup> Week 1 (M) BT Week 1 (F <sup>p</sup> )	VO <sub>2</sub> max 50.4 $\pm$ 8 (mL/kg/ min) VO <sub>2</sub> max 36.8 $\pm$ 6.4 (mL/kg/ min)	NM <sup>n</sup> NM	ND°
Skiller and colleagues <sup>3</sup> (2005)	NA	Start-BT (M+F) End-BT (M+F)	<ul> <li>10:11±1.13 2.4 km run time (minutes:seconds)</li> <li>9.1±1.3 shuttle run (level)</li> <li>10:32±1.02 2.4 km run time (minutes:seconds) shuttle run NM</li> </ul>	<ul> <li>33±12 push-ups (maximum number)</li> <li>93±16 sit-ups (maximum number)</li> <li>67.1±16.9 vertical jump (cm)</li> <li>40±11 push-ups (maximum number)</li> <li>97±10 sit-ups (maximum number)</li> <li>72.1±17.6 vertical jump (cm)</li> </ul>	ND

<sup>a</sup>All results are mean±standard deviation.

<sup>b</sup>WP=whey protein.

<sup>c</sup>supp=supplement.

<sup>d</sup>IET=initial entry training.

<sup>e</sup>post l=post intervention.

<sup>f</sup>M=males.

<sup>g</sup>NR=not reported.

<sup>h</sup>Reports that after controlling for initial run performance there was no significant difference between CHO and WP groups at post I (F=3.64;P=0.06).

Reports that after controlling for initial sit up performance there was no significant difference in sit up performance between CHO and WP groups at postintervention (F=0.02; P=0.90).

<sup>j</sup>CHO=carbohydrate.

<sup>k</sup>Reports that after controlling for initial push up performance there was a significant group difference at post intervention (*F*=10.02; *P*=0.002) with the WP supp group performing more push ups at post I (effect size=0.41 (medium) and CHO group effect size=0.18 (small).

<sup>I</sup>NA=not applicable

<sup>m</sup>BT=basic training <sup>n</sup>NM=not measured.

°ND, not determined.

PF=females.

kcal, with nearly all (five of the six) male study groups reporting 69% to 84% of the MRDI (3,824 kcal). The one study that reported higher EI of 4,070 kcal/day (106% of the MRDI) used more robust method of dietary assessment (ie, weighing and recording all foods on recruits' plates before and after each meal in the army dining facility) and thus may be a more accurate reflection of EI during the early training weeks.<sup>19</sup>

Only two studies, undertaken during initial training in different countries, measured both EI and EE during the early weeks of training, providing an estimation of energy balance.<sup>4,19</sup> The first study was undertaken during week 1 of US Army BCT,<sup>4</sup> and in contrast, the second study was undertaken with Australia recruits during week 1 of BT.<sup>19</sup> Although different methods of estimating EE were employed in these studies, their differing EE findings (~3,200 vs ~4,000 kcal/ day) suggest that the application of the AC 3 energy MRDI for males (3,824 kcal) for all initial army training scenarios may be overestimating the energy requirements in some instances. Despite this, given reported daily EIs ranged from 2,644 to 3,199 kcal in five of the six studies involving male recruits, an estimated EE at the lower end of  $\sim$  3,238 kcal/day would still suggest an average energy deficit ranging from marginal (39 kcal/day) to 595 kcal/day during the early weeks of training across various scenarios.<sup>4,5,16,17,19,22</sup> However, another study using a more rigorous method of EI assessment (ie, photography of recruits' food trays/plates before and after eating) found average EI among male and female recruits to be much higher, at  $\sim$  3,850 kcal/day, during the first week of US Army BCT.<sup>25</sup> Thus,  $\sim$  3,800 kcal/day may be a more accurate reflection of the recruits' EI during the early weeks of training, and based on limited EE data, recruits may only be in minor energy deficit during the early periods of training.

#### El Measured at the Beginning and end of BT and BCT: Does Energy Intake Change over the Course of Training?

Studies using repeated dietary intake assessments at both the beginning and at the end of BT BCT suggest that despite increased nutritional demands for recruits, on average, recruits' EI does not increase to meet such requirements.<sup>2,6,7,14,15,21</sup> Study groups in both Israel and Australia reported a significant decrease in EIs from pre- to post-BT,<sup>2,7,21</sup> whereas the majority of study groups (involving both males and females) in the United States reported no change in EI, with only one male group in the United States showing a small but significant increase in EI of 241 kcal/ day.<sup>5,14,15</sup> The contrasting findings are most likely a reflection of the differing diet recall methods employed in each study, with the type of FFQs, meal-specific food logs, and food diaries implemented generating different EIs. Notwithstanding, the majority of studies suggest that EI does not increase to meet the demands of higher EE due to the nature of basic training.

# EI and Body Mass and Composition Changes during BT and BCT

Although inadequate EIs were found during BT and BCT, there were inconsistent findings regarding its influence on body mass and composition. One study reported a significant increase in mean body mass index,<sup>21</sup> others reported a

significant decrease in body mass,<sup>2,15</sup> and some studies reported no significant changes in body mass and/or body mass index.<sup>5,7,14</sup> In the study by Margolis and colleagues involving males undertaking BCT in the United States, despite an increase in mean EI from pre- to end-BCT–from  $\sim$  1,975 kcal/ day to 2,216 kcal/day (representing  $\sim$  58% of the AC 3 MRDI at the end of BCT)—a significant reduction in body mass was observed, suggesting many were in energy deficit.<sup>15</sup> Conversely, in the same study, females had a marginal (nonsignificant) decrease in mean EI of 35 kcal/day from preto end-BCT (representing 62% of the MRDI at end BCT), and their mean body mass remained relatively stable (+0.1 kg at the end of BCT).<sup>15</sup> On average, their fat mass decreased by  $\sim$ 2.7 kg, whereas 88% of the group increased their fat-free mass, on average by  $\sim 2.8$  kg. It should be noted that body weight stability and favorable body composition changes may not be good indicators that energy requirements are being met, if indeed energy availability is suboptimal (ie, 30 to 45 kcal/kg fat-free mass/day) or low (<30 kcal/kg fat-free mass/ day).<sup>26,27</sup> Several other energy-requiring functions may be compromised and afforded suboptimal energy, which may adversely affect health (eg, reproductive health and hormonal balance) and the magnitude of training adaptations and body composition changes.<sup>9,28</sup>

#### Macronutrient Intake during BT and BCT: Implications for Performance, Training Outcomes, and Injury Risk

**Carbohydrate Intake.** As would be expected in light of the inadequate levels of EI, reported carbohydrate intakes were below the recommendations throughout initial army training. Across all training scenarios, almost all male study groups had carbohydrate intakes between 62% and 76% of the MRDI during Weeks 1 through 3,<sup>4,5,17,19,22</sup> whereas females' carbohydrate intakes varied from 76% to 94% of the MRDI during Weeks 1 through 3.<sup>16,17,22</sup> Among three studies that assessed intakes at the beginning and end of BCT, carbohydrate intakes still remained lower than recommended levels regardless of sex.<sup>5,14,15</sup> Two studies found similar carbohydrate intakes at pre- and post-BCT<sup>5,14</sup>; however, one group in the study by McAdam and colleagues<sup>5</sup> provided carbohydrate supplements to recruits, effectively increasing their total carbohydrate intake.<sup>5</sup> The third study found intakes significantly increased from Week 0 to Week 9 of US BCT in both males and females, by ~46 g/day and ~18 g/day, respectively.<sup>15</sup> However, across both males and females in these three studies, total carbohydrate intakes during BCT represented 49% to 73% of the MRDI.<sup>5,14,15</sup> Carbohydrate intakes of 6 to 10 g/kg/day are recommended to facilitate rapid and maximal repletion of glycogen stores when peak training quality or performance is required in subsequent exercise bouts.<sup>29-31</sup> One study found that 70% of male recruits consumed below the 6 g carbohydrate/kg/day recommendation in the early weeks of army training.<sup>4,29</sup> Suboptimal intakes of carbohydrate coupled with EIs below 30 kcal/kg fat-free mass in the medium to long-term may reduce training quality and performance as well as increase the risk of illness and injury.<sup>6,9,10</sup> Among Israeli recruits, lower intakes of carbohydrate (as well as calcium and vitamin D) were noted among recruits who suffered stress fractures,

compared with those who did not.<sup>6</sup> Musculoskeletal injuries are indeed common during initial army training, with a recent study finding that  $\sim 28\%$  of Australian Army recruits suffered a musculoskeletal injury during their training.<sup>32</sup>

Protein Intake. Protein intakes were found to either meet or almost meet the MRDIs before the commencement of initial training and in the early weeks of training.<sup>2,6,7,14-18,21,22</sup> During training, lower adherences to the protein MRDIs (64% to 80%) by both males and females were reported by two studies undertaken during US BCT,<sup>14,15</sup> and one undertaken during BT in Israel.<sup>7</sup> Conversely, other studies reported protein intakes either meet or almost meet the MRDIs.<sup>2,5,6,20</sup> A commonality among those studies that found lower adherences to the protein MRDI was the use of a self-administered FFQ to assess dietary intake,<sup>7,14,15</sup> whereas the latter studies used more robust methods such as FFQs that were completed by the participants with the assistance of a dietitian,<sup>6</sup> meal-specific diet logs,<sup>5</sup> food diaries that participants completed at the time of each meal and snack,<sup>2</sup> and weighing and recording of all foods participants selected in the dining facility and weighing and recording of all plate waste.<sup>20</sup>

More recent data suggest that protein intakes in the range of 1.6 to 2.4 g/kg/day (higher than the MRDIs) may be required to mitigate skeletal muscle mass loss and optimize training adaptations and performance during times of energy deficit.<sup>33</sup> Only two studies assessed protein intakes per kilogram, finding average intakes below this level,<sup>4,5</sup> with one reporting that  $\sim$  40% of recruits consumed <1.5 g/kg/day.<sup>4</sup> In the other study, one group was provided with protein supplementation, which significantly increased their protein intakes and push-up performance at the end of their training when compared with carbohydrate supplementation.<sup>5</sup> It is not readily apparent to the authors as to whether the increased push-up performance, which requires a combination of strength and endurance, is a reflection of higher protein intakes supporting exercise-induced adaptations, especially muscle growth, over the duration of the training or secondary to the slightly higher, albeit nonsignificant, extra calories (~200 kcal) consumed per day within the same group. Nevertheless, the findings suggest that some recruits, who are in energy deficit, regularly consume suboptimal protein, which could compromise their skeletal muscle mass, training adaptations, and performance.<sup>28,33,34</sup> Further, several studies have shown males with low energy availability have lower levels of testosterone<sup>28,35</sup>; optimal protein intake (ie, 1.6 to 2.4 g/kg/day) during military training may be needed for the restoration of testosterone levels as well as other anabolic hormones (eg, insulin and growth hormone).<sup>33,34</sup>

**Fat Intake.** Dietary intakes of fat before the commencement of army training ranged between the middle and the upper end of the recommended range (ie, 25% to 35% of total EI) for most study groups. During initial training, when the recommended intake of fat drops to 23% to 33% of total energy to allow for the increased recommended intakes of carbohydrate that are commensurate with higher levels of physical activity,<sup>12</sup> recruits' fat intakes differed. Half (n 10) of the study groups displayed fat intakes either close to or at the upper end of the recommended range,<sup>4–6,14–16,21,22</sup> with the

other half (n 10) displaying intakes above the recommended range.<sup>2,6,7,17,19-21</sup> Thus in some instances, recruits are consuming higher than recommended proportions of fat, coinciding with the lower than recommended carbohydrate intakes previously discussed. The higher than recommended intakes of fat may be due to recruits' not adjusting their food selections to meet the higher carbohydrate and lower fat recommendations.<sup>20</sup> Depending on the individual, either increasing carbohydrate, low-fat options, may remedy a higher than recommended proportion of fat contribution to total EI. In addition, recruits should focus on high-carbohydrate, low-fat sources for peak performance during training to promote adequate digestion before exercise and to avoid gastrointestinal discomfort/distress.<sup>36,37</sup>

# Possible Reasons for Inadequate Dietary Intakes during BT and BCT

New recruits are exposed to a different eating environment where time to eat can be limited and, at times, access to food is restricted (in terms of needing to fit between activities or within mealtimes). Factors such as whether meals are consumed in a dining facility or in the field foreseeably influence on recruits' EI, with previous research showing negative energy balance among soldiers undertaking field training while subsisting solely on combat ration packs.<sup>3</sup> Other possible reasons behind the reported inadequate energy and macronutrient intakes include that the demands of training may influence appetite and gut functioning. As described by King and colleagues,<sup>39</sup> increased EE from increased physical activity (above previously normal levels) may only be partially compensated for, if at all, by increased EI, depending on the individual.<sup>39-41</sup> Variability has been shown to exist in appetite changes in response to exerciseinduced increases in EE. Habitual exercisers appear more likely to control EI to match EE, and this may be explained by interindividual differences in compensatory mechanisms, such as the rate of gastric emptying and gut absorption.<sup>39</sup> Given the large volumes of physical activity undertaken during BT (measured at  $\sim$ 7 hours/day of light to vigorous activity in some scenarios)<sup>4,5</sup> certain foods and/or the timing of meals before exercise may lead to gastrointestinal distress during subsequent exercise, depending on the individual.<sup>36,37</sup> Thus, without proper nutritional periodization, it is possible that some recruits' avoid large meals and/or certain foods during the day.<sup>37</sup> Existing nutrition guidance to recruits during initial military training varies between countries, although in both Australia and the United States includes basic performance nutrition concepts delivered through a 1hour lecture as well as in written formats.<sup>43,44</sup> In light of the findings of the present review, additional performance nutrition strategies such dietary supplementation and behavior change strategies should be devised,<sup>45</sup> as discussed further within the Implications for Future Research section.

#### Limitations

In many cases, dietary intakes of army recruits were derived from self-reported information (eg, diet logs, diet recall interviews, and FFQs). Self-reported information is subject to biases such as recall bias and social desirability bias, and thus its interpretation is limited, as suggested by many studies included in this review. In addition, we compared the dietary intakes of recruits during training to the Australian AC 3 MRDIs, which are sufficient to meet the requirements of nearly all healthy individuals, and thus may be above some recruits' dietary requirements.

#### Implications for Further Research

Given the limitations of the dietary assessment tools used in the reviewed studies, where practical, future research should select methods that can accurately quantify energy and macronutrient intakes. These data, together with assessment of energy expenditure, resting metabolic rate, and body composition, could provide a more accurate determination of the energy availability and requirements of army recruits during contemporary training. Concurrent measures on military-relevant performance measures will help determine optimal levels of energy and macronutrient intakes and energy availability for training quality, training adaptations, and performance, as well as reducing risks of illness and injury. Finally, to inform further strategies to improve the dietary intakes of recruits, the contemporary eating behaviors of army recruits and the reasons for suboptimal dietary intakes should be explored. These include behaviors and barriers (eg, limited eating time and opportunities, poor appetite, and stress), attitudes (eg, perceived importance of nutrition for optimizing performance), and self-efficacy (eg, performance nutrition knowledge). Other strategies (both behavioral and practical) that use registered dietitian nutritionists to guide and assist recruits in meeting their increased energy and macronutrient requirements within current nutrition promotion programs could help enhance performance and health during initial training.

#### CONCLUSIONS

The findings of this systematic literature review indicate that army recruits undertaking initial training are likely to underconsume energy compared with the recommended intake for extended periods of their training, with greater deficits in carbohydrate intake compared with other macronutrients. Despite intakes of protein being closer to the MRDIs than carbohydrate intakes, protein intakes still appeared lower than the recommended optimal protein intakes to enhance training adaptations. An important question that could not be answered was the influence of inadequate energy and macronutrient intakes on performance, with few included studies concurrently measuring physical fitness and/or performance outcomes with dietary intake. Notwithstanding, because nutrition is a cornerstone to military capability, our review provides further evidence of the dietary inadequacies that occur in army recruits. Key stakeholders and policy makers should consider such inadequacies when devising nutrition guidance and strategies in the future. Finally, our review also highlights a major gap in the current literature, with the need for further research linking suboptimal energy and macronutrient intakes to key military performance indicators.



#### PRACTICE IMPLICATIONS

#### What Is the Current Knowledge on This Topic?

Militaries have established recommended dietary intakes based on the high physical demands of army training. However, the extent to which army recruits achieve such intakes is unclear, and suboptimal dietary intakes may place them at risk of impaired performance.

## How Does This Research Add to Knowledge on This Topic?

Internationally, a high proportion of army recruits are not meeting military recommended dietary intakes, especially for energy and carbohydrate and to a lesser degree protein. These suboptimal intakes could negatively influence training-induced adaptations in body composition and physical performance.

## How Might This Knowledge Influence Current Dietetics Practice?

Registered dietitian nutritionists could play an integral role in devising and delivering further strategies (eg, behavior change and dietary supplementation) to army recruits and their superiors. Practical guidance should be provided on fueling and rapid refueling strategies surrounding endurance activity, as well as on meeting increased protein requirements through foods and supplements (where necessary).

#### References

- Adler A, Williams J, McGurk D, Moss A, Bliese P. Resilience training with soldiers during basic combat training: Randomisation by pla toon. Appl Psychol Health Well Being. 2015;7(1):85 107.
- Skiller B, Booth C, Coad R, Forbes Ewan C. Assessment of nutritional status and fatigue among Army recruits during the Army Common Recruit Training Course. Part A: Catering services and diet. DSTO TR 1736, https://apps.dtic.mil/sti/pdfs/ADA447856.pdf. Accessed June 17, 2020.
- Skiller B, Booth C, Coad R, Forbes Ewan C. Assessment of nutritional status and fatigue among Army recruits during the Army Common Recruit Training Course. Part B: Psychological and health aspects. DSTO RR 0300, https://apps.dtic.mil/dtic/tr/fulltext/u2/a448187.pdf. Accessed June 17, 2020.
- McAdam J, McGinnis K, Ory R, et al. Estimation of energy balance and training volume during Army Initial Entry Training. J Int Soc Sports Nutr. 2018;15(1):e1 e9.
- McAdam J, McGinnis K, Sefton J, et al. Effect of whey protein sup plementation on physical performance and body composition in Army initial entry training soldiers. *Nutrients*. 2018;10(9):e1248.
- Moran D, Heled Y, Arbel Y, et al. Dietary intake and stress fractures among elite male combat recruits. J Int Soc Sports Nutr. 2012;9:e1 e7.
- Etzion Daniel Y, Constantini N, Finestone A, et al. Nutrition con sumption of female combat recruits in army basic training. *Med Sci* Sports Exerc. 2008;40(Suppl 11):S677 S684.
- Departments of the Army, the Navy, and the Air Force. Nutrition and menu standards for human performance. AR 40 25, https:// armypubs.army.mil/epubs/DR\_pubs/DR\_a/pdf/web/AR40 25\_WEB\_ Final.pdf. Accessed June 17, 2020.

### RESEARCH

- 9. Mountjoy M, Sundgot Borgen J, Burke L, et al. IOC consensus state ment on relative energy deficiency in sport (RED S): 2018 update. *Br J Sports Med.* 2018;52:687 697.
- **10.** Drew M, Vlahovich N, Hughes D, et al. Prevalence of illness, poor mental health and sleep quality and low energy availability prior to the 2016 Summer Olympic Games. *Br J Sports Med.* 2018;52(1):47 53.
- Murphy NE, Carrigan CT, Karl JP, Pasiakos SM, Margolis LM. Threshold of energy deficit and lower body performance declines in military personnel: A meta regression. *Sports Med.* 2018;48(9):2169 2178.
- Forbes Ewan C. Australian defence force nutritional requirements in the 21st century (version 1) DSTO GD 0578. https://apps.dtic.mil/ dtic/tr/fulltext/u2/a502859.pdf. Accessed June 17, 2020.
- **13.** Collins RA, Baker B, Coyle DH, Rollo ME, Burrows TL. Dietary assessment methods in military and veteran populations: A scoping review. *Nutrients*. 2020;12(3):769.
- 14. Gaffney Stomberg E, Lutz L, Rood JC, et al. Calcium and vitamin D supplementation maintains parathyroid hormone and improves bone density during initial military training: A randomized, double blind, placebo controlled trial. *Bone*. 2014;68:46 56.
- **15.** Margolis L, Pasiakos S, Philip Karl J, et al. Differential effects of mil itary training on fat free mass and plasma amino acid adaptations in men and women. *Nutrients*. 2012;4(12):2035 2046.
- King N, Arsenault J, Mutter S, et al. Nutritional Intake of Female Sol diers during the US Army Basic Combat Training. Natick, MA: US Army Research Institute of Environmental Medicine; 1994. Report T94 17.
- Rose R, Baker C, Salter C, Wisnaskas W, Edwards J. Dietary Assessment of US Army Basic Trainees at Fort Jackson, South Carolina. Natick, MA: US Army Research Institute of Environmental Research; 1988. Report T6 89.
- Booth C, Coad R. Army recruit health and diet survey. https://apps. dtic.mil/sti/pdfs/ADA393294.pdf. Accessed June 17, 2020.
- **19.** Morrissey B. Interim Report on Food Intake and Energy Expenditure of Army Recruits. Scottsdale, Tasmania, Australia: Materials Research Laboratory; 1988.
- 20. Forbes Ewan C, Probert B, Booth C, Coad R. Assessment of Adequacy of Rationing during Infantry Initial Employment Training. Fishermans Bend, Vic: Defence Science and Technology Group (formerly Defence Science and Technology Organisation); 2008. DSTO TR 2181.
- Herzman Harari S, Constantini N, Mann G, Lencovsky Z, Stark A. Nutrition knowledge, attitudes, and behaviors of Israeli female combat recruits participating in a nutrition education program. *Mil Med.* 2013;178(5):517 522.
- 22. Israeli E, Merkel D, Constantini N, et al. Iron deficiency and the role of nutrition among female military recruits. *Med Sci Sports Exerc*. 2008;40(Suppl 1):S685 S690.
- US National Heart Lung and Blood Institute. Quality assessment tool for before after studies with no control group. https://www.nhlbi. nih.gov/health topics/study quality assessment tools. Accessed June 17, 2020.
- 24. Evidence Analaysis Manual. Chicago, IL: Academy of Nutrition and Dietetics; 2016.
- **25.** Williamson DA, Martin PD, Allen HR, et al. Changes in food intake and body weight associated with basic combat training. *Mil Med.* 2002;167(3):248 253.
- **26.** Burke L, Lundy B, Fahrenholtz I, Melin A. Pitfalls of conducting and interpreting estimates of energy availability in free living athletes. *Int J Sport Nutr Exerc Metab.* 2018;28(4):350–363.

- 27. Burke LM, Close GL, Lundy B, Mooses M, Morton JP, Tenforde AS. Relative energy deficiency in sport in male athletes: A commentary on its presentation among selected groups of male athletes. Int J Sport Nutr Exerc Metab. 2018;28(4):364 374.
- **28.** Heikura I, Uusitalo A, Stellingwerff T, Bergland D, Mero A, Burke L. Low energy availability is difficult to assess but outcomes have large impact on bone injury rates in elite distance athletes. *Int J Sport Nutr Exerc Metab.* 2018;28(4):403 411.
- 29. Burke L, Hawley J, Wong S, Jeukendrup A. Carbohydrates for training and competition. *J Sports Sci.* 2011;29(Suppl 1):S17 S27.
- **30.** Burke L, Kiens B, Ivy J. Carbohydrates and fat for training and re covery. *J Sports Sci.* 2004;22(1):15 30.
- **31.** Thomas D, Erdman K, Burke L. Position of the Academy of Nutrition and Dietetics, Dietitians of Canada, and the American College of Sports Medicine: Nutrition and athletic performance. *J Acad Nutr Diet.* 2016;116(3):501 528.
- 32. Schram B, Pope R, Orr R. Injuries in Australian Army full time and part time personnel undertaking basic training. *BMC Musculoskelet Disord*. 2019;20(1):6.
- **33.** Pasiakos S, Austin K, Lieberman H, Askew E. Efficacy and safety of protein supplements for US Armed Forces personnel: Consensus statement. *J Nutr.* 2013;143(11 Suppl):S1811 S1814.
- Church DD, Gwin JA, Wolfe RR, Pasiakos SM, Ferrando AA. Mitigation of muscle loss in stressed physiology: Military relevance. *Nutrients*. 2019;11(8):1703.
- Elliott Sale K, Tenforde A, Parziale A, Holtzman B, Ackerman K. Endocrine effects of relative energy deficiency in sport. Int J Sport Nutr Exerc Metab. 2018;28(4):335 349.
- de Oliveira E, Burini R, Jeukendrup A. Gastrointestinal complaints during exercise: Prevalence, etiology, and nutritional recommenda tions. Sports Med. 2014;44(Suppl 1):79 85.
- **37.** Jeukendrup A. Periodized nutrition for athletes. *Sports Med.* 2017;47(1):51 63.
- Tassone EC, Baker BA. Body weight and body composition changes during military training and deployment involving the use of combat rations: A systematic literature review. *Br J Nutr.* 2017;117(6):897 910.
- **39.** King N, Horner K, Hills A, et al. Exercise, appetite and weight man agement: Understanding the compensatory responses in eating behaviour and how they contribute to variability in exercise induced weight loss. *Br J Sports Med.* 2012;46(5):315 322.
- **40.** Long SJ, Hart K, Morgan LM. The ability of habitual exercise to in fluence appetite and food intake in response to high and low energy preloads in man. *Br J Nutr.* 2002;87(5):517–523.
- **41.** Imbeault P, Saint Pierre S, AlméRas N, Tremblay A. Acute effects of exercise on energy intake and feeding behaviour. *Br J Nutr.* 1997;77(4):511 521.
- **42.** Finlayson G, Bryant E, King N, Blundell J. Variability in the acute effect of exercise on appetite, energy intake, liking and wanting for food. *Appetite*. 2008;50(2–3):558.
- Department of the Army. Enlisted initial entry training policies and administration. TRADOC Regulation 350 6, https://adminpubs. tradoc.army.mil/regulations/TR350 6.pdf. Accessed June 17, 2020.
- Booth C. ADF educators guide to healthy eating (ADF EDGE). https:// www.dst.defence.gov.au/sites/default/files/publications/documents/ DSTO GD 0727.pdf. Accessed June 17, 2020.
- **45.** Bentley RNM, Mitchel N, Blackhouse SH. Sports nutrition in terventions: A systematic review of behavioural strategies used to promote dietary behaviour change in athletes. *Appetite*. 2020;150.

Defence FOI 386/22/23

Document 2 RESEARCH

#### **AUTHOR INFORMATION**

B. A. Baker is a military dietitian nutritionist and a doctoral degree candidate, Defence Science and Technology Group, Swinburne University, Scottsdale, Tasmania, Australia. M. B. Cooke is a senior lecturer and R. Belski is a dietetics course director, Swinburne University, Hawthorn, Victoria, Australia. J. E. Carins is a senior research fellow and discipline leader Defence Feeding Systems, Defence Science and Technology, Griffith University, Scottsdale, Tasmania, Australia.

Address correspondence to: Bradley A Baker, MDietSt, APD, AccSD, 74 George St, Scottsdale, TAS, Australia, 7260. E mail: bradley.baker2@dst. defence.gov.au

#### STATEMENT OF POTENTIAL CONFLICT OF INTEREST

No potential conflict of interest was reported by the authors.

#### FUNDING/SUPPORT

Under a Defence Staff PhD Agreement between Defence Science and Technology Group and Swinburne University, this research was supported in the form of in kind support from both parties and a Research Training Program Fees Offset Scholarship from Swinburne University.

The protocol was prospectively registered with the PROSPERO international prospective register of systematic reviews (CRD42019128328).

#### AUTHOR CONTRIBUTIONS

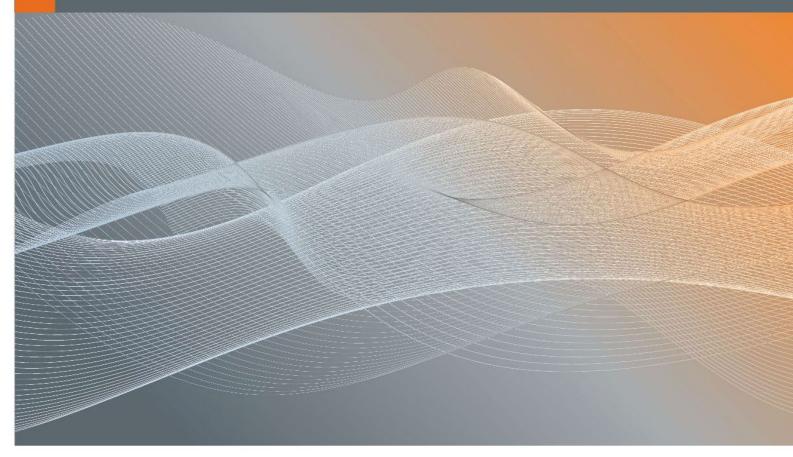
B. Baker, M. Cooke, and R. Belski contributed to study conception and design. B. Baker and M. Cooke contributed to data extraction. B. Baker wrote the original draft of the manuscript and M. Cooke and R. Belski critically reviewed it. All authors were involved in qualitatively synthesizing the results and critically reviewing and editing the manuscript.

Defence FOI 386/22/23 Document 3





# A Supplement Management Framework for Special Operations Command: Project Update



This report provides immediate documentation of results of work performed in Land Division under LD 1508. The report is written for the information of the Client. Secondary distribution within DST Group is subject to approval by the Chief of Division; other requests must be referred to the Client. This report may not be cited in the open literature without the express permission of the Chief of Division. Approved for release: 23<sup>rd</sup> March 2021.

**Defence Science and Technology Group** 

DSTG-CR-2021-0046

Defending Australia and its National Interests www.defence.gov.au



DSTG-CR-2021-0046

Author[s] s47E(d)

Produced by Land Division Defence Science and Technology Group Department of Defence PO Box 7931 Canberra BC ACT 2610

www.dst.defence.gov.au

Telephone: 1300 333 362

#### © Commonwealth of Australia 2021

This work is copyright. Apart from any use permitted under the *Copyright Act 1968* no part may be reproduced by any process without prior written permission from the Department of Defence.

### **Conditions of Release and Disposal**

This document is the property of the Australian Government; the information it contains is released for defence purposes only and must not be disseminated beyond the stated distribution and secondary release statement without prior approval of the Releasing Authority.

The document and the information it contains must be handled in accordance with security regulations, downgrading and delimitation is permitted only with the specific approval of the Releasing Authority.

This information may be subject to privately owned rights.

The officer in possession of this document is responsible for its safe custody.

DSTG-CR-2021-0046

This page is intentionally blank.

Defence FOI 386/22/23 Document 3

DSTG-CR-2021-0046

# CONTENTS

1.	BACKGROUND	1
	1.1.Purpose1.2.The AIS Sports Supplement Framework	
2.	FUTURE WORK	5
3.	CONCLUSION	6
4.	REFERENCES	7



# GLOSSARY

ADF	Australian Defence Force
AIS	Australian Institute of Sport
ADFSSO	ADF School of Special Operations
DHM	Defence Health Manual
DSTG	Defence Science and Technology Group
IOC	International Olympic Committee
JHC	Joint Health Command
NSOs	National Sporting Organisations
SOCOMD	Special Operations Command
WADA	World Anti-Doping Agency

Defence FOI 386/22/23 Document 3

### [OFFICIAL]

DSTG-CR-2021-0046

## 1. BACKGROUND

Special Operations Command (SOCOMD) members often undertake training and deployment involving strenuous physical and mental tasks that require optimal performance and recovery. In such situations, members often have extremely high energy and nutrient demands, whilst having limited opportunities to eat enough food to meet their increased requirements. Consequently, undesired deficits in energy and nutrient intakes are common (Margolis et. al., 2014). Such deficits can have an immediate negative impact on health, such as resistance to injury and infection, bone mineral density and strength, as well as on performance. Prolonged periods of energy and nutrient deficit, which are sometimes endured by SOCOMD members, lead to marked reductions in health and performance (Friedl et. al., 2000; Murphy et al., 2018). As such, poor nutritional intake may impede mission success (Barringer et al., 2018).

Accordingly, to ensure SOCOMD members maintain a performance edge over adversaries, the use of supplements should be considered, particularly when nutritional requirements cannot be met by everyday foods alone (Maughan et al., 2018). Supplements are defined as "a food, food component, nutrient, or non-food compound that is purposefully ingested in addition to the habitually-consumed diet with the aim of achieving a specific health and/or performance benefit" (Maughan et al., 2018, p. 439). Furthermore, supplements may assist members in meeting their nutritional requirements and enable a performance advantage through optimising their health, recovery and/or training adaptations in situations where optimal nutrient intakes cannot be met by diet alone (Maughan et al., 2018). In a consensus statement by the International Olympic Committee (IOC) several supplements are supported by "good to strong" evidence of enhancing aspects of exercise recovery, training adaptations or performance when used correctly (Maughan et al., 2018).

While several supplements are considered both safe and effective for supporting optimal health and performance, a number of supplements sold commercially in Australia have been found to contain substances that are banned by the World Anti-Doping Agency (WADA). In 2016, a report by LGC Group found that of 67 supplements tested, 13 (19%) were contaminated with one or more prohibited substances (LGC, 2018). In addition, a study by Cooper et al. (2018) found that of 112 commercially available supplements, six (5%) contained androgens.

A recent study investigating the prevalence of supplement use in the Australian Army found that approximately 87% of SOCOMD members self-report using at least one dietary supplement at least once a week (Baker et al., 2019). In this study, SOCOMD

DSTG-CR-2021-0046

members were significantly more likely to use any dietary supplement at least once per week than other Australian Army members (87% vs 78%), with the use of individual vitamins and minerals and multivitamin and minerals also significantly higher among SOCOMD members vs other Australian Army members. Adverse side effects resulting from the use of supplements were common, with ~16% of regular supplement users within the Australian Army experiencing one or more side effects, with the most common being heart palpitations (10% of users) (Baker et al., 2019). Self-administration of supplements will likely increase over time, as indicated by reported trends in use in military populations (Lieberman et al., 2010; Knapik et al., 2016; Baker et al., 2019). Increased levels of use, in the absence of expert guidance on safety and efficacy, may lead to an increased prevalence of adverse side effects and an increased risk of a positive drug test, given that many commercially available supplements contain WADA prohibited and border-controlled substances.

Currently, the Defence Health Manual (DHM) contains Defence policy on the use of supplements by Defence personnel (Defence, 2016), with a Defence Determination prohibiting the use of all WADA prohibited substances in the ADF (*Defence Act 1903 s. 93B(1)*, AUST). In addition, the DHM states that health practitioners "are not to prescribe or supply dietary supplements or complementary medicines to Defence members unless there is a clear clinical indication for doing so." Thus, where a Defence member has a diagnosed dietary/nutritional deficiency, Defence policy supports the prescription and supply of medical dietary supplements (e.g. iron, vitamin D and calcium).

In recent years, evidence related to the safety and efficacy of supplements has been translated into robust policies by organisations such as Australian Institute of Sport (AIS) as well as National Sporting Organisations (NSOs). From 2000-2013, the AIS implemented a Sport Supplement Program to guide the provision and use of supplements among Australian athletes. This is an ongoing program that comprises an educational component supported by a supplement classification system based on the efficacy and doping risk and the provision of supplements for use during training and competition (AIS, 2019). A 2016 study evaluated the impact of the AIS Sports Supplement Program on the supplement practices of members of the Australian national swimming team. One group of participants were part of the AIS training program and guided by the supplement program while the supplement practices of a comparison group comprising swimmers who had not been exposed to the AIS supplement program were also evaluated. The findings indicate that the swimmers guided by the supplement program were more likely to use supplements that were recommended by specialist trained health professionals, were classified as evidence-based and were supplied under the authority of the program. The researchers concluded that overall supplement use by participants in the supplement program was influenced by the provision of supplements

DSTG-CR-2021-0046

under the guidance of the program. The supplement program was also found to facilitate the cohesive and consistent delivery of evidence based information to the AIS swimmers by the health professionals involved. The provision of supplements under the authority of the program reduced the risk of the use of contaminated products, banned substances and the misuse of potentially dangerous products (Shaw et al., 2016). This outcome is particularly relevant to SOCOMD due to the reported use of supplements and the high prevalence of adverse side effects, such as combination products and purported prohormones that are not well supported for safety of use or efficacy in enhancing performance (Baker et al., 2019). Consequently, the implementation of similar policy in SOCOMD is likely to improve the supplement practices of SOCOMD members, conferring improved health and performance.

The management of supplement use in SOCOMD is necessary to reduce health risk and accidental ingestion of banned substance. Developing a robust and legal management system for supplement use will result in better outcomes for the SOCOMD community. To further explore the potential for policy change in regard to supplement use in the ADF it is necessary to engage with key stakeholders, in particular Joint Health Command (JHC) the owners of the DHM, and others experienced in the development, delivery and use of health related policy.

### 1.1. Purpose

Under Land 1508: Special Operations Capability Enhancement and Continuous Development, Defence Science Technology Group (DSTG) was tasked to investigate potential mechanisms to provide SOCOMD members with access to supplements in accordance with evidence-based, best practice protocols on their safe and effective use for promoting health and performance. This work presents an opportunity for SOCOMD to adopt a robust supplement management policy.

### 1.2. The AIS Sports Supplement Framework

The AIS Sports Supplement Framework provides NSOs and agencies with a foundation for developing their own policies on supplement use. This document is structured on the knowledge and resources developed during the implementation of the AIS Sports Supplement Program between 2000 and 2013. Since its development, several professional sporting bodies in Australia have adopted the framework to guide their supplement use policies (AIS, 2019).

The framework classifies formulated foods and beverages, performance supplements and medical supplements into four groups (A, B, C and D) based on scientific evidence

and other factors that determine whether a product is safe, legal and effective in improving athletic health and/or performance. Furthermore, the framework provides guidance regarding the use of formulated foods and beverages, performance supplements and medical supplements and on their monitoring by health professionals. In practice, athletes belonging to NSOs and other agencies that have adopted the framework are provided with access to suitably qualified health professionals (e.g. Accredited Sports Dietitians and Sports Physicians) to receive guidance on their supplement use, including the provision of supplements that are known to be safe and effective for enhancing their performance and/or recovery during training and competition, according to the classification system.

Based on the AIS Sports Supplement Framework, DSTG proposes that a SOCOMDspecific policy document be drafted in collaboration with key stakeholders. It is proposed that a SOCOMD-specific supplement framework would aim to meet the specific training, operational and military characteristics of Special Forces, whilst ensuring the legal, safe and efficacious use of supplements.

The intent is to draft, in collaboration with key stakeholders (e.g. JHC, Joint Logistics Command and the ADF School of Special Operations), a policy document that will ensure SOCOMD members and SOCOMD health and support staff (including contractors) understand their obligations regarding, and the benefits, risks and limitations of, supplement use.

Currently, the specific aims of the framework are to:

- 1. align with the Australian Institute of Sport (AIS) Sports Supplement Framework
- support research into certain supplements according to the group they belong to (i.e. A, B, C or D) supplement group
- 3. support SOCOMD member safety and well-being
- 4. support performance nutrition education programs for SOCOMD personnel with a focus on the development of the knowledge and lifestyle skills needed to achieve sound eating patterns and an understanding of the role of nutrition within a high-performance training and deployment environment.
- 5. promote correct and appropriate supplement usage protocols for maximising health, performance, and recovery while reducing the risks of adverse side effects.
- 6. provide a system for the provision of supplements to SOCOMD members.

Defence FOI 386/22/23 Document 3

## [OFFICIAL]

DSTG-CR-2021-0046

## 2. FUTURE WORK

To continue this work, DSTG, in consultation with the ADFSSO, will identify relevant stakeholders, noting the importance of involving ADF stakeholders at a range of levels. It is proposed that key stakeholders be invited to workshop the need and future direction, to enable the safe, legal and efficacious use of supplements in SOCOMD, with the aim of collaborating on devising a SOCOMD-specific supplement framework.

Developing a SOCOMD-specific supplement management framework that is fit for purpose and addresses the complex issues associated with the principles and practice of supplement use is a challenging process. Despite the challenges, supplement programs, in general, have resulted in lower supplement usage, in particular the use of "high risk" supplements. Additionally, the implementation of best practice protocols for supplement use is supported by such management programs (Shaw et al., 2016). For this reason, investigation of the legal and logistic elements of a supplement framework to enable SOCOMD members to access supplements, is required. Thus, to ensure the successful implementation and use of a SOCOMD supplement framework, it is necessary to engage with key stakeholders who are familiar with the health, legal and ethical implications associated with the use and management of supplements in the ADF.

Additionally, DSTG, in consultation with subject matter experts from academia, will write a discussion paper on key considerations relating to the implementation and use of a supplement management framework in an ADF setting. Specifically, this paper will identify the practical and philosophical barriers and facilitators for the implementation and use of a SOCOMD supplement framework. The final product will provide recommendations for the delivery, endorsement, implementation and use of a SOCOMDspecific supplement framework.

# 3. CONCLUSION

This reports details the initial exploration of the development and implementation of a SOCOMD-specific supplement framework which would enable the supply of dietary supplements with a strong evidence base for enhancing human performance. Implementation of such a framework may provide SOCOMD members with a performance edge over adversaries. A policy that is informed by the AIS Sports Supplement Framework should be explored. In practice, where the safe achievement of a health or performance benefit is indicated, such a supplement policy may enable the supply of supplements to SOCOMD members in accordance with best-practice protocols. The framework would also reduce the likelihood of unsafe supplement use and instances of adverse effects.

It is recommended that further investigation into the development and implementation of a SOCOMD-specific supplement framework continue, in particular, facilitated engagement with key stakeholders to further evaluate the merit of this approach in the ADF environment.

Defence FOI 386/22/23 Document 3

## [OFFICIAL]

DSTG-CR-2021-0046

# 4. **REFERENCES**

Australian Institute of Sport (AIS). (2019). AIS Sports Supplement Framework. Available from: <u>https://ais.gov.au/ data/assets/pdf file/0004/698557/AIS-Sports-Supplement-Framework-2019.pdf</u>

Baker, B., Probert, B., Pomeroy, D., Carins, J., & Tooley, K. (2019). Prevalence and Predictors of Dietary and Nutritional Supplement Use in the Australian Army: A Cross-Sectional Survey. Nutrients, 11, 1462.

s33(a)(i)

Cooper, E.R., McGrath, K.C.Y., Li, X.H., & Heather, A.K. (2018). Androgen bioassay for the detection of non-labelled androgenic compounds in nutritional supplements. International Journal of Sport Nutrition and Exercise metabolism. 28(10).

Defence Act 1903 s. 93B(1). (AUST). https://www.legislation.gov.au/Details/F2019L00349

Department of Defence (Defence). (2016). Defence Health Manual, Chapter 2: Use of dietary supplements and complementary medicines by Australian Defence Force personnel. Australian Government. Volume 2, Part 15.

Friedl, K., Moore, R.J., Hoyt, R.W, & Marchitelli, L.J. (2000). Endocrine markers of semistarvation in healthy lean men in a multi-stressor environment. Journal of Applied Physiology, 88(5), 1820. DOI: <u>10.1152/jappl.2000.88.5.1820</u>

s33(a)(i)

LGC. (2018). Australian Supplement Survey 2016. Available online:

https://www.informed-

sport.com/sites/default/files/LGC\_Australian%20Supplement%20Survey\_0.pdf (accessed on 18 August 2020).

s33(a)(i)

## [OFFICIAL]

## [OFFICIAL]

Margolis, L.M., Crombie A.P., McClung H.L., McGraw, S.M, Rood, J.C., Montain, S.J., & Young, A.J. (2014). Energy requirements of US Army Special Operation Forces during military training. Nutrients, 6(5), 1945.

Maughan, R.J., Burke, L.M., Dvorak, J., Larson-Meyer, D.E., Peeling, P., Phillips, S.M., Rawson, E.S., Walsh, N.P., Garthe, I., Geyer, H., et al. (2018). IOC consensus statement: Dietary supplements and the high-performance athlete. British Journal of Sports Medicine, 52, 439.

Murphy, N. E., Carrigan, C. T., Karl, J. P., Pasiakos, S. M., & Margolis, L. M. (2018). Threshold of energy deficit and lower-body performance declines in military personnel: a meta-regression. Sports Medicine, 48(9), 2169.

Shaw, G., Slater, G., & Burke, L. M. (2016). Supplement use of elite Australian swimmers. International Journal of Sport Nutrition and Exercise metabolism, 26(3), 249.

## [OFFICIAL]

DSTG-CR-2021-0046

# **DISTRIBUTION LIST**

A Supplement Management Framework for Special Operations Command: Project Update

s47E(d)

#### **Task Sponsor**

s47E(d)

#### S&T Program

s47E(d)



## [OFFICIAL]

DSTG-CR-2021-0046

Defence FOI 386/22/23 Document 3

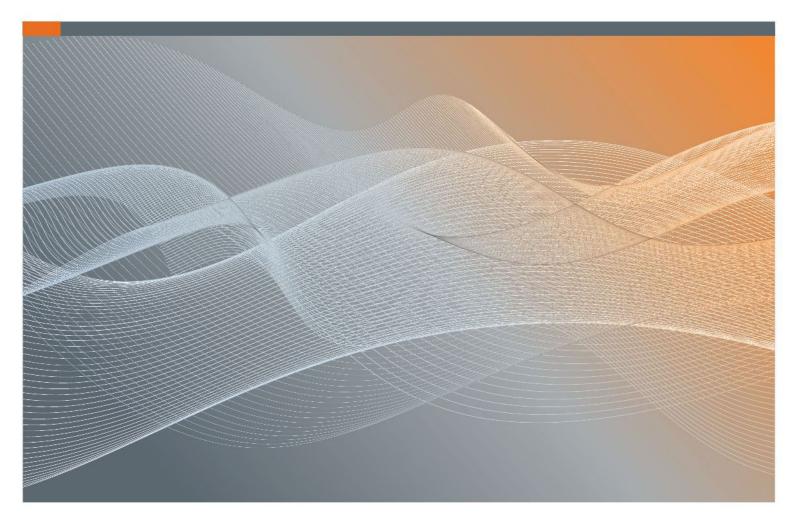
## [OFFICIAL]

DSTG-CR-2021-0046

DEFENCE SCIENCE AND TECHNOLOGY GROUP			IMM/CAVEAT (OF DOCUMENT)		
DOCUMENT CONTROL DATA			[Any IMM or caveat for the report]		
TITLE		SECURITY CLASSIFICATION			
Supplement Management Framework for Special		Document (O)			
Operations Command: Project Update		Title (O)			
		(		(0)	
AUTHOR(S)		PRODUCED BY			
s47E(d)		Defence Science and Technology Group			
		Department of Defence			
		PO Box 7931 Canberra BC ACT 2610			
		Canberra DC			
DSTG NUMBER	REPORT TYPE			DOCUMENT DATE	
DSTG-CR-2021-0046	Client Report			Feb, 2021	
TASK NUMBER	TASK SPONSOR			RESEARCH DIVISION	
s33(a)(i)	SOHQ			Land	
MAJOR SCIENCE AND TECHNOLOG	SCIENCE AND TECHNOLOGY CAPABILITY				
Land Human Systems		Food & Nutrition			
SECONDARY RELEASE STATEMENT OF THIS DOCUMENT					
This report provides immediate documentation of results of work performed in Land Division under L1508. The					
report is written for the information of the SOHQ. Secondary distribution within DST Group is subject to approval					
by Chief of Division: other requests must be referred to SOHQ. This report may not be cited in the open literature					
without the express permission of the Chief of Division.					
ANNOUNCEABLE					
The metadata of this document may be announced to the Defence community.					
CITABLE IN OTHER DOCUMENTS					
No					
RESEARCH LIBRARY THESAURUS					
Special forces, supplements, management					



# The Utility and Safety of Caffeine as an Ergogenic Aid in Australian Defence Force Combat Ration Packs



Defence Science and Technology Group DSTG-GD-1113

Defending Australia and its National Interests www.defence.gov.au



Authors s47E(d)

Produced by Land Division Defence Science and Technology Group Department of Defence PO Box 7931 Canberra BC ACT 2610

#### www.dst.defence.gov.au

Telephone: 1300 333 362

© Commonwealth of Australia 2020 This work is copyright. Apart from any use permitted under the *Copyright Act 1968* no part may be reproduced by any process without prior written permission from the Department of Defence.

#### **Conditions of Release and Disposal**

This document is the property of the Australian Government; the information it contains is released for defence purposes only and must not be disseminated beyond the stated distribution and secondary release statement without prior approval of the Releasing Authority.

The document and the information it contains must be handled in accordance with security regulations, downgrading and delimitation is permitted only with the specific approval of the Releasing Authority.

This information may be subject to privately owned rights.

The officer in possession of this document is responsible for its safe custody.

# EXECUTIVE SUMMARY

Caffeine is a naturally occurring stimulant well known for its effectiveness as an ergogenic aid and fatigue countermeasure. To inform a Safety Case Report on caffeine provision in combat ration packs (CRP), a literature review was conducted to understand its utility and safety as an ergogenic aid in military scenarios. The literature reviewed included research articles as well as guidelines by peak military health and performance bodies relating to caffeine use. The findings revealed that when peak physical performance is required, combatants should use caffeine ~1 hour prior to physical activity. Effective doses include 1–3 mg/kg (i.e. ~80–240 mg of caffeine for an 80 kg combatant) both before and during exercise, or a single 3–6 mg/kg dose (i.e. 240–480 mg for an 80 kg combatant) about 60 minutes before exercise commences.

The utility of caffeine as a fatigue countermeasure during military training and deployment involving sleep deprivation has been studied extensively. Expert panels such as those of s33(a)(iii)

have established clear recommendations on caffeine use during military operations involving sleep deprivation. Repeat doses of 200 mg doses every 3–4 hours, up to a total of 600 mg/day, are recommended by the <sup>\$33(a)(iii)</sup> and the <sup>\$33(a)(iii)</sup> In 2001, the <sup>\$33(a)(iii)</sup>

for use during short duration missions involving sleep deprivation. This guidance underpins the design of in-service special purpose<sup>s33(a)(iii)</sup> combat rations.

The available evidence was reviewed to understand what side effects may be experienced by CRP users (i.e. healthy adolescents and adults) at differing levels of caffeine intake. Possible side effects of caffeine for healthy, non-pregnant adults are:

- disrupted sleep (when ~100 mg is consumed within 6 hours of sleep)
- impaired fine motor control (with single doses of > 300 mg)
- arrhythmias i.e. an irregular, rapid or slow heart beat (currently available evidence indicates that intakes of ~400–450 mg/day are well tolerated without adverse cardiovascular side effects)
- increased risk of fracture in women (with daily intakes of > 400 mg)
- anxiety (with daily intake of > 700 mg)
- fatalities (resulting from single doses of 3,000–10,000 mg).

For pregnant women, there is an increased risk of miscarriage and low birth weight (with daily intakes of > 200–300 mg), and non-habitual caffeine consumers and individuals who are sensitive to caffeine are more likely to suffer from side effects.

Caffeine is widely consumed by Australian civilians and combatants alike. Given its wideranging benefits to military-relevant measures of physical and cognitive performance, general purpose CRP should provide the maximum safe level of caffeine to give users the maximum possible competitive advantage on the battlefield. Considering available evidence on the safe level of daily caffeine intake for healthy, non-pregnant adults (of 400 mg/day, with single doses not exceeding 200 mg) and adolescents and pregnant women (of up to 300 mg/day), we recommend that the caffeine available to combatants delivered via the current general purpose CRP be limited to 300–400 mg per pack, with future forms of supplementation (e.g. an arduous duties supplement) providing up to a total of 600 mg/day (refer to discussion in the final paragraph).

Current general purpose CRP configurations contain ~280 mg—a level close to the lower range of our recommended safe level. However, considering the doses required for ergogenic benefits, current CRP component formulations, as well as current CRP configurations, may be suboptimal for promoting competitive advantage during operations. Thus, it is recommended that a number of alternative CRP menus with improved caffeine delivery be designed and introduced. For example, such menus should target the inclusion of components that can be deliberately consumed at the right time, such as when on-the-move, while providing doses that promote performance benefits (i.e. ~200 mg). As identified in the review presented herein, single doses greater than 200 to 300 mg may result in side effects in some individuals (e.g. individuals who are not habitual caffeine consumers, individuals who are sensitive to caffeine, as well as those with pre-existing conditions such as anxiety). Consequently, CRP components should not contain greater than 100-200 mg/serve (in accordance with the guidance specific to each product type by the s33(a)(iii) Studies are required to evaluate the caffeine intakes of users of such CRP, and to establish strategies that promote caffeine intakes in accordance with the levels needed for ergogenic benefits (e.g. enhanced CRP configurations, educative labelling and behaviour change strategies).

Based on a considerable body of literature and the recommendations by the  $s^{33(a)(iii)}$  the TTCP and others, doses of up to 200 mg every 3–4 hours (up to a total of 600 mg/day) are well-tolerated by healthy adults when used in short bouts (up to 72 hours), with a very low likelihood of adverse side effects. Aligning with guidance from the  $s^{33(a)(iii)}$  and others, future arduous duties supplements (i.e. a module, supplementary to general purpose CRPs, provided as necessitated by the operational situation) and special purpose CRPs would be well placed to make available additional doses of caffeine, up to

a total of 600 mg/day. Provided users of such forms of combat feeding are deemed medically fit for deployment, and thus do not have any pre-existing health conditions which may be exacerbated by high daily caffeine intakes, special purpose CRP and arduous duties supplements for use in short bouts (i.e. up to 72 hours) should include doses of caffeine commensurate with those required to optimally mitigate fatigue during sleep deprivation. Similar to the s33(a)(iii)

and others, such a CRP should include 4 to 5 caffeinated gum or mints per CRP, containing 100 mg per strip or mint, in addition to 1–2 other caffeine containing components (e.g. a caffeinated bar or gel), to provide up to 600 mg of caffeine. This page is intentionally blank.

# CONTENTS

1.	INTRO	DDUCTION1
2.	BACK 2.1. 2.2.	GROUND
	2.3. 2.4.	3 Prohibited Substances in the ADF
3.	CAFE	EINE AND PERFORMANCE
	3.1. 3.2. 3.3. 3.4.	Physical Performance       5         Cognitive Function in the Rested State       7         Caffeine as a Fatigue Countermeasure during Sleep       7         Deprivation       7         Caffeine Sources and Absorption       8
	-	- -
<b>4</b> . <b>5</b> .	POTE 4.1. 4.2. 4.3. 4.4. 4.5. 4.5. 4.6. 4.7. 4.8. 4.9. 4.10. s33(a)(ii	NTIAL SIDE EFFECTS OF CAFFEINE9Fatal Doses9Cardiovascular Effects10Anxiety and Mental Health11Risks to Pregnant Women and the Foetus: Miscarriage and12Low Birth Weight12Caffeine Withdrawal Symptoms in Habitual Users14Sleep Latency and Quality15Risks to Adolescents, Small-statured Individuals, Caffeine-sensitive Individuals and Non-habitual Caffeine Users16Fine Motor Skill16Bone Health and Fracture Risk17Hydration17
6.	CAFF	EINE CONTENT IN CURRENT AUSTRALIAN CRP
7.		MARY AND IMPLICATIONS FOR AUSTRALIAN GENERAL OSE AND SPECIAL PURPOSE CRP25
8.		IOWLEDGEMENTS
9.	REFE	RENCES

# GLOSSARY

3RAR	3 <sup>rd</sup> Battalion Royal Australian Regiment			
ADF	Australian Defence Force			
CR1M	Combat Ration One Man			
CR5M	Combat Ration Five Man			
CR	combat rations			
CRP	combat ration packs			
DSTG	Defence Science and Technology Group			
EFSA	European Food Safety Authority			
FSANZ	Food Standards Australia New Zealand			
s33(a)(iii)				
kg	kilogram			
MEC	medical employment classification			
MRE	Meal, Ready to Eat			
mg	milligram			
MORE	Modular Operational Ration Enhancement			
n	number of participants			
NATA	National Association of Testing Authorities			
NMI	National Measurement Institute			
PR1M	Patrol Ration One Man			
s33(a)(iii)				
WADA	World Anti-Doping Agency			

## 1. INTRODUCTION

Caffeine is a naturally occurring stimulant well known for its effectiveness as an ergogenic aid and fatigue countermeasure (Maughan et al., 2018). It is naturally found in coffee, tea and chocolate, as well as being an additive to beverages (e.g. energy drinks, cola drinks) and some sports supplements (e.g. pre-workout supplements). It is one of the most widely consumed drugs in the world. In Australia, adults consume on average 150 to 170 mg of caffeine per day (ABS, 2015). In 2018, a Defence Science and Technology Group (DSTG) survey of ~300 Combat Arms soldiers found 92% of respondents consumed caffeinated beverages (coffee, tea, cola, energy drinks) and had an average daily caffeine intake of 170 mg/day, with those who consumed caffeinated beverages everyday (47% of respondents) consuming 234 mg/day (Baker & Probert, 2018). Although, as the authors acknowledged, the actual daily intakes of Combat Arms soldiers who are habitual caffeine users may be considerably higher, due to the frequent consumption of highly-caffeinated supplements (such as pre-workout supplements) reported by the soldiers in the same questionnaire, which were not included in the caffeine intake analyses.

Combat ration packs (CRP) are a Class 1 mission-critical supply item used in training and operational environments, and are designed to provide combatants with enough nutritional sustenance to satisfy the daily requirements associated with their intended use (CRUR, 2014). Consequently, they should provide caffeine in optimal levels for their intended users, in foods and beverages that are their preferred options—to satisfy their habitual caffeine usage patterns to avoid the deleterious effects of caffeine withdrawals. Additionally, as caffeine is an effective ergogenic aid and fatigue countermeasure, where safe and effective to do so, combatants should exploit its potential. However, a recent study of Australian combatants' dietary intakes during a 9-day field training exercise found that their caffeine intakes are likely to be considerably less than their habitual intakes. From the total of ~280 mg of caffeine that was contained in the issued CRPs, their average caffeine intakes were 98 mg/day, ranging between an average of 77 mg/day and 124 mg/day across the 9 days (McLaughlin et al, 2018; Baker & Probert, 2018). However, as use may cause side effects, it is important to understand safe levels of use to inform the levels that should be present in CRPs.

The aims of this report are to determine an effective and safe level of caffeine to include in the combat ration feeding system, comprising CRP and supplementary feeding elements, for use by Australian Defence Force (ADF) combatants. To understand its effectiveness and utility, research, guidelines and policies relating to doses required to improve military performance and/or mitigate fatigue were reviewed. Subsequently, the safety of effective doses was reviewed. The implications for the level and distribution of caffeine in CRP are discussed, including the safe total level of caffeine for CRP and the optimal dosing and distribution of caffeine within individual CRP items to achieve ergogenic benefits.

# 2. BACKGROUND

### 2.1. CRP Types and Users

There are currently three types of CRP, Combat Ration One Man (CR1M), Patrol Ration One Man (PR1M) and Combat Ration Five Man (CR5M). The demographics of combatants who subsist on CRP include both adolescents (17–18 years inclusive) and adults (19 years and over) of both sexes (Forbes-Ewan, 2009). Thus, safety issues relating to these demographics have been considered when assessing the safety of caffeine for use in CRP.

## 2.2. World Anti-Doping Agency (WADA) Position on Caffeine Use

The use of caffeine is socially accepted, including for use in competitive sport. It was removed from the WADA list of prohibited substances in 2004 and is classed as belonging to Group A of the Australian Institute of Sport Supplements Evidence Map. Group A supplements are those that are supported by good to strong evidence for being safe and effective for enhancing performance in specific situations using evidence-based protocols (AIS, 2015).

#### 2.3. Prohibited Substances in the ADF

The Defence Determination (Prohibited Substances) 2019 describes the substances that are currently prohibited in the ADF, including all WADA prohibited substances. Thus, caffeine is permitted for use in the ADF (Australian Government, 2019).

## 2.4. Food Standards Australia New Zealand (FSANZ)

The level of caffeine that is permitted in food is regulated by the Food Standards Code (the Code). Specifically, limits apply to the concentration of caffeine that may be present in foods generally and in formulated caffeinated beverages (e.g. cola-type soft drinks, energy drinks and other non-alcoholic drinks with added caffeine).

FSANZ Standard 2.6.4 states that for formulated caffeinated beverages that contain added caffeine (e.g. cola-type soft drinks and energy drinks), they must contain no less than 145 mg/L and no more than 320 mg/L of caffeine. It is to be labelled as a caffeine product, include average quantities of caffeine per serving size and per 100 mL, and if formulated with other vitamins must also contain a 'one day quantity' (amount you are able to safely consume within a day) (FSANZ, 2016b). For items that have naturally

occurring caffeine (tea, coffee, chocolate) no warnings are required on the labelling, however, any formulated caffeinated beverage must state the following warning:

Contains Caffeine. The product is not suitable for young children, pregnant or lactating women or those sensitive to caffeine.

In 2019, FSANZ made recommendations to the Australian Government to regulate the sale of pure and highly concentrated caffeine powders and food products after the death of a young Australian from a caffeine overdose (FSANZ, 2019). The recommendations were developed due to the danger surrounding the consumption of highly concentrated and pure caffeine products. It is difficult to measure a safe dose of caffeine (e.g. 200 mg) from pure caffeine powder, unless in a laboratory, therefore the use of highly concentrated or pure caffeine products can easily result in accidental overdose. A potentially fatal dose of one teaspoon of pure caffeine powder may contain 4,000 mg of caffeine and is equivalent to ~25–50 cups of coffee (FSANZ, 2019).

The recommendations were accepted by the Australian Government and Standard 1.1.1 of the Code was amended, effective from 12 December 2019, to prohibit the sale of a food with a caffeine concentration of 5% or more for solid or semi-solid foods, and 1% or more for liquid foods (Colbeck, 2019; FSANZ, 2016a). The amendment did not affect the provisions for formulated caffeinated beverages. One of the recommendations was for continuing targeted research on caffeine consumption in specific vulnerable population groups (FSANZ, 2019), which may further inform the use of caffeine in CRP.

# 3. CAFFEINE AND PERFORMANCE

There are many physical and cognitive performance benefits of caffeine that are relevant to combatants.

#### 3.1. Physical Performance

A vast number of studies have investigated the effects of caffeine on physical performance in athletes (Burke, 2008, Maughan et al, 2018; Baker et al, 2014; Goldstein et al, 2010; Peeling et al, 2018; Spriet, 2014; Zhang et al, 2015). However, there is a paucity of studies that have investigated the effects of caffeine on measures of physical performance in combatants during field training or deployment (McClung et al, 2011, McLellan et al, 2016). Nevertheless, in leveraging off research conducted in athletes, when determining how combatants should use caffeine to enhance their physical performance, consideration must be given to the type of physical activity (e.g. marching with or without load carriage, combat, fire-and movement, rapid advance and/or withdrawal), intensity (e.g. light, moderate, heavy) and duration for caffeine use to be most effective. The best practice use of caffeine for different exercise scenarios is discussed below.

The ergogenic response to caffeine during prolonged activities (i.e. endurance exercise) is affected by dose, timing and the individual's history of caffeine use and the source of caffeine. It is recommended that caffeine be taken one hour prior to the start of physical activity to reap the most benefits. This provides sufficient time for absorption, with peak caffeine concentration in the blood being reached from 0.5–3 hours after ingestion. Dose response studies have typically reported optimal performance benefits with moderate dosing of 3–7 mg/kg body weight (corresponding to at least 240 mg for an individual with a body weight of 80 kg). For prolonged activities, benefits include increased time to reach exhaustion levels or reduced perception of pain (McLellan et al, 2016; Southward et al, 2018).

To improve endurance capacity and/or performance, a dose of 3–6 mg/kg of body weight (e.g. 240–480 mg for an 80 kg combatant) consumed 60 minutes prior to the activity, or lower dose (i.e. < 3 mg/kg of body weight) both before and during the activity is effective for most individuals. Benefits that can be expected include increased time to fatigue (i.e. exercise capacity) and improved time-trial performance in activities ranging from 5–150 minutes across numerous exercise modalities (e.g. running, cycling, rowing and others) (Maughan et al, 2018; McLellan et al, 2016; Southward et al, 2018).

During exercise lasting 60 minutes or more it has been shown that beneficial effects can be achieved from small to moderate caffeine intakes (1–3 mg/kg of body weight or ~80–240 mg of caffeine for an individual with a body weight of 80 kg), when caffeine is taken at a variety of times (before and/or throughout exercise, or towards the end of exercise or when becoming fatigued) and consumed with carbohydrate (Spriet, 2014).

The effect caffeine has on strength and power activities and brief sprints (10–20 seconds) is unclear (Burke, 2008). The literature is inconsistent and it is unclear whether discrepancies could be due to differences in study design or individual differences among subjects. However, a recent umbrella review of meta-analyses by Grgic and colleagues found that caffeine supplementation may acutely enhance muscular endurance, maximal strength and power in resistance exercise, although further research is required (Goldstein et. al, 2010; Grgic et al, 2018). Furthermore, evidence suggests that caffeine ingestion may have an ergogenic effect across all types of muscle action (Grgic et al, 2018).

However, these findings relate to short term or single exercise bouts and therefore are less applicable to most operational exercises where these types of activities tend to be performed repeatedly over a period. Therefore, combatants partaking in activities involving a mix of power activities and sprints during a prolonged task will likely benefit from supplementation with caffeine in dosing mentioned above (3–6 mg of caffeine/kg of body weight).

There is no evidence to support performance benefits increasing with increases in caffeine doses (Maughan et al, 2018). A larger caffeine dose (> 9 mg/kg) does not appear to increase the performance benefits but does increase the likelihood of negative effects (Peeling et al, 2018, Maughan et al, 2018). It is advisable that combatants should use lower caffeine doses to both maximise performance potential whilst minimising possible side effects. Possible side effects of high levels of caffeine intake will be discussed in <u>Section 4</u>.

In summary, where practicable, to obtain maximum benefits, combatants should use caffeine ~1 hour prior to the start of all modes of physical activity when peak performance is required. Effective doses include 1–3 mg/kg (i.e. ~80–240 mg of caffeine for an 80 kg combatant) both before and during physical activity, or a single 3–6 mg/kg dose (i.e. 240–480 mg for an 80 kg combatant) about 60 minutes before physical activity commences. Lastly, the authors suggest that further educative and behaviour change strategies should be devised for combatants and commanders, and evaluated for enhancing the utilisation of caffeine in accordance with best practice protocols. CRP education and labelling options for caffeine-containing products should be investigated to

enhance users' awareness of caffeine and its safe and appropriate use for enhancing performance.

### 3.2. Cognitive Function in the Rested State

Several measures of cognitive function (e.g. reaction time, alertness, vigilance and attention) can be improved in rested individuals, in particular those experiencing suboptimal arousal, with low (~40 mg or 0.5 mg/kg) to moderate (~300 mg or 4 mg/kg) caffeine doses (McLellan et al, 2016). The optimal dose appears to be up to 300 mg (or 4 mg/kg) (McLellan et al, 2016), with negligible cognitive performance gains resulting from doses greater than 300 mg, and doses beyond this level more likely to produce negative side effects (refer to Section 4).

In doses of 20–200 mg, cognitive attributes such as alertness, self-perceived energy levels, motivation and concentration are improved, and reaction times on visual pattern recognition are reduced when low to moderate doses (i.e. 60–400 mg/day) of caffeine are consumed (Smith et al, 2000).

### 3.3. Caffeine as a Fatigue Countermeasure during Sleep Deprivation

The utility of caffeine as a fatigue countermeasure during sleep deprivation has been studied extensively, including in military scenarios (IOM, 2001; Crawford et al, 2017; Tharion et al, 1997; Kamimori et al, 2015; McLellan et al, 2007; Paech et al, 2015; Grant et al, 2018; Aidman et al, under review; Aidman et al, 2018; Johnson et al, 2016). Based on the studies conducted, <sup>\$33(a)(iii)</sup>

have established clear recommendations for caffeine use in military operations involving sleep deprivation that have been adopted by the <sup>s33</sup>(a)(iii)

The benefits of caffeine on aspects of cognitive function that are integral to safety during military operations involving sleep deprivation (e.g. continuous operations for 50 hours) include improved visual and auditory vigilance, alertness, logical reasoning, live fire marksmanship, as well as improving or maintaining reaction time and reducing driving errors (IOM, 2001; Baranski et al, 2003; Kamimori et al, 2015; Tharion et al, 1997; Paech et al, 2015; McLellan et al, 2007; Aidman et al, under review; Aidman et al, 2018; Johnson et al, 2016; Grant et al, 2018; Killgore & Kamimori, 2020). These effects can be seen from caffeine doses of 200 mg, with research showing no significant differences in performance outcomes when doses of 200 mg vs 300 mg are used (Tharion et al, 1997), indicating doses of 200 mg elicit maximum benefits (Tharion et al, 1997). Repeat doses

of 200 mg doses every 3–4 hours, up to a total of 600 mg/day, are recommended by the s33(a)(iii)

Kamimori et al, 2015; McLellan et al, 2007; Aidman et al, under review; Aidman et al, 2018; Johnson et al, 2016; Paech et al, 2015; Grant et al, 2018; Killgore & Kamimori, 2020). This is due to the half-life of caffeine being between 3 and 7 hours, after which time benefits are no longer observed and repeat doses are required. Such dosage regimens have been deemed safe for healthy adults when used in very short bouts (e.g. up to 72 hours), with very few adverse side effects reported in the studies conducted (IOM, 2001; Baranski et al, 2003).

#### 3.4. Caffeine Sources and Absorption

Caffeine can be ingested from a variety of sources (e.g. beverages, foods, chewing gum and tablets), as shown in Table 1 in <u>Section 5</u>. Caffeine from foods, beverages and tablets is absorbed in the gut whereas from caffeinated chewing gum, it is absorbed through the lining of the mouth, and thereby enters the bloodstream significantly faster than when ingested from other sources (e.g. beverages, foods and tablets) (Kamimori et al, 2002; Wickham et al, 2018). The onset of action for caffeinated gum is 5–10 minutes, and 30–45 minutes for caffeinated beverages (e.g. coffee and cola) (Kamimori et al, 2002; IOM, 2001). A study by Kamimori et al (2002) found that, on average, 85% of the caffeine dose provided in caffeinated gum is absorbed after 5 minutes of chewing. For combatants who have limited opportunities to eat and drink, and who would benefit from rapid performance enhancements and reversal of fatigue during missions, caffeinated gum presents obvious advantages (Kamimori et al, 2002). One such advantage is that it enables combatants to make rapid decisions on an appropriate level of caffeine to ingest to stay alert. \$33(a)(iii)

, and that combatants using it are provided with clear guidance on its safe and effective use.

## 4. POTENTIAL SIDE EFFECTS OF CAFFEINE

Although caffeine can elicit benefits to both physical and cognitive performance, some individuals may experience side effects at certain doses. A vast number of literature reviews and meta-analyses have examined the safety of caffeine. The available evidence indicates that for healthy non-pregnant adults aged 19 years and over, daily intakes of 400 mg are safe and are not associated with any adverse side effects such as toxicity, cardiovascular side effects (e.g. arrhythmias or hypertension), changes in behaviour or an increased incidence of cancer (EFSA, 2015; Temple et al, 2017; Nawrot et al, 2003; Grosso et al, 2017; Poole et al, 2017).

The available evidence was reviewed to understand what side effects may be experienced by CRP users (i.e. healthy adolescents and adults) at differing levels of caffeine intake. Possible side effects of caffeine for healthy, non-pregnant adults are: disrupted sleep (when ~100 mg is consumed within 6 hours of sleep); impaired fine motor control (with doses of > 300 mg); arrhythmias i.e. an irregular, rapid or slow heart beat (currently available evidence indicates that intakes of ~400-450 mg/day are well tolerated without adverse cardiovascular side effects); an increased risk of fracture in women (with daily intakes of > 400 mg), and; anxiety (with daily intake of > 700 mg), with fatalities resulting from single doses of 3,000–10,000 mg. For pregnant women, there is an increased risk of miscarriage and low birth weight (with daily intakes of > 200–300 mg). Meta-analyses have found that other harmful effects that have been reported in the literature to date are largely nullified by adequate adjustment for confounding factors, such as smoking (Grosso et al, 2017; Poole et al, 2017). Interindividual differences exist in responses to caffeine, with some more susceptible to side effects, and habitual users less susceptible to side effects than non-habitual users at equivalent doses (Temple et al, 2017; Nawrot et al, 2003). In addition to dose-dependent side effects, withdrawal symptoms (e.g. headaches, irritability, fatigue) are often observed in habitual users following abstinence from caffeine for as little as 12 hours.

#### 4.1. Fatal Doses

Death from caffeine ingestion is rare, occurring only as a result of intakes at very high levels compared to the levels found in everyday foods and beverages. Death has been shown to occur in rats at intakes of more than 100 mg/kg of body weight/day (Turnbull et al, 2015; Boyd et al, 1965), which corresponds to more than 6,000–10,000 mg/kg/day) in humans (Cappelletti et al, 2015). In a report investigating the safety of pure caffeine, FSANZ states that while the lethal dose of caffeine is considered to be 6,000–10,000 mg, the death of a young Australian occurred after a single 3,000 mg dose resulting from

ingestion of pure caffeine powder (FSANZ, 2019). The likelihood of unintentionally ingesting this level of caffeine from everyday foods and beverages providing ~100–200 mg of caffeine per serve is extremely remote (e.g. an individual would need to consume the equivalent of 70 cups of instant coffee, or 60 energy gels each providing 100 mg of caffeine).

Highly-caffeinated products (e.g. caffeinated supplements) and pure caffeine powder are dangerous and can be lethal if ingested in uncontrolled doses. The Safety Data Sheet for pure caffeine mentions that diarrhoea, vomiting, agitation and headaches occur after absorption of toxic quantities (Sigma-Aldrich, 2019). FSANZ (2019) has stated that 1/16th of a teaspoon of pure caffeine is equivalent to a 200 mg dose, therefore ingesting pure caffeine as an uncontrolled dose can be lethal.

Death is an uncommon occurrence from caffeine consumption, however it can happen, with most of the reported cases being adolescents consuming energy products or diet pills while having an undiagnosed underlying heart condition (Temple et al, 2017). A review undertaken by Cappelletti et al (2015) determined that in the majority of cases where caffeine was the cause of death, it was consumed as a dietary supplement or taken with other drugs or alcohol. For example, in one case, caffeine and nicotine reacted together in the body causing the rapid onset of toxicosis resulting in death. More commonly, deaths occurred from voluntary ingestion of tablets containing high concentrations of pure caffeine resulting in accidental death or suicide (Cappelletti et al, 2015).

The above information on the risk of death from the ingestion of pure caffeine has been included in the present report for completeness and to provide an overview of fatal doses. Whilst there is little likelihood that one can consume a fatal dose of caffeine that is contained in food and beverages, products containing highly concentrated or pure caffeine can be dangerous. FSANZ has recently acted to limit the allowable concentration of caffeine in foods to reduce this risk (see <u>Section 2.4</u> of this report).

#### 4.2. Cardiovascular Effects

Caffeine temporarily stimulates a modest increase in heart rate and blood pressure (Temple et al, 2017; Grosso et al, 2017). Isolated case reports have indicated that individuals with heart abnormalities and conditions are more susceptible to suffering cardiovascular side effects from acute caffeine intake (Cannon et al, 2001; Ward et al, 2014). Consequently, whether intake causes various types of arrhythmias (i.e. an irregular, rapid or slow heart beat) has been widely researched. Specifically, a systematic literature review and meta-analysis of seven observational studies (evaluating a total of 115,993 participants both with and without a history of a diagnosed heart condition) found that low intakes (defined to be < 350 mg), moderate intakes (defined to be 350–699 mg) and high intakes (defined to be  $\geq$  700 mg) were not associated with an increased risk of experiencing atrial fibrillation (an irregular and often rapid heartbeat) in any population (Caldeira et al, 2013). On the contrary, low intakes were found to be associated with a significantly lower risk of atrial fibrillation. Another systematic literature review and metaanalysis, by Zuchinali et al, included seven human experimental studies (involving a total of 290 healthy and unhealthy participants) and found that caffeine doses of < 300 mg and 300-450 mg were not associated with an increased risk of any type of ventricular arrhythmia (abnormal heartbeat) in either healthy or unhealthy participants. The same authors, in separate meta-analysis of two animal studies, demonstrated that very high doses of caffeine (i.e. up to 35 mg/kg of body weight) increased the risk of developing ventricular fibrillation (a life-threatening heart rhythm characterised by a rapid and inadequate heartbeat). Thus, the authors concluded that the effects observed in animals arise due to very high doses of caffeine that are unlikely to be regularly consumed by humans from everyday foods and beverages. Notably, Zuchinali et al (2016) excluded studies investigating the effect of energy drinks and energy shots in order to isolate the effects of caffeine.

Energy drinks and energy shots often contain caffeine in addition to many other active ingredients such as taurine, guarana and ginseng. Importantly, studies indicate that the risk of cardiovascular side effects, such as arrhythmias, increases from energy drink consumption due to their formulation and not the effects of caffeine alone (Kozik et al, 2016; Fletcher et al, 2017; Shah et al, 2016a; Shah et al, 2016b; Shah et al, 2015; Phan & Shah, 2014; Kurtz et al, 2013).

In summary, the available literature indicates that for healthy adults, caffeine intakes (in isolation) of ~400–450 mg/day do not appear to cause any cardiovascular side effects (e.g. arrhythmias and/or high blood pressure) beyond temporarily stimulating a modest increase in blood pressure (Temple et al, 2017; Grosso et al, 2017). In addition, currently available evidence indicates that even high intakes (i.e.  $\geq$  700 mg/day) do not increase the risk specifically for atrial fibrillation.

#### 4.3. Anxiety and Mental Health

Some studies have shown that some individuals may experience anxiety following ingestion of 150–500 mg of caffeine (Turnbull et al, 2015). However, there are mixed findings regarding this, with not all studies finding that caffeine doses in this range increase the risk of experiencing anxiety as a side effect (Turnbull et al, 2015). Factors that can increase an individual's susceptibility to experiencing anxiety following caffeine

ingestion at this level include a pre-existing anxiety disorder, not being a habitual caffeine consumer and genetic predisposition (e.g. individuals with certain adenosine receptor gene polymorphisms). There are more consistent findings regarding a significantly increased risk of experiencing anxiety resulting from higher doses of caffeine, in the range of 700–1,200 mg (10 mg/kg of body weight) (Turnbull et al, 2015).

In summary, the evidence suggests that some people who are sensitive to caffeine may experience anxiety following ingestion of relatively small amounts of caffeine (e.g. 150 mg), however in healthy adults without a pre-existing mental health condition, there is more consistent evidence which suggests there is a greater risk of suffering anxiety as a side effect when doses of 700 mg or more are consumed. Thus, for ADF members who are medically classified as deployable and who do not have a mental health condition (DHM Vol 002 Part 006, 2014), doses of 700 mg or more are more likely to result in anxiety.

# 4.4. Risks to Pregnant Women and the Foetus: Miscarriage and Low Birth Weight

Females account for over 18% of active service members in the ADF (ADF, 2019). The likelihood of pregnant women using CRP is low, as their Medical Employment Classification (MEC) is downgraded and therefore they would not be deployed or undertake field training (DHM Vol 002 Part 006, 2014). However, as unintended pregnancies are common, and women who have recently conceived often do not know they are pregnant during the first trimester of pregnancy, they could theoretically use CRP while their pregnancy is unknown. Thus, it is important to consider the safe level of caffeine intake for pregnant women and the risks to them posed by caffeine in order to understand how they can be mitigated.

The effects of caffeine are longer lasting in pregnant women compared to non-pregnant adults, with levels remaining elevated in the blood of pregnant women for approximately double the time of non-pregnant adults (Temple et al, 2017). Caffeine has a half-life of 3–7 hours in non-pregnant adults, whereas the half-life ranges from 6–16 hours for pregnant women (EFSA, 2015).

Research relating to safety of caffeine for pregnant women has focused on daily habitual intakes, rather than the safety of single doses or intakes in short bouts (e.g. 3–14 days). Of note, CRPs are most frequently used in short bouts. ADF doctrine states that the CR1M, which is the most commonly issued CRP, can be used for a maximum of 20 operational days as the sole source of food, after which time troops must receive fresh foods for equal to or greater than half this period. The CR5M can be used for a maximum

of 42 operational days and the PR1M can be used as necessary. In emergency operational situations, all CRPs may be used for unlimited period (SUPMAN4, 2014). Thus, women who have recently conceived and who are deployed on operations could theoretically be required to subsist exclusively on CRP for prolonged periods in emergency situations before becoming aware they are pregnant; such as during the first trimester of pregnancy, albeit in rare instances.

Over the past two decades, higher daily caffeine intakes have been found to be associated with an increased risk of miscarriage (Wen et al, 2001; Weng et al, 2008; Signorello et al, 2001; Karypidis et al, 2006; Wikoff et al, 2016). A number of confounding factors have also been assessed for increasing the risk of miscarriage, such as nausea during pregnancy and genetic factors related to caffeine metabolism. All studies have investigated the safety of habitual daily caffeine intakes for pregnant women. Differing daily levels of intake have been found to be significantly associated with an increased risk of miscarriage, such as 100–299 mg (compared to < 20 mg) (Wen et al, 2001), 100–299 mg in slow caffeine metabolisers (Signorello et al, 2001), > 200 mg (compared to < 200 mg) (Weng et al, 2008), > 300 mg in women who reported nausea after nausea had started (Wen et al, 2001), and > 500 mg in women with the CYP1B1 432 Val/Val genotype (Karypidis et al, 2006). A study by Weng et al found a significantly higher risk of miscarriage among pregnant women consuming  $\geq$  200 mg/day compared to those consuming < 200 mg/day. Among the 1063 participants in the study, 172 miscarriages occurred, with 57 (33%) of these occurring before 8 gestational weeks.

A small number of studies have found no increased risk of miscarriage at daily intakes ranging from 300-500 mg/day (Wikoff et al, 2016). However, differing methods of obtaining self-reported caffeine intakes from pregnant women have been employed among studies published to date, and thus limitations such as recall bias may influence their results. Considering the total body of evidence, and the greater number of studies that have found that higher intakes of caffeine are associated with an increased risk of miscarriage, overall consistency has been found in the finding that higher caffeine intakes increase the risk of miscarriage (Poole et al, 2017; Chen et al, 2015; Li et al, 2016). Two recent meta-analyses found that caffeine intakes are associated with an increased risk of miscarriage. The first, published in 2015, conducted a meta-analysis of 13 prospective observational studies and found that the risk of miscarriage increases by 16% in women with caffeine intakes in the range of 150–349 mg/day compared to those with no or very low caffeine intakes, or by 7% for every 100 mg consumed per day (Chen et al, 2015). The second, published in 2016, conducted a meta-analysis of 13 prospective observational and 13 retrospective case-control studies, and found that the risk of miscarriage rose by 19% for every 150 mg of caffeine consumed per day (Li et al, 2016).

There is also consistent evidence that higher caffeine intakes during pregnancy increase the risks of low birth weight (Rhee et al, 2015; Poole et al, 2017). A meta-analysis of twelve studies into the effect of caffeine intake on the risk of low birth weight found that for every additional 100 mg consumed per day, there was a 3% increase in the risk (Rhee et al, 2015).

Considering the consistent evidence that higher caffeine intakes increase the risks of miscarriage and low birth weight, a number of food safety and health bodies have set recommended daily limits of caffeine intake for pregnant women. For example, FSANZ, the EFSA and the American College of Obstetricians and Gynaecologists recommend a daily limit of 200 mg (FSANZ, EFSA, 2015; ACOG, 2010), while the Public Health Agency of Canada recommends a limit of 300 mg/day (Health Canada, 2019). The World Health Organisation recommends that pregnant women with high daily intakes above 300 mg/day limit their caffeine intake to reduce the risks of miscarriage and low birth weight (WHO, 2019).

In summary, although it may be uncommon for women who do not yet know they are pregnant to use CRP, it is important to consider the risks to them posed by caffeine intake in order to understand how they can be mitigated. To mitigate the risks to pregnant women and the foetus, and considering the recommendations from peak national and international health and food safety bodies, all women of childbearing age using CRP should receive education on the risks of caffeine intake above 200–300 mg/day during pregnancy. This should be delivered in a variety of formats, such as during alcohol and drug education sessions and in information contained on menu sheets and CRP component labels.

#### 4.5. Caffeine Withdrawal Symptoms in Habitual Users

Abstinence from caffeine by habitual consumers for a little as 12 hours they may give rise to withdrawal symptoms such as headaches, fatigue, anxiety and irritability (Smith et al, 2000; Juliano & Griffiths, 2004). Symptoms often vary between individuals, with onset time varying between 12–24 hours of abstinence. Symptoms tend to be more severe at ~20–51 hours of abstinence and can last for between 2 and 9 days (Juliano & Griffiths 2004, Addicott & Laurienti, 2009; Turnbull et al, 2015). Those with higher habitual caffeine intakes are more likely to experience symptoms and symptoms of greater severity (Juliano & Griffiths, 2004).

Rogers et al performed two experiments investigating the effect caffeine withdrawal had on both habitual and non-habitual users of caffeine. They discovered that after an overnight withdrawal, habitual users self-reported being less alert and more tense compared to non-users. After providing caffeine to both habitual and non-habitual users of caffeine, the results showed that the beneficial effects (which were improved mood, alertness and mental performance as determined by a mood questionnaire and reaction time tasks) of caffeine in habitual users are largely due to a reversal of the negative effects of withdrawal (Rogers et al, 2003).

Whilst caffeine withdrawal symptoms may not be life threatening (Turnbull et al, 2015) they could negatively affect combatants' performance. For example, combatants who habitually consume caffeine in the morning and/or afternoon may be at risk of withdrawals when undertaking high-tempo missions in hot-humid environments if they are limited to the primary caffeine-containing components in CRP. These components, instant coffee and tea, must be brewed and therefore are not conducive to eating while 'on-the-move' or in hot-humid environments, as suggested by the high discard rates of instant coffee and tea bags during a recent study (McLaughlin et al, 2018). Thus, symptoms of withdrawal may present and detrimentally impact their performance. However, research supports the notion that withdrawal symptoms are generally mild and do not have long term effects (Wikoff et al, 2017), and re-administration of caffeine will rapidly and often completely reverse any withdrawal symptoms that are being experienced (Juliano & Griffiths, 2004).

#### 4.6. Sleep Latency and Quality

Caffeine doses above 100 mg close to bedtime is known to impact sleep latency and quality. The EFSA Panel on Dietetic Products, Nutrition and Allergies advises that 100 mg of caffeine can lead to increased sleep latency and reduced sleep duration in some adults, particularly if consumed close to bedtime (EFSA, 2015). Studies have shown that the ability to sleep, or the ability to fall asleep, is reduced when doses exceed 100 mg/day (in some individuals) or if caffeine is consumed close (i.e. within 6 hours) to the normal sleep time s33(a)(iii)

. The ability to sleep and sleep quality are both greatly impaired at high doses (e.g. 500 mg/day).

However, following sleep deprivation, caffeine intake, even at very high dosages, appears to have minimal impact on sleep latency and quality. A recent study involved a 10 hour baseline sleep followed by 50 hours of sleep deprivation. During the 50 hours, at 0100, 0300, 0500 and 0700 hours, 200 mg of caffeine (or placebo) was given to the participants. After sleep deprivation, an 8 hour recovery sleep was observed. The results showed that high dosages of caffeine did not severely disrupt sleep quality following 50 hours of wakefulness. This suggests that the inhibitory effect of caffeine on sleep is minimised after sleep deprivation (Paech et al, 2015).

# 4.7. Risks to Adolescents, Small-statured Individuals, Caffeine-sensitive Individuals and Non-habitual Caffeine Users

It has been suggested that caffeine could adversely affect blood pressure, heart rate, mood, sleep, as well as cause headaches, more readily in adolescents and small-statured individuals. However, due to the limited number of studies conducted in adolescents, there is insufficient evidence to conclusively state the effect caffeine has on this group (Wikoff et al, 2017). Comprehensive literature reviews by Wikoff et al (2017) and Nawrot et al (2003) have suggested that healthy adolescents can safely consume < 2.5 mg/kg of caffeine per day (up to 300 mg per day) without any side effects. In contrast, the EFSA (2015) suggests that 3 mg/kg bodyweight per day may be safe for adolescents (corresponding to 225 mg for a 75 kg adolescent), however it also noted that there is insufficient available evidence to conclusively derive a safe level of caffeine intake for adolescents.

Research demonstrates that some individuals are more sensitive to caffeine, particularly when taken in very high dosages. Following a recent trial involving sleep deprivation and 200 mg doses of caffeine every 2 hours (providing a total of 800 mg of caffeine over an 8-hr period), a small number (n = 2) of participants (n = 24) exhibited very high serum caffeine levels, which can cause negative side effects (e.g. nausea, headaches, shaking and anxiety) (Paech et al, 2015).

Considering the potential for heightened sensitivity to caffeine among adolescents, smallstatured individuals and non-habitual users, the s33(a)(iii)

recommended that when caffeine doses of 100–600 mg are provided to military members, 100 mg dose increments be provided. In practice, this enables members to limit their intake to 200 mg within a 3–4 hour period, by consuming 100 mg, waiting 15 minutes, and consuming a second 100 mg dose if required s33(a)(iii)

#### 4.8. Fine Motor Skill

It has been suggested that caffeine can impair fine motor control, such as hand steadiness, due to an increased state of anxiety. Negative effects appear to occur mostly in individuals who are not habitual caffeine users and/or with doses  $\geq$  300 mg (Bovim et al, 2008; Baker et al, 2014; Smith, 2002). In support of the notion that doses up to 200–300 mg are well-tolerated in healthy adults without compromising fine-motor skill, <sup>\$33(a)</sup>

300 mg enabled SEAL trainees to sight their target and pull the trigger faster without compromising shooting accuracy (Tharion et al, 2003).

#### 4.9. Bone Health and Fracture Risk

High intakes of caffeine may adversely affect bone mineral density and increase the risks of osteoporosis and fracture, especially in women, with intake being associated with increased urinary calcium excretion (Heaney & Pecker, 1982; Heaney & Rafferty, 2001), a small impairment of calcium absorption (Heaney & Pecker, 1982; Heaney, 2002), and decreases in Vitamin D receptor expression in osteoblasts (Rapuri et al. 2007). A 2014 systematic review and meta-analysis which included 15 studies found that dosedependent coffee consumption was associated with an increased risk of fractures in women. Specifically, consumption of 2 and 8 cups/day of coffee was associated with a 2% and 54% higher risk, respectively, compared to in those who are non-consumers of coffee. The authors noted that, while the exact mechanism(s) for this increased risk is unclear, most studies have implicated caffeine, and thus the increased risk may be 'at least partly attributed to the effects of caffeine'. Contrary to the increased risk of fracture in women, the same meta-analysis found that the risk of fractures was 24% lower in males with the highest level of coffee consumption (Lee et al, 2014). Finally, the authors noted that, given the limitations in the published literature to date, further prospective studies are needed to confirm the findings that an increased risk of fracture is associated with higher levels of coffee consumption.

It is possible that higher habitual caffeine intakes (e.g. 330 mg of caffeine per day, the equivalent of 4 cups of coffee) in population subgroups who do not meet calcium requirements could further increase their risks of osteoporotic fractures (Hallström et al, 2006). Whilst further research is required, it appears that low to moderate intakes of caffeine (up to 400 mg/day) do not appear to have any adverse effects on bone health in healthy adults who consume an adequate diet (Wikoff et al, 2017). It should however be emphasised that ensuring CRP contains calcium commensurate with combatants' requirements, and that calcium is distributed across multiple CRP components to increase its consumption, is also important in promoting optimal bone health in CRP users. Therefore, improving the calcium content of CRPs is an important strategy to mitigate any adverse bone health effects of increasing their caffeine content.

#### 4.10. Hydration

Caffeine is known to have a small effect on diuresis in individuals at rest, and intake has been postulated to adversely affect hydration status during exercise as well as and exercise performance in the heat (McLennan et al, 2016; Armstrong, 2002; Maughan &

Griffin, 2003; Ruxton, 2008). A recent meta-analysis found that a median dose of 300 mg corresponded to only small and moderate increases in urine volume in males and females at rest, respectively, corresponding to an average increased urine volume of 109  $\pm$  195 mL, or a 16.0  $\pm$  19.2 % increase (Zhang et al, 2015). On average among both males and females at rest, caffeine doses in the range of 300 to 500 mg also resulted in only a small increase in urine volume. However notably, during exercise, no effect of caffeine on diuresis was found (Zhang et al, 2015). Further, a recent literature review examined the effect of caffeine ingestion in the range of ~250–700 mg on a range of variables during exercise in the heat, including sweat rate, fluid-electrolyte balance, urine volume, and heat storage and core temperature. The authors found no evidence that caffeine intake in this range alters fluid-electrolyte balance or hydration status, concluding that: 'ingestion of caffeine in doses up to 9 mg per kilogram (~700 mg) prior to or during exercise in hot environments should not be avoided due to fear of increased fluid-electrolyte loss or a reduced exercise tolerance in the heat' (Armstrong, 2002).

In summary, during military operations involving exercise, even those that require intense exercise over several hours and in hot climates, caffeine ingestion up to 700 mg/day will not exaggerate overall fluid loss.

5.

## 6. CAFFEINE CONTENT IN CURRENT AUSTRALIAN CRP

As shown in Table 3, the current CR1M builds (i.e. those produced in the 2018/19 and 2019/20 financial years) contain approximately 280 mg of caffeine spread across 2 serves of instant coffee, 2 serves of tea, 1 chocolate bar and 1 packet of candied chocolates. The PR1M produced in the 2018/19 financial year also contained approximately 280 mg of caffeine, but contained 1 caffeinated energy gel instead of a chocolate bar.

It is important to note that the caffeinated energy gel (found only in the 2018/19 REPLEN module) has a negligible amount of caffeine, on par with the amounts found within the chocolate CRP components. Therefore, its inclusion adds to the total level of caffeine contained in each CRP, without being an amount that will directly elicit any beneficial ergogenic effects (as discussed in <u>Section 3</u>).

Product	Amount of	Amount per item Quantity items per CRP			ms per	Caffeine in CRP (mg)		
	Caffeine <sup>1</sup>	in CRP (mg)	CR1M	CR5M	PR1M	CR1M	CR5M	PR1M
Instant coffee (2.5 g)	3400 mg/100 g	85	2	10	2	170	850	170
Tea bag (1 bag)	150 mg/L <sup>2</sup>	45 <sup>3</sup>	2	10	2	90	450	90
Chocolate bar (50 g)	16 mg/100 g	8	1	5	0	8	40	0
Chocolate candy (50 g)	21 mg/100 g	10.5	1	5	1	10.5	52.5	10.5
Sports gel (35 g)	24.8 mg/100 g	8.7	0	0	1 <sup>4</sup>	0	0	8.7
Total Caffeine per CR1M (average mg)278.5								
Total Caffeine per PR1M (average mg)270.5								
			18/	'19 REF	PLEN^			279.18

Table 4	US IOM suggested delivery of ca	affeine to military personnel

1 caffeine analysis of in-service CRP components was carried out by a NATA-accredited laboratory (see footnotes<sup>a,b</sup>) 2 Analysis was carried out on the liquid from a tea bag (2.5 g) steeped in 300 ml water rather than the tea leaves themselves

3 Caffeine per item for tea = 150 mg/L X 0.3 L based on preparation instructions for analysis

4 The sports gel was present in the 18/19 PR1M REPLEN only.

<sup>a</sup> National Measurement Institute (NMI) (2019). Report of Analysis, Report No. RN1247925; Sports Gel, Chocolate Ration, Chocolate Candy, Instant Coffee. Internal Report.

<sup>b</sup> National Measurement Institute (NMI) (2019) Report of Analysis, Report No. RN1247926; Tea Bag. Internal Report.

Whilst there is an adequate total amount of caffeine present in both the CR1M and PR1M for some ergogenic benefits (improvements are observed with ~200 mg doses), almost all caffeine-containing components would have to be consumed at the same time. Therefore, the spread of caffeine, primarily across 4 hot beverage-making components, would be problematic for promoting ergogenic benefits. Instant coffee and tea bags require time to prepare and consume, and have particularly low consumption rates in field environments (Carins & Kullen, 2011; McLaughlin et al, 2018; McLaughlin et al, under review).

During a 9 day field exercise in a hot-humid environment, only 26% of the instant coffee and 9% of the tea bags that were issued to combatants were consumed (Baker and Probert, 2018; McLaughlin et al, under review). In an earlier study, even lower consumption rates of instant coffee, from 6–9%, were reported during a two week jungle warfare training course in a hot-humid environment (Carins & Kullen, 2011). Combatants in this study reported that the common reasons for discarding these components was because they had 'no time' or 'didn't feel like it' (Carins & Kullen, 2011). A possible explanation for the latter is that they are beverages intended to be brewed and consumed hot and are therefore not palatable to some individuals before, during or after physical activity in a hot-humid environment. During the same study, the ration chocolate and the chocolate candy had a relatively high consumption rates (both over 70%) and had moderate to high acceptability ratings.

In a 6 day field exercise in a hot-humid environment, the jack ration most frequently carried by participants was coffee sachets, with 21% of participants consuming coffee from home, suggesting they preferred their own brand of coffee to that provided in CRP (McLaughlin et al, 2018). It was observed that 60–75% of the tea and coffee issued in CRP were discarded by combatants before they entered the field because they were either not liked, not needed or were time consuming to prepare (McLaughlin et al, 2018). In the field, similar to the findings of other trials, the instant coffee and the tea bags were poorly consumed and had low acceptability ratings (McLaughlin et al, 2018).

In contrast, the chocolate candies and ration chocolate were both highly accepted. The dosing of caffeine from these components is not expected to enhance performance, noting the content in chocolate-based components is low and likely well below an effective dose.

As mentioned in the introduction, the caffeine intake of combatants is, on average, likely less when living on CRP compared to free-living on a non-constrained diet. This would be especially so if the items are not well received, potentially hindering combatants' ability to reach their level of habitual caffeine intake (McLaughlin et al, 2018).

# 7. SUMMARY AND IMPLICATIONS FOR AUSTRALIAN GENERAL PURPOSE AND SPECIAL PURPOSE CRP

Caffeine is widely consumed by Australian civilians and combatants alike. Given its wideranging benefits to military-relevant measures of physical and cognitive performance, general purpose CRP should provide the maximum safe level of caffeine to provide users with the maximum possible competitive advantage on the battlefield. Doses of at least ~200 mg (consumed 60 minutes prior to commencement of exercise) are required to enhance endurance exercise performance and capacity. Cognitive performance can also be enhanced, in both rested and sleep deprived individuals, when either single doses of 200 mg or repeated doses of 200 mg every 4 hours (during prolonged sleep deprivation) are consumed.

Possible side effects of caffeine for healthy, non-pregnant adults are:

- disrupted sleep (when ~100 mg is consumed within 6 hours of sleep)
- impaired fine motor control (with single doses of > 300 mg)
- arrhythmias (i.e. an irregular, rapid or slow heart beat) (currently available evidence indicates that intakes of ~400–450 mg/day are well tolerated without adverse cardiovascular side effects)
- an increased risk of fracture in women (with daily intakes of > 400 mg)
- anxiety (with daily intake of > 700 mg)
- fatalities (resulting from single doses of 3,000–10,000 mg).

For pregnant women, there is an increased risk of miscarriage and low birth weight (with daily intakes of > 200–300 mg), and non-habitual caffeine consumers and Individuals who are sensitive to caffeine are more likely to suffer from side effects.

Considering available evidence on the safe level of daily caffeine intake for healthy, nonpregnant adults (of 400 mg/day, with single doses not exceeding 200 mg) and adolescents and pregnant women (of up to 300 mg/day), we recommended that the caffeine content of general purpose CRP be limited to 300–400 mg per pack. To further mitigate the risks of side effects of caffeine use, all CRP users should receive education on the risks of high caffeine intakes—i.e. single doses exceeding 200 mg within a 4-hour period; daily intakes above 400 mg/day for healthy, non-pregnant adults; daily intakes above 300 mg/day for adolescents and small statured individuals; and daily intakes above 200–300 mg/day for pregnant women. In addition to including such guidance on CRP menu sheets and component labels, this should be delivered in a variety of other formats, such as during yearly alcohol and drug education sessions. The delivery of such education does not fall within the remit of DSTG, rather it is a Joint Health Command (JHC) responsibility, and thus engagement with JHC is required to devise suitable education approaches for ADF members.

Current general purpose CRP configurations contain ~280 mg—a level close to the lower range of our recommended safe level. However, current CRP component formulations, as well as current CRP configurations, may be suboptimal for promoting ergogenic benefits and thus a competitive advantage during operations. It is a consistent finding that CRP are seldom consumed in their entirety, and as mentioned earlier, caffeine intakes among combatants using CRP are likely to be substantially below their habitual intakes. Recent data indicates that from CRP containing ~280 mg of caffeine, average caffeine intakes of only 98 mg/day may be expected, even when factoring in caffeine intakes from caffeine-containing jack rations brought into the field by combatants. The two instant coffee sachets and two and tea bags are the highest contributors of caffeine in current CRP, containing ~85 mg and ~45 mg per serve, respectively. Research suggests that these components are poorly consumed in the field, at least in the scenarios that have been studied to date.

We recommend that a number of alternative CRP menus with improved caffeine delivery be designed and introduced. Aligning with guidance from the US IOM, and given combatants have limited opportunities to eat and drink, a variety of caffeine sources should be issued in CRPs to promote both uptake and performance benefits. Currently, all eight menus of the CR1M and all five menus of the PR1M contain two serves of tea and two serves of instant coffee, despite these components being amongst those with the highest discard rates in field environments—with studies indicating ~75% of instant coffee and ~90% of the tea bags are discarded, respectively. Alternative menus should target the inclusion of components that not only provide doses that promote performance benefits (i.e. ~200 mg), but are also in forms that can be deliberately consumed at the right time, such as when on-the-move. This would involve reducing the total number of caffeine-containing components, namely those requiring preparation with boiling water, by removing one or two the serves of tea and one serve of instant coffee. The equivalent level of caffeine (~200 mg, an optimal dose for promoting ergogenic benefits) could then be formulated in a component that is highly accepted in field environments, such as a bar or energy gel that can be quickly and purposefully consumed without preparation when it is needed. To ensure caffeine-containing products provided to CRP users are both safe and efficacious, it is recommended that minimum and maximum caffeine levels are specified within DEF(AUST) documentation for all caffeine-containing CRP components. Studies are required to evaluate the caffeine intakes of users of such CRP, and to

establish strategies that promote caffeine intakes in accordance with the levels needed for ergogenic benefits (e.g. enhanced CRP configurations, educative labelling and behaviour change strategies).

Based on a considerable body of literature and the recommendations by the s<sup>33(a)(iii)</sup> <sup>s<sup>33(a)(iii)</sup> and others, doses of up to 200 mg every 3–4 hours (up to a total of 600 mg/day) are well-tolerated by healthy adults when used in short bouts (up to 72 hours), with a very low likelihood of adverse side effects. Such dosing regimens are an effective fatigue countermeasure during short-duration training and deployment involving sleep deprivation, and thereby enhance operational safety and effectiveness. As identified in the review presented herein, single doses greater than 200 to 300 mg may result in side effects in some individuals (e.g. individuals who are not habitual caffeine consumers, individuals who are sensitive to caffeine, as well as those with pre-existing conditions such as anxiety). Consequently, any CRP components provided should not contain greater than 100–200 mg/serve (refer to guidance specific to each product type by the US IOM).</sup>

Aligning with guidance from the  $s^{33(a)(iii)}$ , future arduous duties supplements (i.e. a module, supplementary to general purpose CRPs, provided as necessitated by the operational situation) and/or special purpose CRPs (both for use in short bouts up to 72 hours) would be well-suited to make available additional doses of caffeine, up to a total of 600 mg/day. Consistent with guidance from the  $s^{33(a)(iii)}$ , quick release caffeinated components, such as chewing gum and/or mints, should contain no more than 100 mg/serve, while sustained release (over ~1 hour) caffeine within components such as food bars should contain no more than 200 mg/serve. In practice, this enables adolescents, small-statured individuals and non-habitual caffeine consumers to limit their intake to well-tolerated levels. It is recommended that labels also include guidance on safe and effective use of caffeine, in line with the  $s^{33(a)(iii)}$  recommendations.

Any individual receiving caffeine provision in a future CRP, above the level provided in general purpose CRP and up to 600 mg/day, should be medically deemed to be deployable in order to safely consume such doses (e.g. have no history of a heart abnormality of condition or a mental health condition). JHC are responsible for deeming ADF members medically fit for deployment, and thus should be engaged regarding the medical considerations that exist related to the provision of such doses of caffeine to ADF members.

DSTG has previously recommended the introduction of a special purpose, light-weight CRP delivering restricted but optimal levels of energy and nutrients to ADF members engaged in high intensity, short-duration operations, such as those involving sleep

deprivation lasting up to 72 hours in duration (see papers by McLaughlin, 2015 and Baker and Probert, 2016). s33(a)(iii)

Although this

capability has been trialled in the ADF, to date, it has not been introduced.

Provided users of such a CRP are deemed medically fit for deployment, and thus do not have any pre-existing health conditions which may be exacerbated by high daily caffeine intakes, a special purpose CRP for use in short bouts of up to 72 hours, could include doses of caffeine commensurate with those required to optimally mitigate fatigue during sleep deprivation.s33(a)(iii)

, such a CRP should include 4 to 5 caffeinated gum or mints per CRP, containing 100 mg per strip or mint, in addition to 1-2 other caffeine containing components (e.g. a caffeinated bar or gel), to provide a total of  $\sim$ 600 mg of caffeine. All such products should be labelled with guidance on their safe and effective use, in line with the labelling of caffeinated gum and mints in s33(a)(iii). All users of such a CRP should also receive guidance on the safe and effective use of caffeine during short-duration missions involving sleep deprivation (i.e. non-habitual caffeine consumers must be aware that use may be more likely to result in adverse side effects; each strip of gum contains 100 mg of caffeine; chew one strip / 100 mg at a time for at least five minutes and then wait 15 minutes and if still not alert then consume a second 100 mg dose; do not exceed a 200 mg dose within a 3-4 hour period; consume a second 100-200 mg dose after 3-4 hours if needed). All users of such a CRP should be educated annually on how to safely and effectively follow use caffeine for optimising performance and countering fatigue, e.g. during alcohol and drug awareness training. JHC are responsible for delivering such education to ADF members, and thus should be engaged on the most appropriate way to deliver such guidance to ADF members. A commander's guide to caffeine should also be developed, including the guidance that they remain cognisant of optimal caffeine dosages during each specific mission and remind troops who choose to use caffeine to use it in dosages that are commensurate with the guidelines.

## 8. ACKNOWLEDGEMENTS

The authors gratefully acknowledge Ross Coad and Tracey McLaughlin their review of, and feedback towards, this report prior to publication, and Eugene Aidman for his review and feedback towards an early draft of this report.

## 9. **REFERENCES**

Addicott, M. A. & Laurienti, P. J. (2009). A comparison of the effects of caffeine following abstinence and normal caffeine use. *Psychopharmacology*, 207(3), 423–431. DOI: 10.1007/s00213-009-1668-3

Aidman, E., Balin, M., Johnson, K., Jackson, S., Paech, G. M., Pajcin, M., Grant, C., Mitchelson, E., Kamimori, G. H., Fidock, J., Della Vedova, C., Banks, S. (under review) Caffeine disrupts the impact of real-time drowsiness on cognitive performance.

Aidman, E., Johnson, K., Paech, G. M., Della Vedova, C., Pajcin, M., Grant, C., Kamimori, G., Mitchelson, E., Hoggan, B. L., Fidock, J., & Banks, S. (2018). Caffeine reduces the impact of drowsiness on driving errors. *Transportation Research Part F: Traffic Psychology and Behaviour*, 54, 236–247. DOI: 10.1016/j.trf.2018.01.008

American College of Obstetricians and Gynecologists. (2010). ACOG committee opinion No. 461: tracking and reminder systems. *Obstetrics and Gynecology*, 116(2 Pt 1), 464. DOI:10.1097/AOG.0b013e3181eeb27a

Australian Bureau of Statistics (ABS), 27 April 2015, Caffeine. Available from: <u>https://www.abs.gov.au/ausstats/abs@.nsf/Lookup/by%20Subject/4364.0.55.008~2011-</u> <u>12~Main%20Features~Caffeine~410</u>

Australian Defence Force (2019). *Women in the ADF Report 2018-19. A supplement to the Defence Annual Report 2018-19.* 

Australian Defence Force, Department of Defence (2014). *Australian Defence Force Ration Scales and Scales of Issue*, SUPMAN4, Edition 7

Australian Defence Force (2016). Defence Health Manual, latest version available from <a href="http://intranet.defence.gov.au/home/documents/data/ADFPUBS/DHM/Complete.pdf">http://intranet.defence.gov.au/home/documents/data/ADFPUBS/DHM/Complete.pdf</a>, accessed 25/05/2020

Australian Institute of Sport (AIS) (viewed 26/11/2019). Group A AIS Sports Supplements Evidence Map, <u>https://ais.gov.au/nutrition/supplements/tiles/group\_a</u>

Australian Government, (2019). Defence Determination (Prohibited Substances) 2019, <u>https://www.legislation.gov.au/Details/F2019L00349</u>

Baker, L. B., Nuccio, R. P., & Jeukendrup, A. E. (2014). Acute effects of dietary constituents on motor skill and cognitive performance in athletes. *Nutrition Reviews*, 72(12), 790–802

Baker, B. & Probert, B. (2016). *The usage and suitability of the patrol ration one man during a short-duration SASR patrol*, Land Division, Defence Science and Technology Group, DST-Group-TN-1538.

Baker, B. & Probert, B. (2018). *Initial findings from a dietary supplements survey: caffeinated beverage use among combat arms soldiers*, Land Division, Defence Science and Technology Group, DST-Group-CR-2018-0053

s33(a)(iii)

Boyd, E. M., Dolman, M., Knight, L. M., Sheppard, E. P. (1965). The chronic oral toxicity of caffeine. *Canadian Journal of Physiology and Pharmacology*, 43(6), 995–1007. DOI: 10.1139/y65-105

Bovim, G, Naess, P, & Helle, J, (1995). Caffeine influence on the motor steadiness battery in neuropsychological tests. *Journal of Clinical and Experimental Neuropsychology*, 17(3), 472–476.

Burke, L. M. (2008). Caffeine and sport performance. Applied physiology, nutrition, and metabolism, 33(6), 1319–34. DOI: 10.1139/H08-130.

Caldeira, D., Martins, C., Alves, L. B., Pereira, H., Ferreira, J. J., & Costa, J. (2013). Caffeine does not increase the risk of atrial fibrillation: a systematic review and metaanalysis of observational studies. *Heart*, 99(19), 1383–1389.

Cannon, M. E., Cooke, C. T., & McCarthy, J. S. (2001). Caffeine-induced cardiac arrhythmia: an unrecognised danger of healthfood products. *Medical Journal of Australia*, 174(10), 520–521.

Cappelletti, S., Piacentino, D., Sani, G., & Aromatario, M. (2015). Caffeine: cognitive and physical performance enhancer or psychoactive drug? *Current Neuropharmacology*, 13(1), 71–88.

Carins, J. E. & Kullen, C. J. (2011). *Field Acceptability and Consumption of CR1M and Potential New Food Items during the Hot Weather Ration Trial*. Defence Science and Technology Organisation, Melbourne. DSTO-TN-1041.

Chen, L. W., Wu, Y., Neelakantan, N., Chong, M. F. F., Pan, A., & van Dam, R. M. (2016). Maternal caffeine intake during pregnancy and risk of pregnancy loss: a categorical and dose–response meta-analysis of prospective studies. *Public Health Nutrition*, 19(7), 1233-1244. DOI: 10.1017/S1368980015002463

Colbeck, R. (Minister for Youth and Sport) (2019). Australia to protect consumers by banning sale of pure caffeine powder, media release, Parliament House, Canberra, 21 September.

Crawford, C., Teo, L., Lafferty, L., Drake, A., Bingham, J. J., Gallon, M. D., ... & Berry, K. (2017). Caffeine to optimize cognitive function for military mission-readiness: a systematic review and recommendations for the field. *Nutrition Reviews*, 75(suppl\_2), 17-35.

Department of Defence (2014). Defence Health Manual (DHM) Chapter 2, medical employment classification system. Vol 002 Part 006.

European Food Safety Authority (EFSA) Panel on Dietetic Products, Nutrition and Allergies, (2015). Scientific opinion of the safety of caffeine. European Food Safety Authority, 13(2), 4102. DOI: 10.2903/j.efsa.2015.4102

Fletcher, E. A., Lacey, C. S., Aaron, M., Kolasa, M., Occiano, A., & Shah, S. A. (2017). Randomized controlled trial of high-volume energy drink versus caffeine consumption on ECG and hemodynamic parameters. *Journal of the American Heart Association*, 6(5), e004448.

Food Standards Australia New Zealand (FSANZ) Australia New Zealand Food Standards Code (2016a). Standard 1.1.1 Structure of the Code and general provisions. Accessible at <u>https://www.legislation.gov.au/Details/F2020C00027</u>

Food Standards Australia New Zealand (FSANZ) Australia New Zealand Food Standards Code (2016b). Standard 2.6.4 Formulated caffeinated beverages. Accessible at <a href="https://www.legislation.gov.au/Details/F2013C00107">https://www.legislation.gov.au/Details/F2013C00107</a>

Food Standards Australia New Zealand (FSANZ) (2019). Australia New Zealand Food Standards Code, Pure and highly concentrated caffeine products, FSANZ review August 2019. Accessible at

https://www.foodstandards.gov.au/Documents/CaffeineReport2019.pdf

Forbes-Ewan, C. (2009). *Australian Defence Force Nutritional Requirements in the 21st Century (Version 1)*. Defence Science and Technology Organisation, Melbourne. DSTO-GD-0578.

Goldstein, E. R., Ziegenfuss, T., Kalman, D., Kreider, R., Campbell, B., Wilborn, C., ... & Wildman, R. (2010). International society of sports nutrition position stand: caffeine and performance. *Journal of the International Society of Sports Nutrition*, 7(1), 1–15. DOI: 10.1186/1550-2783-7-5

Grant, C. L., Coates, A. M., Dorrian, J., Paech, G. M., Pajcin, M., Della Vedova, C., ... & Banks, S. (2018). The impact of caffeine consumption during 50 hr of extended wakefulness on glucose metabolism, self-reported hunger and mood state. *Journal of Sleep Research*, 27(5), e12681. DOI: 10.1111/jsr.12681

Grgic, J., Trexler, E. T., Lazinica, B., & Pedisic, Z. (2018). Effects of caffeine intake on muscle strength and power: a systematic review and meta-analysis. *Journal of the International Society of Sports Nutrition*, 15(1), 11. DOI: 10.1186/s12970-018-0216-0

Grosso, G., Godos, J., Galvano, F., & Giovannucci, E. L. (2017). Coffee, caffeine, and health outcomes: an umbrella review. Annual review of nutrition, 37, 131-156.

Hallström, H., Wolk, A., Glynn, A., & Michaëlsson, K. (2006). Coffee, tea and caffeine consumption in relation to osteoporotic fracture risk in a cohort of Swedish women. *Osteoporosis International*, 17(7), 1055–1064. DOI: 10.1007/s00198-006-0109-y s33(a)(iii)

Health Canada, Caffeine in Food, <u>https://www.canada.ca/en/health-</u> <u>canada/services/food-nutrition/food-safety/food-additives/caffeine-foods/foods.html</u>, (viewed 28/11/19)

Heaney, R. P. (2002). Effects of caffeine on bone and the calcium economy. *Food and Chemical Toxicology*, *40*(9), 1263–1270.

Heaney, R. P., & Recker, R. R. (1982). Effects of nitrogen, phosphorus, and caffeine on calcium balance in women. *The Journal of Laboratory and Clinical Medicine*, 99(1), 46–55.

Heaney, R. P., & Rafferty, K. (2001). Carbonated beverages and urinary calcium excretion. *The American Journal of Clinical Nutrition*, 74(3), 343–347. s33(a)(iii)

Johnson, K., Aidman, E., Paech, G. M., Pajcin, M., Grant, C., LaValle, C., ... & Banks, S. (2016). Early morning repeat-dose caffeine mitigates driving performance impairments during 50 hours of sleep deprivation. *Road & Transport Research: A Journal of Australian and New Zealand Research and Practice*, 25(3), 3.

Juliano, L. M., & Griffiths, R. R. (2004). A critical review of caffeine withdrawal: empirical validation of symptoms and signs, incidence, severity, and associated features. *Psychopharmacology*, 176(1), 1–29. DOI: 10.1007/s00213-004-2000-x

Kamimori, G. H., Karyekar, C. S., Otterstetter, R., Cox, D. S., Balkin, T. J., Belenky, G. L., & Eddington, N. D. (2002). The rate of absorption and relative bioavailability of caffeine administered in chewing gum versus capsules to normal healthy volunteers. *International Journal of Pharmaceutics*, 234(1–2), 159–167.

Kamimori, G. H., McLellan, T. M., Tate, C. M., Voss, D. M., Niro, P., & Lieberman, H. R. (2015). Caffeine improves reaction time, vigilance and logical reasoning during extended periods with restricted opportunities for sleep. *Psychopharmacology*, 232(12), 2031–2042. DOI 10.1007/s00213-014-3834-5

Kelley, R. (Deputy Secretary Defence People) (2019). *Management of the use of prohibited substances in the Australian Defence Force*, MILPERSMAN Part 004, Chapter 3, Ed 2-AL9, 13 December. Accessible at

http://defweb.cbr.defence.gov.au/home/documents/data/DEFPUBS/DEPTMAN/MILPERS MAN/Part\_04/\_MILPERSMAN\_\_\_\_Pt04Cp03.pdf

Killgore, W. D., & Kamimori, G. H. (2020). Multiple caffeine doses maintain vigilance, attention, complex motor sequence expression, and manual dexterity during 77 hours of total sleep deprivation. *Neurobiology of Sleep and Circadian Rhythms*, 9, 100051. DOI: 10.1016/j.nbscr.2020.100051

Kurtz, A. M., Leong, J., Anand, M., Dargush, A. E., & Shah, S. A. (2013). Effects of caffeinated versus decaffeinated energy shots on blood pressure and heart rate in healthy young volunteers. Pharmacotherapy: The Journal of Human Pharmacology and Drug Therapy, 33(8), 779–786.

Lee, D. R., Lee, J., Rota, M., Lee, J., Ahn, H. S., Park, S. M., & Shin, D. (2014). Coffee consumption and risk of fractures: A systematic review and dose–response meta-analysis. *Bone*, 63, 20–28. DOI: 10.1016/j.bone.2014.02.007

Maughan, R. J., Burke L. M., Dvorak, J., Larson-Meyer, D.E., Peeling, P., Phillips, S.M., ... & Engebretsen, L. (2018). IOC consensus statement: dietary supplements and the high-performance athlete. *British Journal of Sports Medicine*, 52(7), 439–455. DOI: 10.1136/bjsports-2018-099027

Maughan, R. J., & Griffin, J. (2003). Caffeine ingestion and fluid balance: a review. *Journal of Human Nutrition and Dietetics*, 16(6), 411–20. DOI: 10.1046/j.1365-277X.2003.00477.x

McLaughlin, T. (2015). *Design and Evaluation of an Energy-Dense, Light-Weight Combat Ration to Sustain Land Forces Involved in High-Intensity, Short-Duration Operations.* Defence Science and Technology Organisation, Scottsdale. DSTO-TR-3109.

McLaughlin, T., De Diana, J., Bulmer, S. & Pike, A. (2018). *Comparative Field Evaluation of the In-service and Prototype Modular Mission Adaptive Combat Ration Packs*. Defence Science and Technology Group, Scottsdale. DST-Group-TR-3453.

McLaughlin, T., Baker, B. & De Diana, J. (under review) *Mission Adaptive Combat Ration Packs; Design and Field Use Evaluation of a Modular Prototype*.

s33(a)(iii)

McLellan, T. M., Caldwell, J.A., & Lieberman, H.R. (2016). A review of caffeine's effects on cognitive, physical and occupational performance. *Neuroscience & Biobehavioral Reviews*, 71, 294–312. DOI: 10.1016/j.neubiorev.2016.09.001

McLellan, T. M., Kamimori, G. H., Voss, D. M., Tate, C. & Smith S. J. R. (2007). Caffeine effects on physical and cognitive performance during sustained operations. *Aviation Space and Environmental Medicine*, 78, 871–7.

s33(a)(iii)

Nawrot, P., Jordan, S., Eastwood, J., Rotstein, J., Hugenholtz, A. & Feeley, M., (2003). Effects of caffeine on human health. *Food Additives and Contaminants*, 20(1), 1–30. DOI: 10.1080/0265203021000007840

NSW Government Health (2013). Caffeine. https://www.health.nsw.gov.au/aod/resources/Pages/caffeine.aspx

Paech, G. M., Della Vedova C., Pajcin, M., Grant, C., Kamimori, G., & Banks, S. (2015). Caffeine has minimal effects on daytime recovery sleep following severe sleep deprivation. *Sleep and Biological Rhythms*, 14(2), 142–156. DOI 10.1007/s41105-015-0031-9

Peeling, P., Binnie, M. J., Goods, P. S. R., Sim, M., & Burke, L. M. (2018). Evidencebased supplements for the enhancement of athletic performance. *International Journal of Sport Nutrition and Exercise Metabolism*, 28(2), 178–187. DOI: 10.1123/ijsnem.2017-0343

Phan, J. K., & Shah, S. A. (2014). Effect of caffeinated versus noncaffeinated energy drinks on central blood pressures. *Pharmacotherapy: The Journal of Human Pharmacology and Drug Therapy*, 34(6), 555–560.

Poole, R., Kennedy, O. J., Roderick, P., Parkes, J., Fallowfield, J. A., & Hayes, P. C. (2017). Coffee consumption and health: umbrella review of meta-analyses of multiple health outcomes. *BMJ (Clinical Research Ed.)*, 359. DOI: 10.1136/bmj.j5024

Rapuri, P. B., Gallagher, J. C., & Nawaz, Z. (2007). Caffeine decreases vitamin D receptor protein expression and 1,25(OH)2D3 stimulated alkaline phosphatase activity in human osteoblast cells. *Journal of Steroid Biochemistry and Molecular Biology*, 103(3-5), 368–71. DOI: 10.1016/j.jsbmb.2006.12.037

Rhee, J., Kim, R., Kim, Y., Tam, M., Lai, Y., Keum, N., & Oldenburg, C. E. (2015). Maternal caffeine consumption during pregnancy and risk of low birth weight: A doseresponse meta-analysis of observational studies. *PLoS ONE*, 10(7). DOI: 10.1371/journal.pone.0132334

Rogers, P. J., Martin, J., Smith, C., Heatherley, S. V., & Smit, H. J. (2003). Absence of reinforcing, mood and psychomotor performance effects of caffeine in habitual non-

consumers of caffeine. *Psychopharmacology*, 167(1), 54–62. DOI 10.1007/s00213-002-1360-3

Ruxton, C. H. S. (2008). The impact of caffeine on mood, cognitive function, performance and hydration: a review of benefits and risks. *Nutrition Bulletin*, 33(1), 15–25. DOI: 10.1111/j.1467-3010.2007.00665.x|

Shah, S. A., Chu, B. W., Lacey, C. S., Riddock, I. C., Lee, M., & Dargush, A. E. (2016a). Impact of acute energy drink consumption on blood pressure parameters: a metaanalysis. *Annals of Pharmacotherapy*, 50(10), 808–815.

Shah, S. A., Nguyen, N. N., & Bhattacharyya, M. (2015). Energy implications of consuming caffeinated versus decaffeinated energy drinks. *Journal of Pharmacy Practice*, 28(5), DOI: 10.1177/0897190015585738

Shah, S. A., Occiano, A., Nguyen, T. A., Chan, A., Sky, J. C., Bhattacharyya, M., O'Dell, K. M., Shek, A & Nguyen, N. N. (2016b). Electrocardiographic and blood pressure effects of energy drinks and Panax ginseng in healthy volunteers: a randomized clinical trial. *International Journal of Cardiology*, 218, 318–323

Sigma-Aldrich, (2019). Safety Data Sheet – Caffeine, Product Number C0750, CAS-No. 58-08-2, Printed 30/10/2019.

Signorello, L. B., Nordmark, A., Granath, F., Blot, W. J., McLaughlin, J. K., Annerén, G., Lundgren, S., Ekbom, A., Rane, A., & Cnattingius, S. (2001). Caffeine metabolism and the risk of spontaneous abortion of normal karyotype fetuses. *Obstetrics and Gynecology*, 98(6), 1059–1066.

Smith, P. F., Smith, A., Miners, J., McNeil, J., & Proudfoot, A. (2000). Report from the Expert Working Group on The Safety Aspect of Dietary Caffeine. Available from: <u>https://www.foodstandards.gov.au/publications/Documents/safety%20aspects%20of%20</u> <u>dietary%20caffeine.pdf</u>

Smith A. (2002). Effects of caffeine on human behavior. *Food and Chemical Toxicology: an International Journal Published for the British Industrial Biological Research Association*, 40(9), 1243–1255. DOI: 10.1016/s0278-6915(02)00096-0

s33(a)(iii)

Southward, K., Rutherfurd-Markwick, K. J., Ali. A. (2018) Correction to: The Effect of Acute Caffeine Ingestion on Endurance Performance: A Systematic Review and Meta-

Analysis. *Sports Medicine*, 48(10):2425-2441. DOI: 10.1007/s40279-018-0967-4. Erratum for: Sports Med, 48(8):1913-1928. PMID: 30094798

Spriet L. L. (2014). Exercise and sport performance with low doses of caffeine. *Sports Medicine*, 44(Suppl 2), S175–S184. DOI: 10.1007/s40279-014-0257-8

Temple, J. L., Bernard, C., Lipsultz, S. E., Czachor, J. D., Westphal, J. A. & Mestre, M. A., (2017). The safety of ingested caffeine: a comprehensive review. *Frontiers in Psychiatry*, 8, 80. DOI: 10.3389/fpsyt.2017.00080
s33(a)(iii)

Turnbull, D., Rodricks, J.V. & Mariano, G.F. (2015). Neurobehavioral hazard identification and characterization for caffeine. *Regulatory Toxicology and Pharmacology*, 74, 81–92, DOI: 10.1016/j.yrtph.2015.12.002

s33(a)(iii)

Department of Defence, *User Requirements for Combat Rations Pack (CRUR)*, Issue 2.0 dated Feb 14, endorsed SO1 Capability Resource, AHQ.

Ward, A. E., Lipshultz, S. E., & Fisher, S. D. (2014). Energy drink–induced near-fatal ventricular arrhythmia prevented by an intracardiac defibrillator decades after operative "repair" of tetralogy of fallot. *The American Journal of Cardiology*, 114(7), 1124–1125.

Wen, W., Shu, X. O., Jacobs, D. R., Jr, & Brown, J. E. (2001). The associations of maternal caffeine consumption and nausea with spontaneous abortion. *Epidemiology*, 12(1), 38–42. DOI: 10.1097/00001648-200101000-00008

Weng, X., Odouli, R., & Li, D. K. (2008). Maternal caffeine consumption during pregnancy and the risk of miscarriage: a prospective cohort study. *American Journal of Obstetrics and Gynecology*, 198(3), 279.e1–279.e2798. DOI: 10.1016/j.ajog.2007.10.803

Wickham, K. A., & Spriet, L. L. (2018). Administration of caffeine in alternate forms. *Sports Medicine*, 48(1), 79–91.

Wikoff, D., Welsh, B. T., Henderson, R., Brorby, G. P., Britt, J., Myers, E., Goldberger, J., Lieberman, H. R., O'Brien, C., Peck, J., Tenenbein, M., Weaver, C., Harvey, S., Urban, J., & Doepker, C. (2017). Systematic review of the potential adverse effects of caffeine consumption in healthy adults, pregnant women, adolescents, and children. *Food and Chemical Toxicology: an International Journal Published for the British Industrial Biological Research Association*, 109(Pt 1), 585–648. DOI: 10.1016/j.fct.2017.04.002

World Health Organisation (WHO). (2019). Restricting caffeine intake during pregnancy. Available from: <u>https://www.who.int/elena/titles/caffeine-pregnancy/en/</u>

Zhang, Y., Coca, A., Casa, D. J., Antonio, J., Green, J. M., & Bishop, P. A. (2015). Caffeine and diuresis during rest and exercise: A meta-analysis. *Journal of Science and Medicine in Sport*, 18(5), 569–574. DOI: 10.1016/j.jsams.2014.07.017

Zuchinali, P., Ribeiro, P. A., Pimentel, M., da Rosa, P. R., Zimerman, L. I., & Rohde, L. E. (2016). Effect of caffeine on ventricular arrhythmia: a systematic review and metaanalysis of experimental and clinical studies. *EP Europace*, 18(2), 257–266.

## **DISTRIBUTION LIST**

The Utility and Safety of Caffeine as an Ergogenic Aid in Australian Defence Force Combat Ration Packs

s47E(d)

Task Sponsor	s47E(d)			
Director, HLTHSPO, CASG				
Chief Engineer/DAAR, HLTHSPO,CASG				
A/Fleet Manager, Combat Rations, HLTHSPO, CASG				
Food Technologist, HLTHSPO, CASG				
S&T Program				
Chief of Land Division	s47E(d)			
Task Leader ARM 17/485 and RL-LHS MSTC				
Group Leader Food & Nutrition STC				
Discipline Leader Defence Feeding Systems				
Author				
Author				
Author				
SOSTA, SOTEC				
Army				
SO1 Human Performance, DCP, AHQ	s47E(d)			
SO2 Sustainment, DCP, AHQ				
SO1 Culture & Diversity, APC Br, AHQ				

#### Joint Health Command

s47E(d)

Senior Medical Advisor, DHP, JHC

Deputy Chief Medical Officer, DFR

DEFENCE SCIENCE AND TECHNOLOGY GROUP DOCUMENT CONTROL DATA			IMM/CAVEAT (OF DOCUMENT) Sensitive		
TITLE	SECURITY CLASSIFICATION				
The Utility and Safety of Caffeine as a	Document (Official		(Official: Sensitive)		
in Australian Defence Force Combat Ration Packs		Title		(Official)	
AUTHOR(S)	PRODUCED BY				
s47E(d)		Defence Science and Technology Group			
		Department of Defence			
		PO Box 7931			
		Canberra BC	CACT	2610	
DSTG NUMBER	REPORT TYPE			DOCUMENT DATE	
DSTG-GD-1113	General Document			December 2020	
TASK NUMBER	TASK SPONSOR			RESEARCH DIVISION	
N/A	Director, HLTHSPO, CASG			Land Division	
MAJOR SCIENCE AND TECHNOLOGY CAPABILITY		SCIENCE AND TECHNOLOGY CAPABILITY			
Land Human Systems		Food and Nutrition			
SECONDARY RELEASE STATEMEN					

SECONDARY RELEASE STATEMENT OF THIS DOCUMENT

Distribution additional to the initial list is limited to Australian Department of Defence and Defence Force Personnel and others engaged in defence activities in Australia and their equivalent in the United States, the United Kingdom, Canada and New Zealand who are suitably security cleared and have a need-to-know. Others inquiring must be referred to the Chief, Land Division

#### ANNOUNCEABLE

Australian Department of Defence and Defence Force Personnel and others engaged in defence activities in Australia and their equivalent in the United States, the United Kingdom, Canada and New Zealand who are suitably security cleared and have a need-to-know.

CITABLE IN OTHER DOCUMENTS

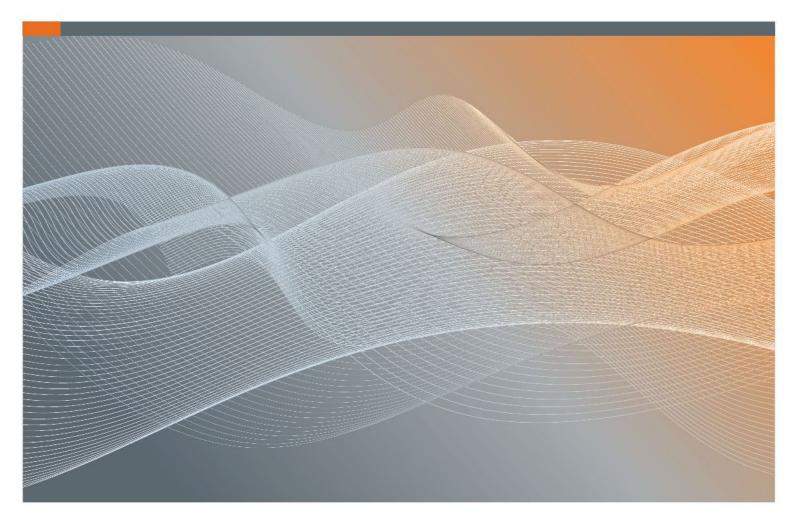
Yes

RESEARCH LIBRARY THESAURUS

Human Performance, Safety, Toxicity, Nutrition, Cognition



# Australian Combatants' Protein and Amino Acid Requirements and Recommendations for Combat Ration Packs



Defence Science and Technology Group DSTG-GD-1174

Defending Australia and its National Interests www.defence.gov.au



DSTG-GD-1174

Authors s47E(d)

Produced by Land Division Defence Science and Technology Group Department of Defence PO Box 7931 Canberra BC ACT 2610

#### www.dst.defence.gov.au

Telephone: 1300 333 362

© Commonwealth of Australia 2022 This work is copyright. Apart from any use permitted under the *Copyright Act 1968* no part may be reproduced by any process without prior written permission from the Department of Defence.

Approved for public release

Defence FOI 386/22/23 Document 5

### **OFFICIAL**

DSTG-GD-1174

## EXECUTIVE SUMMARY

Australian Defence Force (ADF) combatants perform a wide range of physically and cognitively demanding tasks during field training and deployment. Protein is a component of all living cells, and is a nutrient of vital importance to health, performance and recovery from vigorous physical activity. Combatants depend on sufficient daily protein intake to provide the amino acids (AA) required for the maintenance and optimisation of skeletal muscle, ligaments, tendons, collagen and bone, as well as many other bodily processes that are vital to health and performance.

The quantity of protein provided in ADF Combat Ration Packs (CRP) is based on the 2009 Recommended Nutritional Criteria (RNC) set by Forbes-Ewan (2009) of 122–150 g. Since 2009, further research has been conducted related to the protein requirements of combatants, including the quantity, quality and timing of protein needed to maximally facilitate recovery and adaptations following physical activity. Accordingly, this report examines newly published scientific literature relevant to the military-specific benefits, challenges and risks in optimising protein and AA provisions within CRP.

Combatants require protein intakes in the range of 1.5–2.0 g/kg to optimally build, repair, maintain and synthesise skeletal muscle. Based on the evidence presented in this report, it is recommended that Australian CRP should provide at least 144 g protein (translating to 1.7 g/kg for an average 84-kg male combatant, and 1.5 g/kg for a combatant weighing 96-kg). The upper range for Australian CRP should be set at 168 g (or 2.0 g/kg for an average 84-kg combatant; 1.8 g/kg for a 96-kg combatant). Accordingly, a revised RNC of 144–168 g of protein should be adopted for CRP delivering 16–18 MJ. This translates to 15–18% and 13–16% of the total energy content of CRP menus delivering 16 MJ and 18 MJ, respectively.

Further to the total protein provision, evidence is presented in this report on the optimal quantity and quality of protein that should be provided in CRP Main Meals (MM), Light Meals (LM) and high-protein snacks and beverages to enable combatants to best meet their protein requirements. Over the past decade, protein timing strategies have been investigated for their role in supporting training adaptations and recovery following vigorous resistance and endurance activity. This research has shown that by providing sufficient amounts (0.24–0.40 g/kg) of high biological value (HBV) protein at regular intervals (i.e. every 3–4 hours) after vigorous physical activity—both resistance and endurance—optimal types and quantities of AA can be provided to promote recovery and muscular adaptations.

Although a wide range of foods of both animal and plant origin contain protein, they are not equally valuable for maximising muscle protein synthesis (MPS) for skeletal muscle maintenance and growth. It is generally accepted that animal protein sources such as beef, chicken, egg, and milk contain an optimal essential amino acid (EAA) profile and are of HBV. They are able to stimulate MPS to a greater extent than plant-based protein sources (e.g. legumes). Plant-based protein sources, such as legumes and isolated proteins from peas, chickpeas and rice generally lack one or more EAA, have a relatively low digestibility, and contain suboptimal levels of leucine, an important branched chain amino acid (BCAA).

Accordingly, further to the protein RNC, it is recommended (based on the average combatant weighing 84-kg) that CRP contain two MM providing 0.4 g of HBV protein/kg each, one LM providing 0.3 g of HBV protein/kg, and three snacks (including at least one beverage and one styled as a pre-sleep snack) providing 0.24 g of HBV protein/kg each. To meet these recommendations, the following distribution and mode of delivery is recommended for HBV protein in CRP:

- two MM, each containing ≥ 30 g of HBV protein, intended to be consumed at lunch and dinner
- one LM containing ≥ 25 g of HBV protein, styled as a breakfast meal
- one high-protein snack component containing ≥ 20 g of HBV protein
- one high-protein beverage containing ≥ 20 g of HBV protein
- one beverage or snack intended as a pre-sleep component containing ≥ 20 g of HBV protein.

A number of these high-protein LM, MM, snacks and beverages should also be high in carbohydrate in accordance with the recommendations by Keenan et al. (In Preparation), or ideally be consumed in conjunction with high-carbohydrate foods, to preserve AA from oxidation for energy. Ideally, MM, LM and snacks should be consumed every 3–4 hours; however, it is acknowledged that this may not always be possible due to operational, logistical, and tactical constraints, hence CRP should be developed to be easily and rapidly consumed by combatants, for example when they are on-the-move.

Among the individual AA that are required to stimulate MPS, the most extensively studied is leucine. This is the only AA that has been consistently shown to initiate MPS within skeletal muscle. A range of other AA have been extensively studied for their ability to enhance performance. Although AA supplements such as  $\beta$ -alanine and creatine deliver beneficial results to athletic performance when correct dosage protocols are followed,

DSTG-GD-1174

insufficient research has been conducted within the military context to elucidate their efficacy for combatants. The loading and dosage protocols required present clear challenges in unpredictable scenarios, and CRP may not be the most appropriate vehicle for delivering such ergogenic aids.

In-service CRP, including the individual components they provide, were evaluated against the protein recommendations. Presently, DEF(AUST) specifications include protein requirements for ready-to-eat (RTE) MM (including meat-based meals [MBM], vegetable-based meals [VBM], cereal-based meals [CBM]), and also for LM, freeze dried meals (FDM), bread, beef snacks and dairy components. However, these requirements only apply to the total content of protein, and not to the source or quality of the protein.

At 145 g, the mean protein content of the Combat Ration One Man (CR1M) 2021/22 is within the recommended range of protein. However, with a protein content range of 134–151 g, some CR1M 2021/22 menus fall below the recommended range. At 152 g, the mean protein content of the Patrol Ration One Man (PR1M) 2019/20 build is adequate against the total protein recommendation. However, similar to the CR1M 2020/21, not all PR1M 2019/20 menus meet the minimum recommendation (with a protein content range of 141–162).

CR1M menus currently include both MBM and VBM as MM. Of these, only two MBM (Chicken Korma and Lamb and Tomato Sambal) meet the recommendations for protein content and quality. The average protein content of the MBM and VBM is 24 g and 16 g per 250 g serve, respectively. PR1M menus currently include FDM as MM choices. With a mean protein content of 43 g, all in-service FDM meet the recommended minimum amount of protein (30 g per serve), and all contain a HBV source of protein (i.e. beef, lamb, chicken or fish) that provides at least 30 g of protein per serve.

Neither the PR1M nor the CR1M contains a breakfast-type LM meeting the protein recommendations in this report. Current breakfast-type LM foods (natural muesli and porridge variants), even with the addition of sweetened condensed milk, would provide only 50% of the recommended protein for a LM. Being cereal-based formulations, these LM aren't considered HBV protein sources. Within CRP, few LM are good sources of protein for combatants. Tuna varieties provide 14–20 g protein per serve; this is 5–11 g (or 20–40%) below the recommended amount for a LM (Table A.2 in Appendix A).

Snack options within CR1M and PR1M menus primarily contain carbohydrate, are often sweet and contain little protein except for the two beef steak bars, which provide ~8 g of protein per 25 g serve. This provides less than 50% of the protein recommended for a snack. Only one beverage option—the protein drink powder—provides protein (~13 g per serve; 65% of the recommended protein content ( $\geq$  20 g) for a high-protein beverage.

Considering the above, the opportunity exists to improve the protein content and quality of in-service MM, LM, snacks and beverage components, particularly those intended to be protein-rich sources within CRP. Product improvement of existing CRP components should consider the following actions:

- Increase the quantity, and/or improve the quality, of lean meat in MM. Following this, if required, adjust MM serve sizes to ensure the quantity and quality of protein is consistent in providing the minimum amount of HBV protein required to maximally facilitate recovery from, and skeletal muscle adaptations to, vigorous physical activity.
- As an interim measure, increase the quantity of legumes such as lentils and beans in VBM. As these vegetarian protein sources are lower in protein than animal and soy protein sources, it is unlikely that this action alone will provide the minimum recommended level of protein for MM (≥ 30 g) within the constraint of a 250 g serve size. In addition, they are of lower biological value than protein sources of animal and soy origins. It is recommended that the shelf life and acceptability of VBM formulated with alternative vegetarian protein sources such as tofu and textured vegetable protein (TVP) be investigated as a priority action towards meeting the protein recommendations for VBM. VBM formulations containing complementary plant-based protein sources (e.g. a grain and a legume) and that are fortified with complementary plant-based protein isolate powders (e.g. rice and pea protein) should also be evaluated.
- Introduce protein-rich LM, snacks and beverages with either increased or alternative protein sources to boost both the quantity and quality of the protein they provide in order to meet the recommendations. This action is most relevant to the protein-rich LM, snacks and beverages that do not contain protein from dairy, meat or fish, and/or do not contain a sufficient quantity of these protein sources. In the first instance, these components should be formulated with a source of protein of animal origin (i.e. meat, fish, whey protein isolate, or whey protein concentrate), as these sources are of the greatest biological value.
- Increase the quantity of whey protein in the protein drink powder so that it provides ≥ 20 g of HBV protein (e.g. from whey protein isolate or whey protein concentrate).

A review and update of the DEF(AUST) specifications and standards series for CRP is also recommended to ensure that the above recommendations will be met. All individual product specifications for protein-rich foods should identify and specify the quantity and quality of protein in protein-rich food sources.

DSTG-GD-1174

# CONTENTS

1.	INTR	ODUCTION	.1
	1.1.	Importance of Protein	.2
	1.2.	Physiology of Protein Utilisation	.2
	1.3.	Physiology of Skeletal Muscle Recovery and Adaptation	.3
2.	PRO	TEIN AND THE MILITARY	.4
	2.1.	Combatants' Protein Requirements	.4
		2.1.1. Recommended Daily Intakes	.4
		2.1.2. Per-Meal Protein Recommendations during Recovery	.6
		2.1.3. Protein Dose and Timing Recommendations during	
		Recovery	
	2.2.	Protein Quality (Biological Value)	10
		2.2.1. Leucine	12
	2.3.	Protein and Health	
		2.3.1. Immune Function	
		2.3.2. Bone Health and Injury Prevention	14
		2.3.3. Muscle Repair and Recovery	
	2.4.	Protein and Performance	
		2.4.1. Strength and Power	
	2.5.	Combatants' Protein Requirements in Extreme Conditions	
	2.6.	Amino Acid Supplements	
		2.6.1. β-Alanine	
		2.6.2. Creatine	
		2.6.3. Tyrosine	23
		2.6.4. β-Alanine, Creatine and Tyrosine: Summary and	
		Recommendations	23
3.	RECO	OMMENDATIONS FOR CRP	24
		3.1.1. Main Meals	24
		3.1.2. Light Meals	25
		3.1.3. Snacks	
		3.1.4. Beverages	25
4.	EVAL	UATION OF CURRENT CRP AGAINST RECOMMENDATIONS.	26
		4.1.1. Combat Ration One Man (CR1M)	27
		4.1.2. Patrol Ration One Man (PR1M)	27
		4.1.3. Individual Components	28
5.	RECO	OMMENDED CRP INNOVATIONS	30
	5.1.	New Products	31
	5.2.	Specifications and Standards	32

#### DSTG-GD-1174

#### **OFFICIAL**

6. REFERENCE LIST	34
APPENDIX A. PROTEIN CONTENT AND QUALITY OF IN-SERVI	
LM, SNACK AND BEVERAGE COMPONENTS	50
Table A.1 Comparison of the content of in-service CRP M Provisions with the Protein Quantity and Quality	lain Meal
Recommendations	50
Table A.2 Comparison of the content of in-service CRP L Provisions with the Protein Quantity and Quality	ight Meal
Recommendations	51
Table A.3 Comparison of the content of in-service High-P	Protein CRP
Snack Provisions with the Protein Quantity and Qu	uality
Recommendations	51
Table A.4 Comparison of the content of in-service High-P	Protein CRP
Beverage Provisions with the Protein Quantity and	l Quality
Recommendations	51
Table A.5 Other in-service Protein Sources within CRP	52
APPENDIX B. ESSENTIAL AMINO ACID CONTENT OF SELECT	ED CRP
COMPONENTS	53

DSTG-GD-1174

## GLOSSARY

AA	Amino acid(s)
ACTMOD	Activity Module
ADF	Australian Defence Force
AMDR	Acceptable Macronutrient Distribution Range
ATP	Adenosine triphosphate
ВА	β-alanine
BCAA	Branch chain amino acid(s)
BMD	Bone mineral density
СВМ	Cereal-Based Meal(s)
CR1M	Combat Ration One Man
CRP	Combat Ration Pack(s)
DEF(AUST)	Australian Defence Standard Publication
DIAAS	Digestible indispensable amino acid score
DOMS	Delayed onset muscle soreness
DSTG	Defence Science and Technology Group
EAA	Essential amino acid(s)
EB	Energy balance
EE	Energy expenditure
EI	Energy intake
EIMD	Exercise induced muscle damage
FD	Freeze dried
FDM	Freeze Dried Meal(s)
FFM	Fat-free mass
HBV	High biological value
IGF-1	Insulin-like growth factor 1
IOC	International Olympic Committee
LBV	Low biological value

DSTG-GD-1174

LM	Light Meal(s)
MM	Main Meal(s)
MBM	Meat Based Meal(s)
MPS	Muscle protein synthesis
MRDI	Military Recommended Dietary Intake(s)
ΝΑΤΟ	North Atlantic Treaty Organization
NPB	Negative protein balance
NEB	Negative energy balance
NHMRC	National Health and Medical Research Council
PCr	Phosphocreatine
PDCAAS	Protein Digestibility Corrected Amino Acid Score
P:F:C ratio	Protein:Carbohydrate:Fat ratio
PR1M	Patrol Ration One Man
RDA	Recommended Daily Allowance (United States)
RDI	Recommended Dietary Intake(s)
RNC	Recommended Nutritional Criteria
RTE	Ready-to-eat
SSR	Special Support and Reconnaisance
TVP	Textured vegetable protein
VBM	Vegetable-Based Meal(s)

Defence FOI 386/22/23 Document 5

#### **OFFICIAL**

DSTG-GD-1174

## 1. INTRODUCTION

Australian Defence Force (ADF) combatants perform a wide range of physically and cognitively demanding tasks during field training and deployment. Completing these tasks requires endurance, strength, power, agility and vigilance (Nevin 2017). Combatants may experience negative energy balance, thermal stress, mental fatigue, and a range of other physiological and psychological stresses that are metabolically challenging, and thereby influence nutritional requirements. Inadequate nutritional intakes may impede mission success, with potential implications including diminished physical and cognitive performance, decreased productivity, increased risks of illness and injury, and reduced numbers of deployable combatants.

Combat Ration Packs (CRP) are provided during field training and deployments when it is not possible to provide fresh foods. Currently, two 24-hour individual CRP are used by the ADF: the Combat Ration One Man (CR1M) and Patrol Ration One Man (PR1M). The CR1M is a 'general purpose' CRP, suitable for use by ADF members under almost all circumstances other than special operations. The PR1M is a 'special purpose' CRP, reserved almost exclusively for special operations.

The quantity of protein provided in ADF CRP is based on the 2009 Recommended Nutritional Criteria (RNC), which sets a requirement for the total protein content of CRP (Forbes-Ewan 2009). Since 2009, further research has been conducted related to the protein requirements of combatants, including the quantity, quality and timing of protein needed to maximally facilitate recovery and adaptations following vigorous physical activity (Maughan et al. 2018; Jäger et al. 2017; Longland et al. 2016; Burke & Deakin, 2015; Pasiakos et al. 2015a). In particular, studies into protein quality (i.e. amino acid profile), doses and timing have further elucidated how daily protein intake should be distributed in meals and snacks to maximally facilitate muscular recovery and adaptations. The adequacy of the quantity, quality and distribution of protein in current CRP is uncertain, as there are currently no requirements to standardise the quality or distribution of protein in the Main Meals (MM), Light Meals (LM), beverages or snacks provided in CRP. Thus, the opportunity exists to align the protein delivered by CRP with the need to sustain and enhance the health, well-being, and physical and cognitive performance of combatants.

Accordingly, this report examines newly published scientific literature relevant to combatants' protein and amino acid requirements for optimal health and performance. Recommendations are made on the optimal quantities, quality, sources and distribution of protein and amino acids (AA) within CRP, and the optimal timing of protein intake. This

aims to cater for combatants with varied energy requirements due to alterations in operational tempo, duration, stress, climate, and location, thereby providing them with a competitive edge on the battlefield. In closing, the report evaluates the readiness of inservice CRP, including the individual components they provide, to deliver against the protein recommendations. Lastly, recommendations are made for improving the protein provided by CRP.

#### 1.1. Importance of Protein

Protein is a component of all living cells, and is a nutrient of vital importance to health, performance, and recovery from vigorous physical activity. Dietary protein provides the body with the AA required for the maintenance, synthesis and enhancement skeletal muscle, ligaments, tendons, collagen and bone (Young et al. 1994). Proteins of this kind are termed *structural* proteins. Biochemical reactions in the body typically depend on *functional* proteins (enzymes) as catalysts. AA can also be used as metabolic messengers, as well as in transport, storage, signalling, and immune functions (Burke & Deakin 2015; NHMRC 2006; Pasiakos et al. 2015a; Pasiakos et al. 2015b; Young et al. 1994). The protein requirements of combatants may increase during periods of negative energy balance, as well as in response to strength training and prolonged physical activity (Jager et al. 2017).

#### 1.2. Physiology of Protein Utilisation

Unlike carbohydrate and fat, the body does not store excess protein as an energy reserve. Proteins within the human body (e.g. those found in skeletal muscle) are extremely dynamic, and are continuously being catabolised (broken down) to AA and resynthesised. For example, studies show that 1–2% of skeletal muscle mass is turned over each day (Koopman & van Loon 2009). Therefore, combatants depend on sufficient daily intake of protein for the maintenance and optimisation of skeletal muscle, as well as many other bodily processes that are vital to health and performance (Burke & Deakin 2015).

Of the 20 common AA in nature, 11 can be made in the human body, while the remaining 9 must be obtained through the diet (NHMRC 2006). These are designated essential amino acids (EAA). Inadequate protein intake, particularly of the 9 EAA, can have negative consequences on all human tissues and lead to declines in muscle mass, physical power and strength, immunity, and rate of wound healing, and may also result in an increased risk of musculoskeletal injuries (Burke & Deakin 2015; Nindl et al. 2007; Longland et al. 2016). All these factors can adversely affect the health and performance of combatants, and thereby may compromise mission success.

DSTG-GD-1174

## 1.3. Physiology of Skeletal Muscle Recovery and Adaptation

Following vigorous physical activity, such as resistance training and endurance exercise, the rates of both muscle protein synthesis (MPS) and muscle protein breakdown (MPB) increase. MPS refers to the synthesis of new functional muscle from AA, and MPB refers to the degradation of muscle protein back to AA (Witard et al. 2021). The increase in the rate of MPS is approximately 2.5 times that of MPB following resistance training (Biolo et al. 1995). A number of studies have shown that acute rates of MPS are predictive of long-term gains in muscle growth in response to training and nutritional interventions (Damas et al. 2016; Wilkinson et al. 2007; Hartman et al. 2007; Volek et al. 2013). This relationship is apparent in individuals with previous training experience, and becomes apparent in untrained individuals in a time-dependent manner as they progress in a training program (Damas et al. 2016; Brook et al. 2015). MPS is regulated by AA availability (Kimball & Jefferson 2002), which is determined by the quality and quantity of dietary protein intake. As a result, measurements of MPS rates are widely used as a method for determining the effectiveness of nutritional interventions in enhancing muscle repair and growth over the acute period (e.g. 4-6 hours) following vigorous physical activity such as resistance training (Atherton & Smith, 2012; Witard et al. 2021). This report discusses studies that have measured MPS rates to evaluate the effectiveness of manipulating protein intakes in enhancing muscle repair and adaptation in conjunction with physical activity.

## 2. PROTEIN AND THE MILITARY

### 2.1. Combatants' Protein Requirements

#### 2.1.1. Recommended Daily Intakes

In Australia, the Recommended Dietary Intake (RDI) for protein in civilians is based on the estimated requirement in grams per kilogram of body weight (g/kg) per day, as determined by the National Health and Medical Research Council (NHMRC). For the general adult population, the RDI for protein to maintain nitrogen balance and prevent deficiency is based on 0.75 and 0.8 g/kg for women and men, respectively (NHMRC 2006). Protein intakes lower than the RDI may result in net protein catabolism, negatively affecting health and performance. When protein requirements are increased above the RDI, such as during periods of heavy physical activity, higher protein intakes are needed to prevent protein catabolism (Longland et al. 2016; Pasiakos 2020).

Combatants constitute a unique subgroup of the population, requiring protein intakes greater than the general population to cope with the wide range of physically demanding tasks they perform. Forbes-Ewan (2009) adapted the current RDI for the general population to suit the unique needs of ADF combatants and denoted these as Military Recommended Dietary Intakes (MRDI) (Forbes-Ewan 2009). The MRDI established for protein are higher than the RDI for the general population, equating to 1.5–2.0 g/kg for an adult male combatant.

In addition to RDI, the NHMRC defines Acceptable Macronutrient Distribution Ranges (AMDR<sup>1</sup>) for protein, fat and carbohydrate. The AMDR include the recommendation that protein provides 15–25% of energy intake (EI) to ensure that the full range of nutrients are consumed at recommended levels, and to reduce the risk of chronic disease (NHMRC 2006). Forbes-Ewan (2009) provided guidance on adjusting the protein AMDR to account for the higher energy demands of ADF combatants (16–18 MJ/d) while remaining within the daily protein targets expressed relative to body weight (1.5–2.0 g/kg).

For ADF combatants expending 16 MJ/d or 18 MJ/d, Forbes-Ewan (2009) recommended that protein contribute 13-18% and 12-17% of total EI, respectively. Given that the mean weight plus or minus the standard deviation of Australian combatants is  $83.7 \pm 12.5$  kg

<sup>&</sup>lt;sup>1</sup> The AMDR is an estimate of the range of intake for each macronutrient for individuals (expressed as per cent contribution to energy), which would allow for an adequate intake of all the other nutrients whilst maximising general health outcome (NHMRC 2006).



DSTG-GD-1174

(Tomkinson et al. 2017), this corresponds to daily protein intakes of 125–172 g/d (or 1.5-2.0 g/kg for a combatant weighing ~84 kg and expending 16 MJ/d) and 129–183 g/d (or 1.5-2.2 g/kg for a combatant weighing ~84 kg and expending 18 MJ/d), respectively. For general purpose CRP (providing 16 MJ), Forbes-Ewan (2009) suggested that the RNC for protein be 122–150 g (equating to 1.5-1.8 g/kg for an average combatant weighing ~84 kg).

In 2013 a consensus statement was published for the United States military, recommending that combatants consume 1.5–2.0 g/kg during field training and deployment (Pasiakos et al. 2013). Furthermore, the Minimum Nutrition Content Standard established for protein in the 2013 iteration of the North Atlantic Treaty Organization (NATO 2013) nutrition recommendations for operational rations (equivalent to CRP) was based on a protein intake of 1.5–2.0 g/kg in military situations. For NATO soldiers with an average body weight of 79 kg and almost all being less than 92 kg, a protein content for operational rations of 118–185 g (1.5–2.0 g/kg) was set.

The authors of this report recommend that for Australian CRP, based on an average 84-kg male combatant, and to provide the majority of Australian combatants weighing up to 96 kg with at least 1.5 g/kg of protein, the lower level of the range should be 144 g protein (1.7 g/kg for an average 84-kg combatant; 1.5 g/kg for a 96-kg combatant). Further, it is recommended that the upper level of the range of protein for Australian CRP should be set at 168 g (or 2.0 g/kg for an average 84-kg combatant; 1.8 g/kg for a 96-kg combatant).

Recent controlled laboratory studies have shown that even higher protein intakes—of 1.6–2.4 g/kg—maximally mitigate the losses of skeletal muscle that occur in situations involving energy deficits of  $\leq$  40% (Longland et al. 2016; Murphy et al. 2018; Pasiakos 2013; Pasiakos et al. 2015b; Pasiakos 2020; Witard et al. 2014). However, combatants are commonly in even greater negative energy balances while subsisting on CRP during real-world training and deployment (Karl et al. 2021). For example, a study conducted in 2016 found that Australian combatants consumed on average ~8.7 MJ/d during a 6-day period despite provision of  $\geq$  16 MJ/d (corresponding to an EI of ~54% of their estimated EE) (McLaughlin et al. 2018). In a recent Norwegian study, soldiers were reported to be in severe energy deficits over a 10-day field training exercise, corresponding to almost 80% of their estimated EE (Ofsteng et al. 2020). In that study, no differences in body composition were observed following the consumption of high (2.0 g/kg) versus low (1.0 g/kg) protein diets. However, the authors identified methodological uncertainties due to the timing of post-exercise body composition measurements (Ofsteng et al. 2020).

High discard rates of CRP foods corresponding to  $\geq$  40% of their total energy content are common, being an almost universal finding (Booth et al. 2003; Forbes-Ewan 2009; Murphy et al. 2018; O'Leary et al. 2020; Richmond et al. 2014; Tassone & Baker 2017). These high discard rates also lead to energy deficits in combatants, leading to reductions in body weight and body energy reserves. When these occur over a prolonged duration, large cumulative energy deficits can increase the risk of loss of strength and muscular endurance (see <u>Section 2.4 Protein and Performance</u>). Factors contributing to inadequate EI while subsisting on CRP include 'field stripping' of CRP to save space for other mission-specific equipment or to lighten the load carried, as well as suppressed appetite, limited eating opportunities, and dislike of the food provided (McLaughlin et al. 2018).

McLaughlin et al. (2018) found that mean protein intake—76 g/d; 0.9 g/kg—was also inadequate, despite provision of 124–132 g/d. As discussed earlier, daily protein intakes should be in the range 1.5–2.0 g/kg in metabolically challenging situations to optimally build, repair, maintain and synthesise skeletal muscle (Pasiakos et al. 2015a; Pasiakos et al. 2013; Karl et al. 2021). This level of daily protein intake is also applicable to combatants operating in extreme environments, such as temperature extremes, as protein needs do not appear to be greater in such situations (Pasiakos 2020).

#### Key Message

Australian CRP providing either 16 MJ or 18 MJ should provide 144–168 g of protein (or 1.7–2.0 g/kg for an average combatant weighing 84 kg and 1.5–1.8 g/kg for a combatant weighing 96 kg). Accordingly, a revised RNC of 144–168 g of protein should be adopted for CRP delivering 16–18 MJ. This translates to 15–18% and 13–16% of the total energy content of CRP menus delivering 16 MJ and 18 MJ, respectively.

#### 2.1.2. Per-Meal Protein Recommendations during Recovery

Further to recommended total daily protein intake, per-meal protein doses have been recommended to maximally stimulate MPS during recovery following vigorous physical activity, such as resistance and endurance exercise. Combatants are unlikely to engage in structured and periodised resistance or endurance training while undertaking field training or deployment while subsisting on CRP. However, they are often required to undertake physically-demanding tasks in unfamiliar terrain and to carry heavy loads over long distances. These tasks will lead to muscle damage, thus combatants require higher-than-usual protein intakes to promote muscle repair and recovery, and to optimise skeletal muscle function. Moreover, with limited time to recover between tasks, they require rapid and maximal muscular recovery between bouts of physical activity.

DSTG-GD-1174

Per-meal protein recommendations to maximise MPS have been developed based on research conducted in healthy adults during energy balance. A landmark study by Moore et al. (2009) provided varying amounts of protein to healthy young men with resistance training experience following a bout of intense resistance training. A threshold for maximal MPS over the four hours following resistance training was identified as a 20 g dose of high biological value (HBV)<sup>2</sup> whole egg protein, which translated to a dose relative to body weight of 0.23 g/kg per meal (Moore et al. 2009). These per-meal recommendations would appear inadequate for CRP to meet combatants' total daily protein requirements (of 144–168 g). Of greater relevance to combatants is a study by Murphy et al. (2016), which provided evidence for benefits from higher per-meal intakes of protein of approximately 30–40 g (~0.4 g/kg) for older adults, compared with 20 g (0.24 g/kg) for younger adults (Moore et al. 2009). The rationale for this was that it would overcome the age-related, skeletal muscle anabolic resistance which results in loss of muscle mass (sarcopenia) and reductions in muscle strength and function (Murphy et al. 2016). Similar physiological changes in muscle have been observed when combatants move to higher altitudes (Pasiakos et al. 2017). However, as previously mentioned, these studies were conducted among participants in energy balance and therefore may have limited relevance to combatants who are often in significant energy deficits (Gwin et al. 2020).

A recent comprehensive review by Gwin et al. (2020) found only two studies that investigated MPS rates following exercise and a single dose of protein among healthy adults during moderate energy deficit (~30% of energy requirements). The first, by Areta et al. (2014), found 30 g of HBV whey protein stimulated MPS to a greater extent than 15 g of HBV whey protein over the 3 hour period following exercise and protein ingestion. The second found high (0.3 g/kg or ~24 g) EAA ingestion enhanced whole body protein synthesis and net protein balance compared to standard (0.1 g/kg or ~8 g) EAA ingestion over the 3–7 hour period following exercise and protein ingestion (Gwin et al. 2021). Gwin et al. (2020) highlighted the importance of examining MPS rates in addition to whole body protein synthesis, whole body protein breakdown and net protein balance when assessing the effectiveness of nutritional interventions in maximally supporting muscle mass during energy deficit. This is because, in addition to muscle, AA are required elsewhere in the body for protein synthesis to offset the protein breakdown that occurs during energy deficit (Gwin et al. 2020).

<sup>&</sup>lt;sup>2</sup> High biological value (HBV) protein is dietary protein derived from sources of animal origin such as beef, chicken, egg and milk, as well as isolated soy protein. HBV proteins contain an optimal EAA profile to maximally stimulate skeletal and whole-body muscle protein synthesis, compared to lower biological value (LBV) plant-based proteins.



Few studies have investigated the effectiveness of nutritional interventions in maximising MPS and whole body protein status during larger energy deficits of  $\geq$  40% of requirements. A study by Margolis et al. (2016), conducted with Norwegian soldiers during arctic training, found that providing four bars per day containing 20 g of HBV whey protein each resulted in similar levels of whole body protein loss compared with providing four bars per day containing of 20 g of carbohydrate each (Margolic et al. 2016; Gwin et al. 2020). However, as this was a field study, it was not possible to control participants' energy intakes, and those who received the carbohydrate bars consumed significantly greater amounts of total energy which may have influenced the results.

Further research is required to support the development of per-meal protein recommendations for combatants to maximally promote muscle recovery, adaptation and maintenance during periods of energy deficits of  $\geq$  40% of requirements. Until further research is conducted, in accordance with the per-meal protein intakes recommended by Murphy et al. (2016), the authors of this report recommend that two CRP MM should each contain $\geq$  0.4 g/kg, which translates to an absolute dose of  $\geq$  30 g of HBV protein. These should be provided in conjunction with a range of protein-rich snacks, beverages and LM, as discussed in the following subsection, in order to maximally facilitate muscle adaptations and recovery.

#### Key Message

Based on current evidence, it is recommended that combatants subsisting on CRP should be supplied with meals containing 0.4 g/kg per MM. This equates to absolute protein content of 30 g HBV protein per MM based on a combatant with an average weight of 84 kg. These per-meal recommendations may assist combatants in achieving the daily protein intakes recommended (1.5–2.0 g/kg), while promoting an even distribution of HBV protein intake.

### 2.1.3. Protein Dose and Timing Recommendations during Recovery

Over the past decade, protein timing strategies have been investigated for their role in enhancing training adaptations and recovery following vigorous resistance and endurance activity. A single bout of vigorous physical activity, such as resistance exercise, can enhance MPS for at least 24–48 hours. Consequently, over this period dietary protein is required to facilitate adaptations (Phillips et al. 1997). Similarly, protein intake is important during recovery from endurance training, to facilitate improvements in aerobic capacity through increases in the number of mitochondria in skeletal muscle cells (Knuiman et al. 2018). Similar to the studies underpinning the per-meal protein recommendations, much of the research on the timing of repeated protein doses during recovery has focussed on healthy adults during energy balance, rather than combatants

DSTG-GD-1174

who are often in significant energy deficits. This research has shown that by providing sufficient amounts of HBV protein at appropriate regular intervals (every 3–4 hours) after vigorous activity—both resistance and endurance—optimal AA can be provided to enhance MPS, and thereby maximally stimulate recovery and muscular adaptations (Burke & Deakin 2015; Kato et al. 2016; Knuiman et al. 2018; Moore & Stellingwerf 2012; Thomas et al. 2016; Jager et al. 2017).

Early work by Moore et al. (2009) identified 20 g (or 0.23 g/kg) of HBV protein as the threshold at which MPS is maximally stimulated in young adults in energy balance over the early post-exercise period (4 h). Further work by Areta et al. (2013) investigated both the optimal timing and dose of protein consumption in young adults in energy balance over a more prolonged recovery period (12 h) following resistance training. Repeated ingestion of 20 g of protein every 3 hours was found to support greater rates of MPS compared with identical total amounts of protein consumed either as 10 g every 1.5 hours or 40 g every 6 hours (Areta et al. 2013).

Evenly distributing of protein intake throughout the day has also been shown to enhance MPS among older adults in small to moderate energy deficit following resistance exercise. Murphy et al. (2015) provided two groups of participants with energy restricted, protein-matched diets, with one group consuming ~25 g of protein at breakfast, lunch and dinner, and the other consuming 10 g, 15 g and 50 g of protein at breakfast, lunch and dinner, respectively. Despite both groups consuming similar total levels of energy (~10.5 MJ and 9.3 MJ) and protein (1.1 g/kg and 1.0 g/kg), those who had a balanced distribution of protein intake throughout the day displayed a 19% increase in MPS (Murphy et al. 2015).

However, many Australians have a skewed distribution of protein intake over the day, favouring the evening meal, with relatively low intakes at breakfast and lunch (Noakes 2018). These lower protein intakes at breakfast and lunch are at odds with current protein timing and distribution guidelines to maximally stimulate MPS to mitigate losses in muscle mass, strength, and function (Noakes 2018). Combatants using current CRP may also follow this skewed pattern of protein intake over the day. For example, there are large variations in the level of protein provided in the MM, and the breakfast-style components provide little protein. Currently, all eight CR1M menus and all five PR1M menus contain natural muesli, which provides only 8 g of protein per serve. Until further research is conducted, in addition to two MM providing 30 g HBV protein each, CRP should provide a range of protein-rich components that can be eaten by combatants every 3–4 hours to stimulate muscle repair and growth. This will promote an even distribution of protein intake throughout the day to stimulate MPS and whole body protein synthesis (Burke & Deakin 2015; Kato et al. 2016; Knuiman et al. 2018; Moore &

Stellingwerf 2012). To achieve this and meet combatants' total daily protein requirements (of 144–168 g), it is recommended that CRP contain one protein-rich LM, styled as a breakfast component, one protein-rich snack, and one protein-rich beverage. One additional protein-rich snack or beverage styled for pre-sleep consumption represents an additional feeding opportunity to promote muscle adaptations and recovery in combatants by further distributing protein intake throughout the day, and possibly improve whole body protein synthesis rates overnight (Reis et al. 2021). In accordance with other recommendations in this report, these should provide 0.3 g/kg per LM and 0.24 g/kg per snack and beverage (Areta et al. 2013; Jager et al. 2017; Murphy et al. 2018; Pasiakos et al. 2017; Reis et al. 2021).

### **Key Message**

Based on current evidence, combatants require an even distribution of HBV protein intake throughout the day to promote MPS. Further to the protein RNC and in conjunction with the recommendations made in <u>Subsection 2.1.2 Per-Meal Protein</u> <u>Recommendations during Recovery</u>, it is recommended that CRP contain:

- two MM, each providing 0.4 g/kg
- one LM providing 0.3 g/kg
- three snacks (including at least one beverage and one styled as a pre-sleep snack or beverage), each providing 0.24 g/kg.

This translates to absolute HBV protein quantities of  $\geq$  30 g per MM,  $\geq$  25 g per LM and  $\geq$  20 g per snack.

Ideally, MM, LM and snacks should be consumed every 3–4 hours. However, it is acknowledged that this may not always be possible due to operational, logistical, and tactical constraints. CRP should be developed to be easily and rapidly consumed by combatants, for example when they are on-the-move. Education and behaviour change strategies should be explored for their ability to promote protein intake in accordance with the recommendations in this report.

# 2.2. Protein Quality (Biological Value)

Although a wide range of foods of both animal and plant origin contain protein, they are not equally valuable for maximising MPS for skeletal muscle maintenance and growth. As described in <u>Section 2.1.1</u>, it is generally accepted that dietary protein sources of animal origin—such as beef, chicken, egg and milk—as well as isolated soy protein, contain an optimal EAA profile and are therefore HBV proteins (Gwin et al. 2020). These HBV

DSTG-GD-1174

protein sources provide the ideal mix of AA to maximally stimulate skeletal and wholebody muscle protein synthesis, compared to lower biological value (LBV) plant-based proteins (Burke & Deakin 2015). Among the milk proteins, whey protein is the most rapidly digested and absorbed, and thereby stimulates MPS in the acute period (3– 4 hours) following exercise to a greater extent than those which are more slowly digested and absorbed, such as casein (Boirie et al. 1997; Dangin et al. 2001; Tang et al. 2009).

Plant-based protein sources, such as legumes and isolated proteins from peas, chickpeas and rice generally lack one or more EAA, have a relatively low digestibility, and contain suboptimal levels of leucine, an important branched chain amino acid (BCAA) (Berrazaga et al. 2019). All these factors contribute to an inferior MPS response to LBV proteins compared with the same quantity of HBV proteins (Berrazaga et al. 2019).

Protein quality, or biological value, has been traditionally assessed using the Protein Digestibility Corrected Amino Acid Score (PDCAAS), and more recently using the Digestible Indispensable Amino Acid Score (DIAAS) (FAO 2011). These methods evaluate the ability of dietary protein to meet human biological AA requirements (Berrazaga et al. 2019; van Vliet et al. 2015). In theory, protein sources with scores closest to 100% have the greatest ability to support both skeletal muscle and whole-body protein anabolism (growth). However, these methods rely on the minimum amounts of nitrogen and AA needed to prevent whole-body protein deficiency, and their validity for assessing the anabolic response of skeletal muscle to dietary protein source is unknown (van Vliet et al. 2015).

Notably, several studies have established that, despite plant-based protein sources such as those of soy origin having PDAAS/DIAAS scores close to those of beef and milk proteins, there appears to be a difference in their ability to stimulate MPS (Phillips 2012; Tang et al. 2009; Yang et al. 2012). Animal protein sources such as beef, chicken, egg, and milk stimulate MPS to a greater extent than plant-based protein sources (e.g. legumes and soy) and are recommended to be regularly consumed (e.g. every 3–4 hours) by combatants during periods of energy deficit (Pasiakos et al. 2013). This may maximise the preservation of fat-free mass (FFM), in particular skeletal muscle mass (Pasiakos et al. 2013; Gorissen & Witard 2017).

Theoretically, comparable rates of MPS may be observed between HBV protein sources and plant-based sources that are either fortified with leucine or consumed in greater quantities, or mixed with other plant-based protein sources (e.g. pea and rice protein), whose EAA contents complement each other. However, limited research exists in humans at the time of this review, and this remains a theoretical concept (Berrazaga et

al. 2019). Until further research is conducted, it is suggested that vegetable-based meals (VBM) within CRP provide a plant-based protein source that provides all EAA (e.g. those of soy origin), or a combination of plant-based protein sources with EAA contents that complement each other (e.g. grains and legumes) in order to improve their biological value. In the latter instance, plant-based protein isolates, such as pea protein and rice protein, could also be added to improve the quantity and quality of available protein.

#### **Key Message**

Combatants should consume a variety of HBV protein sources, such as those from beef, chicken, egg, and milk, every 3–4 hours and in the quantities discussed in <u>Subsection</u> 2.1.2. Protein Dose and Timing Recommendations during Recovery.

### 2.2.1. Leucine

Among the individual AA that are required to stimulate MPS, the most extensively studied is leucine. This is an EAA and can exist alone in supplemental form (as L-leucine), within branched chain amino acid (BCAA) formulations or naturally in animal-based foods such as red meat, poultry, and dairy foods (Rondanelli et al. 2021). Leucine is the only AA that has been consistently shown to initiate MPS within skeletal muscle (Pasiakos and McClung 2011).

Of relevance to combatants subsisting on CRP are the findings of a number of studies that have shown that MPS is elevated both at rest and after resistance exercise following intake of low-protein foods that are supplemented with adequate leucine (i.e. 3-5 g) (Churchward-Venne et al. 2012b; Murphy et al. 2016). A study by Churchward-Venne et al. (2014) showed that supplementing a low-protein mixed macronutrient beverage (providing 6.75 g of HBV protein) with 5 g of leucine produced the same effect on MPS as a high-protein beverage (providing 25 g of HBV protein and 3 g of leucine) following both resistance exercise and rest (Churchward-Venne et al. 2014). Another study by Murphy et al. (2016) reported on the effects of co-ingestion of 5 g of leucine with breakfast, lunch and dinner on MPS rates at rest and after resistance exercise. Participants in this study were randomised to one of two dietary intervention groups. The first consumed a daily level of protein in accordance with the United States Recommended Daily Allowance (RDA) for protein (0.8 g/kg; low-protein group), while group 2 consumed 1.5 times the RDA (1.2 g/kg; high-protein group). MPS rates were determined by muscle biopsy and via oral isotopes. Both groups showed equally enhanced rates of MPS at rest and following resistance exercise when meals were supplemented with 5 g of leucine, regardless of whether participants consumed a low- or high-protein diet (Murphy et al. 2016). These findings have relevance to combatants who do not meet the protein meal and snack recommendations in this report.

DSTG-GD-1174

To our knowledge, further studies to those discussed above that have examined the effects of supplementing low-protein meals and snacks with leucine among adults undertaking vigorous exercise while in severe energy deficit ( $\geq$  40% of energy requirements) have not been conducted. Nevertheless, consideration should be given to leucine supplementation in MM, LM, snacks and beverages that do not achieve the HBV protein recommendations in this report.

In addition, in Australia, fortification of foods with leucine must adhere to current legislative requirements as specified in The Code (FSANZ 2016). The Code stipulates a maximum daily dose of 490 mg of leucine that may be added to food, or may be in the form of a supplementary sports food. This may present a challenge for current MM and LM within CRP, as the additional fortification recommendation exceeds the maximum permitted daily dose for supplementary sports foods. Investigation is warranted into whether additional leucine may be added to CRP meals, as these may not be classed as 'supplementary sports foods' under The Code.

### Key Message

To achieve maximal MPS when rationing is by CRP, increasing the content of lean, HBV protein sources within protein-rich foods that fall short of the recommendations in this report is required in the first instance.

For MM and LM with HBV protein levels below the recommendations of 30 g and 25 g, respectively, consideration should be given to supplementing them with leucine (to a total of 5 g) to enhance MPS. Similarly, consideration should also be given to whether snacks and beverages may also benefit from leucine fortification (to a total of 2–3 g per snack and beverage) if the recommendation of 20 g of HBV protein is not otherwise achieved. To determine the level of supplemental leucine required in MM, LM and protein-rich snacks and beverages that do not meet the recommendations in this report, their leucine content should be analysed.

# 2.3. Protein and Health

### 2.3.1. Immune Function

To function effectively, the immune system requires adequate dietary protein and energy. Inadequate intakes of protein lead to negative protein balance (NPB)<sup>3</sup>, which results in muscle protein being broken down to supply the AA required to maintain physiological processes such as the immune response (Li et al. 2007). Nearly all immune system

<sup>&</sup>lt;sup>3</sup> Negative protein balance occurs when protein breakdown exceeds protein intake.



responses are negatively impacted by malnutrition arising from prolonged deficits in intake of protein and energy (Calder 2014). When undertaking arduous training or deployment involving extreme environmental stressors (e.g. cold, heat or high altitude), while subsisting exclusively on CRP, suboptimal intakes of protein and energy almost inevitably occur (Baker et al. 2020; Berryman et al. 2018; Forbes-Ewan 2009; McLaughlin et al. 2018). This is a risk factor for a compromised immune system and thereby for increased risk of infection (Montero et al. 2002).

### **Key Message**

CRP should deliver protein in accordance with combatants' requirements to maintain and promote immune function.

### 2.3.2. Bone Health and Injury Prevention

Injuries are an unfortunate but common occurrence among active individuals, including combatants, who engage in regular, intense physical activity (Burke and Deakin 2015). A survey conducted in 2015 on retired ADF personnel (predominantly Army) revealed that 30% of all respondents sustained a bone fracture and 27.9% experienced at least one broken bone during their service (Kelsall et al. 2018).

Nutritional intake modulates bone health, including bone mineral density and bone strength (Sale & Elliot-Sale 2019). Of particular importance are intakes of both energy and protein. When El is suboptimal or low, reduced energy availability (EA) places bone health at risk, and can lead to short-term bone stress injuries and longer-term reductions in bone mass and strength (Sale & Elliot-Sale 2019). EA refers to the level of energy being consumed in the diet that is leftover after the energy cost of physical activity is subtracted (Mountjoy et al., 2018). EA is the amount of energy that is available to support all physiological functions, and can be classified as suboptimal when it is in the range of 125–189 kJ/kg FFM/day and low when it is below 125 kJ/kg FFM/day (Burke et al., 2018a; Burke et al., 2018b). During periods of suboptimal and low EA, insufficient energy is available to optimally maintain all physiological functions and many be impaired, including the maintenance of bone (Mountjoy et al., 2018).

As mentioned above, dietary protein intake is vital in the maintenance of bone mineral density and bone strength. Protein contributes to around 30% of bone mass and 50% of bone volume, with the remaining 50% of bone volume being minerals (especially calcium) (Heany 2002). Almost all (~98%) of protein found in bone comprises collagen type 1 tissue, with the remainder being non-collagenous proteins, which form an integral component of bone structure. The latter are implicated in bone quality and fracture resistance (Bonjour 2016; Morgan et al. 2015). For bone growth and remodelling to occur, regular daily protein ingestion is required to stimulate the bone anabolic hormone

DSTG-GD-1174

insulin-like growth factor-1 (IGF-1) (Bonjour 2016). Stimulation of IGF-1 results in a cascade of physiological processes within the body that prompt kidney production of the active form of vitamin D (1,25-dihydroxyvitamin D) (Bonjour 2016). This in turn boosts intestinal absorption of dietary calcium and phosphorous, which positively influences bone mineralisation for growth and remodelling (Bonjour 2016; Heany 2002; Karpouzos et al. 2017). It is thought that these processes, as initiated by dietary protein intake, are essential for net positive bone accrual and remodelling (Mangano et al. 2014).

Indeed, two meta-analyses have found small but positive impacts of higher dietary protein intakes on measures of bone mineral density (Darling et al. 2009; Shams-White et al. 2017). More recently, a meta-analysis found that vegans had a 44% increased risk of fracture than omnivores (Iguacel et al. 2019). The same study also found small but significant reductions in bone mineral density at the femur neck and lumbar spine among both vegans and vegetarians compared to omnivores. The authors noted that many of the nutrients that are critical for bone health, such as HBV protein, calcium and vitamin D, are found in the highest levels in animal food sources, such as fish, meat, eggs, milk and cheese. For vegans in particular, these findings highlight the importance of appropriate diet planning (Iguacel et al. 2019).

### **Key Message**

To protect bone mineral density and reduce the risk of bone stress injuries, combatants should be provided with adequate HBV protein in accordance with the recommendations in this report (see <u>Section 2.1. Combatants Protein Requirements</u>, <u>Subsection 2.1.1 Per-Meal Recommendations during Recovery</u> and <u>Subsection 2.1.2 Protein Dose and Timing Recommendations during Recovery</u>). They should be encouraged to consume these to get sufficient intakes of protein, calcium and vitamin D, as well as minimise energy deficits, to protect bone mineral density and reduce the risk of bone stress injuries.

### 2.3.3. Muscle Repair and Recovery

Exercise-induced muscle damage (EIMD) occurs when combatants experience sudden, unaccustomed vigorous activity, such as taking part in high-intensity operations in unfamiliar terrains. Damage to skeletal muscle fibres results in reductions in muscle function, exercise capacity and force development, and in delayed onset muscle soreness (DOMS), all of which can last for several days and can negatively affect performance (Owens et al. 2019; Thorlund et al. 2011).

Stimulation of MPS is critical to the repair and recovery of skeletal muscle tissue after vigorous activity (Burke & Deakin 2015). It is preferable to consume a source of protein as soon as practically possible after physical activity to provide the AA needed for the muscle remodelling process. However, protein consumed within 24–48 hours after

physical activity still contributes to the enhancement of skeletal MPS and remodelling processes. This further emphasises the need to ensure that CRP contain protein in accordance with the recommendations in this report.

### **Key Message**

Current MM, VBM, LM, snack and beverage components should be modified to improve both energy and protein content to enable combatants to achieve the energy and protein intakes needed to optimise skeletal muscle repair and recovery (see <u>Section 2.1.</u> <u>Combatant Protein Requirements</u>).

# 2.4. Protein and Performance

### 2.4.1. Strength and Power

As previously discussed, in combination with resistance exercise, protein intake promotes the repair and growth of skeletal muscle, and in turn, improves muscular strength and power (Breen & Phillips 2012; Churchward-Venne et al. 2012a; Moore et al. 2009; Stokes et al. 2018). The growth of skeletal muscle depends on the rate of MPS being greater than the rate of MPB. When MPS is greater than MPB, increases in skeletal muscle size (muscular hypertrophy) occur, whereas when MPB is greater than MPS, loss of skeletal muscle occurs (Stokes et al. 2018). Optimising muscular strength and power is a key consideration for combatants, who are frequently required to carry heavy equipment and supplies over long distances, often while exposed to days or weeks of environmental extremes such as heat, cold and/or high altitude.

However, as discussed earlier, combatants are likely to have low intakes of energy and protein when subsisting exclusively on CRP. This often coincides with high levels of physical activity, resulting in NEB—when EE exceeds EI—and increased NPB. Declines in lower-body power and strength have been shown to occur as combatants' cumulative NEB grows (Murphy et al. 2018). Combatants can tolerate a cumulative NEB of up to - 23.8 to -80.0 MJ, equating to -3.4 to -11.4 MJ/d over 7 days or -1.6 to -5.3 MJ/d over 15 days with no or only small (2%) declines in lower-body strength and power (Murphy et al. 2018). However, moderate (8%) to large (10%) declines in lower-body strength and power have been shown to occur when NEB begins to exceed -164.3 MJ and -248.6 MJ over an entire operation, corresponding to a loss of body mass of  $\geq$  8% (Murphy et al. 2018).

As discussed earlier, when NEB is moderate (EI in the range 60–100% of EE), protein intakes in the range 1.6–2.4 g/kg are required to maximally mitigate the losses of skeletal muscle that occur during these periods of energy deficit. However, when NEB is large (EI

DSTG-GD-1174

≤ 60% of EE), regardless of whether protein intakes are low (e.g. 1.0 g/kg) or high (e.g. 2.0 g/kg), MPB tends to occur at similar rates. This is to release energy from protein and/or to provide the AA for essential physiological functions (Berryman et al. 2018; Karl et al. 2021). Losses of skeletal muscle mass can lead to reduced maximal muscle force and rate of force development (Christensen et al. 2008). Thus, reducing the cumulative NEB may promote the preservation of muscular performance during training and deployment (Christensen et al. 2008; Murphy et al. 2018). Further research should explore strategies to achieve this, and should also seek to understand the implications of large cumulative NEB on combatants' recovery of skeletal muscle mass and readiness for reinsertion.

### Key Message

CRP should provide sufficient energy in the form of optimal protein, carbohydrate and fat. Further research is required into strategies that may further assist combatants in avoiding total NEB > -80 MJ (equating to > -11.4 MJ/d over 7 days or > -5.3 MJ/d over 15 days, or > -1.3 MJ/d over 64 days) that results in loss of  $\geq$  3% of body mass.

# 2.5. Combatants' Protein Requirements in Extreme Conditions

High altitudes (3000+ m above sea level) represent a unique environmental situation that has a direct impact on energy and protein requirements. This impact must be considered when designing CRP, as future CRP must be suitable for use at altitudes up to 4000 m (HMSP-A 2015).

EE for the same level of activity increases when combatants move to high altitudes. This can initially be explained by reductions in the partial pressure of oxygen (PO2) (Bergeron et al. 2012; Burke & Deakin 2015; Cymerman 1996; Wing-Gaia 2014). This limits oxygen availability due to decreases in air (barometric) pressure (Burke & Deakin 2015; Cymerman 1996). The body compensates by increasing breathing frequency and heart rate to deliver more oxygen to metabolically active tissues (Burke & Deakin 2015). This physiological process uses more energy, leading to increased EE and higher basal metabolic rate (Wing-Gaia 2014).

Altitude-induced anorexia (loss of appetite) is common in the first few days at high altitude. This may be explained by the effect of high altitude on brain centres controlling appetite and/or altered satiety hormones (Wing-Gaia 2014). This combination of increased EE and reduced EI results in weight loss and dehydration ('hypoxia induced diuresis') during the initial stages of exposure (Wing-Gaia 2014).

During moderate energy deficits ( $\leq 40\%$ ) at sea level, higher protein intakes in combination with resistance training can preserve FFM and may overcome the skeletal

muscle anabolic resistance experienced at high altitudes (Imoberdorf et al. 2006; Longland et al. 2016; Margolis et al. 2018; Pasiakos et al. 2013; Pasiakos 2020). However, energy deficits have been reported as high as 70% of total daily EE among combatants at an altitude of ~4300 m (Berryman et al. 2018). In that study protein intakes of 1.0 g/kg vs 2.0 g/kg resulted in similar reductions in FFM (in particular, skeletal muscle) (Berryman et al. 2018). As a result, Berryman et al. (2018) and others have speculated that severe NEB results in a shift away from whole body protein synthesis in favour of protein oxidation (Hector & Phillips 2018; Pasiakos et al. 2017; Pasiakos et al. 2010; Pasiakos 2020; Witard et al. 2014).

Further, rapid reductions in weight due to severe NEB can lead to reduced strength and power, and a reduction in anabolic hormones such as testosterone and IGF-1, further accelerating loss of FFM (Degoutte et al. 2006; Koral & Dosseville 2009; Nindl et al. 2007; Pasiakos et al. 2017). To ameliorate this effect, higher daily intakes of protein of 2.4–3.5 g/kg have been suggested in an attempt to preserve FFM and reduce decrements in performance (Helms et al. 2014; Longland et al. 2016; Pasiakos et al. 2020).

However, very high protein intakes (e.g. > 3.5 g/kg) may result in displacement of other key nutrients (especially carbohydrate) which are also required in increased amounts at high altitude. Therefore, carbohydrate intake should also be monitored when protein intakes are increased, as carbohydrate may preserve FFM by sparring AA from oxidation for energy (Margolis et al. 2021). A recent study showed that, following muscle glycogen depletion, low carbohydrate intakes (1.5 g/kg) resulted increased BCAA oxidation for energy compared to adequate carbohydrate intakes (6.0 g/kg). Therefore, protein should be consumed with carbohydrate, to provide an alternative source of fuel to the muscles while preserving AA for muscle recovery and adaptations (Margolis et al. 2021).

#### **Key Message**

Further research is needed to understand the optimal provision of protein in CRP designed for use at high altitude. Until further research is conducted, it is recommended that CRP for use at high altitude should provide 144–168 g/d of protein (or 1.7–2.0 g/kg based on an ADF member of average weight, i.e. ~84 kg).

A number of the high-protein LM, MM, snacks and beverages provided in CRP should also be high in carbohydrate in accordance with the recommendations by Keenan et al (In Preparation), to provide fuel to the muscles and preserve AA from oxidation for energy.

Defence FOI 386/22/23 Document 5

# OFFICIAL

DSTG-GD-1174

# 2.6. Amino Acid Supplements

Combatants, like athletes, often seek to enhance their performance and/or body composition with the use of dietary supplements. Compared to the general Australian population, a high prevalence of dietary supplement use has been found among Australian soldiers, with 76% of males and 86% of females reporting the use of at least one dietary supplement at least once a week (Baker et al. 2019). Many AA supplements are available commercially, and those that have potential benefits for combatants warrant consideration for use when rationing is by CRP. For the purpose of this review, these are considered to be  $\beta$ -Alanine (BA), creatine and tyrosine.

According to a recent consensus statement by the IOC, 'good to strong' evidence supports the use of BA and creatine to improve aspects of physical performance (Maughan et al. 2018). BA is an AA and creatine is a compound derived from the AA glycine, arginine and methionine. Lastly, tyrosine is an AA that has been investigated for its potential to improve cognitive performance. However, any decision to supply AA or creatine supplements within CRP to try to achieve performance advantages on the battlefield must be informed by a risk-benefit analysis (Burke 2017). This involves consideration of each supplement's efficacy, legality, safety, practicality and the optimal dose(s) required to elicit beneficial effects.

### 2.6.1. β-Alanine

BA is produced in the liver, is found in some foods (e.g. chicken and red meat), and exists as a supplement in the form of a powder (Trexler et al. 2015). The beneficial effects of BA lie in its ability to increase muscle carnosine levels, which leads to improved intracellular buffering capacity and delayed fatigue during sustained high-intensity exercise (Maughan et al. 2018).

### 2.6.1.1. β-Alanine and Performance

In a recent IOC consensus statement, BA supplementation is regarded as having 'small, but potentially meaningful performance benefits (of ~0.2–3%) during both continuous and intermittent exercise tasks of 30 seconds to 10 minutes in duration' in sports situations (Saunders et al. 2017; Baguet et al. 2010; Chung et al. 2012; Maughan et al. 2018). In the military context, supplementation has been shown to improve performance in a 50-m casualty carry (Hoffman et al. 2015b). In addition to physical performance, BA supplementation has been investigated for maintaining aspects of cognitive performance, such as reaction time (Varanoske et al. 2018; Pomeroy et al. 2020). However, limited evidence exists to indicate a cognitive benefit in humans (Varanoske et al. 2018; Pomeroy et al. 2020).

### 2.6.1.2. β-Alanine Dose

Effective supplementation protocols involve consuming 3–6 g of BA (in powder form) in divided doses (0.8–1.6 g four times per day) for a period of 4–12 weeks (Hoffman et al. 2015a; Hoffman et al. 2015b; Maughan et al. 2018; Stellingwerff 2020).

The dosing protocols required for an ergogenic response from BA supplementation also present practical challenges within military environments where CRP are used. Firstly, chronic loading doses are required (as described above) before performance benefits are observed, and these may not be practicable given the relatively short notice that combatants may have for deployment. Although CRP may be used for extended periods in emergency situations, they are most frequently used for no more than 16 days, which would be insufficient time to achieve the required loading dose.

Secondly, taking four doses of BA per day—either as a powder or as a food component—while undertaking field training or deployment could be difficult due to competing tasks and time restraints. This is exacerbated by combatants' habitual practice of not meeting energy and nutrient requirements when rationed with CRP. Further, the effect of NEB on the biological fate (and effectiveness) of BA is unknown; therefore, further research is warranted before BA could be recommended for use as an ergogenic aid.

### 2.6.2. Creatine

Creatine is the most used and most thoroughly researched ergogenic aid in human physical performance. In this review, 'creatine' refers to creatine monohydrate, the form of creatine that has been extensively studied and has been shown to improve physical performance (Maughan et al. 2018). It is almost exclusively found in the muscles of animals and in seafood (Kreider et al. 2017). It is beyond the scope of this paper to outline the metabolic role of creatine—for this, the reader is referred to Kreider et al. (2017) for a comprehensive overview.

### 2.6.2.1. Creatine and Performance

Creatine supplementation is highly effective in increasing muscle stores of phosphocreatine (PCr). PCr is the fuel source required for the resynthesis of adenosine-triphosphate (ATP) —a molecule that provides the energy needed for exercise of short duration (< 30 sec) at high intensity (Kreider et al. 2017). Through this mechanism, creatine supplementation is effective in increasing skeletal muscle mass, strength and power in response to chronic resistance training programs (Maughan et al. 2018).

Defence FOI 386/22/23 Document 5

# OFFICIAL

DSTG-GD-1174

### 2.6.2.2. Creatine and Thermoregulation

Creatine may also provide thermoregulatory benefits in the heat, by enhancing heat tolerance due to its osmotic properties (Kreider et al. 2017). Loading creatine in doses of 25 g/d for 7 days (rapid loading phase with 5 x 5-g servings per day) followed by 5 g/d for 21 days (maintenance phase) results in 1–2 kg increase in total body water (Powers et al. 2003). Kilduff et al. (2004) reported increases in intracellular water volume and beneficial thermoregulatory and cardiovascular responses such as reduced heart rate, lower rectal temperature and decreased sweat rate after prolonged vigorous activity in the heat as a result of supplementation with creatine.

This hyperhydration may partially offset the deleterious effects of heat-related illness that can result from exposure to extreme heat, with subsequent decrements in performance. Early anecdotal reports had suggested that supplementation with creatine may actually lead to impaired heat tolerance. However, in a comprehensive review, Lopez et al. (2009) concluded that there were 'no differences in body temperature with creatine supplementation, and some even showed that creatine attenuated the rise in body temperature during vigorous activity in the heat.' However, at the time of writing this report, no evidence exists regarding the thermoregulatory effects of creatine in the military context. Further research would be necessary before creatine supplementation could be recommended for enhanced thermoregulation in combatants.

#### 2.6.2.3. Creatine and Cognitive Performance

Substances that enhance or assist in maintaining cognitive performance are termed cognitive aids, or nootropic substances. Like skeletal muscle, the brain is a highly metabolically active organ that uses ATP for energy (Dolan et al. 2018). Interest has grown in the scientific community on whether creatine supplementation may increase creatine levels in the brain as well as in the muscles, and thereby enhance cognitive performance. Approximately 95% of the body's creatine stores are found in skeletal muscle, with most of the remaining 5% being in the brain (Dolan et al, 2018). Less is known about the potential for nootropic effects from creatine supplementation compared to physical performance enhancement, however preliminary research has been conducted in this area.

Improvements in cognitive function associated with creatine supplementation have been shown after exposure to cognitive stressors such as sleep deprivation and hypoxia (McMorris et al. 2006; McMorris et al. 2007; Turner et al. 2015; Twycross-Lewis et al. 2016). McMorris et al. (2007) reported that creatine supplementation led to partial improvements in cognitive performance involving complex tasks among individuals who were concurrently undertaking moderate-intensity exercise (intermittent stair-climbing,

step-ups and walking) every two hours while sleep-deprived. Therefore, research is limited, and differences between cognitive performance tasks between studies may not be relevant to military operations.

Turner et al. (2015) built a case for a neuroprotective role for supplemental creatine during acute oxygen deprivation. As combatants may operate in extreme environmental conditions such as high altitude while sleep-deprived, the findings of Turner et al. (2015) could have military relevance. Following seven days of creatine supplementation (20 g/d), these researchers found that stores of creatine within the brain increased. This was associated with reduced cognitive decline through enhanced attentional capacity (Turner et al. 2015). These findings could have relevance for combatants deployed on missions at high altitude, but further research is warranted.

A cautious approach would be appropriate in applying the above findings regarding possible cognitive benefits of creatine supplementation in military populations, given that the effects of creatine on cognitive performance during military-specific tasks have not been investigated.

### 2.6.2.4. Creatine Dose

2.6.2.5. Recommended dose protocols for creatine supplementation typically follow a rapid loading phase (5 x 5 g split dose for 5–7 days) followed by a maintenance phase (3–5 g per day for 21 days) to effectively increase and maintain elevated body creatine stores (Kreider et al. 2017; Maughan et al. 2018; Twycross-Lewis et al. 2016). Combining consumption of creatine with 50 g of carbohydrate or protein further accelerates uptake of creatine within skeletal muscle, possibly due to the anabolic effect of insulin (Steenge, Simpson & Greenhaff 2000). Similar to BA, these present practical challenges within military environments where CRP are used (refer to discussion in <u>Section 2.6.1.2. β-Alanine Dose</u>).

### 2.6.2.6. Creatine Safety

Early concerns related to the safety of creatine supplementation have been shown to be largely unfounded, and well-controlled clinical trials are yet to find any adverse effects of creatine supplementation when taken according to the correct protocols (Kreider et al. 2017). Although renal dysfunction resulting from creatine supplementation is commonly reported in the early literature on creatine supplementation, this is limited to individuals with pre-existing renal disease (Kreider et al. 2017). Apart from weight gain associated with acute loading of creatine, there do not appear to be any adverse health or performance effects of creatine supplementation up to 30 g/d for five years (Kreider et al. 2017; Powers et al. 2013).

DSTG-GD-1174

### 2.6.3. Tyrosine

Tyrosine—a non-essential AA that occurs naturally in many high-protein foods—is a key precursor for the synthesis of the catecholamines dopamine and noradrenaline (Pomeroy et al. 2020). These catecholamines are required to facilitate effective cognitive performance in stressful situations such as sleep deprivation, physically-demanding activity, altitude exposure and exposure to extremes of temperature (O'Brien et al. 2007). It is not uncommon for combatants to be exposed to these stressful situations, often in combination.

### 2.6.3.1. Tyrosine Dose and Performance

Studies have reported improvements in cognitive performance with acute ingestion (1–2 hours prior to exercise/stressful event) of tyrosine in doses ranging from 2 g (Colzato et al. 2013; Colzato et al. 2014); Colzato et al. 2015; Deijen et al. 1999; Deijen and Orbleke 1994; Jongkees et al. 2015), to 150 mg/kg (Magill et al. 2003; Steenbergen et al. 2015; Thomas et al. 1999). However, due to methodological differences between studies, and concerns pertaining to the quality of the studies conducted to date, firm conclusions regarding the efficacy of tyrosine supplementation cannot be made (Pomeroy et al. 2020).

Moreover, military environments expose combatants to unpredictable scenarios. Therefore, inclusion in CRP of tyrosine to improve cognitive performance is not recommended at this time.

### 2.6.4. β-Alanine, Creatine and Tyrosine: Summary and Recommendations

Although supplements such as  $\beta$ -alanine and creatine are beneficial to aspects of athletic performance when correct dosage protocols are followed, insufficient research has been conducted within the military context to elucidate their efficacy for combatants. The loading and dosage protocols required present clear challenges in unpredictable military scenarios, and CRP may not be the most appropriate vehicle for delivering such ergogenic aids. Based on current evidence, it is not recommended that AA supplements be provided in CRP. However, in the rapidly changing field of sports and performance nutrition, it is recommended that a watching brief be maintained on the potential of ergogenic and cognitive aids to enhance military performance. Moreover, it is recommended that DSTG take the responsibility for maintaining this watching brief.

# 3. RECOMMENDATIONS FOR CRP

Based on the evidence presented in <u>Section 2. Protein and the Military</u>, the authors recommend that the RNC for CRP be revised to 144–168 g of protein for CRP delivering 16 and 18 MJ. In terms of the percent energy contribution from protein, this translates to 15–18% and 13–16% of the total energy content of CRP menus delivering 16 MJ and 18 MJ, respectively. Further to the protein RNC, to ensure that the quantity and quality of protein in CRP can enable combatants to achieve an even distribution of protein intake over a 24-hour period in accordance with their requirements, the following distribution and mode of delivery for HBV protein provision is recommended:

- main meals; two MM containing ≥ 30 g of HBV protein, intended to be consumed as a lunch and dinner meal
- light meal; one LM containing  $\geq$  25 g of HBV protein, styled as a breakfast meal
- high protein snack components (those considered good sources of protein); one snack containing ≥ 20 g of HBV protein
- high protein beverage (those considered good sources of protein); one containing ≥ 20 g HBV protein
- one beverage or snack intended as a pre-sleep component containing ≥ 20 g of casein or whey protein.

CRP should provide a range of protein-rich components. A number of these high-protein LM, MM, snacks and beverages should also be high in carbohydrate in accordance with the recommendations by Keenan et al. (In Preparation), or ideally be consumed in conjunction with high-carbohydrate foods, to preserve AA from oxidation for energy. For ease of use, where possible, food and beverages should be in the form of readily and rapidly consumable components. Consumption of MM, LM and high-protein snacks and beverages every 3-4 hours should be encouraged, to provide the protein needed to promote recovery and optimal adaptation to extremes of activity and NEB (see <u>Subsection 2.1.1 Per-Meal Recommendations during Recovery</u> and <u>Subsection 2.1.2</u> Protein Dose and Timing Recommendations during Recovery).

### 3.1.1. Main Meals

The recommended content of protein for MM (30 g of HBV protein) is at the lower end of the range of the per-meal recommendations outlined in <u>Subsection 2.1.1. Per Meal</u> <u>Recommendations during Recovery</u> and <u>Subsection 2.1.2 Protein Dose and Timing</u>

DSTG-GD-1174

<u>Recommendations during Recovery</u>). This is to ensure that the minimum quantity and quality of protein required to elicit maximal stimulation of MPS is provided. Ideally, combining a red meat (beef, lamb or pork) MM with a white meat (fish or chicken) MM within each menu would enhance nutritional content and increase variety (thereby mitigating menu fatigue). Having each MM provide 30 g of HBV protein would ensure that MM consistently provide similar quantities and quality of protein, thereby allowing substitution of menu items without variation in protein content.

### 3.1.2. Light Meals

LM could be made from HBV protein sources (e.g. egg) or be cereal-based choices (e.g. porridge and muesli). If cereal-based, LM should also contain a dairy source (e.g. powdered milk or whey protein powder) to ensure the HBV protein recommendations are met. Having a number of LM options, including breakfast-style LM, of equivalent protein quality and quantity ( $\geq$  25 g HBV protein) would enable CRP menus to offer variety and likely lead to increased intake. LM should contain a balance of protein and carbohydrate to assist in meeting combatants' requirements for both (Keenan et al. In Preparation).

### 3.1.3. Snacks

Snack food options must be easily consumable (eat-on-the-go and out-of-packet). Ideally, snack options should be formulated to maximise delivery of replenishment levels of both protein and carbohydrate (Keenan et al. In Preparation) when consumed between meals. When the operational situation allows, protein-rich snacks should be consumed 3–4 hours post meals to ensure optimal protein intake.

### 3.1.4. Beverages

One beverage should contain  $\geq 20$  g HBV protein (preferably whey protein isolate, as it acts rapidly) and should be consumed as a meal accompaniment with a cereal-based LM to help meet HBV protein recommendations. Alternatively, beverages could be consumed at the mid-point between meals to facilitate optimal spread of protein intake over the 24-hr period (i.e. consuming HBV protein every 3-4 hours). A second protein-rich beverage or food—one designed for pre-sleep consumption— should provide  $\geq 20$  g HBV protein (as discussed in <u>Subsection 2.1.2 Protein Dose and Timing Recommendations during Recovery</u>).

# 4. EVALUATION OF CURRENT CRP AGAINST RECOMMENDATIONS

Presently, DEF(AUST) specifications include protein requirements for a selection of CRP components. These include ready-to-eat (RTE) MM (including meat based meals [MBM], vegetable-based meals [VBM], cereal-based meals [CBM]), and also for freeze dried meals (FDM), LM, bread, beef snacks and dairy components. However, these requirements apply only to the total content of protein, and not to the source or quality of the protein. For milk-based products, the type of protein is specified (i.e. *milk protein*). However, no product specification requires a minimum quantity of protein from a HBV protein source/ingredient. The current specification for a protein drink powder does not identify any requirements for protein.

CRP component (current net weight)	DEF(AUST)	Nominal	Recommended
	Specification	protein	protein
		content (g)	content (g)
Meat-based MM (RTE) (250 g)	10432	15–37.5*	≥ 30 HBV
Cereal-based MM (RTE) (250 g)	10615	≥ 5.0	≥ 30 HBV
Vegetable-based MM (RTE) (250 g)	10518	≥ 12.5	≥ 30 HBV
Fish-based MM (RTE) (250 g)	10385	≥ 22.5	≥ 30 HBV
Freeze-dried meals (110 g)	10505	14.3–49.5*	≥ 30 HBV
Cereal-based LM (dry) (90 g)	10349	Not specified	≥ 25 HBV
Cheese, processed cheddar (56 g)	10368	≥ 10.6	
Tuna (85 g)	10385	14	
Long life bread (65 g)	11100	6.5	
Beef snacks (25 g)	10838	8.8	≥ 20 HBV
Hi-protein drink powder (60 g)	10570	Not specified	≥ 20 HBV
Sweetened condensed milk (50 or 85 g)	10377	≥ 4.5 or ≥ 6.8	
Non-dairy creamer (3 or 15 g)	10378	Not specified	
Skim milk powder (3 g)	10378	≥ 1.0	
Concentrated yeast extract (15 g)	10553	≥ 3.6	

Table 1: Current protein requirements for CRP components compared with protein recommendations

\*Products are categorised as low-, medium- or high-protein

Current CRP nutritional standards identify a requirement for a total content of protein (122–150 g) and do not include specifications related to the quality (e.g. HBV sources), distribution or mode of delivery (Forbes-Ewan 2009). Some menus of the in-service

DSTG-GD-1174

CR1M and PR1M contain adequate levels of protein, however the quality, distribution and mode of delivery does not align with the recommendations in this report. The current suite of CRP components does not support the assembly of CR1M and PR1M that would meet the protein recommendations provided in this report.

# 4.1.1. Combat Ration One Man (CR1M)

At 145 g, the mean protein content of the CR1M 2021/22 is within the recommended range (Table 2). However, with a protein content range of 134–151 g, some CR1M 2020/21 menus fall below the recommended range. Protein contributes 13.6–15.4% of the total energy content, also indicating that some menus fall below the recommended range. Encouragingly, compared to the 2018/19 and 2019/20 CR1M builds, the protein content of the 2020/21 and 2021/22 CR1M increased slightly. However, the quality and distribution of protein in current CR1M builds do not meet the recommendations in this report.

	Energy content	Average protein content	Protein range (g)	Protein contribution to total energy
	(MJ)	(g)		(%)
Recommended	16		144–168	15.0–18.0
requirements	18		144–168	13.0–16.0
Content of in-serv	ice CRP a	gainst recommende	d requirements	
2021/22 CR1M	16.4	145	134–151	13.6–15.4
2020/21 CR1M	17.2	147	135–155	13.1–15.0
2019/20 CR1M	17.0	135	120–149	11.8–14.6
2018/19 CR1M	17.3	138	128–149	12.4–14.4
2019/20 PR1M	16.2	153	141–162	14.5–16.7
2018/19 PR1M	17.3	174	160–185	15.5–17.9

Table 2: Comparison of recommended requirements for energy and protein with the content of in-
service CR1M and PR1M

Source: McLaughlin, Forbes-Ewan & White (In Preparation)

### 4.1.2. Patrol Ration One Man (PR1M)

At 153 g, the mean protein content of the most recent PR1M (2019/20) build is adequate against the total protein recommendation (Table 2). However, with a range of 141–162 g, not all PR1M 2019/20 menus meet the minimum recommendation. Protein contributes 14.5–16.7% of the total energy content, also indicating that not all menus fall within the

recommended range. Moreover, compared to the 2018/19 PR1M builds, the 2019/20 PR1M has undergone a decline in protein content.

### 4.1.3. Individual Components

The list of components that are currently approved for CRP is unlikely to deliver menus that will meet the recommendations for protein. In-service MM partially meet the recommendations for MM (Table A.1 in Appendix A). In-service LM, snacks and beverages do not meet the recommendations for protein (Tables A.2–A.4 in Appendix A). CRP do not contain a casein- or whey-rich beverage or food (providing  $\geq$  20 g HBV protein) for pre-sleep consumption.

### 4.1.3.1. Main Meals (MM)

PR1M menus currently include FDM as MM choices. All in-service FDM provide the recommended minimum amount of protein (30 g), and all contain a HBV source of protein (i.e. beef, lamb, chicken or fish) that provides at least 30 g of protein per serve. The average protein content of FDM is 43 g (range 34–59 g/110 g serve).

CR1M menus currently include both meat-based and vegetable-based RTE MM. Of these, only two MBM (chicken korma and lamb and tomato sambal) are adequate in protein content and quality (i.e. contain 30 g of HBV protein) to meet the recommendations for MM (Table A.1 in Appendix A). The average protein content of the RTE MM is 24 g and 16 g per 250 g serve, for meat-based and vegetable-based MM respectively. Total content is in the range 14–31 g and 15–17 g respectively for MBM and VBM. Increasing the content of lean meat in these products is likely to ensure that the minimum recommended amount of protein from a HBV source is provided. Nine RTE MBM (butter chicken, chicken korma, hearty beef stew, lamb & tomato sambal, lamb casserole, lamb korma, Malay lamb curry, Moroccan lamb, savoury mince) are known to contain all nine EAA (Table A.1 in Appendix A) and qualify as HBV sources of protein. AA analysis of other MM has not been undertaken.

With the exception of VBM, the approved list of MM (including both FDM and RTE MM) offers good variety in the sources of HBV protein (e.g. beef, lamb, chicken and fish). Variety in CRP MM is important, to avoid menu fatigue. MM options currently make the most significant contribution to protein content in both CR1M and PR1M menus. VBM require reformulation to improve their quantity and quality of protein.

### 4.1.3.2. Light Meals (LM)

Within CRP, few LM are good sources of protein for combatants. Neither the current CR1M nor PR1M contains a breakfast-type LM that meets the recommendations for protein. Current cereal-based LM choices (i.e. porridge and muesli), with the addition of

DSTG-GD-1174

sweetened condensed milk—the only approved dairy accompaniment for cereal-based LM—provide 50% of the recommended amount of protein for a LM (Table A.2 and A.5 in Appendix A). Cereal-based LM should be reformulated to provide  $\geq$  25 g of HBV protein from dairy sources such as powdered milk and whey protein powder. The inclusion of egg (a HBV protein source) is also worth considering when formulating breakfast-style meals.

Tuna varieties provide 14–20 g protein per serve (Table A.2 in Appendix A), 5–11 g (20–40%) below the recommended amount for a LM (Table A.2 in Appendix A). Adding a bread accompaniment and the processed cheese to make a 'tuna and cheese sandwich' would provide 26–30 g of HBV protein. However, this is unlikely to be a convenient eat-on-the-move option. Increasing the serving size of tuna varieties to 105–130 g (depending on the flavour/variety) will ensure the minimum recommended protein amount of protein from a HBV source is provided.

### 4.1.3.3. Snacks

Snack options within CR1M and PR1M menus primarily contain carbohydrate, are often sweet, and contain little protein except for the two beef steak bars (Table A.3 in Appendix A). Beef steak bars provide combatants with ~8 g of HBV protein per 25 g serve. While this will contribute to protein needs between MM, it provides less than 50% the recommended protein content for a snack.

### 4.1.3.4. Beverages

Only one beverage option—the protein drink powder—provides protein (~13 g per serve) (Table A.4 in Appendix A). This quantity falls short of the recommended minimum protein content for a high-protein beverage, being 65% of that recommended ( $\geq$  20 g HBV protein). Whey protein (a HBV protein source) is an ingredient in this beverage's formulation, however, as the content of this ingredient isn't standardised, its contribution is unknown. Two AA, L-carnitine and taurine, are added ingredients however neither of these is an EAA. The authors of this report have no knowledge of why this beverage has been supplemented with these AA and recommend that they be removed. In the first instance, a formulation that provides  $\geq$  20 g of HBV protein per serve is recommended.

### 4.1.3.5. Meal accompaniment

Within current CRP menus, meal accompaniments can make valuable contributions toward total available protein. For example, the processed cheese provides 10 g of protein per serve (Table A.5 in Appendix A). The cheese has been found to contain all nine EAA (Appendix B). The protein content of this dairy item is below the level that is considered a protein-rich food source (≥ 20 g HBV protein).

# 5. RECOMMENDED CRP INNOVATIONS

CRP innovations in line with the recommendations in this report are required to ensure that optimal quantities and quality of protein are available to provide the potential for improved protein intakes by combatants. The current CRP configurations do not deliver the recommended protein for CRP to support optimal intake. Improvements to both CRP components and doctrine are required to enable the CRP capability to meet the protein requirements of combatants.

The opportunity exists to improve the protein content and quality of in-service MM, LM, snacks and beverage components, particularly those intended to be protein-rich sources within CRP. Product improvement of existing CRP components should consider the following actions:

- Increase the quantity, and/or improve the quality, of lean meat in MM. Following this, if required, adjust MM serve sizes to ensure the quantity and quality of protein is consistent in providing the minimum amount of HBV protein required to maximally facilitate recovery from, and skeletal muscle adaptations to, vigorous physical activity.
- As an interim measure, increase the quantity of legumes such as lentils and beans in VBM. As these vegetarian protein sources are lower in protein than animal and soy protein sources, it is unlikely that this action alone will provide the minimum recommended level of protein for MM (≥ 30 g) within the constraint of a 250 g serve size. In addition, they are of lower biological value than protein sources of animal and soy origins. It is recommended that the shelf life and acceptability of VBM formulated with alternative vegetarian protein sources such as tofu and textured vegetable protein (TVP) be investigated as a priority action towards meeting the protein recommendations for VBM. VBM formulations containing complementary plant-based protein sources (e.g. a grain and a legume) and that are fortified with complementary plant-based protein isolate powders (e.g. rice and pea protein) should also be evaluated.
- Introduce protein-rich LM, snacks and beverages with either increased or alternative protein sources to boost both the quantity and quality of the protein they provide in order to meet the recommendations. This action is most relevant to the protein-rich LM, snacks and beverages that do not contain protein from dairy, meat or fish, and/or do not contain a sufficient quantity of these protein sources. In the first instance, these components should be formulated with a source of protein of animal origin (i.e. meat, fish, whey protein isolate, or whey protein concentrate), as these sources are of the greatest biological value.

DSTG-GD-1174

• Increase the quantity of whey protein in the protein drink powder so that it provides ≥ 20 g of HBV protein (e.g. from whey protein isolate or whey protein concentrate).

VBM that are formulated with legumes and/or grains as the only protein source(s) are unlikely to meet the protein recommendation (of 30 g of HBV protein per serve) within the constraint of a 250 g serve size due to the lower protein content and quality of most plant-based foods compared to animal-based foods. Formulating VBM with a mixture of plant-based protein sources such as tofu, TVP, legumes (e.g. beans and/or lentils), and including appropriate amounts of plant-based protein isolates will increase the likelihood that combatants meet their EAA needs. TVP— a high protein plant-based food, contains approximately 51 g of protein per 100 g<sup>4</sup>—could assist VBM formulations to meet the recommended protein availability from CRP. Ensuring VBM meet combatants' protein requirements, and provide an equivalent quantity and quality of protein to MBM, may increase their acceptability among both vegetarians and omnivores. Anecdotal reports indicate that VBM are disliked due to being low in protein, particularly among omnivores who occasionally have access to only VBM during field training and deployment (i.e. when only vegetarian menus are available).

In-service FDM are formulated with red meat and fish products as the major source of protein. Including FDM based on poultry, vegetable and cereal would increase the variety of MM, and therefore likely reduce the risk of menu fatigue. The next generation CRP will be required to cater for various religious, cultural and dietary preferences, including vegetarians (HMSP-A, 2015). Inclusion of poultry, vegetable, and cereal-based FDM in future CRP menus would enable the ADF to cater to broader dietary needs and preferences, while concurrently offering greater variety in MM choices through FDM products.

# 5.1. New Products

New product development and/or sourcing optimally formulated commercially-available food and beverage components rich in HBV protein should be considered. . Products to consider include:

- A breakfast-type meal; one formulated with whey protein, egg and/or meat as a protein-rich breakfast-type LM.
- High-protein food bars (with 20 g HBV protein per serve)

<sup>44</sup> USDA Food Database; FoodData Central (usda.gov)

• A protein-rich (20 g of HBV protein) beverage or food designed for pre-sleep consumption.

# 5.2. Specifications and Standards

A review and update of the DEF(AUST) specifications and standards series for CRP is required to ensure that the above recommendations will be met. All individual product specifications for protein-rich foods should identify and specify the quantity and quality of protein required. In addition, there are currently three categories of RTE MBM: A (high protein), B (medium protein), and C (low protein/high carbohydrate) within the specifications for MBM in retort pouches (DEF(AUST)10432, 2018). These categories should be withdrawn, and a single requirement created that meet the increased protein needs of combatants. Further, CRP configuration standards should inform the assembly of menus to ensure that they contain appropriate servings of protein-rich MM, LM, snacks and beverages.

DSTG-GD-1174

# ACKNOWLEDGEMENTS

The authors wish to acknowledge and gratefully thank Bianka Probert, Anna Niec as well as our colleagues from The Technical Cooperation Program (TTCP) nations for their helpful feedback and suggestions in finalising the writing of this report.

# 6. REFERENCE LIST

Atherton, P.J., & Smith, K. (2012). Muscle protein synthesis in response to nutrition and exercise. J Physiol, 590(5), 1049–1057.

Areta, J.L., Burke, L.M., Camera, D.M., West, D.W., Crawshay, S., Moore, D.R., Stellingwerff, T., Phillips, S.M., Hawley, J.A. and Coffey, V.G. (2014). Reduced resting skeletal muscle protein synthesis is rescued by resistance exercise and protein ingestion following short-term energy deficit. Am J Physiol Endocrinol Metab, 306(8), E989–E997. https://doi.org/10.1152/ajpendo.00590.2013

Areta, J.L., Burke, L.M., Ross, M.L., Camera, D.M., West, D.W., Broad, E.M., Jeacocke, N.A., Moore, D.R., Stellingwerff, T., Phillips, S.M., Hawley, J.A., & Coffey, V.G. (2013). Timing and distribution of protein ingestion during prolonged recovery from resistance exercise alters myofibrillar protein synthesis. J Physiol, 591(9), 2319–2331. https://doi.org/10.1113/jphysiol.2012.244897

Baguet, A., Bourgois, J., Vanhee, L., Achten, E., & Derave, W. (2010). Important role of muscle carnosine in rowing performance. J Appl Physiol, 109(4), 1096–1101.

Baker, B.A., Cooke, M.B., Belski, R., & Cairns, J.E. (2020). The influence of training on new army recruits' energy and macronutrient intakes and performance: a systematic literature review. J Acad Nutr Diet, 120(10), 1687–1705. https://doi.org/10.1016/j.jand.2020.06.004

Baker, B., Probert, B., Pomeroy, D., Carins, J., & Tooley, K. (2019). Prevalence and predictors of dietary and nutritional supplement use in the Australian army: a cross-sectional survey. Nutrients, 11(7), 1462. <u>https://doi.org/10.3390/nu11071462</u>

Berrazaga, I., Micard, V., Gueugneau, M., & Walrand, S. (2019). The role of the anabolic properties of plant- versus animal-based protein sources in supporting muscle mass maintenance: a critical review. Nutrients, 11(8), 1825. <u>https://doi:10.3390/nu11081825</u>

Bergeron, M.F., Bahr, R., Bärtsch, P., Bourdon, L., Calbet, J.A.L., Carlsen, K.H.,
Castagna, O., González-Alonso, J., Lundby, C., Maughan, R.J., Millet, G., Mountjoy, M.,
Racinais, S., Rasmussen, P., Subudhi, A.W., Young, A.J., Soligard, T., & Engebretsen,
L. (2012). International Olympic Committee consensus statement on thermoregulatory
and altitude challenges for high-level athletes. Br J Sports Med, 46, 770–779.

Berryman, C.E., Young, A.J., Karl, J.P., Kenefick, R.W., Margolis, L.M., Cole, R.E., Carbone, J.W., Lieberman, H.R., Kim, I.Y., Ferrando, A.A., & Pasiako, S.M. (2018).

Severe negative energy balance during 21 d at high altitude decreases fat-free mass regardless of dietary protein intake: a randomized controlled trial. FASEB J, 32(2), 894–905.

Biolo, G., Maggi, S.P., Williams, B.D., Tipton, K.D., & Wolfe, R.R. (1995). Increased rates of muscle protein turnover and amino acid transport after resistance exercise in humans. Am J Physiol Endocrinol Metab, 268(3), E514–E520.

Boirie, Y., Dangin, M., Gachon, P., Vasson, M.P., Maubois, J.L., & Beaufrère, B. (1997). Slow and fastdietary proteins differently modulate postprandial protein accretion. Proc Natl Acad Sci USA, 94, 14930–14935.

Bonjour, J. (2016). The dietary protein, IGF-I, skeletal health axis, HMBCI, 28(1), 39–53. https://doi.org/10.1515/hmbci-2016-0003

Booth, C., & Cairns, J. (2006). Nutritional determinants of bone health: implications for the Australian Defence Force. Australian Military Medicine, 15(1), 9–14.

Booth, C.K., Coad, R.A., Forbes-Ewan, C.H., Thomson, G.F., & Niro, P.J. (2003). The physiological and psychological effects of combat ration feeding during a 12-day training exercise in the tropics. Mil Med, 168(1), 63–70.

Breen, L., & Phillips, S.M. (2012). Nutrient interaction for optimal protein anabolism in resistance exercise. Curr Opin Clin Nutr Metab Care, 15(3), 226–232.

Brook, M.S., Wilkinson, D.J., Mitchell, W.K., Lund, J.N., Szewczyk, N.J., Greenhaff, P.L., Smith, K., & Atherton, P.J. (2015). Skeletal muscle hypertrophy adaptations predominate in the early stages of resistance exercise training, matching deuterium oxide-derived measures of muscle protein synthesis and mechanistic target of rapamycin complex 1 signaling. FASEB J, 29(11), 4485–4496.

Burke, L., & Deakin V. (2015). *Clinical Sports Nutrition* (5th ed.). McGraw-Hill Education (Australia) Pty Ltd.

Burke, L.M. (2017). Practical issues in evidence-based use of performance supplements: supplement interactions, repeated use and individual responses. Sports Med, 47(1), 79–100.

Burke L., Lundy B., Fahrenholtz I., & Melin A. (2018a). Pitfalls of conducting and interpreting estimates of energy availability in free-living athletes. Int J Sport Nutr Exerc Metab, 28(4):350–363.

Burke L.M., Close G.L., Lundy B., Mooses M., Morton J.P., & Tenforde, A.S. (2018b). Relative energy deficiency in sport in male athletes: A commentary on its presentation among selected groups of male athletes. Int J Sport Nutr Exerc Metab, 28(4):364–374.

Calder, P.C. (2014). Very long chain omega-3 (n-3) fatty acids and human health. Eur J Lipid Sci Technol, 116, 1280–1300.

Campbell, B., Kreider, R.B., Ziegenfuss, T., La Bounty, P., Roberts, M., Burke, D., Landis, J., Lopez, H., & Antonio, J. (2017). International Society of Sports Nutrition Position Stand: protein and exercise. J Int Soc Sports Nutr, 14(20). https://doi.org/10.1186/s12970-017-0177-8

Christensen, P.A., Jacobsen, O., Thorlund, J.B., Madsen, T., Moller, C., Jensen, C., Suetta, C., & Aagaard, P. (2008). Changes in maximum muscle strength and rapid muscle force characteristics after long-term special support and reconnaissance missions: a preliminary report. Mil Med, 173(9), 889–894. https://doi.org/10.7205/milmed.173.9.889

Chung, W., Shaw, G., Anderson, M.E., Pyne, D.B., Saunders, P.U., Bishop, D.J., & Burke, L.M. (2012). Effect of 10 week beta-alanine supplementation on competition and training performance in elite swimmers. Nutrients, 4(10), 1441–1453.

Churchward-Venne, T.A., Burd, N.A., & Phillips, S.M. (2012a). Nutritional regulation of muscle protein synthesis with resistance exercise: strategies to enhance anabolism. Nutr Metab, 9(40), 1–8.

Churchward-Venne, T.A., Burd, N.A., Mitchell, C.J., West, D.W., Philp, A., Marcotte, G.R., Baker, S.K., Baar, K., & Phillips, S.M. (2012b). Supplementation of a suboptimal protein dose with leucine or essential amino acids: effects on myofibrillar protein synthesis at rest and following resistance exercise in men. Journal Physiol, 590(11), 2751–65. <u>https://doi.org/10.1113/jphysiol.2012.228833</u>

Churchward-Venne, T.A., Breen, L., Di Donato, D.M., Hector, A.J., Mitchell, C.J., Moore, D.R., Stellingwerff, T., Breuille, D., Offord, E.A., Baker, S.K., & Phillips, S.M. (2014). Leucine supplementation of a low-protein mixed macronutrient beverage enhances myofibrillar protein synthesis in young men: a double-blind, randomized trial. Am J Clin Nutr, 99, 276–86.

Colzato, L.S., De Haan, A., & Hommel, B. (2014a). Food for creativity: tyrosine promotes performance in a convergent-thinking task. Psychol Res, 79(5), 709e714.

Colzato, L.S., Jongkees, B.J., Sellaro, R., & Hommel, B. (2013). Working memory reloaded: tyrosine repletes updating in the N-back task. Front Behav Neurosci, 7, 200. <u>https://doi.org/10.3389/fnbeh.2013.00200</u>

Colzato, L.S., Jongkees, B.J., van den Wildenberg, W.P.M., & Hommel, B. (2014b). Eating to stop: tyrosine supplementation enhances inhibitory control but not response execution. Neuropsychologia, 62, 398e402. http://dx.doi.org/10.1016/j.neuropsychologia.2013.12.027

Cymerman, A. (1996). The physiology of high-altitude exposure. In B.M. Marriott & S.J. Carlson Institute of Medicine (US) Committee on Military Nutrition Research (Eds.), Nutritional needs in cold and in high-altitude environments: applications for military personnel in field operations (295–318), Washington, DC: National Academy of Sciences.

Damas, F., Phillips, S.M., Libardi, C.A., Vechin, F.C., Lixandrão, M.E., Jannig, P.R., Costa, L.A., Bacurau, A.V., Snijders, T., Parise, G., & Tricoli, V. (2016). Resistance training-induced changes in integrated myofibrillar protein synthesis are related to hypertrophy only after attenuation of muscle damage. J Physiol, 594(18), 5209–5222.

Dangin, M., Boirie, Y., Garcia-Rodenas, C., Gachon, P., Fauquant, J., Callier, P., Ballèvre, O., & Beaufrère, B. (2001). The digestion rate of protein is an independent regulating factor of postprandial protein retention. Am J Physiol Endocrinol Metab 280, E340–E348.

Darling, A.L., Millward, D.J., Torgerson, D.J., Hewitt, C.E., & Lanham-New, S.A. (2009). Dietary protein and bone health: a systematic review and meta-analysis. Am J Clin Nutr, 90(6), 1674–1692.

DEF(AUST) 10349 / Issue 1 / Type C, (2013). Cereal-based Breakfast Foods, Australian Defence Standard, Department of Defence.

DEF(AUST) 10368 / Issue 1 / Type C, (2013). Cheese and Cheese Products, Australian Defence Standard, Department of Defence.

DEF(AUST) 10377 / Issue 1 / Type C, (2012). Sweetened Condensed Milk, Australian Defence Standard, Department of Defence.

DEF(AUST) 10378 / Issue 2 / Type C, (2015). Dried Milk Products and Creamers, Australian Defence Standard, Department of Defence.

DEF(AUST) 10385 / Issue 1 / Type C, (2013). Fish and Fish Based Meals, Australian Defence Standard, Department of Defence.

DEF(AUST) 10432 / Issue 3 / Type T, (2018). Meat Based Meals in Retort Pouches, Australian Defence Standard, Department of Defence.

DEF(AUST) 10505 / Issue 2 / Type C, (2015). Freeze Dried Products, Australian Defence Standard, Department of Defence.

DEF(AUST) 10518 / Issue 1 / Type C, (2013). Vegetables and Vegetable Based Meals, Australian Defence Standard, Department of Defence.

DEF(AUST) 10553 / Issue 1 / Type C, (2015). Concentrated Yeast Extract Spread (CYES), Australian Defence Standard, Department of Defence.

DEF(AUST) 10570 / Issue 2 / Type C, (2016). Beverage Base, Australian Defence Standard, Department of Defence.

DEF(AUST) 10615 / Issue 1 / Type C, (2013). Cereal and Cereal-based Products, Australian Defence Standard, Department of Defence.

DEF(AUST) 10838 / Issue 3 / Type C, (2017). Beef Snacks, Australian Defence Standard, Department of Defence.

DEF(AUST) 11100 / Issue 1 / Type C, (2015). Long Life Bread (LLB), Australian Defence Standard, Department of Defence.

Degoutte, F., Jouanel, P., Bègue, R.J., Colombier, M., Lac, G., Pequignot, J.M., & Filaire, E. (2006). Food restriction, performance, biochemical, psychological, and endocrine changes in judo athletes. Int J Sports Med, 27(01), 9–18.

Department of Defence, *Australian Defence Force Ration Scales and Scales of Issue. SUPMAN 4*, Department of Defence. 2014, Defence Publishing Service. Canberra, Australian Capital Territory.

Deijen, J.B., & Orlebeke, J.F. (1994). Effect of tyrosine on cognitive function and blood pressure under stress. Brain Res Bull, 33(3), 319–23. https://doi.org/10.1016/0361-9230(94)90200-3.

Deijen, J.B., Wientjes, C.J., Vullinghs, H.F., Cloin, P.A., & Langefeld, J.J. (1999). Tyrosine improves cognitive performance and reduces blood pressure in cadets after one week of a combat training course. Brain Res Bull, 48(2), 203–9. <u>https://doi.org/10.1016/s0361-9230(98)00163-4</u>.

Dolan, E., Gualano, B., & Rawson, E.S. (2019) Beyond muscle: the effects of creatine supplementation on brain creatine, cognitive processing, and traumatic brain injury. Eur J Sport Sci, 19(1), 1–14. https://doi.org/10.1080/17461391.2018.1500644

FAO Expert Consultation (2011). Dietary protein quality evaluation in human nutrition. FAO Food Nutr Pap, 92: 1–66.

https://web.archive.org/web/20170623021644/http://www.fao.org/ag/humannutrition/3597 8-02317b979a686a57aa4593304ffc17f06.pdf

FSANZ (2016). Australia New Zealand Food Standards Code – Standard 2.9.4 – Formulated Supplementary Sports Foods. Food Standards Australia New Zealand Act 1991 (Cth).

Forbes-Ewan (2009). Australian Defence Force Nutritional Requirements in the 21st Century (Version 1). DSTO-GD-0578, Human Protection and Performance Division, Defence Science and Technology Organisation, Fishermans Bend, Victoria.

Gorissen, S.H.M., & Witard, O.C. (2017). Characterising the muscle anabolic potential of dairy, meat and plant-based protein sources in older adults. Proceedings of the Nutrition Society, 77, 20–31.

Gwin, J.A., Church, D.D., Hatch-McChesney, A., Howard, E.E., Carrigan, C.T., Murphy, N.E., Wilson, M.A., Margolis, L.M., Carbone, J.W., Wolfe, R.R. and Ferrando, A.A. (2021). Effects of high versus standard essential amino acid intakes on whole-body protein turnover and mixed muscle protein synthesis during energy deficit: A randomized, crossover study. Clin Nutr, 40(3), 767–777.

Gwin, J.A., Church, D.D., Wolfe, R.R., Ferrando, A.A., & Pasiakos, S.M. (2020). Muscle protein synthesis and whole-body protein turnover responses to ingesting essential amino acids, intact protein, and protein-containing mixed meals with considerations for energy deficit. Nutrients, 12(8), 2457. https://doi.org/10.3390/nu12082457

Hartman, J.W., Tang, J.E., Wilkinson, S.B., Tarnopolsky, M.A., Lawrence, R.L., Fullerton, A.V., & Phillips, S.M. (2007). Consumption of fat-free fluid milk after resistance exercise promotes greater lean mass accretion than does consumption of soy or carbohydrate in young, novice, male weightlifters. Am J Clin Nutr, 86(2), 373–381.

Head Modernisation and Strategic Plans-Army (HMSP-A). (2015). ADF Combat Ration Packs User Requirement (CRUR), R22018658, Deputy Chief of Army. Available from: https://www.defence.gov.au/FOI/Docs/Disclosures/107\_1516\_Document.pdf

Heaney, R.P. (2002). Protein and calcium: antagonists or synergists? Am J Clin Nutr, 75(4), 609–610. <u>https://doi.org/10.1093/ajcn/75.4.609</u>

Hector, A.J., & Phillips, & S.M. (2018). Protein recommendations for weight loss in elite athletes: a focus on body composition and performance. Int J Sport Nutr Exerc Metab, 28, 170–177. <u>https://doi.org/10.1123/ijsnem.2017-0273</u>

Helms, E.R., Zinn, C., Rowlands, D.S., & Brown, S.R. (2014). A systematic review of dietary protein during caloric restriction in resistance trained lean athletes: a case for higher intakes. Int J Sport Nutr Exerc Metab, 24, 127–138.

Hoffman, J.R., Landau, G., Stout, J.R., Dabora, M., Moran, D.S., Sharvit, N., Hoffman, M.W., Moshe, Y.B., McCormack, W.P., Hirschhorn, G., & Ostfeld, I. (2014). β-alanine supplementation improves tactical performance but not cognitive function in combat soldiers. J Int Soc Sports Nutr, 11(15). <u>https://doi.org/10.1186/1550-2783-11-15</u>

Hoffman, J.R., Landau, G., Stout, J.R., Hoffman, M.W., Shavit, N., Rosen, P., Moran, D.S., Fukuda, D.H., Shelef, I., Carmom, E., & Ostfeld, I. (2015a). β-Alanine ingestion increases muscle carnosine content and combat specific performance in soldiers. Amino Acids, 47, 627–636.

Hoffman, J.R., Stout, J.R., Harris, R.C., & Moran, D.S. (2015b). β-Alanine supplementation and military performance. Amino Acids, 47, 2463–2474. https://doi.org/10.1007/s00726-015-2051-9

Imoberdorf, R., Garlick, P.J., McNurlan, M.A., Casella, G.A., Marini, J.C., Turgay, M., Bartsch, P., & Ballmer, P.E. (2006). Skeletal muscle protein synthesis after active or passive ascent to high altitude. Med Sci Sports Exerc, 38(6), 1082–1087.

Iguacel, I., Miguel-Berges, M. L., Gómez-Bruton, A., Moreno, L. A., & Julián, C. (2019). Veganism, vegetarianism, bone mineral density, and fracture risk: a systematic review and meta-analysis. Nutr Rev, 77(1), 1–18.

Jäger, R., Kerksick, C.M., Campbell, B.I., Cribb, P.J., Wells, S.D., Skwiat, T.M., Purpura, M., Ziegenfuss, T.N., Ferrando, A.A., Arent, S.M. and Smith-Ryan, A.E. (2017). International society of sports nutrition position stand: protein and exercise. J Int Soc Sports Nutr, 14(1), 1–25.

Jongkees, B.J., Hommel, B., Kuhn, S., & Colzato, L.S. (2015). Effect of tyrosine supplementation on clinical and healthy populations under stress or cognitive demands: A review. J Psychiatr Res, 70, 50–57.

Karl, P.J., Margolis, L. M., Fallowfield, J.L., Child, R.B., Martin, N.M., & McClung, J.P. (2021). Military nutrition research: contemporary issues, state of the science and future directions. Eur J Sport Sci, (just-accepted), 1–23.

Karpouzos, A., Diamantis, E., Farmaki, Savvanis, S, & Troupis, T. (2017). Nutritional aspects of bone health and fracture healing. J Osteoporos. <u>https://doi.org/10.1155/2017/4218472</u>

Kato, H., Suzuki, K., Bannai, M., & Moore, D.R. (2016). Protein requirements are elevated in endurance athletes after exercise as determined by the indicator amino acid oxidation method. PLoS One, 11(6), e0157406. https://doi.org/10.1371/journal.pone.0157406

Kelsall, H., Sim, M., Van Hooff, M., Lawrence-Wood, E., Hodson, S., Sadler, N., Benassi, H., Hansen, C., Avery, J., Searle, A., Ighani, H., Iannos, M., Abraham, M., Baur, J., Saccone, E., & McFarlane, A. (2018). Mental health and wellbeing transition study, physical health status summary report. The Department of Defence and The Department of Veterans' Affairs, Canberra, Australia.

Keenan, S., Peterson, R., McLaughlin, T., Baker, B., & Forbes-Ewan, C. (In Preparation). Australian combatants' carbohydrate and dietary fibre requirements and recommendations for combat ration packs, Land Division: Defence Science and Technology Group, Fishermans Bend, Victoria.

Kilduff, L.P., Georgiades, E., James, N., Minnion, R.H., Mitchell, M., Kingsmore, D., Hadjicharlambous, M., & Pitsiladis, Y.P. (2004). The effects of creatine supplementation on cardiovascular, metabolic, and thermoregulatory responses during exercise in the heat in endurance-trained humans. Int J Sport Nutr Exerc Metab, 14(4):443–60. https://doi.org/10.1123/ijsnem.14.4.443

Kimball, S.R., & Jefferson, L.S. (2002). Control of protein synthesis by amino acid availability. Curr Opin Clin Nutr Metab Care, 5(1), 63–67.

Knuiman, P., Hopman, M. T., Verbruggen, C., & Mensink, M. (2018). Protein and the adaptive response with endurance training: wishful thinking or a competitive edge? Front Physiol, 9, 598.

Koopman, R., & van Loon, L.J. (2009). Aging, exercise, and muscle protein metabolism. J Appl Physiol, 106, 2040–2048. https://doi.org/10.1152/japplphysiol.91551.2008

Koral, J., & Dosseville, F. (2009). Combination of gradual and rapid weight loss: Effects on physical performance and psychological state of elite judo athletes. J Sports Sci, 27(2), 115–120.

Kreider, R.B., Kalman, D.S., Antonio, J., Ziegenfuss, T.N., Wildman, R., Collins, R., Candow, D.G., Kleiner, S.M., Almada, A.L. and Lopez, H.L. (2017). International Society

of Sports Nutrition position stand: safety and efficacy of creatine supplementation in exercise, sport, and medicine. J Int Soc Sports Nutr, 14(18). https://doi.org/10.1186/s12970-017-0173-z

Li, P., Yin, Y. L., Li, D., Kim, S. W., & Wu, G. (2007). Amino acids and immune function. Br J Nutr, 98(2), 237-252.

Longland, T.M., Oikawa, S.Y., Mitchell, C.J., Devries, M.C., & Phillips, S.M. (2016). Higher compared with lower dietary protein during an energy deficit combined with intense exercise promotes greater lean mass gain and fat mass loss: a randomized trial. Am J Clin Nutr, 103, 738-46.

Lopez, R.M., Casa, D.J., McDermott, B.P., Ganio, M.S., Armstrong, L.E., & Maresh, C.M. (2009). Does creatine supplementation hinder exercise heat tolerance or hydration status? A systematic review with meta-analysis. J Athl Train, 44(2), 215-223. https://doi.org/10.4085/1062-6050-44.2.215

Magill, R.A., Waters, W.F., Bray, G.A., Volaufova, J., Smith, S.R., Lieberman, H.R., McNevin, N., & Ryan, D.H. (2003). Effects of tyrosine, phentermine, caffeine Damphetamine, and placebo on cognitive and motor performance deficits during sleep deprivation. Nutr Neurosci, 6(4):237-46. https://doi.org/10.1080/1028415031000120552

Mangano, K.M., Sahni, S., & Kerstetter, J.E. (2014). Dietary protein is beneficial to bone health under conditions of adequate calcium intake: an update on clinical research. Curr Opin Clin Nutr Metab Care, 17(1), 69–74.

https://doi.org/10.1097/MCO.00000000000013

Margolis, L.M., Carbone, J.W., Berryman, C.E., Carrigan, C.T., Murphy, N.E., Ferrando, A.A., Young, A.J., & Pasiakos, S.M., (2018). Severe energy deficit at high altitude inhibits skeletal muscle mTORC1-mediated anabolic signaling without increased ubiguitin proteasome activity. FASEB J, 32(11), 5955-5966.

Margolis, L.M., Karl, J.P., Wilson, M.A., Coleman, J.L., Whitney, C.C. and Pasiakos, S.M. (2021). Serum Branched-Chain Amino Acid Metabolites Increase in Males When Aerobic Exercise Is Initiated with Low Muscle Glycogen. Metabolites, 11(12), 828.

Margolis, L.M., Murphy, N.E., Martini, S., Gundersen, Y., Castellani, J.W., Karl, J.P., Carrigan, C.T., Teien, H.K., Madslien, E.H., Montain, S.J. and Pasiakos, S.M. (2016). Effects of supplemental energy on protein balance during 4-d arctic military training. Med Sci Sports Exerc, DOI: 10.1249/MSS.00000000000944.

DSTG-GD-1174

Maughan, R.J., Burke, L.M., Dvorak, J., Larson-Meyer, D.E., Peeling, P., Phillips, S.M., Rawson, E.S., Walsh, N.P., Garthe, I., Geyer, H. and Meeusen, R., & Engebretsen, L. (2018). IOC consensus statement: dietary supplements and the high-performance athlete. Int J Sport Nutr Exerc Metab, 28(2), 104–125.

McLaughlin, T., Diana, J.D., Bulmer, S., & Pike, A. (2018). Comparative field evaluation of the in-service and prototype modular mission adaptive combat ration packs. DST-Group-TR-3453. Land Division, Defence Science and Technology Group, Scottsdale, Australia.

McLaughlin, T., Forbes-Ewan, C. & White, A. (In Preparation). Australian Combat Ration Packs: Meeting Nutritional Requirements. Land Division: Defence Science and Technology Group, Fishermans Bend, Victoria.

McMorris, T., Harris, R.C., Swain, J., Corbett, J., Collard, K., Dyson, R.J., Dye, L., Hodgson, C., & Draper, N. (2006). Effect of creatine supplementation and sleep deprivation, with mild exercise, on cognitive and psychomotor performance, mood state, and plasma concentrations of catecholamines and cortisol. Psychopharmacology, 185, 93–103. <u>https://doi.org/10.1007/s00213-005-0269-z</u>

McMorris, T., Harris, R.C., Howard, A.N., Langridge, G., Hall, B., Corbett, J., Dicks, C., & Hodgson, C. (2007). Creatine supplementation, sleep deprivation, cortisol, melatonin and behaviour. Physiol Behav, 90(1): 21–8. <u>https://doi.org/10.1016/j.physbeh.2006.08.024</u>

Moore, D.R., Robinson, M.J., Fry, J.L., Tang, J.E., Glover E.I., Wilkinson, S.B., Prior, T., Tarnopolsky, M.A., & Phillips, S.M. (2009). Ingested protein dose response of muscle and albumin protein synthesis after resistance exercise in young men. Am J Clin Nutr, 89, 161–8.

Moore, D.R., & Stellingwerff, T. (2012). Protein ingestion after endurance exercise: the evolving needs of the mitochondria. J Physiol, 590(8), 1785–1786.

Morgan, S., Poundarik, A. A., & Vashishth, D. (2015). Do non-collagenous proteins affect skeletal mechanical properties? Calcif Tissue Int, 97(3), 281–291. <u>https://doi.org/10.1007/s00223-015-0016-3</u>

Montero, A., López-Varela, S., Nova, E., & Marcos, A. (2002). The implication of the binomial nutrition-immunity on sportswomen's health. Eur J Clin Nutr. 56(3), S38–41. https://www.doi.org/10.1038/sj.ejcn.1601483

Mountjoy M., Sundgot-Borgen J.K., Burke L.M., Ackerman K.E., Blauwet C., Constantini N., Lebrun C., Lundy B., Melin A.K., Meyer N.L., & Sherman R.T. (2018). IOC consensus

statement on relative energy deficiency in sport (RED-S): 2018 update. Br J Sports Med, 52:687–697.

Murphy, N.E., Carrigan, C.T., Karl, J.P., Pasiakos, S., & Margolis, L. (2018). Threshold of energy deficit and lower-body performance declines in military personnel: a meta-regression. Sports Med, 48, 2169–2178.

Murphy, C.H., Churchward-Venne, T.A., Mitchell, C.J., Kolar, N.M., Kassis, A., Karagounis, L.G., Burke, L.M., Hawley, J.A. and Phillips, S.M. (2015). Hypoenergetic diet-induced reductions in myofibrillar protein synthesis are restored with resistance training and balanced daily protein ingestion in older men. Am J Physiol Endocrinol Metab, 308(9), E734–E743.

Murphy, C.H., Saddler, N.I., Devries, M.C., McGlory, C., Baker, S.K., & Phillips, S.M. (2016). Leucine supplementation enhances integrative myofibrillar protein synthesis in free-living older men consuming lower- and higher-protein diets: a parallel-group crossover study. Am J Clin Nutr, 104(6), 1594–1606. https://doi.org/10.3945/ajcn.116.136424

NHMRC (2006). Nutrient Reference Values for Australia and New Zealand Including Recommended Dietary Intakes. Canberra: National Health and Medical Research Council. Canberra, ACT.

NATO (2013). NATO STANDARD AMedP-1.11, Allied Medical Publication. Requirements of individual operational rations for military use. NATO Standardisation Agency (NSA), October 2013.

Nevin, J. (2017). The tactical athlete: optimising physical preparedness for the demands of combat. Strength Cond J, 44, 25–34.

Nindl, B.C., Barnes, B.R., Alemany, J.A., Frykman, P.N., Shippee, R.L., & Friedl, K.E. (2007). Physiological consequences of U.S. Army Ranger training. Med Sci Sports Exerc, 38(9), 1380–7. <u>https://doi.org/10.1249/MSS.0b013e318067e2f7</u>

Noakes, M, (2018). Protein balance: new concepts for protein in weight management; CSIRO, Australia.

O'Brien, C., Mahoney, C., Tharion, W.J., Sils, I.V., & Castellani, J.W. (2007). Dietary tyrosine benefits cognitive and psychomotor performance during body cooling. Physiol Behav, 90, 301–307.

Ofsteng, S.J., Garthe, I., Josok, O., Knox, S., Helkala, K., Knox, B., Ellefsen, S., & Ronnestad, B.R. (2020). No effect of increasing protein intake during military exercise

DSTG-GD-1174

with severe energy deficit on body composition and performance. Scand J Med Sci Sports, 30(5), 865–877.

O'Leary, T.J., Wardle, S.J., & Greeves, J.P. (2020). Energy Deficiency in Soldiers: The Risk of the Athlete Triad and Relative Energy Deficiency in Sport Syndromes in the Military. Front Nutr, *7*, 142. <u>https://doi.org/10.3389/fnut.2020.00142</u>

Owens, D.J., Twist, C., Cobley, J.N., Howatson, G., & Close, G.L. (2019). Exerciseinduced muscle damage: What is it, what causes it and what are the nutritional solutions? Eur J Sport Sci, 19(1), 71–85. <u>https://doi.org/10.1080/17461391.2018.1505957</u>

Pasiakos, S.M., Austin, K.G., Lieberman, H.R., & Askew, E.W. (2013). Efficacy and safety of protein supplements for US Armed Forces personnel: consensus statement. J Nutr, 143(11), 1811S–1814S.

Pasiakos, S.M., Vislocky, L.M., Carbone, J.W., Altieri, N., Konopelski, K., Freake, H.C., Anderson, J.M., Ferrando, A.A., Wolfe, R.R., & Rodriguez, N.R. (2010). Acute energy deprivation affects skeletal muscle protein synthesis and associated intracellular signaling proteins in physically active adults. J Nutr, 140(4), 745–51. https://doi.org/10.3945/jn.109.118372

Pasiakos, S.M., Sepowitz, J.J., & Deuster, P.A. (2015a). US military dietary protein recommendations: a simple but often confused topic. J Spec Oper Med, 15(4), 89–95.

Pasiakos, S.M., Margolis, L.M., & Orr, J.S. (2015b). Optimized dietary strategies to protect skeletal muscle mass during periods of unavoidable energy deficit. FASEB J, 29(4), 1136–1142.

Pasiakos, S.M., Berryman, C.E., Carrigan, C.T., Young, A.J., & Carbone, J.W. (2017). Muscle protein turnover and the molecular regulation of muscle mass during hypoxia. Med Sci Sports Exerc, 49(7), 1340–1350.

Pasiakos, S.M. (2020). Nutritional requirements for sustaining health and performance during exposure to extreme environments. Annu Rev Nutr, 40(1), 1.1–1.24

Pasiakos, S.M., & McClung, J.P. (2011). Supplemental dietary leucine and the skeletal muscle anabolic response to essential amino acids. Nutr Rev, 69(9): 550–7. https://doi.org/10.1111/j.1753-4887.2011.00420.x

Phillips, S.M. (2012). Nutrient-rich meat proteins in offsetting age-related muscle loss. Meat Sci, 92(3), 174–178.

Phillips, S.M., Tipton, K.D., Aarsland, A., Wolf, S.E., & Wolfe, R.R. (1997). Mixed muscle protein synthesis and breakdown after resistance exercise in humans. Am J Physiol, 273, E99–E107.

Pomeroy, D.E., Tooley, K.L., Probert, B., Wilson, A., & Kemps, E. (2020). A systematic review of the effect of dietary supplements on cognitive performance in health young adults and military personnel. Nutrients, 12(2), 545.

Powers, M.E., Arnold, B.L., Weltman, A.L., Perrin, D.H., Mistry, D., Kahler, D.M., Kraemer, W., & Volek, J. (2003). Creatine supplementation increases total body water without altering fluid distribution. J Athl Train, 38(1), 44–50.

Reis, C.E., Loureiro, L.M., Roschel, H., & da Costa, T.H. (2021). Effects of pre-sleep protein consumption on muscle-related outcomes—A systematic review. J Sci Med Sport, 24(2), 177–182.

Richmond, V.L., Horner, F.E., Wilkinson, D.M., Rayson, M.P., Wright, A., & Izard, R. (2014). Energy balance and physical demands during an 8-week arduous military training course. Mil Med, 179(4), 421. <u>https://doi.org/10.7205/MILMED-D-13-00313</u>

Roberts, B.M., Helms, E.R., Trexler, E.T., & Ftischen, P.J. (2020). Nutritional recommendations for physique athletes. J Hum Kinet, 71, 79–108. https://doi.org/10.2478/hukin-2019-0096

Rondanelli, M., Nichetti, M., Peroni, G., Faliva, M.A., Naso, M., Gasparri, C., Perna, S., Oberto, L., Di Paolo, E., Riva, A., & Petrangolini, G., Guerreschi, G., & Tartara, A. (2021). Where to find leucine in food and how to feed elderly with sarcopenia in order to counteract loss of muscle mass: practical advice. Front Nutr, *7*:622391. <u>https://doi.org/10.3389/fnut.2020.622391</u>

Rutherfurd, M.S., Fanning, A.C., Miller, B.J., & Moughan, P.J. (2015). Protein digestibility-corrected amino acid scores and digestible indispensable amino acid scores differentially describe protein quality in growing male rats. J Nutr, 145(2), 372–379. https://doi.org/10.3945/jn.114.195438

Sale, C., & Elliott-Sale, K. J. (2019). Nutrition and Athlete Bone Health. Sports Med, 49(2), 139–151. <u>https://doi.org/10.1007/s40279-019-01161-2</u>

Saunders, B., Elliott-Sale, K., Artioli, G.G., Swinton, P.A., Dolan, E., Roschel, H., Sale, C., & Gualano, B., 2017. β-alanine supplementation to improve exercise capacity and performance: a systematic review and meta-analysis. Br J Sports M, 51(8), 658–669.

Schaafsma, G. (2000) The Protein Digestibility–Corrected Amino Acid Score. J Nutr, 130(7), 1865S–1867S, https://doi.org/10.1093/jn/130.7.1865S

Shams-White, M.M., Chung, M., Du, M., Fu, Z., Insogna, K.L., Karlsen, M.C., LeBoff, M.S., Shapses, S.A., Sackey, J., Wallace, T.C., & Weaver, C.M. (2017). Dietary protein and bone health: a systematic review and meta-analysis from the National Osteoporosis Foundation. Am J Clin Nutr, 105(6), 1528–1543.

Steenbergen, L., Sellaro, R., Hommel, B., & Colzato, L.S. (2015). Tyrosine promotes cognitive flexibility: evidence from proactive vs. reactive control during task switching performance. Neuropsychologia, 69, 50–5.

https://doi.org/10.1016/j.neuropsychologia.2015.01.022

Steenge, G.R., Simpson, E.J., & Greenhaff, P.L. (2002). Protein- and carbohydrateinduced augmentation of whole body creatine retention in humans. J Appl Physiol, 89(3):1165–71. <u>https://doi.org/10.1152/jappl.2000.89.3.1165</u>

Stellingwerf, T. (2020). An update on beta-alanine supplementation for athletes. SSE, 29(208), 1–6.

Stokes, T., Hector, A.J., Morton, R.W., McGlory, C., & Phillips, S.M. (2018). Recent perspectives regarding the role of dietary protein for the promotion of muscle hypertrophy with resistance exercise training. Nutrients, 10(2), 180. https://doi.org/10.3390/nu10020180

Tang, J.E., Moore, D.R., Kujbida, G.W., Tarnopolsky, M.A., & Phillips, S.M. (2009). Ingestion of whey hydrolysate, casein, or soy protein isolate: effects on mixed muscle protein synthesis at rest and following resistance exercise in young men. J Appl Physiol, 107, 987–992.

Tarnopolsky, M.A., Atkinson, S.A., MacDougall, J.D., Chesley, A., Phillips, S., & Schwarcz, H.P. (1992). Evaluation of protein requirements for trained strength athletes. J Appl Physiol, 73(5), 1986-95. <u>https://www.doi.org/10.1152/jappl.1992.73.5.1986</u>

Tassone, E.C., & Baker, B.A. (2017). Body weight and body composition changes during military training and deployment involving the use of combat rations: a systematic literature review. Br J Nutr, 117, 897-910.

TGA (2020). Changes to the regulation of sports supplements in Australia. Department of Health, Therapeutics Goods Administration. Available from: <u>https://www.tga.gov.au/node/912254</u>

Thomas, D.T., Erdman, K.A., & Burke, L.M. (2016). American college of sports medicine joint position statement. Nutrition and athletic performance. Med Sci Sports Exerc, 48(3), 543–568.

Thomas, J.R., Lockwood, P.A., Singh, A., & Deuster, P.A. (1999). Tyrosine improves working memory in a multitasking environment. Pharmacol Biochem Behav, 64(3), 495-500. <u>https://doi.org/10.1016/s0091-3057(99)00094-5</u>

Thorlund, J.B., Jakobsen, O., Madsen, T., Christensen, P.A., Nedergaard, A., Andersen, J.L., Suetta, C., & Aagaard, P. (2011). Changes in muscle strength and morphology after muscle unloading in Special Forces missions. Scand J Med Sci Sports 21(6): e56–63. https://doi.org/10.1111/j.1600-0838.2010.01149.x

Tomkinson, G.R., Daniell, N., Fulton, A., & Furnell, A. (2017). Time changes in the body dimensions of male Australian Army personnel between 1977 and 2012. Appl Ergon, 58, 18–24. <u>https://doi.org/10.1016/j.apergo.2016.05.008</u>

Trexler, E.T., Smith-Ryan, A.E., Stout, J.R., Hoffman, J.R., Wilborn, C.D., Sale, C., Kreider, R.B., Jäger, R., Earnest, C.P., Bannock, L., Campbell, B., Kalman, D., Ziegenfuss, T.N., & Antonio, J. (2015). International society of sports nutrition position stand: Beta-Alanine. J Int Soc Sports Nutr, 12(30). <u>https://doi.org/10.1186/s12970-015-0090-y</u>

Turner, C.E., Byblow, W.D., & Gant, N. (2015). Creatine supplementation enhances corticomotor excitability and cognitive performance during oxygen deprivation. J Neurosci, 35(4), 1773–1780. <u>https://doi.org/10.1523/JNEUROSCI.3113-14.2015</u>

Twycross-Lewis, R., Kilduff, L.P., Wang, G., & Pitsiladis, Y.P. (2016). The effects of creatine supplementation on thermoregulation and physical (cognitive) performance: a review and future prospects. Amino Acids 48(8):1843–55. https://doi.org/10.1007/s00726-016-2237-9

Van Vliet, S., Burd, N.A., & van Loon, L. (2015). The Skeletal Muscle Anabolic Response to Plant- versus Animal-Based Protein Consumption. J Nutr, 145(9), 1981–1991.

Varanoske, A.N., Wells, A.J., Kozlowski, G.J., Gepner, Y., Frosti, C.L., Boffey, D., Coker, N.A., Harat, I., & Hoffman, J.R. (2018). Effects of b-alanine supplementation on physical performance, cognition, endocrine function, and inflammation during a 24 h simulated military operation. Physiol Rep, 6(24), e13938. <u>https://doi.org/10.14814/phy2.13938</u>

Volek, J.S., Volk, B.M., Gómez, A.L., Kunces, L.J., Kupchak, B.R., Freidenreich, D.J., Aristizabal, J.C., Saenz, C., Dunn-Lewis, C., Ballard, K.D., & Quann, E.E. (2013). Whey

DSTG-GD-1174

protein supplementation during resistance training augments lean body mass. J Am Coll Nutr, 32(2), 122–135.

Whitney, E., Rolfes, S.R., & Crowe, T. (2020). *Understanding Nutrition* (4<sup> h</sup> ed). Cengage Learning AUS.

Wilkinson, S.B., Tarnopolsky, M.A., MacDonald, M.J., MacDonald, J.R., Armstrong, D., & Phillips, S.M. (2007). Consumption of fluid skim milk promotes greater muscle protein accretion after resistance exercise than does consumption of an isonitrogenous and isoenergetic soy-protein beverage. Am J Clin Nutr, 85(4), 1031–1040.

Wing-Gaia, S. L. (2014). Nutritional strategies for the preservation of fat free mass at high altitude. Nutrients, 6(2), 665–681.

Witard, O.C., Jackman, S.R., & Breen, L. (2014). Myofibrillar muscle protein synthesis rates subsequent to a meal in response to increasing doses of whey protein at rest and after resistance exercise. Am J Clin Nutr, 99, 86–95.

Witard, O.C., Bannock, L., & Tipton, K.D. (2021). Making Sense of Muscle Protein Synthesis: A Focus on Muscle Growth During Resistance Training. Int J Sport Nutr Exerc Metab, 1(aop), 1–13.

Yang, Y., Churchward-Venne, T.A., Burd, N.A., Breen, L., Tarnopolsky, M.A., Phillips, & S.M. (2012). Myofibrillar protein synthesis following ingestion of soy protein isolate at rest and after resistance exercise in elderly men. Nutr Metab, 9(1), 57.

Young, V.R., El-Khoury, A.E., Sanchez, M., & Castillo, L. (1994). The biochemistry and physiology of protein and amino acid metabolism, with reference to protein nutrition. Nestle Nutrition Workshop Series (USA), 33, 1–28.

## APPENDIX A. PROTEIN CONTENT AND QUALITY OF IN-SERVICE MM, LM, SNACK AND BEVERAGE COMPONENTS

Table A.1 Comparison of the content of in-service CRP Main Meal Provisions with the protein quantity and quality recommendations

	Serve	Protein	Protein Quality	
	Size (g)	Content (g)		
Recommendation		≥30	HBV*	EAA*
MBM				
Asian Beef with Vegetable and Black	250	27	Y	NA
Beef and Gravy	250	38	Y	NA
Butter Chicken	250	17	Y	Y
Chicken and Wild Rice	250	22	Y	NA
Chicken Korma	250	30	Y	Y
Chilli Con Carne	250	27	Y	NA
French Lamb Stew	250	21	Y	NA
Hearty Beef Stew	250	22	Y	Y
Lamb Casserole	250	14	Y	Y
Lamb & Tomato Sambal	250	31	Y	Y
Lamb Korma	250	23	Y	Y
Malay Lamb Curry	250	26	Y	Y
Meatballs with Baked Beans	250	17	uncertain	NA
Moroccan Lamb	250	28	Y	Y
Savoury Mince	250	28	Y	Y
Spaghetti Bolognese	250	22	Y	NA
VBM				
Potato and Chickpea Curry	250	17	Ν	NA
Sweet Potato Thai Red Curry	250	14	Ν	NA
FDM				
Beef and Black Bean	110	59	Y	NA
Beef and Green Beans	110	43	Y	NA
Beef Teriyaki	110	56	Y	NA
Lamb Casserole	110	40	Y	NA
Mango Lamb Curry	110	40	Y	NA
Savoury Beef	110	50	Y	NA
Spaghetti and Meat Sauce	110	34	Y	NA
Tuna Mornay	110	38	Y	NA
Tuna Tetrazzini	110	38	Y	NA
Veal Italienne	110	36	Y	NA

\* Y = yes (Refer Appendix B); N = no; NA = not analysed; green text = meets or exceeds recommendation; red text = does not meet recommendation

DSTG-GD-1174

	Serve Size (g)	Protein Content (g)	Protein Quality	
Recommendation		≥25	HBV*	EAA*
Natural muesli with fruits	90	8	Ν	NA
Porridge, Apple & Cinnamon	120	9	Ν	NA
Porridge, Banana & Maple	120	8	Ν	NA
Tuna with Dried Tomato and Basil	85	14	Y	NA
Tuna with Dried Tomato and Herb	85	18	Y	Y
Tuna with Lime & Black Pepper	85	16	Y	Y
Tuna with Spring Water	85	20	Y	Y

Table A.2 Comparison of the content of in-service CRP Light Meal Provisions with the protein quantity and quality recommendations

\* Y = yes (Refer Appendix B); N = no; NA = not analysed; green text = meets or exceeds recommendation; red text = does not meet recommendation

# Table A.3 Comparison of the content of in-service High-Protein CRP SnackProvisions with the protein quantity and quality recommendations

	Serve	Protein	Protein Quality	
	Size (g)	Content (g)		
Recommendation		≥20	HBV*	EAA*
Beef Steak Bar, Teriyaki	25	8	Y	NA
Beef Steak Bar, Peppered	25	8	Y	Y

\* Y = yes (Refer Appendix B); N = no; NA = not analysed; green text = meets or exceeds recommendation; red text = does not meet recommendation

# Table A.4 Comparison of the content of in-service High-Protein CRP BeverageProvisions with the Protein Quantity and Quality Recommendations

	Serve	Protein	Protein Quality	
	Size (g)	Content (g)		
Recommendation		≥20	HBV*	EAA*
Protein Drink, Coffee	60	13	Y	NA
Protein Drink, Chocolate	60	13	Y	NA

\* Y = yes (Refer Appendix B); N = no; NA = not analysed; green text = meets or exceeds recommendation; red text = does not meet recommendation

## Table A.5 Other in-service protein sources within CRP

	ServeProteinSize (g)Content (g)		Protein Quality	
			HBV*	EAA*
Bread, Long Life, White	60	6	Ν	NA
Bread, Long Life, Wholegrain	60	7	Ν	NA
Cheese, Cheddar	56	10	Y	Y
Sweetened Condensed Milk	50	4	Y	NA

\* Y = yes (Refer Appendix B); N = no; NA = not analysed; green text = meets or exceeds recommendation; red text = does not meet recommendation

DSTG-GD-1174

## APPENDIX B. ESSENTIAL AMINO ACID CONTENT OF SELECTED CRP COMPONENTS

					Essential a	mino acid			
Main meal	Histidine	Threonine	Valine	Lysine	Isoleucine	Leucine	Phenylalanine	Methoinine	Tryptophan
					(g/se	erve)			
Moroccan Lamb	0.8	1.2	1.1	1.3	1.0	2.1	1.1	0.6	0.3
Butter Chicken	0.5	0.8	0.7	0.8	0.7	1.3	0.7	0.4	0.2
Lamb Korma	0.6	0.9	0.9	1.0	0.8	1.6	0.8	0.5	0.2
Chicken Korma	1.0	1.1	1.1	1.2	1.0	1.9	0.9	0.7	0.3
Savoury Mince	0.8	1.0	1.0	1.2	0.9	1.8	1.0	0.5	0.3
Hearty Beef Stew	0.6	0.8	0.8	0.9	0.7	1.4	0.7	0.4	0.2
Malay Lamb Curry	0.6	0.8	0.9	0.9	0.8	1.4	0.7	0.4	0.2
Lamb & Tomato Sambal	0.8	1.2	1.2	1.4	1.1	2.1	1.1	0.7	0.3
Lamb casserole	0.5	1.0	1.0	1.1	0.9	1.6	0.8	0.5	0.2
Cheese, Cheddar	0.3	0.4	0.5	0.5	0.4	0.9	0.5	0.3	0.1
Tuna with Spring Water	1.4	0.8	0.8	1.0	0.7	1.4	0.7	0.5	0.2
Tuna with Dried Tomato & Herb	1.1	0.7	0.7	0.8	0.6	1.1	0.6	0.4	0.2
Tuna with Lime & Black Pepper	1.2	0.6	0.7	0.8	0.6	1.1	0.5	0.4	0.2
Beef steak bar, peppered	0.3	0.4	0.4	0.4	0.3	0.6	0.3	0.2	0.1

## **DISTRIBUTION LIST**

Australian Combatants' Protein and Amino Acid Requirements and Recommendations for Combat Ration Packs

s47E(d)

<b>Task Sponsor</b> SO1 Human Performance, DCP, AHQ	s47E(d)
<b>S&amp;T Program</b> Chief of Land Division	
Task Leader ARM 17/485 and RL-HP MSTC	
Group Leader Physical Ergonomics	
Discipline Leader Defence Feeding Systems and Author	
Discipline Leader Nutrition	
ADFSSO SOSTA, SOCOMD	
Author	
Author	
Author	
Author	
<b>Army</b> SO1 Human Performance, SCSP, AHQ	
SO1 Human Performance, HQ FORCOMD	
SO2 Human Performance, HQ FORCOMD	
SO2 Sustainment, DCP, AHQ	
CO ADFSSO, SOCOMD	
SO HPO Manager, SOCOMD	

DSTG-GD-1174

Physiotherapist, SOCOMD	s47E(d)
ADFSSO SOSTA, SOCOMD	
CASG Chief Engineer/DAAR, HLTHSPO	
National Fleet Manager, Combat Rations, HLTHSPO	
Technical Specialist, Combat Rations, HLTHSPO	
Joint Logistics Command SO1 Catering, DLST	
<b>Navy</b> Navy Catering Technical Advisor, NPB	
<b>Air Force</b> Snr Sports Science Program Manager, HQ Air Command	
Joint Health Command Senior Medical Advisor Population Health, DHP	

DSTG-GD-1174

DEFENCE SCIENCE AND T DOCUMENT CON		DUP	IMM/CAVEAT (OF DOCUMENT)		
TITLE		SECURITY CLASSIFICATION			
Australian Combatants' Protein and A	mino Acid	Doci	ument (O)		
Requirements and Recommendations	s for Combat	Title	e (O)		
Ration Packs					
AUTHOR(S)		PRODUCED	) BY		
s47E(d)		Defence Scie	ence and Technology Group		
		Department			
		PO Box 793 <sup>°</sup> Canberra BC			
DSTG NUMBER	REPORT TYPE		DOCUMENT DATE		
DSTG-GD-1174	General Documer	nt	February 2022		
TASK NUMBER	TASK SPONSOR		RESEARCH DIVISION		
ARM 17/485	s47E(d)		Land Division		
MAJOR SCIENCE AND TECHNOLO	GY CAPABILITY	SCIENCE AND TECHNOLOGY CAPABILITY			
Human Performance		Food and Nutrition			
SECONDARY RELEASE STATEMEN	NT OF THIS DOCU	MENT			
Approved for public release.					
ANNOUNCEABLE					
No limitations.					
CITABLE IN OTHER DOCUMENTS					
Yes					
RESEARCH LIBRARY THESAURUS					
Nutrition, Human Performance, Health, Food, Military, Rations					



Australian Government

## Supplement Use in the Royal Australian Air Force

### S&T Summary Report

DSTG-STS-0079 December 2022 Approved for public release Bianka Probert, Rosa Peterson and Bradley Baker Food and Nutrition, Human Systems Performance, Human and Decision Sciences Division

## **Key Points**

- A cross-sectional survey was employed to investigate RAAF members' supplement use.
- Supplement use was reported by 73% of respondents, with a greater proportion
  of females (83%) compared to males (70%) reporting having used a supplement
  once in the previous 6 months. This result is similar to that reported in the
  Australian Army (77%) and higher than that reported in the general Australian
  population (43%).
- The mean weekly number of any supplement used by participants was 3.2 (SD ±3.9), with 26% indicating they simultaneously used 5 or more supplements per week.
- The most commonly used supplements were Group A (those supported by strong scientific evidence for being safe and effective in specific situations when following evidence-based protocols) and Group C supplements (those with little or no scientific evidence to support any benefits of their use).
- Group D supplements (those that are WADA banned or at high risk of contamination with banned substances) were used by 7% of participants.
- Adverse symptoms were experienced by 8% of participants including; increased heart rate (7%), tremors, numbness in fingers and legs, flushing, stomach pain and headache (2%).
- The findings of this study, when taken together with similar findings from Army, indicate that Defence-wide policy changes and public health initiatives, such as access to expert guidance from an accredited Sports Dietitian, and education and behaviour change strategies, are required to improve supplement use behaviours and to reduce the risk of adverse outcomes of RAAF members.

Defence FOI 386/22/23 Document 6

### **OFFICIAL**

## **Executive Summary**

The prevalence of dietary supplement use is high in the general and military population, with trends of increasing use. The prevalence of dietary supplement use has been investigated in overseas military groups [1, 2], the Australian Army [3, 4], deployed forces [5] and veterans [6], however, use within the Royal Australian Air Force (RAAF) has not been previously explored. Anecdotal evidence indicates that supplement use is prevalent within the RAAF, which may be detrimental to mission performance and the health and safety of RAAF members, given the wide-ranging side effects dietary supplement use may have.

Federal legislation prohibits the use of all substances registered on the World Anti-Doping Agency (WADA) prohibited substances and methods list by Australian Defence Force (ADF) members [7]. In support of this legislation, the ADF has a policy to control the use of dietary supplements by its members, detailed in the Defence Health Manual (Vol 002, Part 015, Chapter 2) [8].

In Australia, supplements are regulated under the Therapeutic Goods Administration (TGA) (<u>https://www.tga.gov.au/</u>) and the Food Standards Australia New Zealand (FSANZ) Food Standards Code (<u>http://www.foodstandards.gov.au/Pages/default.aspx</u>). Regulation of dietary supplements in Australia is less rigorous to that of substances classified as pharmaceuticals [9]. Adverse outcomes from the use of dietary supplements may be due to limited regulation of supplements relating to the safety and quality of ingredients and dangerous patterns of use (e.g. simultaneous use of multiple supplements, contraindications with prescription medicines) [9-11]. Contamination of supplements found on the Australian commercial market have been detected, including contaminants associated with health risk, banned and illegal substances [12, 13], and heavy metals [9]. Many supplements also found to contain substances not listed on the ingredient list or to contain levels of the active ingredient below purported efficacy [9].

The aim of this study was to characterise supplement use in the RAAF, highlighting extent of use, quantity used, demographic and military characteristics of users and self-reported effects of use. The tool employed in this study has been previously used to characterise dietary and nutritional supplement use in the Australian Army [14] and is based on a questionnaire used with US Armed Forces [15].

A cross-sectional survey study of members from the Combat Support Group, RAAF, was employed. Both electronic (distributed via email) and paper based (distributed at RAAF Base Amberley) surveys were administered. A total of 244 (183 online and 61 paper) completed surveys were received from an original population of 1,109, resulting in an overall response rate of 22%.

Ethical approval was received from the Curtin University Human Research Ethics Committee (Curtin low risk ethics approval #16475). In addition, an amendment to DDVA HREC protocol #847-16 was also accepted and approved for the conduct of this study with RAAF members.

For analysis, participants were grouped by having used one or more supplements in the previous 6 months ('non-user' or 'user') or by the use of one or more supplements per week ('non-regular user' or 'regular user'). The supplements included in the questionnaire were grouped into four categories; Group A (strong scientific evidence for use in specific situations using evidence-based protocols); Group B (emerging scientific evidence, merits further research); Group C (little or no scientific evidence to support benefit of use) and Group D (banned or at high risk of contamination with banned substances) as defined in the Australian Institute of Sport Supplement Framework [16].

The population was predominantly male (72%), with a mean ( $\pm$ SD) age 37.0 $\pm$ 14.1 years, height 175.5 $\pm$ 9.2 cm, weight 83.6 $\pm$ 16.0 kg and a body mass index (BMI) 25.0 $\pm$ 7.9 kg/m<sup>2</sup>. Junior and senior non-commissioned officers represented 55% of the participants. The majority of participants had completed an undergraduate degree or higher qualification (43%), were non-smokers (92%), lived off base (94%), had served between 6 and 15 years in the RAAF (42%), had been deployed at least once (64%), and rated their health (90%), fitness (77%) and eating habits (71%) as either 'good' or 'excellent'. The majority of participants reported meeting the recommended levels of cardiorespiratory exercise (55%) [17], whilst all participants meet the recommended two sessions of strength training per week (100%) [17]. The population in this study was older with a greater proportion of females compared to other military studies [2-4, 18-22]. However, according to the 2015 Australian Defence Census this is a common trait of the RAAF. Females made up 19% of the RAAF population and a median age of 34 years for the population. RAAF having the oldest median age and equal highest proportion of females with Navy out of the three Australian services [23].

Supplement use (n=179) was reported by 73% of respondents, with a greater proportion of females (83%) compared to males (70%) reporting having used a supplement once in the previous 6 months. Regular supplement use (n=170) was reported by 70% of participants, with a greater proportion of females (80%) compared to males (66%) indicating regular use. The mean weekly number of any supplement used by participants per week was 3.2 (SD  $\pm$ 3.9), with 26% indicating they used 5 or more supplements per week. This level of regular supplement use similar to that reported in a recent survey using a similar tool in the Australian Army, where 77% (86% female; 76% male) of respondents indicated the regular use of dietary supplements [3]. However, this level of use is higher than that reported in the general Australian population that found 43% (50% female; 35% males) of the general population reporting regular use of dietary supplements [24].

Group A supplements were the most commonly used supplements, with 59% (n=145) of participants indicating having used and regular use of this group of supplements. The most popular Group A supplements used were multivitamin/minerals (52%), protein powders (48%), electrolyte drinks (16%), vitamin D (14%), zinc (13%) and sports drinks (12%). The second most reported group of supplements used by participants was Group C, with 45% (n=110) and 41% (n=99) of participants indicating having used once or regularly use, respectively. The most commonly reported Group C supplements were magnesium (30%), pre-workouts (21%), and branched chain amino acids (12%). Group

B supplement use was reported by 39% (n=96) with regular use reported by 34% (n=82). Fish oils (27%) and vitamin C (27%) the most commonly used Group B supplements. Group D supplements were used by 7% (n=16) of participants with regular use of Group D supplements reported by 6% (n=15) of participants. The stimulants ginseng and gingko biloba and the prohormones maca and testosterone boosters the most commonly reported (all 2%) by users of Group D supplements.

Adverse symptoms were experienced by 8% of participants. The most common adverse symptom reported as the result of supplement use is increased heart rate (7%), whilst 2% of users indicated experiencing tremors, numbness in fingers and legs, flushing, stomach pain, and headache. The majority of participants (55%) were 'extremely confident'/'very confident' that supplements are safe. Participants were split on whether supplements do as they claim, with 32% 'extremely confident'/'very confident' and 35% 'somewhat confident'/'not confident at all'. Reasons for using any supplement were general health (51%), more energy (31%), top-up diet (29%), enhance performance (26%), greater muscle strength (24%), increased endurance (20%), greater muscle size (16%), recommended by health professional (16%) and enhance brain function (10%).

The most popular options for the purchase of supplements were Australian websites (34%) and pharmacies (29%). The internet was the most popular source for information on supplements with 36% of supplement users indicating this option as their source of information. Of concern, only 1% of supplement users sourced supplement information from a GP or dietitian.

In this study we found that prevalence of use of supplements and the use of multiple supplements to be high in the RAAF population. This level of use similar to that reported in the Australian Army [3], but much higher than that reported in the general Australian population [24]. The level of use, type of supplements used, reported side effects, and preference for online supplement purchases reported herein is of concern, particularly when considered in light of the limited regulation of supplements in Australia, the large number of supplements accessible on the commercial market and the no-tolerance stance Defence has on WADA banned supplements. A combination that places RAAF supplement users at greater risk of adverse outcomes that may be detrimental to overall health, military career and performance, with the potential to impact operational success. This study further highlights a need for public health initiatives, such as access to expert guidance from an accredited sports dietitian, and education and behaviour change strategies, to improve the safety of supplement use in this population. The results from this study will inform Defence policy and public health interventions to improve the safety and efficacy of supplement use in the RAAF.

This study was conducted to fulfil the requirements of a Master of Public Health (Curtin University).

## References

- 1. Boos, C., et al., *Self-administration of exercise and dietary supplements in deployed British military personnel during Operation TELIC 13.* Journal of the Royal Army Medical Corps, 2010. **156**(1): p. 32-6.
- 2. Austin, K., et al., *Demographic, Lifestyle Factors, and Reasons for Use of Dietary Supplements by Air Force Personnel.* Aerospace Medicine and Human Performance, 2016. **87**(7): p. 628-637.
- 3. Baker, B., et al., *Prevalence and Predictors of Dietary and Nutritional Supplement Use in the Australian Army: A Cross-Sectional Survey.* Nutrients, 2019. **11**(7): p. 1462.
- 4. Kullen, C., T. Prvan, and H. O'Connor, *Dietary Supplement Use in Australian Army Personnel.* Military Medicine, 2019. **184**(5-6): p. e290-e297.
- 5. Lui, C.-W., et al., *Retrospective self-reported dietary supplement use by Australian military personnel during deployment to Iraq and Afghanistan: results from the Middle East Area of Operations Health Study.* Applied Physiology, Nutrition, and Metabolism, 2019. **44**(6): p. 674-680.
- 6. van der Pols, J.C., et al., *Current dietary supplement use of Australian military veterans of Middle East operations.* Public Health Nutrition, 2017. **20**(17): p. 3156-3165.
- 7. *Defence Act 1903 s. 93B(1)*. AUST.
- 8. Department of Defence, *Defence Health Manual, Chapter 2: Use of dietary supplements and complementary medicines by Australian Defence Force personnel.* 2016, Australian Government.
- 9. Binns, C.W., M.K. Lee, and A.H. Lee, *Problems and Prospects: Public Health Regulation of Dietary Supplements.* Annu Rev Public Health, 2018. **39**(1): p. 403-420.
- 10. Ronis, M.J.J., K.B. Pedersen, and J. Watt, *Adverse Effects of Nutraceuticals and Dietary Supplements*. Annu Rev Pharmacol Toxicol, 2018. **58**(1): p. 583-601.
- 11. Maughan, R., et al., *IOC consensus statement: dietary supplements and the high-performance athlete*. British Journal of Sports Medicine, 2018. **52**(7): p. 439-455.
- 12. Cooper, E., et al., *Androgen bioassay for the detection of nonlabeled androgenic compounds in nutritional supplements.* International Journal of Sport Nutrition and Exercise Metabolism, 2018. **28**: p. 10-18.
- 13. LGC, Australian Supplement Survey. 2016, LGC Group.
- 14. Baker, B., et al., *Prevalence, predictors and extent of dietary and nutritional supplement use in Army*. 2018.
- 15. Lieberman, H., et al., *Use of dietary supplements among active-duty US Army soldiers*. Vol. 92. 2010. 985-95.
- 16. Australian Institute of Sport (AIS), *AIS Sports Supplement Framework*. 2019.
- 17. Australian Government Department of Health. *Australia's Physical Activity and Sedentary Behaviour Guidelines and the Australian 24-Hour Movement Guidelines*. 2020 [cited 19 September 2020]; Available from: <u>https://www1.health.gov.au/internet/main/publishing.nsf/Content/health-pubhlth-strateg-phys-act-guidelines</u>.
- Austin, K., E. Farina, and H. Lieberman, Self-reported side-effects associated with use of dietary supplements in an armed forces population. Drug Testing and Analysis, 2016. 8(3-4): p. 287-295.
- 19. Austin, K., et al., *Predictors of Dietary Supplement Use by U.S. Coast Guard Personnel.* PLOS ONE, 2015. **10**(7): p. e0133006.

- 20. Casey, A., et al., *Supplement use by UK-based British Army soldiers in training.* British Journal of Nutrition, 2014. **112**(7): p. 1175-1184.
- 21. Lieberman, H., et al., *Use of dietary supplements among active-duty US Army soldiers.* American Journal of Clinical Nutrition, 2010. **92**(4): p. 985-995.
- 22. Varney, S., et al., *Self-reported dietary supplement use in deployed United States service members pre-deployment vs. during deployment, Afghanistan, 2013-2014.* Military Medical Research, 2017. **4**.
- 23. Australian Survey Research Group, *Defence Census 2015: public report.* 2016.
- 24. O'Brien, S., et al., *The Prevalence and Predictors of Dietary Supplement Use in the Australian Population*. Vol. 9. 2017.

efence FOI 386/22/23 Document

# Supplement Guidance

# **Executive Summary – Use of Supplements**

The Defence policy on use of supplements is available at <u>Chapter 11—Dietary supplements</u> and complementary medicines (defence.gov.au)

For the majority of Air Force personnel, a good diet can provide all the nutrients required to perform your role (mentally and physically, including recovery) to a high standard.

If you believe you require supplements, consult your Air Force medical practitioner and only use Group A products listed on the Australian Institute of Sport (AIS) website: https://www.ais.gov.au/nutrition/supplements.

### What are Supplements?

Supplements are substances used to correct or enhance dietary intake. They come in varied forms (tablets, powders, liquids, food products). Many supplements are easily identified as they are consumed in single, purified forms such as tablets. Others in the form of bars, drinks or other food-type products are not always recognised as supplements despite containing the same active ingredients.

### General reasons for Supplement Use

**9**1

# Supply nutrients in a convenient form

e.g. a protein-energy shake can be a practical option when unable to access a meal



### Prevent/manage micronutrient deficiencies

e.g. a B12 supplement is mportant if consuming a vegan diet



### Support a restricted dietary intake

e.g. a multivitamin supplement can be useful when restricting intake to lose body fat



### Enhance performance

e.g. caffeine can enhance concentration and/or physical performance



## **Think Food First**

A focus on the whole diet is more important than eating any one nutrient, substance or food. Each food provides a unique combination of nutrients and other chemicals. Consuming a varied diet is the best way to obtain all required substances in balanced combinations. In some circumstances consuming a concentrated source of one substance can compromise absorption of other nutrients, reduce the body's ability to adapt to stress or even increase disease risk. Defence in agreement with major organisations such as the Australian Institute of Sport (AIS), World Cancer Research Fund International (WCRFI), National Health & Medical Research Council (NHMRC) and Heart Foundation support a food first approach to nutrition. This means that nutrient needs should be primarily met through a mixed diet with use of supplements only when supported by strong evidence and under the guidance of a health professional.

### **Trustworthy Information on Supplements**

The following organisations provide evidence-based information regarding supplements.

World Anti-Doping Agency (WADA)	https://www.wada-ama.org/en/who-we-are The WADA Prohibited List documents substances banned in sport, which is also the same guidance used by the ADF.
Sport Integrity Australia	https://www.sportintegrity.gov.au/what-we-do/anti- doping Previously known as ASADA. Provides information regarding safe and banned substances which also guides ADF supplement policies.
AIS Sports Supplement Framework	<u>https://www.ais.gov.au/nutrition/supplements</u> Provides an evidence-based assessment of the risk and benefits of supplements related to sports performance Provides advice on how to use non-banned supplements effectively
Examine	<u>https://examine.com/</u> Independently reviews research regarding supplement use
Sports Dietitians Australia	https://www.sportsdietitians.com.au/factsheets/ Provide fact sheets on a range of sports nutrition topics including supplements



### **Risks with Supplement Use**

In Australia, regulation of supplements is the responsibility of either the Therapeutic Goods Administration (TGA) or Food Standards Australia New Zealand (FSANZ). These organisations assess the safety of supplements to some degree, however there are still risks associated with using supplements:

- Compromised absorption of other nutrients – e.g. consuming a high dose of a single nutrient such as zinc can reduce absorption of a nutrient such as iron
- Compromised physiological adaptation

   e.g. use of antioxidant supplements can
   impair rather than improve recovery from
   exercise
- 3. Health risk due to contamination e.g. substantial evidence indicates that some supplements contain substances that are not listed on their ingredient list - there are numerous cases of medical conditions e.g. liver damage caused by a variety of supplements perceived to be safe by consumers
- 4. Positive drug test due to contamination -there is a risk of testing positive in routine drug tests when taking supplements that have not been independently tested. The prohibited substance testing program is implemented throughout the ADF (Defence Act 1903 s. 93B(1), AUST). It is a requirement that AF units randomly test at least 25% of the unit strength per financial year, whilst 100% of AF recruits and trainees are to be tested (Department of Defence, 2017).
- 5. **Financial burden**-the cost of supplement use can be expensive and for the cost you may not achieve what has been promised on the label e.g. supplements can be sold without strong proof of efficacy, some supplements contain very low levels of active ingredients listed on labels

- 6. Distraction from other more important areas to enhance health and/or performance – e.g. supplements are very easy to purchase and are heavily marketed, some people neglect more important action in the hope that supplements will provide a 'quick-fix'
- 'More is Better' mentality e.g. higher doses than recommended are often consumed in an attempt to achieve a greater benefit, there is no benefit to exceeding an effective dose





## Reducing Risks of Supplement Use

1	Anyone interested in using a supplement should speak with a trusted health practitioner such as a General Practitioner (GP), Accredited Sports Dietitian, Accredited Practicing Dietitian or Pharmacist. It is important to take a holistic view of health when establishing if there is value or risk associated with use of any particular supplement.
2	Consult the AIS Sports Supplement Framework <u>https://www.ais.gov.au/nutrition/</u> <u>supplements</u> . This provides strong guidance on whether or not there is value in using any particular supplement and outlines evidence-based regimes for using particular supplements.
3	Double check if supplements are permitted to be used in the ADF. Supplements on the WADA Prohibited List are not permitted for use in the ADF. The GlobalDro website allows substances to be checked against the WADA Prohibited List. <u>https://www.globaldro.com/AU/search</u>
4	Where possible, only use supplements that have been tested by an independent organisation such as Informed Sport <u>https://sport.wetestyoutrust.com/</u> or Human and Supplement Testing Australia (HASTA) <u>https://hasta.org.au/</u> These organisations test for all substances listed on the WADA Prohibited List. This does not guarantee safety but does reduce risk.
5	Review ongoing supplement use with a health practitioner. Report any adverse effects to the Therapeutic Goods Administration. <u>https://www.tga.gov.au/</u>



## A Quick Review of 5 Popular Supplements

Protein Powder	Active people, working to increase or maintain a higher muscle mass require more protein than sedentary people. Food should always be the first choice for delivering protein with many foods including meat, fish, eggs, dairy foods, nuts, grains, cereals, lentils and legumes providing good amounts. Protein powders can be a convenient option when access to food is limited or a concentrated source of protein is needed (people with small energy needs). Protein requirements are often over-estimated – 20-40g per shake is likely to be more than sufficient.
Creatine	Creatine is important for fuelling repeated, high-intensity exercise. Supplementation can elevate muscle levels and enhance the quality of high-intensity workouts, including strength sessions. This may help to build muscle mass and strength. Creatine is obtained from animal foods such as meat and fish. People who consume high protein diets might not benefit from creatine supplementation.
Caffeine	Small doses of caffeine (~3mg/kg) have been shown to enhance performance in a wide range of exercise situations. For example, an 85kg aviator would require ~250mg of caffeine. Higher doses of caffeine are unlikely to offer additional benefits. A wide range of foods and beverages provide effective amounts of caffeine however, the amount of caffeine in beverages such as coffee and tea can vary widely depending on how they are prepared. For example, a short black typically provides ~100mg of caffeine per serve but might vary from 25-215mg. For predictable results, sources that provide a consistent, known dose of caffeine (e.g. caffeinated gum) are preferable to beverages such as tea and coffee. Some people experience adverse reactions to caffeine. The timing and dose need to be carefully considered to gain the benefits without adversely affecting sleep etc.
Probiotics	Regular consumption of food sources of probiotics such as yoghurt, fermented milks and fermented foods may support a healthy gut and strong immune function. Use of a concentrated probiotic supplement prior to and during travel might reduce risk of gastrointestinal and respiratory illness. Probiotic supplements need to be consumed for approximately 2 weeks prior to travel to build up good bacteria in the gut.
Pre-Workout	Pre-workout supplements are multi-ingredient products that claim to boost energy, increase fat utilisation and enhance performance. Each pre-workout contains different combinations of ingredients. Substances such as caffeine, beetroot juice, creatine, branched chain amino acids, green tea extract and taurine are common. The effect of combining multiple supplements has not been well tested. Any effect obtained from a pre-workout is most likely due to the caffeine. Defence and the AIS Sports Supplement Framework does not currently support use of pre-workout supplements.







## Article Motivators of Indiscriminate and Unsafe Supplement Use among Young Australians

Alexander Campbell <sup>1,\*</sup>, Julia Carins <sup>1</sup>, Sharyn Rundle-Thiele <sup>1</sup>, Sameer Deshpande <sup>1</sup> and Bradley Baker <sup>2</sup>

- <sup>1</sup> Social Marketing at Griffith, Griffith Business School, Griffith University, Nathan, QLD 4111, Australia; j.carins@griffith.edu.au (J.C.); s.rundle-thiele@griffith.edu.au (S.R.-T.); s.deshpande@griffith.edu.au (S.D.)
- <sup>2</sup> Defence Science & Technology Group, Land Division, Scottsdale, TAS 7260, Australia; Bradley.Baker2@dst.defence.gov.au
- \* Correspondence: alexander.campbell@griffith.edu.au; Tel.: +61-7-37358449

Abstract: Background: There is growing concern about the self-administration of supplements, which can often be indiscriminate, counterproductive to health, and serve as a gateway to more harmful drugs and substances. Research suggests that high uptake of performance- and image-enhancing drugs (PIEDs) is correlated with body image to accentuate masculinity. This study provides insights into limiting unhealthy supplement usage. This research identifies reasons for casual unhealthy supplement use among young adult Australians through the Theory of Planned Behavior (TPB) lens, providing practitioners with insights into developing interventions to deter their use. Method: Semi-structured in-depth interviews were conducted with ten participants aged between 18 and 40, using a convenience sample. Leximancer analysis was used to assess word co-occurrence and map to TPB constructs. Results: Leximancer identified positive attitudes, social norms, and perceived behavioral control towards supplement usage. Key themes that influenced supplement use were weight loss, body image, nutrition, training, education, challenges, need, and time. Furthermore, using TPB constructs, affective and instrumental attitudes and prevailing norms were observed when investigating what would cause an individual to use supplements in an unhealthy manner. Conclusion: Through understanding the motivations of indiscriminate supplement use across the Australian population, the study has uncovered several social factors that may reduce or limit the practice of unsafe supplement usage.

Keywords: Theory of Planned Behavior; supplements; theory; program planning

### 1. Introduction

In Western societies, the use of supplements that pose health risks is increasing [1–4]. This may involve indiscriminate self-administration of substances that are often untested, unlikely to pass a "risk-benefit assessment", not recommended by a health professional, banned in sport, and illegal [5]. Broadly, supplements have been defined as "a food component, nutrient, or non-food compound that is purposely ingested in addition to the habitually-consumed diet to achieve specific health and performance benefit" [6]. This definition covers a wide range, from vitamins and minerals to performance- and image-enhancing drugs (PIEDs). Commonly used PIEDs are growth hormones, peptides, and anabolic–androgenic steroids [7,8].

Australia has witnessed increasing use of PIEDs and lifetime usage rates of anabolicandrogenic steroids [9]. Moreover, users of PIEDs commonly consume many supplements simultaneously (often referred to as stacking), increasing the risks of adverse side effects [10]. There is a high prevalence of supplement usage in Australia, with vitamins, fish oils, herbal supplements, multivitamins, and multi-minerals being commonly used [11]; thus, usage could be considered as normalized within the young Australian population, defined in this study as 18 to 40 years of age.



Citation: Campbell, A.; Carins, J.; Rundle-Thiele, S.; Deshpande, S.; Baker, B. Motivators of Indiscriminate and Unsafe Supplement Use among Young Australians. *Int. J. Environ. Res. Public Health* 2021, *18*, 9974. https:// doi.org/10.3390/ijerph18199974

Academic Editor: Juan Del Coso

Received: 4 August 2021 Accepted: 16 September 2021 Published: 22 September 2021

Publisher's Note: MDPI stays neutral with regard to jurisdictional claims in published maps and institutional affiliations.



Copyright: © 2021 by the authors. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (https:// creativecommons.org/licenses/by/ 4.0/). Most users of supplements such as anabolic–androgenic steroids use them to enhance appearance [12]. Additional motivations for anabolic–androgenic steroid consumption include a desire for masculinity and dissatisfaction with body image [13–15]. Gender differences have been identified, where men use supplements to build muscle mass, decrease recovery time and increase overall power and strength. In contrast, women seek to overcome nutritional deficiency, enhance beauty, lose weight, and maintain energy [16,17]. For young adult athletes, supplement use is split into two predominant areas: healing/recovery and sports performance. For example, protein and creatine are used to enhance athletic performance, and vitamins and minerals are considered to assist during recovery [18]. Factors influencing an athlete's decision to use supplements may include enhancing strength and endurance, reducing recovery from injury, and dietary intake substitution [18]. External influences include recommendations through a personal network, merchants, or the internet [19]. In summary, there is a range of reasons why people commence or continue to use supplements.

Supplement use has recently increased due to the misconception that all plant-derived ingredients pose no health risks [20]. The use of lower-risk supplements (e.g., nutritional supplements) for muscle gain by young people can represent a pathway to unhealthy supplement usage such as anabolic–androgenic steroids [21]. For athletes, legal supplements can act as a gateway to banned or illegal substances [22]. Competitive athletes that use legal supplements (e.g., nutritional supplements) versus those who do not are three and a half times more likely to engage in doping [22], which is defined as the illegitimate use of PIEDs by athletes, amateurs, or professional sportspeople for competitive advantage [23]. Significant differences in beliefs and attitudes towards supplements exist between users are more likely to engage in unsafe supplement use than non-users [22]. This indicates that understanding why users consume supplements can be informative when aiming to prevent use or practices involving health risks.

Common side effects experienced by supplement users include numbness, tremors, shaking, flushing, headaches, abdominal pain, anxiety, dizziness, mood swings, acne, and constipation [24]. There have also been reports of sports supplements causing serious health issues. For example, a young, healthy male experienced a hemorrhagic stroke after taking a sports supplement that lacked a defined disclaimer [25]; other symptoms include palpitations, chest pain, or tachycardia [26]. PIEDs' adverse health effects include cardiotoxic events, cerebral strokes, and psychiatric symptoms [27]. In addition, anabolicandrogenic steroids have adverse effects on the cardiovascular system, atherosclerosis, hypertension, arrhythmia, thrombosis, and erythrocytosis [28]. Although there are supplements that do not pose health risks when used in the prescribed or recommended way, there are some (e.g., anabolic-androgenic steroids) that pose a serious threat to health and well-being [29] and others that pose risks when used indiscriminately (e.g., consumption of multiple supplements, leading to harmful levels of specific substances or interactions between substances) [30]. In addition to health risks, there is the risk of punitive action for PIED users, who, despite the legislative prohibition, are able to obtain PIEDs illegally in the fitness industry [31]. This emphasizes the need for more behavior change interventions to demarket risky supplement usage among identified at-risk and current user groups.

In a bid to design more effective behavioral interventions, an extended understanding of why users are attracted to supplement use is required, particularly for identified at-risk and current user groups. It has been claimed that behavior change efforts are enhanced by applying theory, as theory allows for a rich and robust understanding of how things work [32]. Willmott and Rundle-Thiele [33] synthesize theory application, explaining why and how theory should be used across planning, design, implementation and evaluation phases. Adopting a theory-based approach to guide formative research and program design will allow drivers of the focal behavior to be identified and targeted during intervention, and will support detailed evaluation of programs, leading to refinement for future iterations [34]. This study demonstrates how theory could potentially be applied in

program planning and design. Specifically, this study seeks to understand what factors -should be targeted to elicit the desired change in behavior (e.g., reduction in indiscriminate and unsafe supplement use).

The Theory of Planned Behavior (TPB) [35] was selected as the guiding theoretical framework for this study. The TPB has been found to explain intentions across a range of intentional, planned behaviors. For example, TPB has been used to explain binge drinking among under-aged university students [36,37]. Alcohol drinking is a deliberate and planned behavior requiring effort to access alcohol for purchase and later consumption. TPB has also demonstrated an ability to identify factors to target for change in other intentional contexts, including exercise during pregnancy [38], dietary supplement consumption among HIV-positive black women [39], cervical cancer screening [40], obesity preventions [41], and quitting of smoking, which is a highly addictive substance requiring strong, intentional effort [42].

Taken together, a review of the literature identified that many studies demonstrate the capacity for TPB to explain and predict behavior through a set of clearly defined factors. Meta-analytic studies indicate that the TPB framework can effectively predict health behavior across many behaviors, explaining 19% variation in action and 43% in intentions [43]. TPB is a popular framework with social marketers [44,45] because of its power to predict behavior through understanding attitudes, subjective norms, and perceived behavioral control. According to the TPB, three key factors contribute to intentions: attitudes towards the behavior, perceived behavioral control (PBC), and subjective norms [35], and in turn, intentions explain behavior. Figure 1 explores the two-concept TPB model [46], where:

- Affective attitude—the behavior enjoyable to the individual;
- Instrumental attitudes—the behavior beneficial to the individual;
- Descriptive norms—if other individuals conduct the same behavior;
- Injunctive norms—if others influence the behavior;
- Perceived behavioral control—the individual's confidence in executing an action, and how those constructs can shift intentions.

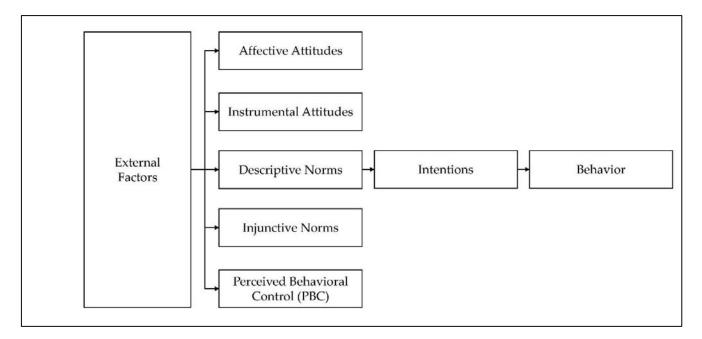


Figure 1. Adaption of Ajzen's Theory of Planned Behavior (TPB). 2011.

With many substances banned for use in Australia, it is hypothesized that supplement use is an intentional behavior requiring cognitive effort to decide to take supplements and deliberate action to purchase substances for consumption. Given the intentionality of the behavior and evidence indicating TPB's potential to explain intentional behaviors, the objective of this study was to apply the TPB framework to identify which theoretical constructs are involved in supplement use, and therefore, which could be targeted during the design of interventions that seek to reduce or limit indiscriminate and unsafe supplement use.

Semi-structured interviews designed using the TPB framework were used to uncover the reasons behind unhealthy supplement usage in an at-risk young adult population. Unhealthy supplement usage was introduced to participants as supplements with known health risks or practices known to increase health risks. This study demonstrates how theory can be applied to identify factors to inform intervention planning and design.

### 2. Materials and Methods

This study follows a qualitative research approach using semi-structured interviews to understand the phenomenon of unhealthy and indiscriminate supplement usage from participants' perspectives, rather than generalizing a large dataset [47]. In qualitative data, saturation (where no new data or constructs of interest emerge) can be reached with approximately 6 to 12 interviews [48,49].

A semi-structured discussion guide was developed based on the TPB model. Table A1 in Appendix A outlines the complete discussion guide linking questions to the TPB model to provide a clear guide on how the theory was applied to identify factors to inform intervention planning and design. Furthermore, the discussion guide seeks to understand the motivations and influences of unhealthy supplement usage, where the user is consuming a level of supplements that are deemed unsafe, and indiscriminate usage, where the user is consuming supplements without careful consideration of the ingredients [29,30].

The following conditions screened participants: level of participation in physical activity, have engaged or witnessed unhealthy supplement usage, under 40 years, and reside in Australia. The recruitment of participants (n = 10) was conducted through a convenience sample method and utilized networks involved in physical activity. Participants were recruited through a social network post via LinkedIn and Facebook, direct email, and inperson recruitment. The semi-structured in-depth interviews were conducted in a 30-min timeframe, voice recorded and later transcribed for analysis. The ten interviews reached data saturation and provided suitable insights to understand the motivator of indiscriminate and unsafe supplement usage. Consent was received before the commencement of the interview, and all data were anonymized to safeguard participant privacy.

The collected data were analyzed using the word association platform, Leximancer. In the study, we used the Leximancer platform to group words, themes, and concepts via co-occurring association from the interview transcripts [50]. Leximancer was selected based on the premise that co-occurring word analysis offers statistical advantages over other qualitative techniques [51]. After the initial analysis, a thematic approach was taken to identify, analyze, and report patterns across the interview dataset [52]. The strategy of pairing the Leximancer platform with thematic content analysis was undertaken to enable the option of textual analysis [53] while remaining firm in analyzing the data objectively [54].

### 3. Results

#### 3.1. Participants

Participants recruited through convenience sampling were primarily men aged from 22 to 39 years, resided in Brisbane, Queensland, Australia, and represented diverse professions (Table 1). The interviews, on average, ran for 25 min.

	Age	Gender	Profession	Supplement Use	Exercise Rate
Participant 1	22	Male	University Student	Moderate	Greater than 3 times per week
Participant 2	28	Male	Scientist	Limited	Once per week
Participant 3	39	Male	Small Business Owner	Limited	Once per week
Participant 4	35	Male	General Practitioner	Limited	Greater the three times per week
Participant 5	34	Male	Mental Health Nurse	Moderate	Twice a week
Participant 6	33	Male	Martial Arts Instructor	Previous user	Greater the three times per week
Participant 7	34	Male	Chef	Undisclosed	Greater the three times per week
Participant 8	26	Female	Retail Worker	Moderate	Greater the three times per week
Participant 9	32	Female	Retail Manager	Moderate	Twice a week
Participant 10	35	Female	Salsa Instructor	Limited	Greater the three times per week

Table 1. Participant profile.

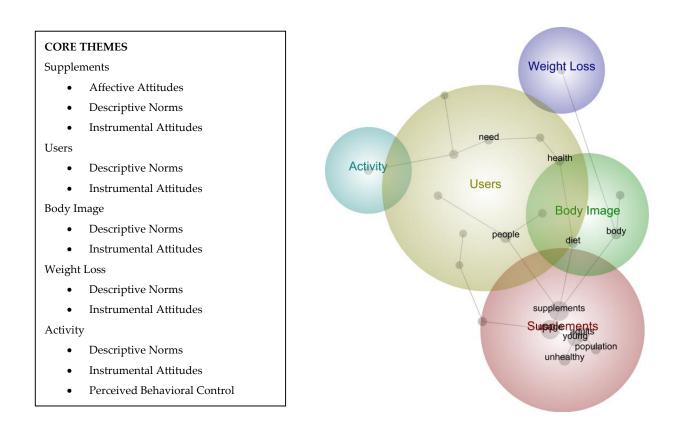
### 3.2. Visual Concept Map, Counts, and Probabilities

Data revealed several concepts reflecting the participants' thoughts and opinions, with each key concept contributing to the overall narrative of response. Table 2 breaks down the concepts by word-like, count, and relevance. Any concept with less than 10% relevance was excluded from the overall results.

Word-Like	Count	Relevance
Supplements	230	100%
Ûsage	204	89%
Adults	90	39%
Young	90	39%
Body	82	36%
People	81	35%
Unhealthy	51	22%
Gym	47	20%
Health	43	19%
Work	37	16%
Education	36	16%
Need	34	15%
Diet	30	13%
Population	26	11%
Training	26	11%
Protein	24	10%
Nutrition	23	10%
Trying	22	10%

Table 2. Ranked themes—semi-structured interviews.

The top-ranked concepts are supplements (230 counts at 100% relevance), usage (204 counts at 89% relevance), adults (90 counts at 39% relevance), young (90 counts at 39% relevance), body (82 counts at 36% relevance), people (81 counts at 35% relevance), unhealthy (51 counts at 22% relevance), gym (47 counts at 20% relevance), health (43 counts at 19% relevance), and work (37 counts at 16% relevance). Five core themes emerged from these concepts. These were supplements, users, activity, weight loss, and body image (Figure 2).



### Figure 2. Leximancer theme map output.

### 3.3. Interview Responses

The five key themes (supplements, users, body image, weight loss, activity) were examined in the TPB constructs of attitudes, subjective norms, and perceived behavioral control to understand how the identified themes influence behavioral intention and action.

### 3.3.1. Supplements

The supplement theme offers the foundational layer to explore TPB concepts. Reference to supplements permitted detailed analysis of the remaining themes. Within the supplement theme, the following co-occurrences of words appeared in the participant dialogue: unhealthy (100%), population (100%), implemented (100%), usage (93%), adults (83%), young (83%), diet (80%), challenges (75%), education (58%), and training (50%) (Table 3). All respondents indicated an unhealthy trend in supplement usage across the population. In addition, respondents highlighted the challenges in education, training, and diet concerning usage levels.

Word-Like	Count	Relevance
unhealthy	51	100%
population	26	100%
implemented	2	100%
usage	189	93%
adults	75	83%
young	75	83%
diet	24	80%
challenges	3	75%
education	21	58%
training	13	50%

### These quotes further illustrate the identified themes.

*The term "unhealthy" has quite a broad meaning. To clarify that for you, and it's your opinion of unhealthy usage instead of my opinions.* 

### Affective Attitudes, Male, 34 Years, Mental Health Nurse, Weightlifter

In terms of scientific studies, there are not nearly enough peer-review scientific studies on the impact of supplements and not just the short term but also the long-term impact of supplements. They say creatine in large doses affects your liver, for example. I don't take large doses, but theoretically, I would be interested, yes.

#### Instrumental Attitudes, Male, 34 Years, Chef, Rock Climber

*My view (assumption) of supplements is if you have a balanced diet, they're not needed. The word supplement means you're supplementing something that's missing from your diet, so look at your diet first.* 

### Instrumental Attitudes, Male, 39 Years, Small Business Owner

I do use supplements. I use an organic protein powder during recovery days and after an extended workout. When I'm training for power, I use micro-doses of concrete creatine. It increases your overall weight, but when I'm training for power, I don't mind having that extra weight very briefly. And I use Codrug. And then, I also use Glutamine for joint recovery because joints get fucked climbing.

### Instrumental Attitudes, Male, 34 Years, Chef, Rock Climber

People who get interested in supplements often do research by themselves, and there is a wealth of knowledge on the internet, but you do get people who just walk into your supplement stores and grab the first thing that is suggested to them. During my creatine use, I read stories of people who used way too much of it and then ran into problems down the line.

Descriptive Norms, Male, 33 Years, Martial Arts Instructor

Respondents indicated a lack of information available on supplements, and if supplements are harmful, they would like to know. Other respondents demonstrated awareness that supplements are not needed if their diet is balanced and delivering needs. These responses gave insight into the perspective of supplement use. The above quotes indicate the instrumental and affective attitudes of supplement usage. Moreover, respondents' attitudes towards supplements seem to be influenced by health, diet, recovery, and nutrition, with one quote questioning the notion of what is unhealthy. Respondents also showed a clear line of questioning regarding body image and unhealthy supplement usage, contesting the evidence, being uncertain, and formulating evidence-based assumptions—thus demonstrating skepticism and the need for further research. Furthermore, instrumental and affective attitudes provide evidence that health, fitness, and nutrition influence unhealthy supplement usage.

### 3.3.2. Users

The term "users" refers to the participants' thoughts and opinions on supplements by other users. The probability of the sub-term being referred to in the Leximancer analysis is as follows: work (32%), protein (29%), time (27%), gym (26%), health (21%), body (21%), need (18%), nutrition (17%), and education (17%). Thus, this indicates that supplements users are influenced to reduce or increase usage based on education levels, nutrition value, body image, and recovery time. This is also substantiated by the evidence of subjective norms in the participants' responses in injunctive and descriptive norms. When referring to the co-occurring words across sub-concepts and the primary concept, body (17), gym (12), and work (12) were all regularly used. The following quotes emphasize the respondents' opinions about users.

I think the number one reason why people do supplements is because of body image and how they perceive themselves, and how they compare themselves to others, because I think a lot of people who use supplementation have specific body images in mind, and they compare themselves to their peers.

### Descriptive Norms, Male, 28 Years, Scientist, Futsal Player

People need to be realistic, and I think that it's just that whole macho bravado across men and women, where women want to be, or they want to compete with men, and social media allows them to compare and constantly. This person's lifting 325 so, they have to do that.

### Descriptive Norms, Male, 35 Years, General Practitioner, Weightlifter

I know it fairly well, and my usage is fairly limited, I would say, so yes, I would benefit, potentially. I would say there's never a bad situation to have more information about it. More information is always helpful. In terms of scientific studies, there are not nearly enough peer-review scientific studies on the impact of supplements and not just the short term but the long-term impact of supplements. They say creatine in large doses affects your liver, for example. I don't take large doses, but theoretically, I would be interested, yes.

Instrumental Attitudes, Male, 34 Years, Chef, Rock Climber

Respondents indicated a linkage between behavior and awareness regarding health implications with supplement use and made the correlation that people who have a poor diet are inadequately educated in nutrition. Furthermore, the respondents also indicated descriptive norms regarding the concerning competitiveness within the alpha dominant genders. In addition, descriptive norms also indicated how body image is a driver of comparison between the individual and their peers, which also links back to the competitiveness of individuals. Instrumental attitudes were also identified, corroborating the need for additional educational materials.

### 3.3.3. Body Image

Body image is another key theme featured in the Leximancer analysis. The term aligns closely with health, weight, need, and nutrition. Sub-terms related to body image are population (35%), weight (33%), need (24%), trying (23%), people (21%), health (21%), adults (19%), young (19%), nutrition (17%), and diet (17%). Therefore, one could postulate that weight gain or loss could influence unsafe supplement usage, circumventing nutrition and healthy diets, and the need to compete with their peers, emphasizing body dysmorphia. When reviewing the co-occurring word count, body image was found to be aligned with people (17), young adults (17), and population (9).

*Of course, it does. Again, it goes back to body image. It's about how many likes you get and how many videos or responses you'll get at the end of the day.* 

### Instrumental Attitudes, Female, 32 Years, Salsa Instructor

*If it's excess, you urinate it out, and it's purely a waste of money. Regarding those guys who want to be professional bodybuilders or in that industry, yes, they need those supplements because there is no way for someone to eat, say, 7000 or 6000 calories to support an extra 15 kilos.* 

Instrumental Attitudes, Male, 35 Years, General Practitioner, Weightlifter

Mostly personality reason and alpha males tend to try and gain an advantage to maintain their alpha status, and they tend to be the ones to end up being gym junkies, and in my experience, the ones more likely to take your heavier supplements such as steroids and that sort of thing to try and short-cut a way to a bigger body and better image.

Descriptive Norms, Male, 39 Years, Small Business Owner, Runner

These results further establish the theme that young adults have opinions of body image relating to health, weight, and diet. The respondents' body image and alpha male status were drivers of supplement use, indicating affective attitudes. Other respondents

reflected instrumental attitudes, stating that overdosing is a waste of money if you are not a professional athlete and that supplements are attractive for obtaining fitness, performance, and body image goals. Considering instrumental attitudes and descriptive norms indicates that the concepts of challenging alpha gender stereotypes or alpha-dominated aspirations could potentially circumvent unhealthy supplement usage.

### 3.3.4. Weight Loss

The weight loss terms have the lowest probability of the five major themes, highlighting them as lower priorities. However, the relationship between body and weight was represented in the co-occurring word count, as it has been identified to have seven different instances within the two concepts. Leximancer uncovered the following probability of cooccurring word associations: trying (14%), training (12%), body (9%), need (6%), gym (4%), protein (4%), people (4%), health (2%), and supplements (2%). Individuals are influenced by supplements for weight loss regarding training, gym, health, and body image. The following quotes reflect upon the respondents' opinions about weight loss.

*Certainly, young people are looking to radically change their body image. Young athletes and young people who are looking to shed weight rapidly and easily.* 

### Descriptive Norms, Male, 33 Years, Martial Arts Instructor

*Like I said, body image, especially if you want to go into tournaments, you'll need something to start with, so if you're trying to lose weight fast as well.* 

### Instrumental Attitudes, Female, 32 Years, Salsa Instructor

If I had a specific goal, it would be interesting to know what the specifically indicated supplements would be that you would need to achieve that goal. For instance, when your body's trying to lose weight, put on muscle mass, or try to improve certain fitness aspects.

### Instrumental Attitudes, Male, 28 Years, Scientist, Futsal Player

These are generally gym people, not so many climbers. I know someone who takes eight to ten tablets a day when he's cutting weight and a ridiculous amount of protein powders and Glutamine and creatine when he's gaining weight. It's ridiculous.

Descriptive Norms, Male, 34 Years, Chef, Rock Climber

The respondents connected body image and weight loss, perceived as a personal emotional response and can incur harmful health outcomes. Moreover, respondents indicated that instrumental attitudes and descriptive norms could influence behavioral intentions to lose weight.

### 3.3.5. Activity

Activity refers to the thoughts and actions relating to physical activity and the relationship with supplement use. It is a secondary trigger to using unhealthy supplements due to the low co-occurring word count. The probability of the co-occurring concepts between activity and sub-concepts is: implemented (50%), challenges (25%), protein (21%), work (19%), people (15%), time (13%), need (12%) and weight (10%). The co-occurring concepts indicated that work and time are potential challenges that may influence the use of unsafe supplements. The following quotes emphasize the relationship that adults under 40 years have with physical activity.

I think young men would not like the changes at all, particularly those that actively use it. I think I would struggle with that, and young men involved in sports looking for performance enhancements.

Instrumental Attitudes, Female, 35 Years, Retail Manager, Pole Fitness

You could bring education into the gyms, but the gyms would need to bring it in. You can't expect the gym to be talking about nutrition, but that is probably where it needs to be implemented.

### Perceived Behavioral Control, Male, 26 Years, Retail Worker, Body Building

I would say it would be males over females. People that have low self-confidence or put a lot of pressure on themselves to succeed. As a result, they turn to illegal substances or unhealthy supplements.

Instrumental Attitudes, Male, 22 Years, University Student, Local AFL

The respondents focused on education and nutrition, and emotions. Other respondents noted the instrumental attitudes of users as they are not receptive to health advice regarding supplements. This was further substantiated with the affective attitudes of users concerning the external pressures to succeed. Participants indicated low ability and, hence, low perceived behavioral control to avoid supplements when not provided with nutritional education.

### 3.4. Synthesis of Themes

The Leximancer analysis uncovered strong themes and concepts. The information gathered from the semi-structured interviews helped understand the influences that encouraged supplement usage through the lens of the TPB constructs, namely behavioral intentions, social norms, attitudes, and perceived behavioral control. Perceived behavioral control was observed to a limited extent in the themes.

The key themes that influenced supplement use were weight loss, body image, nutrition, training, education, challenges, need, and reduced recovery time. The analysis helped understand what influences a young adult to start using supplements. From a TPB perspective, affective and instrumental attitudes were observed frequently. Affective attitudes were directed to alpha gender stereotypes and their emotional reactions to unhealthy supplements, whereas instrumental attitudes were concerned with health and nutrition. At the same time, descriptive norms were central to health and education about users. The perceived behavioral control constructs were influenced by the educational, community, and fitness benefits of users.

From the themes, two underlining narratives were identified as alpha dominant and health. These narratives could inform messaging for two intervention strategies to reduce unhealthy supplement usage.

The majority of the TPB constructs aligned with identified themes, as illustrated in Figure 3. However, injunctive norms were not explicit. The response data could identify the individual's feelings (affective attitude) if the behavior was beneficial (instrumental attitudes), if others conduct the same behavior (descriptive norms) and if the action of the behavior is in their control (perceived behavioral control). It was not clear whether the behavior of supplement usage was influenced by others (injunctive norms), presenting a gap within the dataset.

Other gaps were evident. The behavioral intention was present, but not well-defined in participants responses. The instrumental attitudes of participants were clear; however, affective attitudes had limited presence. Furthermore, perceived behavioral control output was also identified but limited within the dataset.

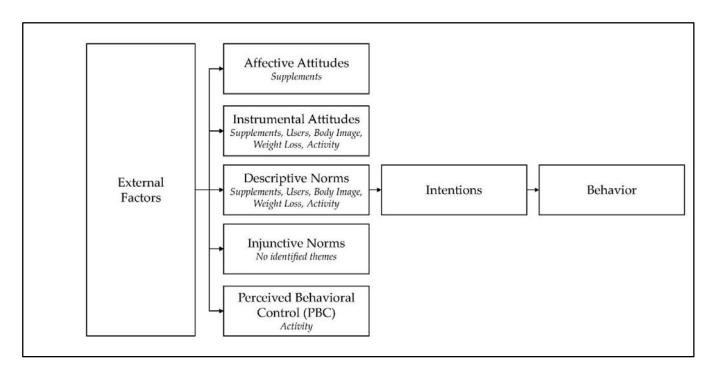


Figure 3. Theory of Planned Behavior with established concepts.

### 4. Discussion

This research aimed to identify the reasons for unhealthy supplement use among young Australians through the TPB lens to design interventions, aiming to limit, reduce, and eliminate harmful supplement usage.

Specifically, the study uncovered an individual's motivations to use supplements linked to the desire to excel, physically dominate (an alpha-dominant aspiration) and improve health and recovery. These insights are valuable and indicate that not all users may respond to messages promoting health or identifying the risks or consequences of taking supplements due to competing desires for performance, excellence, and body dysmorphia.

This study has furthered the literature for the TPB in the health and supplement field by offering qualitative evidence that developing alpha-dominant and health-based interventions could potentially shift an individual's motivations to use supplements in an indiscriminate and potentially unsafe manner. Whilst scholars have investigated supplements in terms of consumption, motivations, attitudes, and influences [55–59], this study contributes theoretical concepts that can be used to limit or reduce supplement usage within a health-focused intervention. In addition, this study contributes to both the health and social marketing literature, as the TPB constructs were used to inform potential messaging strategies to reduce or limit indiscriminate and unhealthy supplement usage. There is limited research that connects theory with a behavioral intervention, with scholars calling for more theory-led design for interventions [45,60].

Furthermore, this study corroborates a TPB supplement study by Nagar [55]. It found that attitudes affect supplement purchase intentions, and those attitudes are guided by risk–benefit, social influences, and health consciousness. Our study validates how the TPB constructs of instrumental and affective attitude, injunctive and descriptive norms, and perceived behavioral control can be used to limit or reduce unhealthy supplement usage levels through a phenomenological approach. By establishing reciprocity between interview and interviewee [61], the study uncovered a vital secondary viewpoint and perspective from participants on limiting or reducing unhealthy usage levels of supplements, giving insight on motivations and influences [62] instead of general characteristics.

In terms of method, this study used Leximancer to identify co-occurring associations within the semi-structured interviews. This allowed the analysis to theoretically link critical

themes and their associations with TPB constructs, leading to a deeper understanding of behavioral intentions and influences, and better informing social marketing interventions.

# 4.1. Implication for Interventions and Program Development

This study indicates the need for a social marketing intervention highlighting the importance of diet and nutrition, supplemented with a demonstration of adverse outcomes to users of unhealthy supplements to address an individual's attitudes towards health or physical performance.

These messages could be delivered at gyms that young people frequent via trainers and communication materials available on site. Fitness magazines, books, websites, blogs, and sports endorsements could deliver these messages. These recommendations imply the need to enhance a training curriculum that combines the dual messages of health and alpha dominance. Organizations that employ young men for their physical fitness (such as federal defense and state police) should undertake employee wellness initiatives to ensure their employees are not at risk. Finally, supplement manufacturers should push for appropriate supplements and supplement use as part of their corporate social responsibility initiatives. Potential messaging strategies could utilize affective and instrumental attitudes with the application of an alpha-dominant and health-based messaging strategy to (1) target alternative body types and challenge negative perceptions of body image, (2) define unhealthy supplement usage while highlighting the negative consequences of shortcuts, and (3) place emphasis on educational material on safe usage levels and alternative dietary options.

# 4.2. Limitations and Future Research

This study provided valuable insights into supplement use. However, some limitations must be acknowledged. These limitations offer avenues for future research. This study (n = 10) had a small sample size, which was sourced through a convenience sample. In addition, there was an uneven distribution between male and female participants, which limited the comparison between gender responses. However, the sample was sufficient as respondents' responses reached a point of saturation, irrespective of the gender distribution. Qualitative research with small samples provides an opportunity to examine concepts in-depth and presents challenges for generalization beyond the samples achieved, while allowing for a deeper phenomenological understanding of the influences and motivations or unhealthy and indiscriminate supplement usage [46]. A larger, representative sample should be pursued to verify these findings and determine whether these insights apply to groups that differ demographically. Furthermore, future research could investigate participants who only witnessed supplement use, allowing for a greater understanding of how others perceive indiscriminate and unsafe supplements, better informing social norms. The study could have explored the TPB model constructs in more detail, specifically perceived behavioral control and subjective norms.

Leximancer's automated analysis through statistical properties allows for identifying emerging themes via the output [63,64]. However, Leximancer has been critiqued for interpreting the data due to how the analysis is performed [65]. Compared to Leximancer, NVivo is labor intensive in the initial analysis, as the user is required to code to develop the themes or categories [54,64,66]. However, this step coaxes the researchers to be more discrete in their analysis. Therefore, using both NVivo and Leximancer in sequence would provide a more rigorous qualitative analysis through the triangulation of results and enhance understanding of the influences and motivations behind unhealthy supplement use.

Furthermore, TPB could be paired with the Social-Ecological Model (SEM) to investigate supplement use, which can help social marketers extend beyond the downstream approaches and explore potential interventions in the social and built environments [67]. SEM benefits health promotions and helps social marketers extend design thinking beyond the individuals whose behavior needs to change. SEM allows researchers to extrapolate how social influences from friends, family members, personal trainers, other gym members, and the surrounding built environment impact the behavior under study [68,69]. SEM assists when health initiatives are complex and cannot be understood from a single view [68].

Future research is needed to determine whether an intervention based on the theoretically informed insights generated in this study can effectively reduce or limit supplement use compared to a no-treatment control or an information-only intervention. There is also an opportunity to investigate if a theoretically informed social marketing intervention, such as a TPB framework, can reduce or limit unhealthy supplement usage compared to a theoretical intervention, as there are academic calls to utilize theory in intervention design and reporting [44,45,70].

In addition, future TPB studies in supplement usage could implement a longitudinal approach to address the identified gaps within the response data. Going beyond the cross-sectional dataset provided in this study will allow the TPB attitude constructs to be explored in greater detail and address the knowledge gap of injunctive norms, affective attitudes, and perceived behavioral control.

# 5. Conclusions

This study has identified factors that can be used in social marketing programs to lower the indiscriminate and unsafe supplement usage across the young Australian population. The TPB constructs of instrumental and affective attitudes delivered insight into the motivators of supplement usage. Across the synthesized themes, the reoccurring factors which influenced supplement usage were inadequate levels of education, body dysmorphia, cynicism to alternative diets, physical performance, and dietary shortcuts. Addressing these drivers of unsafe supplement usage could potentially limit supplement stacking and the use of PIEDs among the young Australian community. Furthermore, the Leximancer analysis has provided a deep analysis of core concepts and themes through linking co-occurring word-like relationships, offering statistical interpretations of TPB constructs, specifically with affective and instrumental attitudes. These results conclude that young adults have opinions of body image relating to health, weight, and diet. This can be translated to defining the critical narratives of health-based (instrumental attitudes) and alpha-dominant (affective attitudes) messaging for potential intervention strategies. Therefore, using a combination of messaging strategies based on instrumental and affective attitudes, a potential campaign could be developed to help limit or reduce unsafe supplement usage within the young Australian adult population.

**Author Contributions:** Conceptualization, A.C., J.C. and S.R.-T.; method, A.C., J.C., S.R.-T. and S.D.; software, A.C.; formal analysis, A.C., J.C. and S.R.-T.; investigation, A.C.; writing—original draft preparation, A.C.; writing—review and editing, A.C., J.C., S.R.-T., S.D. and B.B.; visualization, A.C.; supervision, J.C. and S.R.-T.; project administration, A.C. and J.C. All authors have read and agreed to the published version of the manuscript.

**Funding:** This research is supported by the Commonwealth of Australia as represented by the Defence Science and Technology Group of the Department of Defence.

**Institutional Review Board Statement:** The study was conducted according to the guidelines of the Declaration of Helsinki and approved by the Defence Science and Technology (DST), the Departments of Defence and Veterans' Affairs Human Research Ethics Committee (protocol reference: 054-18, date of approval 13/04/2018) and Ethics Committee of Griffith University (protocol reference: 2018/599, date of approval 11/07/2018).

Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.

**Data Availability Statement:** The data presented in this study are available on request from the corresponding author. The data are not publicly available due to privacy and ethical reasons.

**Conflicts of Interest:** The authors declare no conflict of interest. The funders had no role in the study's design, in the collection, analysis, or interpretation of data, in the writing of the manuscript, or in the decision to publish results.

# Appendix A

# Table A1. Unhealthy supplement usage semi-structured interview guide.

Stimuli	TPB Constructs
Q1. Can you tell me briefly about yourself and what physical activity you undertake?	Investigating all TPB constructs To open the conversation, establish rapport, and obtain background information about the interviewee and their relationship with physical exercise
<ul> <li>Q2. To begin, I would like to gain your first thoughts on a few different topics. Can you tell me what first comes to mind when I say?</li> <li>Gym</li> <li>Fasting</li> <li>Healthcare</li> <li>Nutrition</li> <li>Cross Fit</li> <li>Cardio</li> <li>Weightlifting</li> <li>Endurance</li> <li>Aerobic</li> <li>Balance</li> <li>Calisthenics</li> <li>Body Image</li> <li>Supplement</li> <li>Attitude</li> <li>Rhythm</li> </ul>	Investigating all TPB constructs To relax the participant and create an environment that encourages them to share their thoughts and opinions openly Direct the interviewee's attention towards the topic of interest Encourages forthrightness in answers Insights into true feelings as answers will be their first thoughts
Q3. Regarding diet, what do you think about the use of supplements in your training regime?	Investigating instrumental attitudes
Q4. If using supplements, what supplements are they?	Gaining young Australians' perspective on unhealthy supplement usage
Q5. Would you benefit from supplement usage education?	Investigating perceived behavioral control
Q6. What do you see as disadvantages to reducing supplement usage?	Identifying emotional barriers and enablers
Q7. What comes to mind when curbing risky supplement usage across young adults?	Investigating affective and instrumental attitudes Identifying cognitive, actual barriers, enablers, exploring individual behavioral responses, and identifying underlying attitudes

Stimuli	TPB Constructs		
<i>Q8. What challenges do you foresee if an initiative is implemented to reduce or curb risky supplement usage?</i>	Investigating perceived behavioral control _ Identifying the level of perceived control over young adult unhealthy supplement usage, and a		
Q9. What factors would cause young adults to start or continue to use risky supplements?	internal or external barriers to these perceptions		
Q10. If you want to reduce unhealthy supplement usage levels within the young adult population, whom do you turn to?			
Q11. What is the least beneficial resource when educating young adults about unhealthy supplement usage?	Investigating descriptive and injunctive norms		
Q12. Within the young adult population, who do you think are using supplements for performance enhancements?	Understanding key influencers may be determining the use of risky supplements within the young adult population.		
Q13. Within the young adult population, who do you think are using supplements to improve body image?	_		
Q14. When it comes to educating unhealthy supplement usage within the young adult population, who do you believe would be opposed to change, and who would be receptive?	Investigating behavioral intentions This section refers directly to opinions on supplement usage within the young adult population to ascertain their normatively held beliefs		

# References

- 1. Brennan, B.P.; Kanayama, G.; Pope, H.G., Jr. Performance-enhancing drugs on the web: A growing public-health issue. *Am. J. Addict.* **2013**, 22, 158–161. [CrossRef]
- 2. Seear, K.; Fraser, S.; Moore, D.; Murphy, D. Understanding and responding to anabolic steroid injecting and hepatitis C risk in Australia: A research agenda. *Drugs Educ. Prev. Policy* **2015**, *22*, 449–455. [CrossRef]
- 3. Underwood, M. Exploring the social lives of image and performance enhancing drugs: An online ethnography of the Zyzz fandom of recreational bodybuilders. *Int. J. Drug Policy* **2017**, *39*, 78–85. [CrossRef]
- 4. Yager, Z.; McLean, S. Muscle building supplement use in Australian adolescent boys: Relationships with body image, weight lifting, and sports engagement. *BMC Pediatrics* **2020**, *20*, 1–9. [CrossRef]
- 5. Burke, L.M. Practical issues in evidence-based use of performance supplements: Supplement interactions, repeated use and individual responses. *Sports Med.* **2017**, *47*, 79–100. [CrossRef] [PubMed]
- Maughan, R.J.; Burke, L.M.; Dvorak, J.; Larson-Meyer, D.E.; Peeling, P.; Phillips, S.M.; Rawson, E.S.; Walsh, N.P.; Garthe, I.; Geyer, H. IOC consensus statement: Dietary supplements and the high-performance athlete. *Int. J. Sport Nutr. Exerc. Metab.* 2018, 28, 104–125. [CrossRef] [PubMed]
- Van de Ven, K.; Maher, L.; Wand, H.; Memedovic, S.; Jackson, E.; Iversen, J. Health risk and health seeking behaviours among people who inject performance and image enhancing drugs who access needle syringe programs in Australia. *Drug Alcohol Rev.* 2018, *37*, 837–846. [CrossRef]
- 8. Larance, B.; Degenhardt, L.; Copeland, J.; Dillon, P. Injecting risk behaviour and related harm among men who use performanceand image-enhancing drugs. *Drug Alcohol Rev.* 2008, 27, 679–686. [CrossRef]
- 9. Australian Institute of Health and Welfare. *National Drug Strategy Household Survey 2016: Detailed Findings;* AIHW: Canberra, Australia, 2017.
- Sagoe, D.; McVeigh, J.; Bjørnebekk, A.; Essilfie, M.-S.; Andreassen, C.S.; Pallesen, S. Polypharmacy among anabolic-androgenic steroid users: A descriptive metasynthesis. *Subst. Abus. Treat. Prev. Policy* 2015, 10, 1–19. [CrossRef]
- 11. O'Brien, S.K.; Malacova, E.; Sherriff, J.L.; Black, L.J. The prevalence and predictors of dietary supplement use in the Australian population. *Nutrients* **2017**, *9*, 1154. [CrossRef]
- 12. Kanayama, G.; Pope, H.G., Jr. History and epidemiology of anabolic androgens in athletes and non-athletes. *Mol. Cell. Endocrinol.* **2018**, *464*, 4–13. [CrossRef] [PubMed]
- 13. Neumark-Sztainer, D.; Cafri, G.; Wall, M. Steroid use among adolescents: Longitudinal findings from Project EAT. *Pediatrics* 2007, 119, 476–486.
- 14. Irving, L.M.; Wall, M.; Neumark-Sztainer, D.; Story, M. Steroid use among adolescents: Findings from Project EAT. J. Adolesc. Health 2002, 30, 243–252. [CrossRef]
- 15. Mooney, R.; Simonato, P.; Ruparelia, R.; Roman-Urrestarazu, A.; Martinotti, G.; Corazza, O. The use of supplements and performance and image enhancing drugs in fitness settings: A exploratory cross-sectional investigation in the United Kingdom. *Hum. Psychopharmacol. Clin. Exp.* **2017**, *32*, e2619. [CrossRef]
- 16. Attlee, A.; Haider, A.; Hassan, A.; Alzamil, N.; Hashim, M.; Obaid, R.S. Dietary supplement intake and associated factors among gym users in a university community. *J. Diet. Suppl.* **2018**, *15*, 88–97. [CrossRef] [PubMed]
- 17. Kobayashi, E.; Sato, Y.; Umegaki, K.; Chiba, T. The prevalence of dietary supplement use among college students: A nationwide survey in Japan. *Nutrients* 2017, *9*, 1250. [CrossRef]
- 18. Burns, R.D.; Schiller, M.R.; Merrick, M.A.; Wolf, K.N. Intercollegiate student athlete use of nutritional supplements and the role of athletic trainers and dietitians in nutrition counseling. *J. Am. Diet. Assoc.* 2004, 104, 246–249. [CrossRef]
- 19. Laure, P.; Binsinger, C. Adolescent athletes and the demand and supply of drugs to improve their performance. *J. Sports Sci. Med.* **2005**, *4*, 272.
- 20. Rocha, T.; Amaral, J.S.; Oliveira, M.B.P. Adulteration of dietary supplements by the illegal addition of synthetic drugs: A review. *Compr. Rev. Food Sci. Food Saf.* **2016**, *15*, 43–62. [CrossRef]
- 21. Hildebrandt, T.; Harty, S.; Langenbucher, J.W. Fitness supplements as a gateway substance for anabolic-androgenic steroid use. *Psychol. Addict. Behav.* 2012, 26, 955. [CrossRef]
- 22. Backhouse, S.; Whitaker, L.; Petróczi, A. Gateway to doping? Supplement use in the context of preferred competitive situations, doping attitude, beliefs, and norms. *Scand. J. Med. Sci. Sports* **2013**, *23*, 244–252. [CrossRef]
- 23. Lazuras, L.; Barkoukis, V.; Rodafinos, A.; Tzorbatzoudis, H. Predictors of doping intentions in elite-level athletes: A social cognition approach. *J. Sport Exerc. Psychol.* **2010**, *32*, 694–710. [CrossRef] [PubMed]
- 24. Baker, B.; Probert, B.; Pomeroy, D.; Carins, J.; Tooley, K. Prevalence and Predictors of Dietary and Nutritional Supplement Use in the Australian Army: A Cross-Sectional Survey. *Nutrients* **2019**, *11*, 1462. [CrossRef] [PubMed]
- Young, C.; Oladipo, O.; Frasier, S.; Putko, R.; Chronister, S.; Marovich, M. Hemorrhagic stroke in young healthy male following use of sports supplement Jack3d. *Mil. Med.* 2012, 177, 1450–1454. [CrossRef]
- Geller, A.I.; Shehab, N.; Weidle, N.J.; Lovegrove, M.C.; Wolpert, B.J.; Timbo, B.B.; Mozersky, R.P.; Budnitz, D.S. Emergency department visits for adverse events related to dietary supplements. *N. Engl. J. Med.* 2015, 373, 1531–1540. [CrossRef] [PubMed]
- 27. Brennan, R.; Wells, J.S.; Van Hout, M.C. The injecting use of image and performance-enhancing drugs (IPED) in the general population: A systematic review. *Health Soc. Care Community* **2017**, *25*, 1459–1531. [CrossRef]

- 28. Goldman, A.; Basaria, S. Adverse health effects of androgen use. *Mol. Cell. Endocrinol.* **2018**, 464, 46–55. [CrossRef]
- 29. Momaya, A.; Fawal, M.; Estes, R. Performance-enhancing substances in sports: A review of the literature. *Sports Med.* **2015**, *45*, 517–531. [CrossRef] [PubMed]
- 30. Garthe, I.; Maughan, R.J. Athletes and supplements: Prevalence and perspectives. *Int. J. Sport Nutr. Exerc. Metab.* 2018, 28, 126–138. [CrossRef]
- 31. Illicit Drug Markets in Queensland: 2015–16 Intelligence Assessment; Crime and Corruption Commision: Fortitude Valley, Australia, 2016.
- 32. Michie, S.; Prestwich, A. Are interventions theory-based? Development of a theory coding scheme. *Health Psychol.* **2010**, *29*, 1. [CrossRef]
- 33. Willmott, T.; Rundle-Thiele, S. Are we speaking the same language? Call for action to improve theory application and reporting in behaviour change research. *BMC Public Health* **2021**, *21*, 1–8. [CrossRef] [PubMed]
- 34. Rundle-Thiele, S.; Pang, B.; Knox, K.; David, P.; Parkinson, J.; Hussenoeder, F. Generating new directions for reducing dog and koala interactions: A social marketing formative research study. *Australas. J. Environ. Manag.* **2019**, *26*, 173–187. [CrossRef]
- 35. Ajzen, I. The theory of planned behavior. Organ. Behav. Hum. Decis. Process. 1991, 50, 179–211. [CrossRef]
- 36. Deshpande, S.; Rundle-Thiele, S. Segmenting and targeting American university students to promote responsible alcohol use: A case for applying social marketing principles. *Health Mark. Q.* **2011**, *28*, 287–303. [CrossRef] [PubMed]
- 37. Ross, A.; Jackson, M. Investigating the theory of planned behaviour's application to binge drinking among university students. *J. Subst. Use* **2013**, *18*, 184–195. [CrossRef]
- 38. Walker, C.; Mills, H.; Gilchrist, A. Experiences of physical activity during pregnancy resulting from in vitro fertilisation: An interpretative phenomenological analysis. *J. Reprod. Infant Psychol.* **2017**, *35*, 365–379. [CrossRef]
- Lino, S.; Marshak, H.H.; Herring, R.P.; Belliard, J.C.; Hilliard, C.; Campbell, D.; Montgomery, S. Using the theory of planned behavior to explore attitudes and beliefs about dietary supplements among HIV-positive Black women. *Complementary Ther. Med.* 2014, 22, 400–408. [CrossRef]
- Roncancio, A.M.; Ward, K.K.; Sanchez, I.A.; Cano, M.A.; Byrd, T.L.; Vernon, S.W.; Fernandez-Esquer, M.E.; Fernandez, M.E. Using the theory of planned behavior to understand cervical cancer screening among Latinas. *Health Educ. Behav.* 2015, 42, 621–626. [CrossRef]
- 41. Didarloo, A.; Sharafkhani, N.; Gharaaghaji, R.; Sheikhi, S. Application of theory of planned behavior to improve obesitypreventive lifestyle among students: A school-based interventional study. *Int. J. Pediatr.* **2017**, *5*, 6057–6067.
- 42. Rise, J.; Kovac, V.; Kraft, P.; Moan, I.S. Predicting the intention to quit smoking and quitting behaviour: Extending the theory of planned behaviour. *Br. J. Health Psychol.* **2008**, *13*, 291–310. [CrossRef]
- 43. McEachan, R.R.C.; Conner, M.; Taylor, N.J.; Lawton, R.J. Prospective prediction of health-related behaviours with the theory of planned behaviour: A meta-analysis. *Health Psychol. Rev.* 2011, *5*, 97–144. [CrossRef]
- 44. Truong, V.D. Social marketing: A systematic review of research 1998–2012. Soc. Mark. Q. 2014, 20, 15–34. [CrossRef]
- 45. Truong, V.D.; Dang, N.V. Reviewing research evidence for social marketing: Systematic literature reviews. In *Formative Research in Social Marketing*; Springer: Berlin/Heidelberg, Germany, 2017; pp. 183–250.
- 46. Courneya, K.S.; Conner, M.; Rhodes, R.E. Effects of different measurement scales on the variability and predictive validity of the "two-component" model of the theory of planned behavior in the exercise domain. *Psychol. Health* **2006**, *21*, 557–570. [CrossRef]
- 47. McGrath, C.; Palmgren, P.J.; Liljedahl, M. Twelve tips for conducting qualitative research interviews. *Med. Teach.* **2019**, *41*, 1002–1006. [CrossRef] [PubMed]
- 48. Guest, G.; Bunce, A.; Johnson, L. How many interviews are enough? An experiment with data saturation and variability. *Field Methods* **2006**, *18*, 59–82. [CrossRef]
- 49. Draper, A.; Swift, J.A. Qualitative research in nutrition and dietetics: Data collection issues. *J. Hum. Nutr. Diet.* **2011**, 24, 3–12. [CrossRef] [PubMed]
- Smith, A.E.; Humphreys, M.S. Evaluation of unsupervised semantic mapping of natural language with Leximancer concept mapping. *Behav. Res. Methods* 2006, 38, 262–279. [CrossRef] [PubMed]
- 51. Cretchley, J.; Gallois, C.; Chenery, H.; Smith, A. Conversations between carers and people with Schizophrenia: A qualitative analysis using Leximancer. *Qual. Health Res.* **2010**, *20*, 1611–1628. [CrossRef]
- 52. Braun, V.; Clarke, V. Using thematic analysis in psychology. Qual. Res. Psychol. 2006, 3, 77–101. [CrossRef]
- 53. Biroscak, B.J.; Scott, J.E.; Lindenberger, J.H.; Bryant, C.A. Leximancer software as a research tool for social marketers: Application to a content analysis. *Soc. Mark. Q.* 2017, *23*, 223–231. [CrossRef]
- 54. Sotiriadou, P.; Brouwers, J.; Le, T.-A. Choosing a qualitative data analysis tool: A comparison of NVivo and Leximancer. *Ann. Leis. Res.* **2014**, *17*, 218–234. [CrossRef]
- 55. Nagar, K. An Examination of Gym Supplement Choice: Using the Modified Theory of Planned Behaviour. *J. Food Prod. Mark.* **2020**, *26*, 499–520. [CrossRef]
- 56. van der Horst, K.; Siegrist, M. Vitamin and mineral supplement users. Do they have healthy or unhealthy dietary behaviours? *Appetite* **2011**, *57*, 758–764. [CrossRef]
- 57. Wu, W.-Y.; Linn, C.T.; Fu, C.-S.; Sukoco, B.M. The role of endorsers, framing, and rewards on the effectiveness of dietary supplement advertisements. *J. Health Commun.* **2012**, *17*, 54–75. [CrossRef] [PubMed]

- 58. Garthe, I.; Ramsbottom, R. Elite athletes, a rationale for the use of dietary supplements: A practical approach. *PharmaNutrition* **2020**, *14*, 100234. [CrossRef]
- 59. Santos, G.H.; Coomber, R. The risk environment of anabolic–androgenic steroid users in the UK: Examining motivations, practices and accounts of use. *Int. J. Drug Policy* **2017**, *40*, 35–43. [CrossRef]
- 60. Willmott, T.; Pang, B.; Rundle-Thiele, S.; Badejo, A. Reported theory use in electronic health weight management interventions targeting young adults: A systematic review. *Health Psychol. Rev.* **2019**, *13*, 295–317. [CrossRef] [PubMed]
- 61. Høffding, S.; Martiny, K. Framing a phenomenological interview: What, why and how. *Phenomenol. Cogn. Sci.* **2016**, *15*, 539–564. [CrossRef]
- 62. Fuchs, T. The phenomenology and development of social perspectives. Phenomenol. Cogn. Sci. 2013, 12, 655–683. [CrossRef]
- 63. Jones, M.; Diment, K. *The CAQDA Paradox: A Divergence between Research Method and Analytical Tool*; Merlien Institure: Utrecth, The Netherlands, 2010.
- 64. Wilk, V.; Soutar, G.N.; Harrigan, P. Tackling social media data analysis: Comparing and contrasting QSR NVivo and Leximancer. *Qual. Mark. Res. Int. J.* 2019, 22, 94–113. [CrossRef]
- 65. Hansson, T.; Carey, G.; Kjartansson, R. A multiple software approach to understanding values. J. Beliefs Values 2010, 31, 283–298. [CrossRef]
- 66. McKeown, T.; Mazzarol, T.; Soutar, G. The Future of Work: An Australian Small Business View. In Proceedings of the ICSB World Conference Proceedings, Cairo, Egypt, 18–21 June 2019; pp. 1–13.
- 67. Wymer, W. Developing more effective social marketing strategies. J. Soc. Mark. 2011, 1, 17–31. [CrossRef]
- 68. Robinson, T. Applying the socio-ecological model to improving fruit and vegetable intake among low-income African Americans. *J. Community Health* **2008**, *33*, 395–406. [CrossRef] [PubMed]
- 69. Stokols, D. Translating social ecological theory into guidelines for community health promotion. *Am. J. Health Promot.* **1996**, *10*, 282–298. [CrossRef]
- 70. Luca, N.R.; Suggs, L.S. Theory and model use in social marketing health interventions. *J. Health Commun.* **2013**, *18*, 20–40. [CrossRef]



Review



# A Systematic Review of the Effect of Dietary Supplements on Cognitive Performance in Healthy Young Adults and Military Personnel

# Diane E. Pomeroy <sup>1,\*</sup>, Katie L. Tooley <sup>1</sup>, Bianka Probert <sup>2</sup>, Alexandra Wilson <sup>3</sup> and Eva Kemps <sup>3</sup>

- <sup>1</sup> Cognition and Behaviour, Land Division (Edinburgh), Defence Science & Technology, Department of Defence, Edinburgh, South Australia 5111, Australia; Katie.Tooley@dst.defence.gov.au
- <sup>2</sup> Food and Nutrition, Land Division (Scottsdale), Defence Science & Technology, Department of Defence, Scottsdale, Tasmania 7260, Australia; Bianka.Probert@dst.defence.gov.au
- <sup>3</sup> School of Psychology, Flinders University, Bedford Park, South Australia 5042, Australia; wils0602@flinders.edu.au (A.W.); Eva.Kemps@flinders.edu.au (E.K.)
- \* Correspondence: Diane.Pomeroy@dst.defence.gov.au

Received: 17 January 2020; Accepted: 14 February 2020; Published: 20 February 2020



Abstract: Intake of dietary supplements has increased, despite evidence that some of these have adverse side effects and uncertainty about their effectiveness. This systematic review examined the evidence for the cognitive benefits of a wide range of dietary supplements in healthy young adult samples; the aim was to identify if any might be useful for optimising cognitive performance during deployment in military personnel. Searches were conducted in 9 databases and 13 grey literature repositories for relevant studies published between January 2000 and June 2017. Eligible studies recruited healthy young adults (18–35 years), administered a legal dietary supplement, included a comparison control group, and assessed cognitive outcome(s). Thirty-seven of 394 identified studies met inclusion criteria and were included for synthesis. Most research was deemed of low quality (72.97%; SIGN50 guidelines), highlighting the need for sound empirical research in this area. Nonetheless, we suggest that tyrosine or caffeine could be used in healthy young adults in a military context to enhance cognitive performance when personnel are sleep-deprived. Caffeine also has the potential benefit of improving vigilance and attention during sustained operations offering little opportunity for sleep. Inconsistent findings and methodological limitations preclude firm recommendations about the use of other specific dietary supplements.

Keywords: dietary supplements; cognition; cognitive performance enhancement; military; healthy young adults

# 1. Introduction

A dietary supplement is broadly defined as "a food, food component, nutrient, or non-food compound that is purposefully ingested in addition to the habitually-consumed diet with the aim of achieving a specific health and/or performance benefit" [1]. More specifically, dietary supplements include multivitamins/minerals, individual vitamins/minerals, protein and amino acids, purported prohormones, herbal (plant derived) substances, joint health products, combination products and non-categorical dietary supplements (plant, animal and synthetic derived substances) [2,3]. These may be consumed by mouth as powders, liquids, capsules or tablets. The dietary supplements market has been estimated at 132.8 billion USD in 2016, with projections this will increase to 220.3 billion USD in 2022 [4].

The use of dietary supplements is generally self-prescribed and easily accessible, with consumption increasing, particularly among healthy young adults. Consumption rates of dietary supplements in an

Australian university population were found to be approximately 70% [5], with similar but lower rates identified in military populations [6,7]. Interestingly, a recent report of Australian military personnel observed an increase in the use of supplements, where 76% of men and 87% of women reported using a dietary supplement for a health benefit, indicating that usage within the Australian Army is high [8].

The observed overall increase in the use of dietary supplements within the community is alarming and has occurred despite little empirical evidence for their effectiveness and the observation of adverse effects [2,9–21]. Such adverse effects include insomnia (ginseng) [22], liver damage (unspecified supplements) [23], an increased risk of bleeding (gingko biloba, fish oil) [19,22], interactions with ibuprofen (gingko biloba) [24] and death (caffeine and energy supplements, respectively) [25,26]. Of particular concern is a report stating that an increasing number of dietary supplements contain unlisted potentially life threatening ingredients [27]. Nonetheless, some studies do suggest that dietary supplements may modulate some aspects of cognitive performance in healthy young adults. Supplements that have shown some cognitive benefits result from omega-3 [28,29], multivitamins and minerals [30,31] and caffeine [32].

Concurrently, defence organisations recognise the need to prepare or enhance the cognitive performance of their soldiers whilst in complex or uncertain operational environments. These commonly encompass increased exposure to a variety of stressors including sleep deprivation, climatic extremes, inadequate nutrition, physiological exhaustion and cognitive demands. Decrements in cognitive performance as a result of these stressors can be costly to the individual and the unit. For example, intense field training can increase response time by 20 milliseconds [33], which could be significant in a fire fight. Likewise, sleep deprivation can increase reaction time and errors [32], as well as negatively affect moral judgment [34] and emotional response [35]. As mistakes can be costly, it is important to identify evidence-based means of preserving or enhancing the cognitive performance of military personnel. The effectiveness, durability, and acceptability of other methods, such as computer-based cognitive training and mindfulness training are still being investigated. These other methods are also time intensive and require practice to prevent skill fade. Scientifically supported dietary supplements may provide an alternative to other methods that might be used. Given the widespread use of such supplements by healthy young adults, including military personnel, appropriate ingestion of these is likely to be more acceptable than other means of cognitive enhancement.

The high consumption of dietary supplements by the military, the equivocal empirical evidence for a positive effect on cognitive performance, and a desire to maintain or improve cognitive performance during deployment warrant further investigation into the relationship between legal dietary supplements and cognitive performance in healthy young adults.

This literature review was undertaken in response to a request from the Australian Army for evidenced-based information on the effects of dietary supplementation on cognitive performance. Accordingly, its overall aim was to identify whether legal dietary supplements may enable a military cohort to achieve and maintain optimal cognitive performance during deployment, and which specific aspects of cognitive function can be enhanced. Thus, the focus on a 'military context' and how the Army could implement information was imperative and as such has been discussed throughout with this specific focus.

#### 2. Materials and Methods

Methods employed in this review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [36]. The review protocol was registered with the International Prospective Register of Systematic Review (PROSPERO) on 19 April 2017 and was last updated 9 September 2017 (registration number CRD42017060300). The protocol modification was to (a) remove an erroneous reference to a clinical population; (b) remove a reference to a detailed analysis of the current status of supplement use and the health status of Australian Defence Force personnel, as another large study was commenced within Defence Science and Technology addressing these questions; and (c) extend the scope of keywords describing the review. The review was conducted by subject matter

experts with sufficient expertise to properly evaluate the efficacy of various dietary supplements on cognitive performance. The Participants, Interventions, Comparisons, Outcomes, Study Design (PICOS) method was used to define the scope of the review (see Table 1). Papers were evaluated for beneficial outcomes in terms of one or more aspects of cognitive performance. Any adverse effects were noted to allow consideration of cost-benefits of potentially unsafe supplements.

**Table 1.** Criteria (Participants, Interventions, Comparisons, Outcomes, Study Design–PICOS) used to define the scope of the review.

Parameter	Description
Population	Healthy young adults in both military and civilian populations aged 18–35 years to reflect the age of military personnel likely to be deployed. Reports using experimental or control groups outside the 18–35 age range were included where results for this age group could be clearly identified.
Intervention	Oral administration of legal dietary supplements, used a sole nutritional element, with the aim of enhancing cognitive performance. Multivitamin and/or multi-mineral supplements were included as they are consumed by a large number of military personnel.
Comparison	Age-matched controls with placebo or no treatment, or repeated samples designs and placebo.
Outcome	Cognitive domains: psychomotor, information processing speed, attention/vigilance, memory, and executive function.
Study design	Peer-reviewed randomised control trial

# 2.1. Search Strategy

The search terms used to search databases and relevant repositories were: military personnel, soldier, sailor, airmen, marine, armed forces, coast guard, submariners, army, navy, air force, combined with nutrition, dietary supplements, Dietary supplement (DS), vitamin, mineral, amino acid, protein, herb, herbal, sport drink, sport bar, nutriceuticals, food supplements, ergogenic aids, nutraceuticals, nootropics, pharmaceuticals, performance enhancement, cognitive enhancement, cognition, attention, memory, military, special forces, elite military, operations, nutritional armour/armor, and deployed. Searches were conducted of the following databases: Medline, PubMed, Scopus, Web of Science, PsycINFO, Cochrane Database of Systematic Reviews, Ovid, PsycArticles, and Science Direct. The search also included report repositories, in particular National Technical Information Service (NTIS), Defense Technical Information Centre (DTIC), RAND, National Academies Press, USAIREM, TNO, dSTL, NATO, Defence Science & Technology, Swedish Defence, Canadian Defence, French Defence and Google Scholar. Publication status was not a limitation; however, searches were limited to papers published or prepared during the period 2000–2017, with the final search completed in June 2017. The year 2000 was chosen as the early start point, because: (1) studies investigating supplement use within the military cohort were conducted after that date; (2) systematic literature reviews on some single supplements were published after that date and, with the exception of one on caffeine that covered the period 1998 onwards, most of those reviews searched databases from their inception, going back as early as the 1950s; and (3) the growth in consumption of dietary supplements is relatively new. Full search terms and key words are available in the online supplementary information. Due to the small number of papers identified, a second search was conducted including the following terms: macronutrients, micronutrients, calcium, magnesium, potassium, omega-3, omega-6, Vitamin D, Vitamin B, folate, probiotics, gut-brain axis, caffeine, flavonoids, vitamins, gingko biloba, bacopa, curcumin, ginseng, protein and tyrosine (see online Supplementary material Table S1 for a full example of the search strategy).

#### 2.2. Inclusion Screening

Initially, two authors conducted independent searches of the databases. All authors were involved in the secondary search. Outcomes of both searches were collated. One author (AW) screened all identified records for relevance according to the PICOS elements. Reasons for rejection of all full-text articles were recorded. The other authors independently conducted random checks on the screening process and rationale for rejection.

# 2.3. Data Extraction and Synthesis

At least two authors were involved during the stages of data extraction and synthesis. The abstracts of all records identified in the searches were assessed for relevance and exclusion criteria. Records were excluded if: participants were outside the age range of 18–35 years (unless there was a comparison group within this age range); there were no cognitive outcome measures; apart from multivitamin and guarana papers, a combination of dietary supplements was used (unless there was a pure supplement group to compare to placebo); and the study used a clinical population. Where the abstract provided incomplete information on these exclusion criteria the method section was read to determine if the paper should be excluded. Empirical papers passing this initial exclusion screen were read in full and included in the review unless a reason for exclusion was found on reading the paper (e.g., poor study design, confounds). Review and meta-analytical papers passing the initial screen were assessed for relevant papers fitting the inclusion criteria, and supplemented by papers produced subsequent to the original review or meta-analysis.

#### 2.4. Quality Assessment

Two researchers independently evaluated the risk of bias and methodological quality of included papers. The Grading of Recommendations, Assessment, Development and Evaluation (GRADE) [37] approach was used to assess risk of bias of all relevant papers based on these bias categories: selection, performance, attrition and reporting. Papers were judged to have a high risk of bias if they failed to use adequate randomisation methods, such as a coin toss, failed to conceal allocation, and it was unclear if blinding occurred. Overall, the risk of bias was high in 8.11% and unclear in 62.16% of papers included in this review (see Table 2). Methodological quality for all included papers including previous review or meta-analytical papers was assessed by the Scottish Intercollegiate Guidelines Network (SIGN) 50 Checklist [38]. As can be seen from Table 2, very few of the included papers were of high quality (10.81%), with the majority of low or very low quality (70.27%).

The purpose of our systematic literature review was to evaluate the potential utility of any known dietary supplements that have demonstrated efficacy for enhancing cognitive performance, and broadly, which overarching cognitive functions might be enhanced. A formal meta-analysis was not appropriate in this case due to the high number of poor quality studies. Reasons for a low-quality ranking included: an unknown risk of bias, and the heterogeneity in methodologies, and cognitive outcome measures across the included studies. Accordingly, a meta-analysis was not performed as would produce misleading results [75,76]. Studies are therefore grouped according to supplement used with a narrative synthesis of findings. However, to assist the formulation of recommendations, the total number of outcomes across all included studies and participants involved was calculated for each cognitive domain. In so doing, recommendations adopting the GRADE approach were based on the consistency of outcome findings. Outcomes could be an improvement, deterioration, or no change in cognitive performance measures. All records were documented, and all included papers were summarised according to author, design, objectives, sample, supplement information, confounds measured, outcome measures, results, and adverse effects (see Table 3; a full version of the table of evidence of included studies is provided in Table S2 of the online Supplementary material). A record was kept of excluded papers and their reason for exclusion (See Table S3 in the online Supplementary

material). The PRISMA checklist was completed once the review was complete (Table S4 of the online Supplementary material) and the risk of bias was documented for all included papers.

**Table 2.** Grading of Recommendations, Assessment, Development and Evaluation (GRADE) risk of bias and Scottish Intercollegiate Guidelines Network (SIGN) quality of randomised controlled trials evaluations.

	Random Sequence Generation (Selection Bias)	Allocation Concealment (Selection Bias)	Blinding of Participants and Personnel (Performance Bias)	Incomplete Outcome Data (Attrition Bias)	Selective Reporting (Reporting Bias)	Other Sources of Bias	Risk of Bias	SIGN Quality Evaluation
Beta-Alanine Hoffman 2014 [39]	-	-	?	+	+	+Funding		?
Caffeine	-	-	÷	Ŧ	<b>–</b>	Truituing	-	÷
Aidman 2018 [40]	+	+	?	+	+	+	+	+
Brunye 2010 [41]	+	?	?	+	+	+Funding	?	-
Hussain 2015 [42]	-	-	?	+	+	+	-	?
Kahathuduwa 2017 [43]	+	+	?	+	+	+	+	+
Kamimori 2015 [44]	-	?	?	+	+	+	?	-
Reyner 2000 [45]	+	?	+	+	+	+	+	+
Soar 2016 [46]	+	?	+	+	+	+	+	+
Flavonoids								
Lamport 2017 [47]	+	+	+	+	+	+Funding	+	++
Scholey 2010 [48]	+	?	?	+	+	+Funding	?	-
Watson 2015 [49]	+	+	+	+	+	+Funding	+	++
Wightman 2012 [50]	+	?	?	+	+	+	?	-
Gingko Biloba						+		
Elsabagh 2005 [51] Kennedy 2000 [52]	-	?	+ ?	+	+	+ +Funding	?	-
Kennedy 2000 [52]	+	?	?	+	+	+Funding	?	-
Kennedy 2002 [55]	++	?	?	+ ?	+	+Funding	?	-
Moulton 2001 [55]	-	?	+	+	+	+Funding	?	-
Scholey 2002 [56]	+	?	?	+	+	+Funding	?	-
Ginseng						0		
Yeo 2012 [57]	-	-	-	+	+	+Funding	-	?
Guarana								
Haskell 2007 [58]	+	?	?	+	+	+Funding	?	-
Kennedy 2004 [59]	+	?	?	+	+	+Funding	?	-
Kennedy 2008 [60]	-	+	+	+	+	+Funding	?	-
Veasey 2015 [61]	+	?	?	+	+	+Funding	?	-
Nitrate			-		-			
Thompson 2014 [62]	+	?	+	+	+	+Funding	+	+
Wightman 2015 [63] Omega-3	+	+	+	+	+	+	+	++
Bauer 2014 [28]	-	+	+	+	+	+Funding	+	++
	-							
Giles 2015 [64]	+							
Giles 2015 [64] Prebiotics	+	?	?	+	+	+Funding	?	-

6 of 32

Table 2. Cont.

	Random Sequence Generation (Selection Bias)	Allocation Concealment (Selection Bias)	Blinding of Participants and Personnel (Performance Bias)	Incomplete Outcome Data (Attrition Bias)	Selective Reporting (Reporting Bias)	Other Sources of Bias	Risk of Bias	SIGN Quality Evaluation
Tyrosine Colzato 2013 [66]	+	?	?	+	+	+	?	-
Colzato 2014 [67]	+	?	?	+	+	+	?	-
Colzato 2015 [68]	+	?	?	+	+	+	?	-
Coull 2015 [69]	+	?	?	+	+	+	?	-
Kishore 2013 [70]	+	?	+	+	+	+	+	+
Steenbergen 2015 [71]	+	?	?	+	+	+	?	-
Watson 2012 [72]	-	?	+	+	+	+	?	-
Jongkees 2017 [73]	?	?	+	+	+	+	?	-
<b>B</b> Vitamins								
Bryan 2002 [74]	-	?	?	+	+	+	?	-

**Risk of Bias Criteria:** -: Not done/poorly done; +: Done; ?: Unclear. **Risk of Bias Judgement:** -: High Risk; ++: Acceptable Risk; ?: Unclear Risk. **SIGN Quality Evaluation:** ++: High Quality; +: Acceptable Quality; -: Low Quality; ?: Very Low Quality.

Table 3. Summary of evi	dence of included studies.
-------------------------	----------------------------

Supplement/Autho and Referenc	Population <sup>a</sup> (Sample r Size ( <i>n</i> ), Age Range (mean ± SD), <i>n</i> = Male/Female)	Intervention (dose (Supplier), Placebo, Frequency (f))	Moderator Description	Outcome Summary Positive (+), Negative (-), Inconclusive (<>), Null (0)
Beta-Alanine Hoffman et al. (2014) [39]	(n = 1  study) n = 20 M age = beta-alanine: 20.1 years (0.7); placebo: 20.2years(1.1) 20 Males; 0 Females	6 g beta-alanine tablet (CarnoSyn <sup>TM</sup> ; Natural Alternatives International) Placebo (rice flour) $f = 3/day$ (2 g/serve), 28 day	Fatigue (physical and cognitive)	Information processing speed (+) Memory (0)
Caffeine Aidman et al.	(n = 7  studies) n = 11	subsequent from lit review 800 mg of caffeine gum (Military Energy Gum)	Sleep deprivation	Attention (+)
(2018) [40]	M age = 22.5 years (2.7) 6 Males; 5 Females	Placebo gum f = 200  mg  4/day, 2  hrly (0100-0700h), 2  days	(period)	Executive function (+)
Brunye et al. (2010) [41]	n = 36 M age = 20.1 years (ND) 10 Males; 26 Females	Caffeine capsule: 0, 100, 200 or 400 mg Placebo (capsule) f = single dose	Habitual caffeine intake	Executive function 400 mg only (+) Attention (+)
Hussain and Cole (2015) [42]	n = 26 M age = caffeine: 22.9 years (0.9); placebo: 24 years (0.8) 12 Males; 14 Females	200 mg caffeine placebo f = capsule, single dose	24-h recall	Memory (0) Executive function (0)
Kahathuduwa et al. (2017) [43]	n = 20 M age = 21.9 years (ND) 20 Males; 0 Females	160 mg caffeine drink placebo drink f = single dose 5-way crossover	No moderator	Memory (+) Executive function (+) Information processing speed (0)

Supplement/Author and Referenc	Population <sup>a</sup> (Sample r Size ( <i>n</i> ), Age Range (mean ± SD), <i>n</i> = Male/Female)	Intervention (dose (Supplier), Placebo, Frequency (f))	Moderator Description	Outcome Summary Positive (+), Negative (-), Inconclusive (<>), Null (0)
Kamimori et al. (2015) [44]	n = 20 M age = 28.6 years (4.7) 20 Males; 0 Females	200 mg caffeine gum (Stay Alert <sup>®</sup> ) Placebo gum f = 2145, 0100, 0345 and 0700 h (total 800 mg/day), 3 days	3 nights of sustained wakefulness	Attention (+) Executive function (+)
Reyner and Horne (2000) [45]	n = 16 (2 studies); n = 8/study M age = 23 years (2) 8 Males; 8 Females	200 mg caffeine (2–3 cups of coffee) Placebo f = single dose	Restricted sleep (study 1) and sleep deprivation (study 2)	Attention (+) Sleep restriction only (Study 1)
Soar et al. (2016) [46]	n = 43 M age = 28.1 years 17 Males; 26 Females	1 cup (50 mg caffeine) of caffeinated coffee Placebo (decaffeinated) f = single dose	Habitual caffeine intake	Information processing speed (+) Executive function (<>) Memory (+)
<i>Flavonoids</i> Lamport et al. (2017) [47]	(n = 5  studies) Study 1: $n = 28$ M age = 22 years (2.2) 4 Males; 24 Females Study 2: $n = 16$ ; M age = 22 years (1.9) 8 Males; 8 Females	70.5 mg (500 mL) flavonoid drink (Tropicana Ruby Breakfast Juice; PepsiCo Inc.;) placebo f = single dose	Time since ingestion	Information processing speed (+) Memory (0) Attention (0) Executive function (0)
Scholey et al. (2010) [48]	n = 30 M age = 21.9 years (0.6) 13 Males; 17 Females	Dairy cocoa drink (dose: 520 mg and 994 mg Cocoa Flavanols) placebo (nutrient-matched, low flavanol) f = single dose $525 \pm 5$ mg of polyphenols /60	High cognitive demand	Memory (<>) Information processing speed 994 mg only (+) at 30 and 40 min
Watson et al. (2015) [49]	n = 36 M age = 24.8 years (3.9) M: F not disclosed	kg body weight (anthocyanin-enriched blackcurrant extract; 1.66 g of DelCyan) or from 142 mL of blackcurrant fruit juice (Blackadder), Placebo (0 mg polyphenols) drink; $f =$ single dose	No moderator	Attention (+)
Wightman et al. (2012) [50]	n = 27 M age = 22 years 11 Males; 16 Females	135 mg or 270 mg of epigallocatechin (green tea; DSM Nutritional Products) placebo (not disclosed) f = single dose (2 capsules)	No moderator	Information processing speed (0) Memory (0) Executive function (0)
Gingko Biloba Elsabagh et al. (2005) [51]	( $n = 7$ studies) Study 1: $n = 52$ M age = gingko 21.3 years (0.3); Placebo 21.7 years(0.4) 26 Males; 26 Females Study 2: $n = 40$ M age = gingko 21.2 years (0.3); Placebo 21.5 (0.3) 21 Maley: 19 Females	120 mg of standardised gingko extract (LI 1370; Lichtwer Pharma) Placebo ND <i>f</i> = Study 1 single dose; Study 2 daily for 6 wk.	No moderator	Study 1: Attention (+) Memory (<>) Executive function (0) Study 2: Attention (0) Memory (0) Executive function (0)
Kennedy et al. (2002) [53]	21 Males; 19 Females <i>n</i> = 20; M age = 21.2 years (3.9) 5 Males; 15 Females	60 mg of gingko biloba (GK501, pharmaton), 100 mg P. ginseng extract (G115, Pharmaton), 160 mg ginkgo/ginseng combination (100 mg ginseng/60 mg ginkgo per capsule, Pharmaton) Placebo inert (ND) f = Single dose (6 capsules); 360 mg ginkgo, 400 mg ginseng, 960 mg ginkgo/ginseng, inert placebo	No moderator	Attention (<>) Memory (<>) Information processing speed (<>)
Kennedy et al. (2000) [52]	n = 20 M age = 19.9 years (ND) 2 Males; 18 Females	60 mg standardised gingko extract (GK501, Pharmanton,) Placebo inert (ND) f = Single dose (6 capsules); 120, 240, 360 mg gingko, or inert placebo	No moderator	Attention (<>) Memory (<>) Information processing speed (<>)

# Table 3. Cont.

Table 3. Cont.

Supplement/Author and Referenc	Population <sup>a</sup> (Sample Size ( <i>n</i> ), Age Range (mean ± SD), <i>n</i> = Male/Female)	Intervention (dose (Supplier), Placebo, Frequency (ƒ))	Moderator Description	Outcome Summary Positive (+), Negative (-), Inconclusive (<>), Null (0
Kennedy et al. (2007) [54]	n = 28; M age = 20.4 years (1.2) 10 Males; 18 Females	120 mg standardised gingko biloba extract (60 mg ginkgo per capsule); complexed with 360 mg of phosphatidylserine OR 360 mg of phosphatidylcholine OR Placebo (Indena SpA, Milan) f = single dose (2 capsules)	Complexed extract with two phospholipids	Information processing speed (+); phosphatidylserine only Attention (0) Memory (<>)
Moulton et al. (2001) [55]	n = 60 M age = Gingko: 20.6y (1.9); placebo: 20.4 years (1.8) 60 Males; 0 Females	120 mg of BioGinkgo 27/7 (LI 1370) Placebo = fillers (Pharmanex Inc.) f = once daily (2 tablets), 5 days 120, 240, or 360 mg of	No moderator	Memory (<>) Information processing speed (0)
Scholey and Kennedy (2002) [56]	n = 20 (study 1) M age = 19.9 years (1.5) 2 Males; 18 Females	standardized gingko biloba extract (GK501, Pharmaton SA, 60 mg ginkgo biloba/capsule) Placebo = ND f = single dose 6 capsules (60 mg/capsule)	Serial arithmetic tasks with different cognitive loads	Memory (<>)
<i>Ginseng</i> Yeo et al. (2012) [57]	(n = 1  study) n = 15 M age = ND15 Males; 0 Females	subsequent from lit review 4500 mg/day of Korean red ginseng Placebo = ND f = 5 capsules (300 mg/capsule) 3 doses/day; 2 wk	No moderator	Attention (+); brain activity Memory (+); brain activity Information processing speed (0)
Guarana / Guarana + Multivitamin	(n = 4  studies)			
Haskell et al. (2007) [58]	n = 26 M age = 21.4 years (0.6) 8 Males; 18 Females	37.5, 75, 150 and 300 mg standardize guarana extract (PC-102, Pharmaton, SA) Placebo = ND f = single dose; 1 capsule/day; 6 days	No moderator	Memory (<>) Attention (0) Information processing speed (0)
Kennedy et al. (2004) [59]	n = 28 M age = 21.4 years (0.8) 9 Males; 19 Females	75 mg of a standardised guarana extract (Pharmaton) Placebo = ND f = single dose (2 capsules)	No moderator	Memory (<>) Attention (<>) Information processing speed (<>) Executive function (<>)
Kennedy et al. (2008) [60]	n = 130 M age = 20.9 years (1.6) 60 Males; 70 Females	Berocca Boost®multivitamin + mineral complex (222.2 mg guarana) Placebo = inert effervescent tablet f = single dose, effervesce tablet in 200 mL water	Cognitive demand	Attention (+) Memory (0) Information processing speed (<>) Executive function (<>)
Veasey et al. (2015) [61]	n = 40 M age = 21.4 years 40 Males; 0 Females	Berocca Boost®multivitamin + mineral complex (222.2 mg guarana) Placebo = inert effervescent tablet f = single dose, effervesce tablet in 250 mL water	Exercise	Attention (0) Memory (<>) Information processing speed (<>)
Nitrate	(n = 2  studies)	5 mmol nitrate drink (450 mL		
Thompson et al. (2014) [62]	n = 16 M age = 24.4 years (4.0) 16 Males; 0 Females	beetroot juice, 50 mL low calorie blackcurrant cordial; James White Drinks, Ipswich UK) Placebo (50 mL blackcurrant cordial, 45 mL apple juice, 405 mL water) f = single dose	Mental fatigue and exercise intensities	Attention (0) Executive function (0)

Supplement/Author and Referenc	Population <sup>a</sup> (Sample size (n), Age Range (mean ± SD), n = Male/Female)	Intervention (dose (Supplier), Placebo, Frequency (ƒ))	Moderator Description	Outcome Summary Positive (+), Negative (-), Inconclusive (<>), Null (0)
Wightman et al. (2015) [63]	n = 40 Mean = 21.3 years (0.7) 13 Males; 27 Females	5.5 mmol nitrate drink (450 mL beetroot juice, 50 mL low calorie apple and blackcurrant cordial; James White Drinks, UK) Placebo (50 mL apple and blackcurrant cordial, 50 mL apple juice, 400 mL water) f = single dose	No moderator	Memory (<>) Attention (0)
Omega-3	(n = 2  studies)			
Bauer et al. (2014) [28] Giles et al. (2015) [64]	n = 13 M age = 23.8 years (3.5) 4 Males; 9 Females n = 72 M age = Omega-3: 20.8 years (2.4); Placebo: 20.5 years (1.7) 27 Males; 45 Females	EPA-rich (590 mg EPA, 137 mg DHA; 4.3:1; Eye-Q <sub>TM</sub> , Novasel); DHA-rich (417 mg DHA 159 mg EPA; 3:1; Efalex <sup>TM</sup> , Efamol) Placebo—NONE f = 6/day, 30 days 2800 mg fish oil (1680 mg EPA, 1120 mg DHA; Compound Solutions, CT Placebo (2800 mg olive oil; Compound Solutions, CT)	No moderator Stress	Executive function (+) Memory (<>) Attention (0)
Prebiotics	(n = 1  study)	f = 7 capsules/day, 35 days		
Smith et al. (2015) [65]	n = 50 M age = 23.0 years (ND) 19 Males; 28 Females	5 g oligofructose-enriched inulin powder (ORAFTI, Tienen, Belgium) Placebo powder (ORAFTI, Tienen, Belgium) f = single dose, added to decaffeinated tea or coffee	No moderator	Memory (<>) Information processing speed (0) Attention (0) Executive function (0)
Tyrosine	(n = 8  studies)	0 ( ) (P    P		
Colzato et al. (2013) [66]	n = 22 M age = 19.7 years (ND) 0 Males; 22 Females	2 g tyrosine (Bulk Powders Ltd.) Placebo 2 g microcrystalline cellulose (Sigma-Aldrich) f = single dose, dissolved in 400 mL of orange juice	Cognitive stress	Memory (<>)
Colzato et al. (2014) [67]	n = 22 M age = 20.4 years (ND) 0 Males; 22 Females	2 g tyrosine (Bulk Powders Ltd.) Placebo 2 g microcrystalline cellulose (Sigma-Aldrich LLR, Zwijndrecht, Netherlands f = single dose, dissolved in 400 mL of orange juice	No moderator	Executive function (<>)
Colzato et al. (2015) [68]	n = 32 M age = 19.4 years (ND) 8 Males; 24 Females	2 g tyrosine (Bulk Powders Ltd.) Placebo 2 g microcrystalline cellulose (Sigma-Aldrich) f = single dose, dissolved in400 mL of orange juice	No moderator	Executive function (<>)
Coull et al. (2015) [69]	<i>n</i> = 8 M age = 21.0 years (1.0) 8 Males	Total of 150 mg/kg tyrosine (Myprotein.co.uk) mixed with 250 mL of sugar-free lemon squash (Tesco, UK) Placebo 250 mL of sugar-free lemon squash (Tesco, UK) f = single dose	Exercise in a hot environment	Vigilance (+)

Table 3. Cont.

Supplement/Author and Referenc	Population <sup>a</sup> (Sample size ( <i>n</i> ), Age Range (mean ± SD), <i>n</i> = Male/Female)	Intervention (dose (Supplier), Placebo, Frequency (f))	Moderator Description	Outcome Summary Positive (+), Negative (-), Inconclusive (<>), Null (0)
Kishore et al. (2013) [70]	n = 10 M age = not stated 10 Males; 0 Females	100 mg/kg tyrosine 50 g low fat, high-energy bar (containing 6.5 g of L-tyrosine; Defence Food Research Laboratory, Defence Research and Development Organization, India) Placebo 50 g low fat, high-energy bar (Defence Food Research Laboratory, Defence Research and Development Organization, India) f = single dose	Heat stress	Brain Activity: Attention (+) Executive function (+)
Steenbergen et al. (2015) [71]	n = 22 M age = 19.3 years (1.5) 0 Males; 22 Females	2 g tyrosine (Bulk Powders Ltd.) Placebo 2 g microcrystalline cellulose (Sigma-Aldrich) <i>f</i> = single dose, dissolved in 400 mL of orange juice	No moderator	Executive function (+)
Watson et al. (2012) [72]	n = 8 M age = 23.0 years (3.0) 8 Males; 0 Females	Total 150 mg/kg tyrosine (SHS Intl., Liverpool, UK) in a sugar-free fruit drink (Tesco Ltd., Chestnut, UK) Placebo sugar-free fruit drink (Tesco Ltd., Chestnut, UK) f = 2 doses 30 min apart to yield total of 150mg/kg	Exercise in a warm environment	Attention (0) Memory (0) Executive function (0)
Jongkees et al. (2017) [73]	Study 1: <i>n</i> = 36 M age = Tyrosine 22.2 (2.4); Placebo 20.8 (1.9), 2 Males; 34 Females	2 g tyrosine (Bulk Powders Ltd.) Placebo 2 g microcrystalline cellulose (Sigma-Aldrich) <i>f</i> = single dose, dissolved in 400ml of orange juice	Study 1: No Moderator	Study 1: Memory (+)
<i>B Vitamins</i> Bryan et al. (2002) [74]	(n = 1 study) n = 56 M age = 25.2 years (3.2) 0 Males; 56 Females	750 µg folate, 15 µg $B_{12}$ , 75 mg $B_6$ capsule (Technical Consultancy Services, NSW, Australia) Placebo microcrystalline cellulose, calcium phosphate, soy polysaccharide and magnesium capsule (Technical Consultancy Services, Australia) f = single dose, 5 weeks healthy participants who gave	No moderator	Information processing speed (0) Memory (0) Executive function (0)

Table 3. Cont.

<sup>a</sup> All studies used healthy participants who gave informed consent.

# 3. Results

# 3.1. Literature Search

The literature search was conducted according to the PRISMA statement. The flow of information through the different phases of the systematic review is shown in Figure 1. Varied cognitive domains were assessed (see Table 4), and included psychomotor, information processing speed, attention/vigilance, memory, and executive function, using an assortment of established cognitive tasks. The search and inclusion criteria resulted in the inclusion of papers investigating the following dietary supplements: macronutrients–carbohydrates, proteins (beta-alanine, tyrosine), fats (omega-3); micronutrients–B vitamins, multivitamins, nitrate; herb (plant)-based caffeine, flavonoids, guarana, gingko biloba, ginseng; and prebiotics. Papers investigating the following supplements were excluded due to not assessing cognitive outcomes, participant age, or use of non-human participants: protein, ampakine, bacopa, curcumin, iron, nigella sativa, polyphenol, tryptophan, vitamin D, vitamin E, and zinc. The literature search also found no relevant papers for the following supplements: biotin, calcium,

choline, chromium, copper, fluoride, iodine, iron, magnesium, manganese, molybdenum, niacin, pantothenic acid, phosphorus, potassium, selenium, sodium, vitamin A, vitamin C and vitamin K. Across studies, adverse effects of supplementation were generally not assessed (guarana), not reported (beta-alanine), or not observed (vitamin B, nitrate, caffeine, flavonoids, prebiotics). Only one study on beta-alanine supplementation reported physical side effects (i.e., paraesthesia (tingling) in four participants, which was due to inappropriate administration of the supplement) [39].

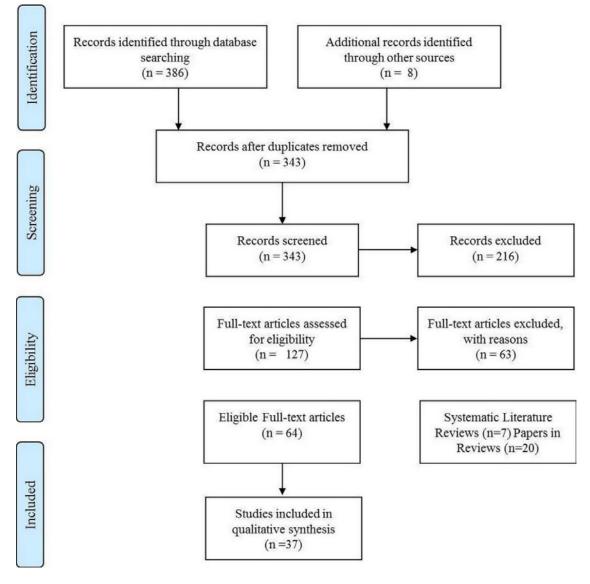


Figure 1. PRISMA 2009 Flow Diagram. Adapted from: Moher D., Liberati A., Tetzlaff J., Altman D.G., The PRISMA Group (2009). *Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement*. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097. For more information, visit www.prisma-statement.org/.

12 of 32

Higher-Order Cognitive Function	Lower-Order Cognitive Function		
Information Processing Speed	Simple Reaction Time (RT)		
	Choice/Complex RT		
Psychomotor	Fine motor control		
	Hand-eye coordination		
	Gross motor control		
	(Marksmanship involves first two)		
Attention/Vigilance	Selective Attention		
u u u u u u u u u u u u u u u u u u u	Sustained Attention (vigilance)		
	Divided Attention		
	Target Detection		
Memory	Procedural		
-	Episodic		
	Semantic		
	Prospective		
	Short-Term Memory		
	Visual Discrimination		
Executive Function	Running Memory		
	Working Memory		
	Map Reading (orienteering)		
	Inhibitory Control: Self-Control (emotions)		
	Resistance to Interference		
	Response Inhibition		
	Logical reasoning		
	Planning		
	Cognitive Flexibility:		
	Verbal Reasoning		
	Numerical Reasoning (math ability)		
	Spatial Reasoning		
	Problem Solving		
	Task Switching		
	Cognitive Shifting		

**Table 4.** Higher-order cognitive functions and associated lower-order cognitive functions used in this review.

# 3.2. Overview of Cognitive Effects by Supplement

# 3.2.1. Macronutrients

The primary macronutrients are carbohydrates, proteins and lipids, and they are required by humans to maintain health and energy. They are termed macronutrients due to the relative large amounts required (i.e., grams) for a normal diet, and are found in fruit, dairy foods, vegetables, pulses, grains, fish, and meat. Very few studies met our search criteria. The only papers that met our criteria with respect to proteins related to two of the amino acids, specifically beta-alanine and tyrosine. The only papers that met our criteria with respect to fats related to omega-3.

# Carbohydrates

Hoyland, Lawton and Dye (2008) [77] noted in their systematic literature review that the majority of previous reviews assessing the relationship between macronutrients and cognitive performance focused on carbohydrates, with very few studies looking at the effects of proteins or lipids. In their review they focused on identifying measures that were used to assess the impact of carbohydrate, protein, and/or lipid manipulations on cognitive function. They found 31 studies involving 1367 participants that examined acute effects of macronutrient manipulations (most notably glucose) on a range of cognitive outcome measures, including psychomotor, information processing speed, attention/vigilance, executive function, and, in particular, memory. The most consistent beneficial

effects were found for memory, particularly from glucose on short-term memory, delayed memory and non-verbal memory. Nonetheless, several studies found no impact of carbohydrate supplementation on memory performance. Findings for other cognitive domains tended to be mixed, likely as a result of insufficient studies that examined these domains, and/or the use of different macronutrient manipulation across studies. More generally, beneficial effects of macronutrients tended to be more commonly observed under conditions of greater cognitive task demands. Our search failed to identify additional studies published since 2008 examining the relationship between macronutrient intake and cognitive performance in healthy young adults.

# Beta-Alanine (Protein)

Beta-alanine is an amino acid produced naturally in the body that can also be acquired via the diet from meat and/or dietary supplements [78]. Due to its presence in other tissues, such as the brain, it is postulated that the beta-alanine precursor, carnosine, may have potential cognitive effects. Early animal studies indicate there may be a link to focus, alertness and cognitive function during stress and fatigue [79].

Only one known study to date has investigated the effects of beta-alanine (see Table 3) on cognitive performance in healthy young humans [39], where both physical and cognitive performance were assessed after four weeks of 6 g beta-alanine supplementation in a sample of military personnel. Twenty male soldiers were assessed on a variety of military tasks and a working memory task (serial subtraction) after induced fatigue from military training. Beta-alanine supplementation did not enhance working memory performance, but significant improvements in marksmanship and reaction time were found within the military context of operational task performance. GRADE and SIGN 50 evaluations of this single study employing beta-alanine was deemed low quality (See Table 2).

### Tyrosine (Protein)

Tyrosine is a non-essential amino acid that is used by cells to synthesise proteins. Briefly, tyrosine is found in high-protein food sources and is synthesised from phenylalanine [80]. Most importantly, tyrosine is the precursor for catecholamine synthesis, which occurs mainly in the brain or adrenal medulla. The catecholamines dopamine and noradrenaline are recognised as modulators of executive function, and are also released in response to stress. An appropriate level of dopamine and noradrenaline facilitates effective cognitive performance whereas an over- or under-abundance of either of these neurotransmitters can have an adverse effect. "Central fatigue hypothesis" [81] is a relevant military problem, where prolonged exercise and/or exposure to extreme stress (extreme temperatures, etc.) alter the synthesis and level of catecholamines. Taken together, this provides good evidence to support that tyrosine, delivered appropriately and at the right dose, can evoke positive cognitive enhancement effects. Indeed, a recent review [82] identified that tyrosine mitigated the impact of stressors such as sleep deprivation, noise, extreme climates and military combat training on a range of cognitive processes including memory, perceptual motor skills, and logical reasoning. The poor quality of papers, as assessed by SIGN criteria, and lack of physiological measures related to uptake of tyrosine meant they were unable to make firm recommendations about tyrosine supplementation; nonetheless they concluded that tyrosine may enhance cognitive performance and warranted further investigation. The current review focuses on papers published since 2000 that are not included in the Attipoe et al. [82] review.

A further eight studies (see Table 3), involving 160 participants and investigating the effect of tyrosine on cognitive processing were found to fit the inclusion criteria. Apart from one study using a single-blind crossover design [72], all studies employed a double-blind placebo-controlled crossover design to examine the role of tyrosine in mitigating stress-induced cognitive declines. Mainly female participants were recruited across the eight studies: three recruited male participants, three used female participants, and two had a mix of both sexes. Tyrosine was administered using different methods: powders, capsules and bars; and at different doses from 2 g to a total dose of 150 mg/kg (approximately

12 g for 80 kg participant) as single or double doses. Tyrosine supplementation has been demonstrated to be most effective in situations of significant stress, physical, cognitive or otherwise. As such, the studies covered: cognitive demand [66–68,71] and external stressors such as noise and thermal changes [69,70,72]. One study evaluated whether tyrosine would modulate the effect of transcranial direct current stimulation on working memory performance [73].

Under cognitively stressed conditions tyrosine improved working memory [66] and various aspects of executive function, namely inhibitory control [67], cognitive flexibility (smaller switching costs) [71] and creative convergent thinking [68]. Although tyrosine had no impact on cognitive performance in warm/hot environments [72], when heat stress was combined with physical exertion, tyrosine supplementation enhanced vigilance [69]. Changes in the event-related potentials N100, P300 and Contingent Negative Variation (CNV), also reflected enhanced attention and executive function related to stimulus evaluation and decision-making [70]. Tyrosine also improved working memory in unstressed individuals [73].

SIGN 50 and GRADE evaluations (see Table 2) revealed that detail pertaining to allocation concealment and appropriate blinding methodology was consistently missing amongst the included studies, resulting in the quality of the research being downgraded. However, the general finding is that tyrosine supplementation might be useful for improving some cognitive functions, specifically psychomotor skills and memory, when individuals are experiencing cumulative stress such as would occur during extended military operations with little opportunity for sleep. Although there are promising indications that tyrosine might be advantageous for improving other aspects of cognition in both stressful and stress-free environments, SIGN 50 and GRADE evaluations (see Table 2) highlight that there is insufficient quality research at this stage to reach firm conclusions or recommendations.

#### Omega-3 (Fats)

Omega-3 is a polyunsaturated fatty acid that must be obtained through dietary intake as it is not produced naturally in the human body [83]. Eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) are essential fatty acids present in omega-3 [84]; DHA makes up 97% of the brain's total omega-3 fatty acid content [84], particularly in brain regions involved in attention and memory [85]. Omega-3 is important for normal cognitive development in early life and may be associated with a reduced decline in cognitive function in older adults [86]. A large proportion of the population fails to consume sufficient amounts of omega-3 [87], in particular the long chain omega-3 fatty acids found in fatty fish such as salmon, tuna or sardines, or via supplementation.

Military personnel work in conditions where maintaining optimal cognitive functioning is critical. Evidence that omega-3 can enhance cognitive performance would support moves to incorporate a greater amount of omega-3 (via food components or supplements) into operational ration packs [83]. Despite evidence that omega-3 supplementation enhances cognitive development during childhood, a recent systematic literature review found no evidence for omega-3 enhancing cognitive performance in healthy adults [88]. The current review focuses on research papers published since 2014, which was the most recent paper included in that earlier review [88].

Two further studies (see Table 3) that met inclusion criteria were identified [28,64]. In both studies participants were drawn from normal, well-rested populations, who either did not use omega-3 supplements or restrained from taking them for four weeks prior to testing. Overall 85 participants received omega-3 supplementation in these studies (54 female, 31 male). Although fish oil capsules were administered in both studies, one used an EPA-rich fish oil [64] (1680 mg EPA:1120 mg DHA per day for 35 days); and the other compared EPA-rich and DHA-rich fish oil [28] (590 mg EPA:137 mg DHA or 159 mg EPA:417 mg DHA per day for 30 days). One study assessed omega-3 uptake via changes in plasma phospholipids [28] and assessed performance on an executive function (Stroop) and spatial working memory task while recording brain activation [28]. The other study evaluated attentional control and emotional regulation [64].

Omega-3 supplementation had no effect on attentional control [64]. Supplementation with a high EPA:DHA ratio (3:1) for 30 days improved the selective attention and cognitive flexibility aspects of executive function as assessed with the Stroop task: reaction time decreased and fMRI patterns of brain activation indicative of increased cognitive efficiency were observed [28]. This contrasts with previous findings by Karr, Grindstaff and Alexander [89] (reported by Teo et al. [88]) that supplementation with a smaller ratio of EPA:DHA (720 mg:480 mg) had no impact on Stroop performance.

Regarding SIGN 50 and GRADE evaluations overall for the additional two papers reviewed applying an omega-3 intervention (see Table 2), the risk of bias and research quality was mixed. On the whole, although some studies have found improvements in some cognitive functions, there is little firm evidence to suggest that omega-3 supplementation can reliably enhance cognition in healthy young adults. More research is required in the future to provide a recommendation.

# 3.2.2. Micronutrients

Micronutrients are essential elements required in small quantities, but necessary to remain healthy. They include vitamins and minerals. Very few papers met our search criteria.

#### **B** Vitamins

The B vitamins are a group of water soluble vitamins comprising thiamine ( $B_1$ ), niacin ( $B_3$ ), pantothenic acid ( $B_5$ ), vitamin  $B_6$ , biotin ( $B_7$ ), folate ( $B_9$ ), and vitamin  $B_{12}$ . The B vitamins collectively play a critical role at all levels of brain function as co-enzymes and precursors of enzymatic processes. They are important for energy production, DNA/RNA synthesis/repair, genomic/non-genomic methylation, and the production of neurochemicals and signalling molecules [30,90]. The mechanisms by which B vitamins affect cognition are still unknown. The B vitamins folate,  $B_6$ , and  $B_{12}$  are known to be involved in the modulation of homocysteine levels; this is important as elevated plasma homocysteine has been associated with poor cognition. Although there is no firm evidence of this relationship, it is likely that the association of the B vitamins with homocysteine metabolism is a by-product of other unknown biological factors that impact on cognitive function [91].

There is a shortage of well-controlled studies assessing the impact of supplementation of B vitamins on healthy young adults (see Table 3). One study assessed the effect of folate, vitamin  $B_6$ , and vitamin  $B_{12}$  supplementation [74] on cognitive function in 56 healthy young females with no external stressors. High doses of B vitamins (750 µg folate, 15 µg vitamin  $B_{12}$ , 75 mg vitamin  $B_6$ ) were administered using tablets or capsules, for five weeks [74]. Information processing speed, attention, memory and executive function were measured. There was a trend towards supplementation with folate, vitamin  $B_6$  and vitamin  $B_{12}$  enhancing aspects of memory performance. There was no impact on other cognitive measures. GRADE and SIGN 50 evaluations (see Table 2) revealed this study to be of low quality with a high level of bias risk. More research is required to determine the effect of the vitamin Bs on cognitive performance.

#### Nitrate

Nitrate is obtained in the diet through the consumption of nitrate-rich vegetables, including beetroot, broccoli, lettuce, and spinach [63]. Although there is limited research on the effects of nitrate supplementation on cognitive functions in humans, the beneficial effect of nitrate on cognition appears to be related to its conversion to nitric oxide. Nitric oxide is involved in the modulation of cerebral blood flow, which is important for optimal brain function. In older adults, dietary nitrate supplementation resulted in improved cerebral blood flow to areas of the brain related to executive functioning [92].

Two studies involving 56 participants have assessed the effect of a dietary nitrate supplementation on cognitive performance in healthy young adults (see Table 3). A double-blind crossover design [62] and a double-blind, placebo-controlled, parallel groups design [63] were employed. Participants were non-military and were either recreationally active men [62] or a mixed male and female sample [63].

Nitrate supplementation was assessed under different conditions: during a physically demanding task (cycling) [62] and in response to a cognitive demand battery [63] to measure cognition. Both studies assessed the effect of single doses of a similar nitrate-rich drink (beetroot juice with added apple and blackcurrant juice; containing 5 to 5.5 mmol of nitrate). Performance on measures of attention (rapid visual information processing test, RVIP) [62,63], working memory (serial subtraction) [63], and executive function (Stroop) [62] were assessed.

The beetroot juice did not enhance attentional performance [63], nor did it mitigate the deterioration in attentional abilities as a result of increasing exercise intensity [62]. Wightman et al. [63] observed greater accuracy on serial threes subtraction but not serial sevens subtraction. However, this effect should be interpreted with caution as the nitrate group underperformed at baseline. No positive effects of beetroot juice on executive functioning were observed [62]. GRADE and SIGN 50 assessments (Table 2) of research on nitrates denoted the studies to be of acceptable-high quality and had low risk of bias, indicating well designed and executed research. Although negligible improvements were found, the small number of papers investigating the impact of nitrates and cognitive performance indicate more research in this domain is warranted.

## 3.2.3. Herbal (Plant-Based) Supplements

Herbal supplements include plant-based extracts such as caffeine, flavonoids, Gingko biloba, ginseng and guarana. Of these, the majority of papers focused on caffeine.

## Caffeine

Caffeine is a plant alkaloid that is quickly absorbed and found in food and drinks such as coffee, tea, energy drinks, soft drinks, and chocolate [93]; peak caffeine concentrations are reached between 15 and 120 min after ingestion [94,95]. The energising and concentration boosting qualities of caffeine are well-known and are the reason caffeine is the most commonly used psychostimulant [41,96]. A growing body of literature has investigated the effects of caffeine on cognitive performance, particularly during/after sleep deprivation. Caffeine works by blocking adenosine receptors within the brain and has demonstrated positive changes (at varying doses) on the alerting, orienting and executive control attention networks within the brain, specifically enhancing alertness, vigilance and reaction time. It has not demonstrated improvements in memory performance or other executive functions, such as decision-making [94]. A recent systematic literature review found caffeine supplementation to be promising for maintaining or improving several aspects of cognitive performance in sleep-deprived people. These are tasks requiring attention, executive function and information processing speed [97]. The current review extends that of Crawford et al. [97] by including studies they omitted and/or were published after 2014.

A further seven studies (see Table 3) were found that examined the effect of caffeine on cognition in healthy young adults. Four studies used crossover designs and three utilised independent group designs. All studies considered acute effects of caffeine and had a relatively even distribution of male and female participants. Two studies recruited men only [43,44] and one recruited military personnel [44], with a combined total number of 172 participants. Participants' caffeine consumption was heterogeneous across all included studies, examining low, moderate, high and mixed users. Caffeine was commonly dosed at 200 mg (range 50–400 mg), with a maximum daily administration of 800 mg. A range of administration modes was used, including capsules, chewing gum, prepared beverage (decaffeinated coffee and caffeinated coffee), or dissolved in distilled water. Four studies examined caffeine in the context of sleep deprivation, or compared well-rested and sleep-deprived subjects [40,44,45]. (The Aidman et al. (2018) [40] paper was under review at the time of conducting the literature search for this systematic review. It has since been published.) The assessed areas of cognition were: psychomotor, information processing speed, attention/vigilance, memory, executive function, and a combination of cognitive abilities required for a practical test of simulated driving ability.

In sleep-deprived participants, caffeine enhanced the performance of military personnel on attentional tests [44]. Further, repeated doses of caffeine mitigated the decline in information processing speed, vigilance, and logical reasoning associated with sleep deprivation [44]. Similar results have been found during a driving task undertaken by sleep-deprived [40,45] and sleep-restricted (Study 1) [45] university students. Driving a vehicle requires attentional control functions of alertness, orienting and executive attention, all of which can be impaired by sleep deprivation. Despite one of the driving studies measuring drowsiness objectively with the Johns Drowsiness Scale [40], and the other measuring subjective sleepiness [45], both studies found that drowsiness/sleepiness after sleep deprivation impaired driving ability. Caffeine mitigated this effect, and subsequently, driving ability did not deteriorate to the same extent after caffeine was consumed. Caffeine also mitigated the effect of sleepiness on driving ability after restricted sleep (Study 1) [45]. Similar improvements in executive control performance were found in sleep-deprived and well-rested participants, with caffeine ameliorating the effect of sleep deprivation on logical reasoning [44].

In well-rested individuals, caffeine improved memory (recognition) and aspects of information speed, specifically, choice reaction time but not simple reaction time [43]. In addition, 400 mg of caffeine enhanced executive function (conflict resolution) and alertness, but not selective attention (as measured by the Attention Network Task–ANT) [41]. Furthermore, although one standard cup of caffeinated coffee improved executive function when measured by the ecologically valid Jansari Assessment of Executive Function (JEF), it failed to do so when assessed by the Stroop task [46]. This suggests that one standard cup of coffee does not influence executive function, or that traditional tests of executive function such as the Stroop task may lack the sensitivity to detect the enhancing effects of caffeine. Caffeine was found to have no effect on other aspects of memory performance in well-rested participants [42].

Taken together, findings from the well-controlled studies suggest that the appropriate dose of caffeine might enhance attention, memory, problem solving and logical reasoning in sleep-deprived young adults. Further, this supplement might also be used to mitigate the joint effect of sustained operations and sleep deprivation on attention and vigilance. Further quality research is necessary before definitive conclusions can be reached about other cognitive functions or contexts.

#### Flavonoids

Flavonoids are natural polyphenol compounds found in fruits and other plants such as berries, apples, wine, tea, and cocoa [48]. Sub-classes of flavonoids include isoflavones (in soybeans and peanuts), flavanols (in tea and cocoa), flavonols (in fruits and vegetables), flavones (in cereals and herbs), anthocyanidins (in berries), and flavanones (in citrus fruits) [98]. The actions of dietary flavonoids on cognition appear to be related to various potential actions on the brain, including neuroprotection from neurotoxins and neuro-inflammation, synaptic signalling activation and improved cerebrovascular blood flow. These actions are driven by the apparent ability of flavonoids to interact with neuronal signalling cascades in the brain, resulting in the inhibition of cell death via exposure to neurotoxic species, the promotion of neuronal survival and differentiation, and an enhancement of peripheral and cerebral blood perfusion. Effects of flavonoids on cognition are likely the result of optimal maintenance of brain morphology due to the regulation of neuronal signalling and protection against neuronal losses [99].

Four included studies considered acute effects of flavonoids on cognitive performance in a total of 137 young healthy adults. All studies utilised crossover designs and were conducted in non-military populations. Although each study used participants from both genders, there was a greater proportion of female participants. The sub-classes of flavonoids investigated were flavanones, cocoa flavanols, anthocyanins, and epigallocatechin gallate (EGCG; a flavonoid typically found in green tea). The flavonoid dose and administration methods were as follows: 70.5 mg flavonones in a commercial citrus juice [47],  $525 \pm 5$  mg of polyphenols per 60 kg of body weight in a blackcurrant extract and a blackcurrant fruit juice, [49] 520 mg and 994 mg of cocoa flavanols in a dairy-based cocoa

drink [48], and 135 mg and 270 mg of EGCG in capsules [50]. All studies investigated the effects of single doses of flavonoids. Information processing speed, attention/vigilance, memory, and executive function were measured. Two studies used cognitive test batteries intended to increase the cognitive demand placed on participants [48,49].

Flavonone supplementation in citrus juice improved information processing speed (digit symbol substitution task) but not inhibitory control (Go/No-Go task) [47,49]. Blackcurrant extract mitigated deteriorating accuracy in sustained attention (RVIP). In addition, Scholey et al. [48] found that the optimal dose of cocoa flavanols (520 mg) improved working memory, in terms of serial threes subtraction, but not serial sevens. Conversely, Wightman et al. [50] found no effect of EGCG on working memory (either serial threes or serial sevens subtraction). Across all studies, flavonoids had no impact on executive function [47,50]. Despite the high quality of two of the included papers (see Table 2), there still remains insufficient quality empirical support to allow us to make any recommendations regarding flavonoid supplementation.

# Gingko biloba

Gingko biloba is an herbal supplement derived from extracts in the leaves of the gingko biloba tree [52] and is commonly used in a standardised form in clinical studies [100]. Unless otherwise specified, the studies included in this review administered a standardised gingko biloba extract. The active molecules of gingko biloba are believed to be linked to an array of potential physiological effects which can influence cognition. These physiological effects include [54]: the scavenging and inhibition of free radicals, anti-platelet activating factor, reducing neuronal death, improved blood circulation, increased cerebral perfusion, and protection against hypoxia. Gingko biloba has been claimed to improve short-term memory, rate of learning, and reaction time [52].

Six articles (comprising seven studies) met inclusion criteria and examined the effect of gingko biloba supplementation on cognition in healthy young non-military adults (see Table 3). There were three male-only studies and four that comprised predominantly female participants. In total, the impact of gingko biloba on cognitive performance was assessed in 240 participants (126 male; 114 female). Crossover (four) and independent group (three) designs were employed. Generally, a single administration of gingko biloba (tablet or capsule: 120–360 mg) was examined with the exception of two studies which applied extended supplementation for six weeks [51] or five days [55]. Kennedy et al. [54] also administered two gingko biloba extracts complexed with phospholipids in addition to the commonly used gingko biloba extract.

Apart from the vigilance component, neither gingko biloba nor ginkgo biloba complexed with phospholipids consistently improved speed of attention [53,54]. A dose-dependent effect of gingko biloba was found with 240 mg and 360 mg improving speed of attention at 2.5 and 6.5 hours post dosing [52]. Reaction time in a sustained attention task was improved after a single dose of 120 mg of gingko biloba; however, this effect may have been due to differences between the intervention and placebo conditions at baseline [51].

All studies assessed the effect of gingko biloba on memory; whilst improvements were found, this was not consistent across all memory tasks; dose-dependent effects were observed for gingko biloba, and in some cases differential effects were found for gingko biloba and ginkgo biloba complexed with phospholipids. A 360 mg dose of gingko biloba enhanced speed of memory, whereas a 240 mg dose degraded performance [52]. A 120 mg dose of ginkgo biloba or 120 mg gingko biloba complexed with phosphatidycholine generally had no impact on overall speed of memory [52–54]. Conversely, gingko biloba complexed with phosphatidylserine enhanced overall speed of memory, as well as memory accuracy in picture recognition [54]. Longer durations of gingko biloba supplementation (six weeks [51] or five days [55] also failed to enhance memory ability. Working memory (serial sevens subtraction speed) was enhanced four to six hours post-dose [53]; however, this is in contrast to Scholey and Kennedy [56], who observed improved accuracy. A single 120 mg dose of gingko biloba improved secondary memory, a composite score derived from performance accuracy on delayed word/picture

recognition, and immediate/delayed word recall tasks, with this effect being maximal one hour post supplementation [54]. Nil or minimal effects were observed for: reaction time [55], attention [51], working memory (including serial threes subtraction) [53–55], and executive function (mental flexibility or planning ability) [51].

In addition, extended supplementation of gingko biloba (>1 week) failed to elicit any cognitive improvement [51]. It should be noted that Kennedy et al.'s studies [52–54] combined results from individual tests into the cognitive factors of speed of attention, accuracy of attention, speed of memory and quality of memory, all derived from a factor analysis of the Cognitive Drug Research computerised assessment battery. However, in some of their studies they evaluated performance on underlying tasks when there was no impact on the overall cognitive factor [54].

In summary, the studies investigating the impact of gingko biloba on cognitive performance yielded mixed results. This fact, together with the uncertainty about risk of bias and poor paper quality (see Table 2), prevents us from making any recommendations about the use of gingko biloba as a means of enhancing cognitive performance. Nonetheless, further quality research is warranted that examines in more detail the dose- and time-dependent effects.

#### Ginseng

The plant Panax ginseng, commonly known as ginseng, is a traditional Chinese treatment and herbal supplement derived from ginseng roots [53]. The major active molecules of Panax ginseng are ginsenosides (saponins), comprising of 30 identified types [101]. Currently, the mechanisms that explain the cognitive effects of ginseng are not known [102]. Ginsenosides have been demonstrated to cause many forms of physiological effects, including modulation of the cardiovascular immune response systems, deceleration of platelet aggregation, modulation of neurotransmission, and nitric oxide synthesis [102].

A recent literature review identified that the included controlled studies consistently found that ginseng enhances cognitive performance, particularly aspects of working memory and speed of attentional processing [103]. Indeed, this review identified that ginseng was as effective, if not moreso, at enhancing working memory and reaction time than was the pharmaceutical modafinil, which is commonly used to enhance cognitive performance in sleep-deprived individuals and more recently in rested people. Nonetheless, Neale et al. [103] also identified that there is limited evidence available to form strong conclusions on the efficacy of ginseng for cognitive enhancement. An earlier systematic literature review reached similar conclusions: empirical studies have identified a potential benefit of ginseng for cognitive enhancement; however, there are too few randomly controlled crossover designed studies to enable strong recommendations on the use of ginseng for cognitive enhancement—or the durability of such enhancement [104]. The current review extends that of Geng et al. [104] and Neale et al. [103] by including studies they omitted and/or were published after 2011.

One additional study (see Table 3), subsequent to those reviewed in earlier systematic reviews, was found that assessed the cognitive enhancing effects of ginseng supplementation in 15 healthy young adults. This study used a randomised double-blind independent groups design with a placebo control and administered Korean ginseng at a dose of 4500 mg per day for two weeks. No effects were found on vigilance; however, ginseng administration had beneficial effects on brain activity related to attention and working memory, as indexed by the P300 event-related potential [57]. SIGN and GRADE evaluations (Table 2) of this single study highlighted the need for caution in interpretation as it was found to be of high risk and very low quality. In summary, findings from the included study will not change the findings from the previously performed systematic reviews of ginseng [103,104]; limited evidence is available to support that ginseng is efficacious in enhancing cognition in healthy young adults.

#### Guarana and Multivitamins

Guarana is a plant extract used predominantly as a food additive and is generally consumed with other herbal supplements, such as ginseng [60]. Guarana's stimulant properties have been attributed to its caffeine content and high quantities of saponins and tannins [60]. The cognitive benefit of guarana is proposed to be related to its ability to decrease the physiological response to physical or psychological stressors [59]. It has been proposed that the impact of guarana on cognition is due to the synergistic effect of its constituents, such as caffeine [105] and theanine [106].

Four studies, involving a total of 224 participants, examined the effect of acute doses of guarana on cognition (see Table 3). Two utilised crossover designs [59,61] and two used an independent groups design [58,61]. Sample compositions varied across the studies: predominantly female (two studies), approximate even gender distribution (one study), and active males only (one study). A standardised guarana extract was used by Kennedy et al. [59] (75 mg) and Haskell et al. [58] (37.5 mg, 75 mg, 150 mg, 300 mg). The other two studies administered a multivitamin + guarana supplement (Berocca Boost®, hereby referred to as MVM + G) in the form of an effervescent tablet dissolved in water. The MVM + G contained 222.2 mg of guarana (including 40 mg caffeine), and equal to or above the recommended dietary allowance (RDA) of B vitamins. The two MVM + G studies induced fatigue using a traditional cognitive demand battery [60] or exercise in combination with a repeated battery of cognitive tests [61]. Attention, memory, working memory, and executive function were measured.

Both MVM + G studies measured attention using RVIP. While Kennedy et al. [60] found an improvement in RVIP speed and accuracy, Veasey et al. [61] did not, nor on choice reaction time. Veasey et al. suggested that this was likely due to a lower number of repetitions completed on the tasks, as compared to Kennedy et al. Alternatively, in contrast to Kennedy et al.'s traditional cognitive demand battery, Veasey et al.'s battery in combination with their exercise regime may not have induced enough mental fatigue to detect any beneficial effects of the MVM + G drink on attention.

Kennedy et al. [59] also found mixed results from pure guarana extract supplementation: speed, but not accuracy, of attention was enhanced by guarana. Speed of attention was a composite of simple reaction time, choice reaction time and digit vigilance, whereas accuracy of attention was a composite of choice reaction time and digit vigilance. In addition, secondary memory (a composite of immediate and delayed recall and recognition tasks) was improved 2.5 h post-supplementation, and at three time points specifically for picture recognition (1, 2.5 and 4 h post-supplementation).

Inconsistent results were also found for memory performance. MVM + G had no effect on working memory (serial threes and serial sevens subtraction) [60]; however, it improved accuracy on numeric working memory [61]. MVM + G did not improve word recall, word recognition, or picture recognition accuracy, but it did improve speed of picture recognition [61]. A standardised guarana extract, however, improved performance on serial sevens subtraction, a sentence verification task, and secondary memory, but had no effect on working memory, speed of memory, or serial threes subtraction performance. Apart from working memory, executive function was not assessed in the MVM + G studies. However, Kennedy et al. [59] and Haskell et al. [58] did examine one aspect of executive functioning, logical reasoning, which was not enhanced by the pure guarana extract.

Overall SIGN and GRADE evaluations of the included studies for guarana intervention (see Table 2) identified that the risk of bias was unclear and the quality of the studies to be low. Although no recommendation can be given for the efficacy of guarana for cognitive enhancement, further research using well-controlled studies might shed more light on the dosage and time effects of this supplement on cognitive performance.

### 3.2.4. Prebiotics

Prebiotics are non-digestible foods/compounds that are found in a range of foods, such as asparagus, banana, garlic, onion, beans, and lentils. They are comprised of carbohydrates or short chains of saccharide molecules [107]. An important characteristic of dietary prebiotics is that they must be a selectively (i.e., preferential to gut microbiota populations including Lactobacillus and Bifidobacteria)

fermentable ingredient which aids the composition and/or activity of the gut microbiota [108]. Different forms of prebiotics exist that commonly include inulin, fructo-oligo-saccharides (FOS), and galacto-oligo-saccharides (GOS). Early evidence suggests that through post-fermentation by resident gut microbiota, prebiotics are capable of modulating a central brain growth factor (BDNF) among other plasticity-related proteins, neurotransmitters, cytokines, as well as anxiety, and emotional processing [107].

Only one study to date (see Table 3) has examined the effect of prebiotics on cognition in 50 healthy young adults. Smith et al. [65] used a crossover design to assess the effect of an acute dose of oligofructose-enriched inulin on reaction time, attention, and memory. A 5 g dose of the inulin supplement was administered in the form of powder added to a decaffeinated tea or coffee which was consumed with breakfast. There was no effect of oligofructose-enriched inulin on simple reaction time or measures of attention [65]. Inulin supplementation enhanced episodic memory (free recall and delayed recognition); however, it did not improve semantic processing, spatial memory, or executive function (logical reasoning). SIGN50 and GRADE assessments (see Table 2) of this one study on prebiotics identified that it was of acceptable risk and acceptable quality. More quality research in the area of utilising a prebiotic for cognitive enhancement in healthy young adults is required for appropriate recommendations to be made.

# 4. Discussion

### 4.1. Scope of Review

The aim of this systematic review was to investigate the relationship between legal dietary supplements and cognitive performance in healthy young adults. Specifically, we sought to determine whether the intake of any such supplements could preserve or enhance cognitive performance with a view to optimising such performance during deployment for the modern war fighter. Our review extended previous reviews in two important ways. First, it included studies of healthy young adult samples more generally, as the results have wider applicability beyond the military. Second, our review included a wide range of dietary supplements, such as various macronutrients and micronutrients, as well as biologically active non-nutrients. Studies included in the current review covered a range of cognitive areas. Individual studies generally focused on one or more of the following cognitive domains: psychomotor, information processing speed, attention/vigilance, memory, and executive function.

#### 4.2. Overall Synthesis

Overall there appears to be some evidence of cognitive enhancement from dietary supplements in healthy young adults. Several studies reported beneficial effects on information processing speed, in particular from supplementation with flavonoids [47] and guarana [60]. Others showed positive effects on memory following supplementation with tyrosine [66,73], caffeine [43], flavonoids [48], gingko biloba [54,56], ginseng [57], and prebiotics [65]. In addition, enhanced effects on attention were observed in some studies that supplemented with tyrosine [69,70], caffeine [44] or ginseng [57], and a handful of studies showed improved executive function with tyrosine [67,68,71], omega-3 [28], or caffeine supplementation [43,44].

However, as shown in Table 5, these beneficial effects were not observed either across all cognitive domains or for all aspects of a particular cognitive domain. For example, Veasey et al. [61] found no effect of guarana on visual information processing speed but they did for recognition memory. In addition, the single study on prebiotics found positive effects only for episodic memory but not semantic memory [65]. Furthermore, Hoffman et al. [39] found that beta-alanine enhanced psychomotor performance, but not working memory. Likewise, flavonoids enhanced information processing speed [47], but not executive function [47,50].

Dietary Supplement	Cognitive Domain					
	Psychomotor	Information Processing Speed	Attention/ Vigilance	Memory	Executive Function	
Beta-alanine	+(20(1))			<>(20(1))		
Tyrosine						
Stress						
Heat			+(10(1))		$+(10(1))^{a}$	
Cognitive				<>(22(1))		
Heat and Physical		<>(16(2))	?(16(2))	<>(8(1))	<>(8(1))	
No Stress				+(36(1))		
Omega-3			?(85(2))	-(13(1))	?(85(2))	
Vitamin B		-(56(1))		<>(56(1))	-(56(1))	
Nitrate						
Stress						
Cognitive/Physical					<>(16(1))	
No Stress			<>(40(1))		<>(40(1))	
Caffeine						
Stress						
Sleep Deprivation			+(39(3))		+(31(2))	
No Stress	+(43(1))	<>(20(1))	?(36(1))	?(46(2))	?(125(4))	
Flavanoids		+(28(1))	+(36(1))	?(57(2))	<>(55(2))	
Gingko biloba		?(120(4))	<>(48(2))	?(240(7))	?(52(1))	
Ginseng		<>(15(1))	+(15(1))			
Guarana						
Stress						
Mental Fatigue		?(130(1))	+(130(1))	<>(130(1))	?(130(1))	
Physical Fatigue		?(40(1))	<>(40(1))	?(40(1))		
No Stress		?(54(2))	?(54(2))	?(54(2))	?(28(1))	
Prebiotics		<>(29(1))	<>(29(1))	?(29(1))	<>(29(1))	

**Table 5.** Summary of impacts of reviewed dietary supplements on cognitive domains (# of participants (# of studies)). Improvement (+), decrease (-), no change (<>), or uncertain (?).

<sup>a</sup> Effect seen for working memory and logical reasoning.

For the majority of dietary supplements included in this review, findings were inconsistent across studies. While some studies showed positive effects of supplementation on psychomotor, information processing speed, attention/vigilance, memory, and/or executive function, others did not. This was notably the case for tyrosine [66–73], caffeine [40–46] and guarana [58–61]. By contrast, several supplements, namely omega-3 [64], B vitamins [74], and nitrates [62,63] showed very little, if any effect on cognitive performance in healthy young adults. However, in terms of military specific tasks, supplementation with beta-alanine was shown to improve marksmanship [39].

# 4.3. Situational Effects

Interestingly, several studies showed enhanced cognitive performance from supplementation under specific conditions. In particular, when macronutrient manipulations involving carbohydrates yielded beneficial effects, this occurred specifically under high cognitive task demand [77]. Furthermore, supplementation with tyrosine improved some aspects of memory and executive function following exposure to a cognitive stressor, but had no impact on the effect of a physical stressor (see Table 5) [66–71]. However, [69] did find that tyrosine improved vigilance during physical exercise in the heat. Thus, unless a certain threshold of physiological stress is reached, tyrosine by itself does not improve cognition. In addition, flavonoid supplementation produced stronger cognitive effects in the two studies that induced cognitive demand [48,49]. Although Kennedy et al. [60] observed stronger cognitive effects from guarana supplementation administered under cognitive demands, Veasey et al. [61] did not when participants also exercised; however, the cognitive load in the latter study may have been insufficient to induce mental fatigue. Likewise, a number of studies found that caffeine mitigated the effects of sleep deprivation on reaction time, recognition, vigilance and overall executive functioning, including in military samples [40,44,45]. In addition, some recent studies showed improvements in memory and

executive function from caffeine consumption in well-rested individuals [43]; however, others did not [42].

#### 4.4. Limitations

The studies included in the review are subject to various limitations. First, there was substantial variability in sample size and composition across studies. Sample sizes ranged from as few as 11 participants to more than 200 participants, with small sample size a frequent occurrence, yielding insufficient power to detect enhanced cognitive effects. Military samples were predominantly made up of men, whereas samples of healthy young adults typically included roughly equal gender ratios, or slightly more women.

Second, the quality, purity, ratio, duration, dose, and timing of the supplements varied widely across studies. In terms of quality, some studies did not administer the supplement in its pure form; it also contained other active ingredients, which could have been responsible for, or have contributed to, any enhanced cognitive effects. For example, the guarana extract can also naturally contain up to four times the amount of caffeine as found in coffee beans [109], with some studies also combining it with B vitamins [60,61], while the nitrate-rich beetroot juice not only contained nitrate but also flavonoids and flavonols [63]. Relatedly, different sub-classes of flavonoids were used across flavonoid supplementation studies [47–50], while omega-3 supplementation studies have been found to suffer from varied EPA to DHA ratios [88], as well as the use of oxidised supplements in some studies [110]; all of these could have contributed to the current state of mixed findings. In addition, potential cognitive effects could have been masked by (a) under-dosing, both in terms of low dosages, and (b) short supplementation periods. Doses considered to be low were used in several omega-3 [28], flavonoid [47,48,50], and ginseng [111] studies, whilst the short supplementation period in Lamport et al. [47] resulted in insufficient absorption time, as the cognitive effects of flavonone-infused citrus juice were evaluated only two hours after supplementation. Finally, although the majority of included studies did use a placebo-control group or a crossover design, the timing of supplementation (i.e., time of day of administration) was not always mentioned, and thus variations in circadian rhythms could have minimised or amplified any cognitive effects. As the gastrointestinal system and metabolism are regulated by circadian rhythms [112,113], it is important to control for the impact of the circadian system on the absorption and metabolism of the ingested supplement.

Third, studies varied in terms of the cognitive domains that were assessed, with limited or no investigation of executive function following supplementation with beta-alanine, gingko biloba, ginseng and guarana. Relatedly, different tasks were used to measure a particular cognitive function across studies.

Fourth, study designs did not consistently control for practice effects (ginseng) [57] or pre-existing baseline differences between the supplementation and placebo groups (gingko biloba) [51], or did not include a placebo-control group altogether (omega-3) [28].

Finally, SIGN50 scoring identified a substantial number of included papers of low quality (see Table 2). To make firm recommendations about the use of dietary supplements for cognitive enhancement, it is crucial that researchers are aware of the need to provide full information on their methodology, especially randomization and blinding techniques, to ensure papers are of high quality and reduce liability of risk and bias. Teo et al. [88] made a similar recommendation in their review on the effect of omega-3 on cognition and highlighted the importance of researchers following agreed reporting guidelines.

These methodological limitations could account for some of the conflicting results regarding cognitive effects from dietary supplementation. Methodological variations among studies also make it difficult to directly compare them, and thus draw firm conclusions. Moreover, the risk of bias assessment deemed the risk of the majority of studies to be unclear. In addition, the quality assessment indicated considerable variability in the quality of studies, with very few studies of high quality.

Of interest, two studies on the cognitive effects of probiotic supplementation were excluded for inappropriate study design [114] and being outside of age-range [115]. Nevertheless, evidence in animals and clinical populations suggests that further research into the cognitive effects of probiotics is warranted. Finally, the cognitive effects of many dietary supplements, such as protein, iron, magnesium, trace elements (e.g., selenium), and many others have not previously been investigated in quality randomised control studies in a cohort of healthy young adults aged 18–35 years. This in itself offers potential scope for future research.

# 4.5. Recommendations

At present there is limited high-quality research on the cognitive effects of dietary supplements in military samples, and in healthy young adults more generally. Nevertheless, the current review suggests that some legal dietary supplements could benefit the cognitive performance of healthy young adults, thus military personnel. First, based on the conditional GRADE evaluation (Table S5 in online Supplementary material), we suggest tyrosine could be used to mitigate the impact of physiological stress (particularly sleep deprivation) on psychomotor and memory performance. Second, a conditional recommendation can also be given for caffeine as it was commonly effective for mitigating the effects of sleep deprivation on attention, vigilance and aspects of executive function. Caffeine potentially also has the additional advantage of enhancing attention and vigilance when military personnel are on sustained operations, so not only working intensively for long periods but also sleep-deprived. However, the quality of caffeine studies was much more varied than that of the tyrosine studies with a mixture of acceptable, unclear and low-quality studies, as also reported in the review by Crawford et al. [97]. Further, although rare, large doses of caffeine can be fatal [25]. We therefore suggest that although caffeine could be used to reduce the impact of sleep deprivation and physiological fatigue on cognitive performance, the dosage provided should take into consideration other sources of caffeine intake. Finally, the lack of quality randomised controlled studies precludes us from offering any qualified recommendations about other supplements covered in this review.

# 4.6. Future Directions

Future directions would encompass a three-pronged approach. First, there is a clear need for sound research into the cognitive benefits of legal dietary supplements, especially among healthy young adults, including military personnel, who increasingly take such supplements despite limited scientific evidence for their efficacy. In particular, future research should consist of adequately powered and well-conducted randomised double-blind placebo-controlled studies. Studies should use adequately dosed high-quality supplements, and determine the appropriate time of day of administration. Furthermore, studies would ideally use crossover designs with appropriate duration to allow for wash-out effects, and focus on the effect of supplements on cognitive functions that have been identified as critical for the military operational environment. With respect to military contexts, study designs should include military specific tasks and conditions that mimic operational stress, such as cognitive load and exposure to stressors, both external (e.g., climatic extremes, noise, vibration) and internal (e.g., sleep deprivation, inadequate nutrition, dehydration)). Nutritional intake both in garrison and during field/operational deployments is commonly found to be inadequate within military populations [116,117] and should therefore be considered in future analyses. To ensure findings generalise to healthy young adults more broadly, the cognitive effects of dietary supplementation should also be tested in individuals who have had adequate sleep (duration and quality), as this will also identify which, if any, supplements would be useful for enhancing cognitive performance as opposed to mitigating its decline when a person is in a stressful environment.

Second, research should address the safety considerations of any supplements that do demonstrate cognitive benefits, and thus weigh up the pros and cons of taking them. The current review identified very few adverse effects from dietary supplementation, indicating that the wide range of supplements reviewed here are generally considered to be safe. However, anecdotal evidence from military samples,

and some empirical evidence [2,9–13,15–21], indicate that some dietary supplements may be harmful, and worryingly, people continue to take a supplement even if they experience bad side effects. Further, despite warnings about their potential harmful effects and the lack of regulation, a recently reported study in the United States found that 50% of people surveyed in 2004–2015 believed that dietary supplements were regulated, safe, and that manufacturers were required to provide visible information on their side effects [26]. A recent study found that the National Institutes of Health (US) Dietary Supplements Label Database identified supplements that claimed to enhance cognition but contained potentially dangerous ingredients such as vinocetine, huperzine A, and picamilon [118]. Thus, it is imperative that future studies report adverse effects to enable the creation of a database to inform regulators of the need for better control of dietary supplements.

Third, because of the potential adverse effects of dietary supplements, research should focus on developing appropriate behaviour change programs designed to equip healthy young adults with the skills and/or support structures needed to make informed safe choices on dietary supplements that they may become exposed to through marketing hype and/or word of mouth.

Having a cognitive edge will help defence personnel achieve superiority in demanding and uncertain environments. Although firm recommendations cannot be made due to a shortage of well-designed studies, conditional recommendations can be made for caffeine and tyrosine, which can enhance aspects of cognition under specific conditions. Further high-quality research is needed to ascertain whether caffeine and/or tyrosine can enhance a broader range of cognitive function more generally. Comparative studies comparing the benefits of caffeine and tyrosine are also warranted, as these would identify whether a single dietary supplement would suffice across a range of stressful and non-stressful situations. In addition, nitrates and omega-3 appear to have little benefit for cognition in healthy young adults. Nevertheless, sufficient evidence exists to warrant further research into the effects of some supplements in healthy young adults. Some critical questions that need be addressed in future research include: (1) Can tyrosine mitigate psychomotor deficits due to sleep deprivation? (2) What are the appropriate protocols for caffeine to ameliorate the detrimental effects of sleep deprivation on attention, memory, and executive function? (3) Can caffeine enhance memory and executive function in well-rested individuals? and (4) What are the appropriate EPA:DHA ratios that result in omega-3 enhancing memory and inhibitory control, and to what extent is this task-dependent?

**Supplementary Materials:** The following are available online at http://www.mdpi.com/2072-6643/12/2/545/s1, Table S1: Example of full search strategy used in the literature search; Table S2: Full table of evidence for included studies; Table S3: Excluded papers and reasons for exclusion; Table S4: PRISMA 2009 checklist; Table S5: GRADE analysis: Overall evidence synthesis for the impact of reviewed dietary supplements on cognitive domains.

Author Contributions: Conceptualization, D.E.P., K.L.T., B.P. and E.K.; methodology, D.E.P., K.L.T., B.P. and E.K.; data curation, A.W.; formal analysis, D.E.P. and E.K.; investigation, D.E.P., K.L.T., B.P., A.W. and E.K.; writing—original draft preparation, D.E.P., K.L.T., B.P., A.W. and E.K.; writing—review and editing, D.E.P., K.L.T., B.P. and E.K.; visualization, D.E.P., K.L.T., B.P., A.W. and E.K.; project administration, D.E.P. and K.L.T. All recommendations were jointly agreed upon by the authors and are based on information emerging from the review. All authors have read and agreed to the published version of the manuscript.

**Funding:** The contribution of A.W. was partially funded under a Collaborative Project Agreement between Defence Science and Technology and Flinders University (ID6867 Nutrition, supplements and Cognitive Fitness).

Acknowledgments: This work was undertaken in response to questions asked of the Defence Science and Technology by the Australian Army. Any opinions, findings, conclusions, or recommendations in this paper are those of the authors and should not be construed as official Department of Defence decisions. The authors would like to thank Eugene Aidman for checking our description of higher-order, and associated lower-order, cognitive functions. We also thank David Crone and Geoffrey Fraser for reading the review paper and checking it against the SIGN checklist for Systematic Literature Reviews. Appreciation is also forwarded to Julia Carins for advice on behaviour change and effective use of programs in support of informed safe choice.

**Conflicts of Interest:** The authors have no interests to declare. None of this work has been presented before in any journal; however, to fulfil Australian Army client reporting requirements, it has been summarised at the Defence Human Sciences Symposium, Adelaide, South Australia November 2017.

#### References

- 1. Maughan, R.J.; Burke, L.M.; Dvorak, J.; Larson-Meyer, D.E.; Peeling, P.; Phillips, S.M.; Rawson, E.S.; Walsh, N.P.; Garthe, I.; Geyer, H.; et al. IOC consensus statement: dietary supplements and the high-performance athlete. *Br. J. Sports Med.* **2018**, *52*, 439–455. [CrossRef]
- 2. Knapik, J.J.; Trone, D.W.; Austin, K.G.; Steelman, R.A.; Farina, E.K.; Lieberman, H.R. Prevalence, Adverse Events, and Factors Associated with Dietary Supplement and Nutritional Supplement Use by US Navy and Marine Corps Personnel. *J. Acad. Nutr. Diet.* **2016**, *116*, 1423–1442. [CrossRef]
- Lieberman, H.R.; Stavinoha, T.B.; McGraw, S.M.; White, A.; Hadden, L.S.; Marriott, B.P. Use of dietary supplements among active-duty US Army soldiers. *Am. J. Clin. Nutr.* 2010, *92*, 985–995. [CrossRef] [PubMed]
- Zion Market Research. Dietary supplements market by ingredients (Botanicals, Vitamins, Minerals, Amino Acids, Enzymes) for additional supplements, medicinal supplements and sports nutrition applciations - Global industry perspective, Comprehensive analysis and forecast, 2016-2022. Available online: https: //www.zionmarketresearch.com/report/dietary-supplements-market. (accessed on 23 June 2017).
- 5. Barnes, K.; Ball, L.; Desbrow, B.; Alsharairi, N.; Ahmed, F. Consumption and reasons for use of dietary supplements in an Australian university population. *Nutrition* **2016**, *32*, 524–530. [CrossRef] [PubMed]
- 6. Kjertakov, M.; Hristovski, R.; Racaj, M. The use of dietary supplement among soldiers from the macedonian special operations regiment. *J. Spec. Oper. Med.* **2013**, *13*, 19–24. [PubMed]
- Knapik, J.J.; Steelman, R.A.; Hoedebecke, S.S.; Farina, E.K.; Austin, K.G.; Lieberman, H.R. A systematic review and meta-analysis on the prevalence of dietary supplement use by military personnel. *BMC Complement*. *Altern. Med.* 2014, 14, 143. [CrossRef] [PubMed]
- Baker, B.; Probert, B.; Pomeroy, D.; Carins, J.; Tooley, K. Prevalence and Predictors of Dietary and Nutritional Supplement Use in the Australian Army: A Cross-Sectional Survey. *Nutrients* 2019, *11*, 1462. [CrossRef] [PubMed]
- 9. Austin, K.G.; Farina, E.K.; Lieberman, H.R. Self-reported side-effects associated with use of dietary supplements in an armed forces population. *Drug Test. Anal.* **2016**, *8*, 287–295. [CrossRef]
- 10. Cellini, M.; Attipoe, S.; Seales, P.; Gray, R.; Ward, A.; Stephens, M.; Deuster, P.A. Dietary supplements: physician knowledge and adverse event reporting. *Med. Sci. Sports Exerc.* **2013**, *45*, 23–28. [CrossRef]
- 11. Chatham-Stephens, K.; Taylor, E.; Chang, A.; Peterson, A.; Daniel, J.; Martin, C.; Deuster, P.; Noe, R.; Kieszak, S.; Schier, J.; et al. Hepatotoxicity associated with weight loss or sports dietary supplements, including OxyELITE Pro United States, 2013. *Drug Test. Anal.* **2016**. [CrossRef]
- 12. Deuster, P.A.; Lieberman, H.R. Protecting military personnel from high risk dietary supplements. *Drug Test. Anal.* 2016, *8*, 431–433. [CrossRef] [PubMed]
- Eliason, M.J.; Eichner, A.; Cancio, A.; Bestervelt, L.; Adams, B.D.; Deuster, P.A. Case reports: Death of active duty soldiers following ingestion of dietary supplements containing 1,3-dimethylamylamine (DMAA). *Mil. Med.* 2012, 177, 1455–1459. [CrossRef] [PubMed]
- Geller, A.I.; Shehab, N.; Weidle, N.J.; Lovegrove, M.C.; Wolpert, B.J.; Timbo, B.B.; Mozersky, R.P.; Budnitz, D.S. Emergency Department Visits for Adverse Events Related to Dietary Supplements. *N. Engl. J. Med.* 2015, 373, 1531–1540. [CrossRef] [PubMed]
- 15. Guallar, E.; Stranges, S.; Mulrow, C.; Appel, L.J.; Miller, E.R. Enough is enough: Stop wasting money on vitamin and mineral supplements. *Ann. Intern. Med.* **2013**, *159*, 850–851. [CrossRef] [PubMed]
- Hughes, J.; Shelton, B.; Hughes, T. Suspected dietary supplement injuries in special operations soldiers. J. Spec. Oper. Med. 2010, 10, 14–24. [PubMed]
- 17. Klein, E.A.; Thompson, I.M., Jr.; Tangen, C.M.; Crowley, J.J.; Lucia, M.S.; Goodman, P.J.; Minasian, L.M.; Ford, L.G.; Parnes, H.L.; Gaziano, J.M.; et al. Vitamin E and the risk of prostate cancer: the Selenium and Vitamin E Cancer Prevention Trial (SELECT). *JAMA* **2011**, *306*, 1549–1556. [CrossRef] [PubMed]
- Magee, C.D.; Witte, S.; Kwok, R.M.; Deuster, P.A. Mission Compromised? Drug-Induced Liver Injury From Prohormone Supplements Containing Anabolic-Androgenic Steroids in Two Deployed U.S. Service Members. *Mil. Med.* 2016, 181, e1169–e1171. [CrossRef]
- 19. Stanger, M.J.; Thompson, L.A.; Young, A.J.; Lieberman, H.R. Anticoagulant activity of select dietary supplements. *Nutr. Rev.* 2012, *70*, 107–117. [CrossRef]

- 20. Urban, K.R.; Gao, W.J. Performance enhancement at the cost of potential brain plasticity: neural ramifications of nootropic drugs in the healthy developing brain. *Front. Syst. Neurosci.* **2014**, *8*, 38. [CrossRef]
- 21. van der Voet, G.B.; Sarafanov, A.; Todorov, T.I.; Centeno, J.A.; Jonas, W.B.; Ives, J.A.; Mullick, F.G. Clinical and analytical toxicology of dietary supplements: a case study and a review of the literature. *Biol. Trace Elem. Res.* **2008**, *125*, 1–12. [CrossRef]
- 22. Cohen, P.A.; Ernst, E. Safety of Herbal Supplements: A Guide for Cardiologists. *Cardiovas. Ther.* **2010**, *28*, 246–253. [CrossRef] [PubMed]
- 23. Navarro, V.J.; Khan, I.; Björnsson, E.; Seeff, L.B.; Serrano, J.; Hoofnagle, J.H. Liver injury from herbal and dietary supplements. *Hepatology* **2017**, *65*, 363–373. [CrossRef] [PubMed]
- 24. Izzo, A.A.; Ernst, E. Interactions Between Herbal Medicines and Prescribed Drugs. *Drugs* **2009**, *69*, 1777–1798. [CrossRef] [PubMed]
- 25. Kerrigan, S.; Lindsey, T. Fatal caffeine overdose: two case reports. *Forensic Sci. Int.* **2005**, *153*, 67–69. [CrossRef]
- 26. Or, F.; Kim, Y.; Simms, J.; Austin, S.B. Taking Stock of Dietary Supplements' Harmful Effects on Children, Adolescents, and Young Adults. *J. adolesc. Health* **2019**, *65*, 455–461. [CrossRef]
- Newmaster, S.G.; Grguric, M.; Shanmughanandhan, D.; Ramalingam, S.; Ragupathy, S. DNA barcoding detects contamination and substitution in North American herbal products. *BMC Med.* 2013, 11, 222. [CrossRef]
- Bauer, I.; Hughes, M.; Rowsell, R.; Cockerell, R.; Pipingas, A.; Crewther, S.; Crewther, D. Omega-3 supplementation improves cognition and modifies brain activation in young adults. *Hum. Psychopharmacol.* 2014, 29, 133–144. [CrossRef]
- 29. Muldoon, M.F.; Ryan, C.M.; Yao, J.K.; Conklin, S.M.; Manuck, S.B. Long-chain omega-3 fatty acids and optimization of cognitive performance. *Mil. Med.* **2014**, *179*, 95–105. [CrossRef]
- 30. Kennedy, D.O.; Stevenson, E.J.; Jackson, P.A.; Dunn, S.; Wishart, K.; Bieri, G.; Barella, L.; Carne, A.; Dodd, F.L.; Robertson, B.C.; et al. Multivitamins and minerals modulate whole-body energy metabolism and cerebral blood-flow during cognitive task performance: a double-blind, randomised, placebo-controlled trial. *Nutr. Metabol.* **2016**, *13*, 11. [CrossRef]
- 31. Pipingas, A.; Camfield, D.A.; Stough, C.; Scholey, A.B.; Cox, K.H.; White, D.; Sarris, J.; Sali, A.; Macpherson, H. Effects of multivitamin, mineral and herbal supplement on cognition in younger adults and the contribution of B group vitamins. *Hum. Psychopharmacol.* **2014**, *29*, 73–82. [CrossRef]
- Lieberman, H.R.; Tharion, W.J.; Shukitt-Hale, B.; Speckman, K.L.; Tulley, R. Effects of caffeine, sleep loss, and stress on cognitive performance and mood during U.S. Navy SEAL training. *Psychopharmacology* 2002, 164, 250–261. [CrossRef] [PubMed]
- 33. Lowe, M.; Harris, W.; Kane, R.L.; Banderet, L.; Levinson, D.; Reeves, D. Neuropsychological assessment in extreme environments. *Arch. Clini. Neuropsychol.* 2007, 22 *Suppl* 1, S89–S99. [CrossRef]
- 34. Killgore, W.D.; Killgore, D.B.; Day, L.M.; Li, C.; Kamimori, G.H.; Balkin, T.J. The effects of 53 hours of sleep deprivation on moral judgment. *Sleep* 2007, *30*, 345–352. [CrossRef] [PubMed]
- 35. Orzel-Gryglewska, J. Consequences of sleep deprivation. *Intern. J. Occupat. Med. Environ. Health* **2010**, 23, 95–114. [CrossRef]
- 36. Shamseer, L.; Moher, D.; Clarke, M.; Ghersi, D.; Liberati, A.; Petticrew, M.; Shekelle, P.; Stewart, L.A.; the PRISMA-P Group. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. *Br. Med. J.* **2015**, *350*, 1–25. [CrossRef] [PubMed]
- 37. Schünemann, H.; Brożek, J.; Guyatt, G.; Oxman, A. GRADE Handbook: Introduction to GRADE Handbook: Handbook for Grading the Quality of Evidence and the Strength of Recommendations Using the GRADE Approach; Schünemann, H., Brożek, J., Guyatt, G., Oxman, A., Eds.; 2013; Available online: https://med.mahidol.ac.th/ ceb/sites/default/files/public/pdf/journal\_club/2017/GRADE%20handbook.pdf (accessed on 30 July 2017).
- 38. Scottish Intercollegiate Guidelines Network. SIGN 50: A Guideline Developer's Handbook. Available online: http://www.sign.ac.uk/methodology/checklists.html (accessed on 1 May 2017).
- 39. Hoffman, J.R.; Landau, G.; Stout, J.R.; Dabora, M.; Moran, D.S.; Sharvit, N.; Hoffman, M.W.; Ben Moshe, Y.; McCormack, W.P.; Hirschhorn, G.; et al. beta-alanine supplementation improves tactical performance but not cognitive function in combat soldiers. *J. Intern. Soc. Sports Nutr.* **2014**, *11*, 15. [CrossRef] [PubMed]

- Aidman, E.; Johnson, K.; Paech, G.M.; Della Vedova, C.; Pajcin, M.; Grant, C.; Kamimori, G.H.; Mitchelson, E.; Hoggan, B.L.; Fidock, J.; et al. Caffeine reduces the impact of drowsiness in driving errors. *Transp. Res. Part F: Traffic Psychol. Behav.* 2018, 54, 236–247. [CrossRef]
- 41. Brunye, T.T.; Mahoney, C.R.; Lieberman, H.R.; Giles, G.E.; Taylor, H.A. Acute caffeine consumption enhances the executive control of visual attention in habitual consumers. *Brain Cogn.* **2010**, *74*, 186–192. [CrossRef]
- 42. Hussain, S.J.; Cole, K.J. No Enhancement of 24-Hour Visuomotor Skill Retention by Post-Practice Caffeine Administration. *PLoS ONE* 2015, *10*, e0129543. [CrossRef]
- 43. Kahathuduwa, C.N.; Dassanayake, T.L.; Amarakoon, A.M.; Weerasinghe, V.S. Acute effects of theanine, caffeine and theanine-caffeine combination on attention. *Nutr. Neurosci.* **2017**. [CrossRef]
- 44. Kamimori, G.H.; McLellan, T.M.; Tate, C.M.; Voss, D.M.; Niro, P.; Lieberman, H.R. Caffeine improves reaction time, vigilance and logical reasoning during extended periods with restricted opportunities for sleep. *Psychopharmacology* (*Berlin*) **2015**, *232*, 2031–2042. [CrossRef] [PubMed]
- Reyner, L.A.; Horne, J.A. Early morning driver sleepiness: Effectiveness of 200 mg caffeine. *Psychophysiology* 2000, 37, 251–256. [CrossRef] [PubMed]
- 46. Soar, K.; Chapman, E.; Lavan, N.; Jansari, A.S.; Turner, J.J.D. Investigating the effects of caffeine on executive functions using traditional Stroop and a new ecologically-valid virtual reality task, the Jansari assessment of Executive Functions (JEF). *Appetite* **2016**, *105*, 156–163. [CrossRef] [PubMed]
- Lamport, D.J.; Pal, D.; Macready, A.L.; Barbosa-Boucas, S.; Fletcher, J.M.; Williams, C.M.; Spencer, J.P.; Butler, L.T. The effects of flavanone-rich citrus juice on cognitive function and cerebral blood flow: an acute, randomised, placebo-controlled cross-over trial in healthy, young adults. *Br. J. Nutr.* 2017, *116*, 2160–2168. [CrossRef]
- Scholey, A.B.; French, S.J.; Morris, P.J.; Kennedy, D.O.; Milne, A.L.; Haskell, C.F. Consumption of cocoa flavanols results in acute improvements in mood and cognitive performance during sustained mental effort. *J. Psychopharmacol.* 2010, 24, 1505–1514. [CrossRef]
- 49. Watson, A.W.; Haskell-Ramsay, C.F.; Kennedy, D.O.; Cooney, J.M.; Trower, T.; Scheepens, A. Acute supplementation with blackcurrant extracts modulates cognitive functioning and inhibits monoamine oxidase-B in healthy young adults. *J. Functional Foods* **2015**, *17*, 524–539. [CrossRef]
- 50. Wightman, E.L.; Haskell, C.F.; Forster, J.S.; Veasey, R.C.; Kennedy, D.O. Epigallocatechin gallate, cerebral blood flow parameters, cognitive performance and mood in healthy humans: a double-blind, placebo-controlled, crossover investigation. *Hum. Psychopharmacol.* **2012**, *27*, 177–186. [CrossRef]
- Elsabagh, S.; Hartley, D.E.; Ali, O.; Williamson, E.M.; File, S.E. Differential cognitive effects of Ginkgo biloba after acute and chronic treatment in healthy young volunteers. *Psychopharmacology (Berlin)* 2005, 179, 437–446. [CrossRef]
- 52. Kennedy, D.O.; Scholey, A.B.; Wesnes, K.A. The dose-dependent cognitive effects of acute administration of Ginkgo biloba to healthy young volunteers. *Psychopharmacology* **2000**, *151*, 416–423. [CrossRef]
- 53. Kennedy, D.O.; Scholey, A.B.; Wesnes, K.A. Modulation of cognition and mood following administration of single doses of Ginkgo biloba, ginseng, and a ginkgo/ginseng combination to healthy young adults. *Physiol. Behav.* **2002**, *75*, 739–751. [CrossRef]
- 54. Kennedy, D.O.; Haskell, C.F.; Mauri, P.L.; Scholey, A.B. Acute cognitive effects of standardised Ginkgo biloba extract complexed with phosphatidylserine. *Hum. Psychopharmacol.* **2007**, *22*, 199–210. [CrossRef] [PubMed]
- 55. Moulton, P.L.; Boyko, L.N.; Fitzpatrick, J.L.; Petros, T.V. The effect of Ginkgo biloba on memory in healthy male volunteers. *Physiol. Behave.* **2001**, *73*, 659–665. [CrossRef]
- 56. Scholey, A.B.; Kennedy, D.O. Acute, dose-dependent cognitive effects of Ginkgo biloba, Panax ginseng and their combination in healthy young volunteers differential interactions with cognitive demand. *Hum. Psychopharmacol.: Clin. Expe.* **2002**, *17*, 35–44. [CrossRef] [PubMed]
- Yeo, H.B.; Yoon, H.K.; Lee, H.J.; Kang, S.G.; Jung, K.Y.; Kim, L. Effects of Korean Red Ginseng on Cognitive and Motor Function: A Double-blind, Randomized, Placebo-controlled Trial. *J. Ginseng Res.* 2012, *36*, 190–197. [CrossRef]
- Haskell, C.F.; Kennedy, D.O.; Wesnes, K.A.; Milne, A.L.; Scholey, A.B. A double-blind, placebo-controleld, multi-dose evaluationm of the acute behavioural effects of guarana in humans. *J. Psychopharmacol.* 2007, 21, 65–70. [CrossRef]

- 59. Kennedy, D.O.; Haskell, C.F.; Wesnes, K.A.; Scholey, A.B. Improved cognitive performance in human volunteers following administration of guarana (Paullinia cupana) extract: comparison and interaction with Panax ginseng. *Pharmacol. Biochem. Behave.* **2004**, *79*, 401–411. [CrossRef]
- 60. Kennedy, D.O.; Haskell, C.F.; Robertson, B.; Reay, J.; Brewster-Maund, C.; Luedemann, J.; Maggini, S.; Ruf, M.; Zangara, A.; Scholey, A.B. Improved cognitive performance and mental fatigue following a multi-vitamin and mineral supplement with added guarana (Paullinia cupana). *Appetite* **2008**, *50*, 506–513. [CrossRef]
- 61. Veasey, R.C.; Haskell-Ramsay, C.F.; Kennedy, D.O.; Wishart, K.; Maggini, S.; Fuchs, C.J.; Stevenson, E.J. The Effects of Supplementation with a Vitamin and Mineral Complex with Guarana Prior to Fasted Exercise on Affect, Exertion, Cognitive Performance, and Substrate Metabolism: A Randomized Controlled Trial. *Nutrients* **2015**, *7*, 6109–6127. [CrossRef]
- 62. Thompson, K.G.; Turner, L.; Prichard, J.; Dodd, F.; Kennedy, D.O.; Haskell, C.; Blackwell, J.R.; Jones, A.M. Influence of dietary nitrate supplementation on physiological and cognitive responses to incremental cycle exercise. *Respir. Physiol. Neurobiol.* **2014**, *193*, 11–20. [CrossRef]
- Wightman, E.L.; Haskell-Ramsay, C.F.; Thompson, K.G.; Blackwell, J.R.; Winyard, P.G.; Forster, J.; Jones, A.M.; Kennedy, D.O. Dietary nitrate modulates cerebral blood flow parameters and cognitive performance in humans: A double-blind, placebo-controlled, crossover investigation. *Physiol. Behav.* 2015, 149, 149–158. [CrossRef]
- 64. Giles, G.E.; Mahoney, C.R.; Urry, H.L.; Brunye, T.T.; Taylor, H.A.; Kanarek, R.B. Omega-3 fatty acids and stress-induced changes to mood and cognition in healthy individuals. *Pharmacol. Biochem. Behav.* **2015**, 132, 10–19. [CrossRef]
- Smith, A.P.; Sutherland, D.; Hewlett, P. An Investigation of the Acute Effects of Oligofructose-Enriched Inulin on Subjective Wellbeing, Mood and Cognitive Performance. *Nutrients* 2015, 7, 8887–8896. [CrossRef] [PubMed]
- 66. Colzato, L.S.; Jongkees, B.J.; Sellaro, R.; Hommel, B. Working memory reloaded: tyrosine repletes updating in the N-back task. *Front. Behav. Neurosci.* **2013**, *7*, 200. [CrossRef] [PubMed]
- Colzato, L.S.; Jongkees, B.J.; Sellaro, R.; van den Wildenberg, W.P.; Hommel, B. Eating to stop: tyrosine supplementation enhances inhibitory control but not response execution. *Neuropsychologia* 2014, 62, 398–402. [CrossRef] [PubMed]
- Colzato, L.S.; de Haan, A.M.; Hommel, B. Food for creativity: tyrosine promotes deep thinking. *Psycholog. Res.* 2015, 79, 709–714. [CrossRef] [PubMed]
- Coull, N.; Watkins, S.L.; Aldous, J.W.; Warren, L.K.; Chrismas, B.C.; Dascombe, B.; Mauger, A.R.; Abt, G.; Taylor, H. Effect of tyrosine ingestion on cognitive and physical performance utilising an intermittent soccer performance test (iSPT) in a warm environment. *Euro. J. Appl. Physiol.* 2015, *115*, 373–386. [CrossRef] [PubMed]
- Kishore, K.; Ray, K.; Anand, J.P.; Thakur, L.; Kumar, S.; Panjwani, U. Tyrosine ameliorates heat induced delay in event related potential P300 and contingent negative variation. *Brain Cogn.* 2013, *83*, 324–329. [CrossRef] [PubMed]
- Steenbergen, L.; Sellaro, R.; Hommel, B.; Colzato, L.S. Tyrosine promotes cognitive flexibility: evidence from proactive vs. reactive control during task switching performance. *Neuropsychologia* 2015, 69, 50–55. [CrossRef]
- Watson, P.; Enever, S.; Page, A.; Stockwell, J.; Maughan, R.J. Tyrosine supplementation does not influence the capacity to perform prolonged exercise in a warm environment. *Intern. J. sport nutr. Exerc. Metabol.* 2012, 22, 363–373. [CrossRef]
- 73. Jongkees, B.J.; Sellaro, R.; Beste, C.; Nitsche, M.A.; Kuhn, S.; Colzato, L.S. L-Tyrosine administration modulates teh effect of transcranial direct current stimulation on working memory in healthy humans. *Cortex* 2017, 103–114. [CrossRef]
- 74. Bryan, J.; Calvaresi, E.; Hughes, D. Short-term folate, vitamin B-12 or vitamin B-6 supplementation slightly affects memory performance but not mood in women of various ages. *J. Nutr.* **2002**, *132*, 1345–1356. [CrossRef] [PubMed]
- 75. Higgins, J.P.T.; Green, S. (Eds.) *Cochrane Handbook for Systematic Reviews of Interventions*; Version 5.1.0 [updated March 2011]; The Cochrane Collaboration, 2011; Available online: www.handbook.cochrane.org (accessed on 17 January 2020).

- Stautz, K.; Zupan, Z.; Field, M.; Marteau, T.M. Does self-control modify the impact of interventions to change alcohol, tobacco, and food consumption? A systematic review. *Health Psychol. Rev.* 2018, 12, 157–178. [CrossRef] [PubMed]
- 77. Hoyland, A.; Lawton, C.L.; Dye, L. Acute effects of macronutrient manipulations on cognitive test performance in healthy young adults: a systematic research review. *Neurosci. Biobehav. Rev.* 2008, 32, 72–85. [CrossRef] [PubMed]
- 78. Ko, R.; Low Dog, T.; Gorecki, D.K.; Cantilena, L.R.; Costello, R.B.; Evans, W.J.; Hardy, M.L.; Jordan, S.A.; Maughan, R.J.; Rankin, J.W.; et al. Evidence-based evaluation of potential benefits and safety of beta-alanine supplementation for military personnel. *Nutr. Rev.* **2014**, *72*, 217–225. [CrossRef]
- 79. Murakami, T.; Furuse, M. The impact of taurine and beta-alanine supplemented diets on behavioral and neurochemical parameters in mice: antidepressant versus anxiolytic-like effects. *Amino Acids* **2010**, *39*, 427–434. [CrossRef]
- 80. Jongkees, B.J.; Hommel, B.; Kuhn, S.; Colzato, L.S. Effect of tyrosine supplementation on clinical and healthy populations under stress or cognitive demands–A review. *J. Psychiatr. Res.* **2015**, *70*, 50–57. [CrossRef]
- 81. Meeusen, R.; Watson, P.; Hasegawa, H.; Roelands, B.; Piacentini, M.F. Central fatigue: the serotonin hypothesis and beyond. *Sports Med.* **2006**, *36*, 881–909. [CrossRef]
- Attipoe, S.; Zeno, S.A.; Lee, C.; Crawford, C.; Khorsan, R.; Walter, A.R.; Deuster, P.A. Tyrosine for mitigating stress and enhamcing performance in healthy adult humans, a Rapid Evidence Assessment of the Literature. *Mil. Med.* 2015, *180*, 754–765. [CrossRef]
- 83. Davis, B.A.; Prall, B.C. The challenges of incorporation of omega-3 fatty acids into ration components and their prevalence in garrison feeding. *Military medicine* **2014**, *179*, 162–167. [CrossRef]
- 84. Bailes, J.E.; Patel, V. The potential for DHA to mitigate mild traumatic brain injury. *Mil. Med.* **2014**, 179, 112–116. [CrossRef]
- 85. Stonehouse, W.; Conlon, C.A.; Podd, J.; Hill, S.R.; Minihane, A.M.; Haskell, C.; Kennedy, D. DHA supplementation improved both memory and reaction time in healthy young adults: a randomized controlled trial. *Am. J. Clin. Nutr.* **2013**, *97*, 1134–1143. [CrossRef] [PubMed]
- Jackson, P.A.; Reay, J.L.; Scholey, A.B.; Kennedy, D.O. DHA-rich oil modulates the cerebral haemodynamic response to cognitive tasks in healthy young adults: a near IR spectroscopy pilot study. *Br. J. Nutr.* 2012, 107, 1093–1098. [CrossRef]
- 87. Stonehouse, W. Does consumption of LC omega-3 PUFA enhance cognitive performance in healthy school-aged children and throughout adulthood? Evidence from clinical trials. *Nutrients* **2014**, *6*, 2730–2758. [CrossRef]
- Teo, L.; Crawford, C.; Yehuda, R.; Jaghab, D.; Bingham, J.J.; Chittum, H.K.; Gallon, M.D.; O'Connell, M.L.; Arzola, S.M.; Berry, K. Omega-3 polyunsaturated fatty acids to optimize cognitive function for military mission-readiness: a systematic review and recommendations for the field. *Nutr. Rev.* 2017, 75, 36–48. [CrossRef] [PubMed]
- 89. Karr, J.E.; Grindstaff, T.R.; Alexander, J.E. Omega-3 polyunsaturated fatty acids and cognition in a college-aged population. *Exp. Clin. Psychopharmacol.* **2012**, *20*, 236–242. [CrossRef] [PubMed]
- 90. Kennedy, D.O.; Haskell, C.F. Vitamins and cognition: what is the evidence? *Drugs* **2011**, *71*, 1957–1971. [CrossRef]
- 91. Kennedy, D.O. B Vitamins and the Brain: Mechanisms, Dose and Efficacy–A Review. *Nutrients* **2016**, *8*, 68. [CrossRef]
- Presley, T.D.; Morgan, A.R.; Bechtold, E.; Clodfelter, W.; Dove, R.W.; Jennings, J.M.; Kraft, R.A.; King, S.B.; Laurienti, P.J.; Jack, W. Acute effect of a high nitrate diet on brain perfusion in older adults. *Nitric Oxide* 2011, 24, 34–42. [CrossRef]
- 93. Glade, M.J. Caffeine-Not just a stimulant. Nutrition 2010, 26, 932–938. [CrossRef]
- 94. McLellan, T.M.; Caldwell, J.A.; Lieberman, H.R. A review of caffeine's effects on cognitive, physical and occupational performance. *Neurosci. Biobehav. Rev.* **2016**, *71*, 294–312. [CrossRef]
- 95. Nehlig, A. Is caffeine a cognitive enhancer? *J. Alzheimer's Dis.* **2010**, *20* (Suppl. 1), S85–S94. [CrossRef] [PubMed]
- 96. Ullrich, S.; de Vries, Y.C.; Kuhn, S.; Repantis, D.; Dresler, M.; Ohla, K. Feeling smart: Effects of caffeine and glucose on cognition, mood and self-judgment. *Physiol. Behav.* **2015**, 151, 629–637. [CrossRef] [PubMed]

- 97. Crawford, C.; Teo, L.; Lafferty, L.; Drake, A.; Bingham, J.J.; Gallon, M.D.; O'Connell, M.L.; Chittum, H.K.; Azorla, S.M.; Berry, K. Caffeine to optimize cognitive function for military mission-readiness: a systematic review and recommendations for the field. *Nutr. Rev.* **2017**, *75*, 17–35. [CrossRef] [PubMed]
- Bell, L.; Lamport, D.J.; Butler, L.T.; Williams, C.M. A Review of the Cognitive Effects Observed in Humans Following Acute Supplementation with Flavonoids, and Their Associated Mechanisms of Action. *Nutrients* 2015, 7, 10290–10306. [CrossRef]
- Spencer, J.P.E. Flavonoids and brain health: multiple effects underpinned by common mechanisms. *Genes Nutr.* 2009, 4, 243–250. [CrossRef] [PubMed]
- Ude, C.; Paulke, A.; Nőldner, M.; Schubert-Zsilavecz, M.; Wurglics, M. Plasma and brain levels of terpene trilactones in rats after an oral single dose of standardized Gingko biloba extract EGb 761(R). *Planta Medica* 2011, 77, 259–264. [CrossRef]
- 101. Tachikawa, E.; Kudo, K.; Harada, K.; Kashimoto, T.; Miyate, Y.; Kakizaki, A.; Takahashi, E. Effects of ginseng saponins on responses induced by various receptor stimuli. *Euro. J. Pharmacol.* **1999**, *369*, 23–32. [CrossRef]
- Reay, J.L.; Scholey, A.B.; Kennedy, D.O. Panax ginseng (G115) improves aspects of working memory performance and subjective ratings of calmness in healthy young adults. *Hum. Psychopharmacol.* 2010, 25, 462–471. [CrossRef] [PubMed]
- 103. Neale, C.; Camfield, D.; Reay, J.; Stough, C.; Scholey, A. Cognitive effects of two nutriceuticals Ginseng and Bacopa benchmarked against modafinil: a review and comparison of effect sizes. *Br. J. Clin. Pharmacol.* 2012, 75, 728–737. [CrossRef] [PubMed]
- 104. Geng, J.; Dong, J.; Ni, H.; Lee, M.S.; Wu, T.; Jiang, K.; Wang, G.; Zhou, A.L.; Malouf, R. Ginseng for cognition. *Cochrane Database Syst. Rev.* 2010. [CrossRef] [PubMed]
- 105. Weckerle, C.A.; Stutz, M.A.; Baumann, T.W. Purine alkaloids in Paullinia. *Phytochemistry* **2003**, *64*, 735–742. [CrossRef]
- 106. Espinola, E.B.; Dias, R.F.; Mattei, R.; Carlini, E.A. Pharmacological activity of Guaranan (Paullinia cupana Mart) in laboratory animals. *J. Ethnopharmacol.* **1997**, *55*, 223–229. [CrossRef]
- Kao, A.C.; Harty, S.; Burnet, P.W. The Influence of Prebiotics on Neurobiology and Behavior. *Intern. Rev. Neurobiol.* 2016, 131, 21–48. [CrossRef]
- 108. Gibson, G.R.; Scott, K.P.; Rastall, R.A.; Tuohy, K.M.; Hotchkiss, A.; Dubert-Ferrandon, A.; Gareau, M.; Murphy, E.F.; Saulnier, D.; Loh, G.; et al. Dietary prebiotics: current status and new definition. *Food Sci. Technol. Bull.* **2010**, *7*, 1–19. [CrossRef]
- 109. Moustakas, D.; Mezzio, M.; Rodriguez, B.R.; Constable, M.A.; Mulligan, M.E.; Voura, E.B. Guarana provides additional stimulation over caffeine alone in the planarian model. *PLoS ONE* 2005, *10*, e0123310. [CrossRef] [PubMed]
- 110. Albert, B.B.; Cameron-Smith, D.; Garg, M.L.; Derraik, J.G.B.; Hofman, P.L.; Cutfield, W.S. Marine oils: Complex, confusing, confounded? *J. Nutr. Intermed. Metab.* **2016**, *5*, 3–10. [CrossRef]
- Kennedy, D.O.; Scholey, A.B.; Wesnes, K.A. Dose dependent changes in cognitive performance and mood following acute administration of Ginseng to healthy young volunteers. *Nutritional Neurosci.* 2001, *4*, 295–310. [CrossRef]
- Huang, W.; Ramsey, K.M.; Marcheva, B.; Bass, J. Circadian rhythms, sleep, and metabolism. *J. Clin. Invest.* 2011, 121, 2133–2141. [CrossRef] [PubMed]
- 113. Potter, G.D.M.; Cade, J.E.; Grant, P.J.; Hardie, L.J. Nutrition and the circadian system. *Br. J. Nutr.* **2016**, *116*, 434–442. [CrossRef]
- 114. Kelly, J.R.; Allen, A.P.; Temko, A.; Hutch, W.; Kennedy, P.J.; Farid, N.; Murphy, E.; Boylan, G.; Bienenstock, J.; Cryan, J.F.; et al. Lost in translation? The potential psychobiotic Lactobacillus rhamnosus (JB-1) fails to modulate stress or cognitive performance in healthy male subjects. *Brain Behav. Immun.* 2017, *61*, 50–59. [CrossRef]
- 115. Allen, A.P.; Hutch, W.; Borre, Y.E.; Kennedy, P.J.; Temko, A.; Boylan, G.; Murphy, E.; Cryan, J.F.; Dinan, T.G.; Clarke, G. Bifidobacterium longum 1714 as a translational psychobiotic: modulation of stress, electrophysiology and neurocognition in healthy volunteers. *Transl. Psychiatry* 2016, *6*, e939. [CrossRef] [PubMed]
- 116. Booth, C.K.; Coad, R.A.; Roberts, W. Evaluation of an Australian combat ration pack as a sole nutrition source during 23 days of military adventurous training in the tropics. *Nutr. Diet.* **2004**, *60*, 239–247.

- 117. Booth, C.K.; Probert, B.; Forbes-Ewan, C.F.; Coad, R.A. Australian Army recruits in training display symptoms of overtraining. *Mil. Med.* **2006**, *171*, 1059–1064. [CrossRef] [PubMed]
- 118. Scott, J.M.; Lindsey, A.T.; Costello, R.B.; Deuster, P.A. Using the Dietary Supplement Label Database to Identify Potentially Harmful Dietary Supplement Ingredients. *Nutr. Today* 2018, 53, 229–233. [CrossRef] [PubMed]



© 2020 by the authors. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (http://creativecommons.org/licenses/by/4.0/).

### [OFFICIAL]

#### **Dietary Supplement Use in the ADF: time for change?**

Bianka Probert, Rosa Peterson & Bradley Baker DSTG, Land Division, Human Performance, Food & Nutrition <u>bianka.probert@dst.defence.gov.au</u>; <u>rosa.peterson@dst.defence.gov.au</u>; <u>bradley.baker2@dst.defence.gov.au</u>

#### Background

Dietary supplements are defined as "a food, food component, nutrient, or non-food compound that is purposefully ingested in addition to the habitually-consumed diet with the aim of achieving a specific health and/or performance benefit" (Maughan et al., 2018). ADF members use dietary supplements at higher rates than the general Australian population (Baker et al., 2019; Kullen et al., 2019, Probert, 2020) and likely to increase, in line with the increasing trends in use observed in military populations (Lieberman et al., 2010; Knapik et al., 2016; Baker et al., 2019; Probert, 2020).

Several dietary supplements are supported by "good to strong" evidence for enhancing aspects of performance, e.g. caffeine and creatine. Others may be recommended by Medical Practitioners or Dietitians to treat and/or prevent nutrient deficiencies e.g. iron and calcium (Maughan et al., 2018). Moreover, protein supplements and sports drinks can provide convenient sources of nutrients to enhance aspects of performance and/or recovery when it is impractical to consume everyday foods. ADF members can often experience periods of poor energy and nutrient intakes during training and deployment that may lead to compromised health and performance. Thus, to maintain a performance edge over adversaries, the use of dietary supplements that are safe, effective and appropriate should be considered, particularly when nutritional requirements cannot be met by everyday foods during training and deployment (Maughan et al., 2018).

The indiscriminate self-administration of dietary supplements can be dangerous, with many commercially available supplements linked to adverse side effects or contaminated with substances that are banned by the World Anti-Doping Agency (WADA) and/or border-controlled (LGC, 2016; Ronis et al., 2018). Thus, increased demand for dietary supplements in the ADF, in the absence of expert guidance on their safety and efficacy, may coincide with increased prevalence of adverse side effects and members failing mandatory drug tests.

The use of health- and performance-related dietary supplements among athletes is managed by robust policies based on evidence on their safety and efficacy, however there is currently no ADF-wide system in place for providing members with access to expert guidance on dietary supplements. Moreover, it is unclear whether Defence health policies would support the prescription and supply of performance-related dietary supplements by Medical Practitioners or Accredited Sports Dietitians.

#### Aim

To determine whether policies developed by sporting organisations may be applicable to the future management of dietary supplement use in the ADF.

#### Results

Evidence related to the safety and efficacy of supplements has been translated into a robust framework by the Australian Institute of Sport (AIS), which has been used as basis by National Sporting Organisations (NSOs) to develop policies on dietary supplement use. Provision of supplements in accordance with the AIS framework has been shown to reduce the risk of individuals using contaminated products, banned substances and the misuse of potentially dangerous products. Whilst ensuring the consistent delivery of evidence based information by health professionals employed under the program (Shaw et al., 2016).

#### Conclusions

If developed, a bespoke ADF supplement management framework, based on those developed for athletic populations, has the potential to improve the supplement practices of ADF members by acting as an evidenced-based guidance system delivered by appropriately qualified health professionals.

### [OFFICIAL]

Improved systems to manage supplement use in the ADF are necessary to maintain a performance edge over adversaries and reduce the risks of adverse events resulting from dietary supplement use. Engagement with a wide range of ADF health and performance stakeholders is required to understand how this may be achieved.

### References

- Baker, B., Probert, B., Pomeroy, D., Carins, J., & Tooley, K. (2019). Prevalence and Predictors of Dietary and Nutritional Supplement Use in the Australian Army: A Cross-Sectional Survey. Nutrients, 11, 1462.
- Kullen, C., Prvan, T., & O'Connor, H. (2019). Dietary Supplement Use in Australian Army Personnel. Military Medicine, 184(5-6), e290-e297.
  - https://doi.org/https://dx.doi.org/10.1093/milmed/usy266
- LGC. (2016). Australian Supplement Survey. Retrieved from: http://drugfreesport.org.za/wpcontent/uploads/2018/04/LGC Australian-Supplement-Survey 0-1.pdf (accessed on 03 July 2021).
- Maughan, R.J., Burke, L.M., Dvorak, J., Larson-Meyer, D.E., Peeling, P., Phillips, S.M., Rawson, E.S., Walsh, N.P., Garthe, I., Geyer, H., et al. (2018). IOC consensus statement: Dietary supplements and the high-performance athlete. British Journal of Sports Medicine, 52, 439.
- Probert, B (2020). Dietary and Nutritional Supplement use in the Royal Australian Air Force. Masters Thesis, Curtin University, Western Australia.
- Ronis, M. J. J., Pedersen, K. B., & Watt, J. (2018). Adverse Effects of Nutraceuticals and Dietary Supplements. Annu Rev Pharmacol Toxicol, 58(1), 583-601. https://doi.org/10.1146/annurevpharmtox-010617-052844
- Shaw, G., Slater, G., & Burke, L. M. (2016). Supplement use of elite Australian swimmers. International Journal of Sport Nutrition and Exercise metabolism, 26(3), 249.

#### **Presentation Preferences**

DHSS will be held as a hybrid live/virtual event. Presentations can be delivered live or pre-recorded. Please indicate your preference.



Standard oral presentation

Mini oral (electronic poster) presentation



Either standard or mini oral presentation

### Effect of a dual action hydration strategy containing high amylose starch on hydration status in an extreme military training environment: a randomised crossover study

### \*Rosa Peterson, Bianka Probert and Bradley Baker

Food & Nutrition, Land Division, Defence Science and Technology \*rosa.peterson@dst.defence.gov.au

**Background:** Optimal hydration is critical for soldiers. During sustained operations in hot climates, exertional heat illness (EHI) poses a significant threat. Soldiers are often subjected to environmental extremes such as hot and humid conditions that may compromise body fluid levels (Lindseth et al.,2013). It is well established that a 5–10% fluid loss and inadequate ingestion of fluids can be potentially detrimental to health, as well as cognitive and physical performance. Cognitive performance is reduced when a 1–3% body weight loss of fluid occurs (Lindseth et al.,2013). Military nutrition research into improving hydration has revolved around supplementation with beverages containing carbohydrates and electrolytes to replace energy, minerals (sodium and potassium) and reducing the onset of fatigue during prolonged periods of exercise (Montain et al., 1997). However, it is known that the volume ingested and the carbohydrate and electrolyte concentration of the fluid is critical to the conditional efficacy of the beverage, lending to opportunity to explore ways of optimising the rate of gastric emptying and intestinal fluid absorption (Binder et al., 2014).

PREPD is a commercially available, dual-action hydration solution that contains resistant starch (RS), glucose and electrolytes. Previous research has shown that RS may increase water absorption in the large intestine, which is capable of absorbing upwards of 5 L/day (Binder et al., 2014). Hydration/sports drinks that utilise the absorptive capacity of both the large and small intestine by incorporating RS have been shown to be effective in improving hydration in athletes undertaking intense physical training in a hot climate (O'Connell et al., 2018) and adults suffering diarrhoea (Ramakrishna et al., 2000). Field deployed soldiers are often exposed to a variety of stressors such as, extreme environments (i.e. heat and humidity), preventative antibiotics (which may lead to gastrointestinal upset and diarrhoea), change in diet (i.e. combat rations), reduced dietary fibre intake, and intense physical activity. Such stressors may further increase dehydration risk and subsequently impair gut health and performance.

**Aim:** This study aims to assess, in an extreme environment, if a novel dual-action hydration strategy containing RS improves the hydration status of personnel immediately before training and during recovery, gut health and cognitive performance.

**Method:** Participants will be recruited from three platoons of the Australian Army who will be at the Combat Training Centre – Jungle Training Wing (CTC-JTW), Tully (Northern Queensland), to complete a Soldiers Under Training (SUT) course. Participants will be undertaking a varied training schedule including navigation, patrolling, webbing runs, quick attacks/searches, ambushes, night orders and 'true grit' as part of the program. Participants will also be taking the antibiotic Doxycycline throughout the training programme.

The intervention consists of participants consuming the PREPD 'Prime' beverage (containing 33 g of RS) the day before they deploy into the field, and the 'Recover' beverage (16 g RS) immediately after training. A series of assessments will be performed including hydration testing, fluid balance monitoring, Urine Specific Gravity, activity monitoring, gut health questionnaires and cognitive performance testing.

**Results:** Initial results of the field trial will be presented. Future directions will be discussed.

**Conclusions:** The following are the projected outcomes for Army.

i) Optimisation of dietary strategies to enhance hydration, with potential to enhance cognitive performance.

ii) Improved understanding of the health benefits of RS, specific to Army.

iii) Improved understanding of the suitability of a novel hydration strategy for soldiers to improve hydration status during training/operations in sustary environments.

hydration status during training/operations in austere environments.

#### **References:**

Binder H, Brown I, Ramakrishna B. Oral Rehydration Therapy in the Second Decade of the Twenty-first Century. Curr Gastroenterol Rep. 2014;16(376).

Lindseth PD, Lindseth GN, Petros TV, Jensen WC, Caspers J. Effects of Hydration on Cognitive Function of Pilots. MILITARY MEDICINE. 2013;178(7):792-798.

Montain SJ, Shippee RL, Tharion WJ. Carbohydrate-electrolyte solution effects on physical performance of military tasks. Aviation Space and Environmental Medicine. 1997;68(5):384-391.

O'Connell S.M., Woodman R.J., Brown I.L., Vincent D.J., Binder H.J., Ramakrishna B.S., Young G.P. (2018) Comparison of a sports-hydration drink containing high amylose starch with usual hydration practice in Australian rules footballers during intense summer training. Journal of the International Society of Sports Nutrition, 15, pp. 46.

Ramakrishna BS, Venkataraman S, Srinivasan P, Dash P, Young GP, Binder HJ (2000) Amylase-resistant starch plus oral rehydration solution for cholera, N Engl J Med. 342:308-13.

#### **Presentation Preference**

Oral Presentation	Х
Poster	
Oral Presentation or Poster	Х



Australian Government Department of Defence Science and Technology

# Prevalence and Predictors of Dietary and Nutritional Supplement Use in the Australian Army: A Cross-Sectional Survey

Brad Baker<sup>1</sup>, Bianka Probert<sup>1</sup>, Diane Pomeroy<sup>2</sup>, Julia Carins<sup>1,3</sup> & <u>Katie Tooley<sup>2</sup></u>

<sup>1</sup> Food and Nutrition, Land Division, DST, Australia
 <sup>2</sup> Cognition and Behaviour, Land Division, DST, Australia
 <sup>3</sup> Social Marketing @ Griffith, Griffith Business School, Griffith University, Australia



### What are 'dietary supplements'

*"a food, food component, nutrient, or non-food compound that is purposefully ingested in addition to the habitually-consumed diet with the aim of achieving a specific health and/or performance benefit"*<sup>1</sup>

<sup>1</sup> Maughan, R.J., et al. Br J Sports Med 2018, 52, 439–455.

2 \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*



# What are 'dietary supplements' and 'nutritional supplements'?

- Categories of dietary supplements (DS) include:
  - Multivitamin/multimineral
  - Protein or amino acid
  - Individual vitamin or mineral
  - Herbal supplements
  - Purported prohormones
  - Combination (of above) products
  - Joint health products



Defence FOI 386/22/23



- Other dietary supplements (plant or animal derived or synthethic)
- Categories of nutritional supplements include:
  - Sports drinks, bars and gels
  - Meal replacements



### **DS and NS and Performance**

Defence FOI 386/22/23 Document 12

- The International Olympic Committee consider several DS and NS have "good to strong" evidence in support of their safety and effectiveness in enhancing performance when used in <u>specific quantities</u> for <u>specific purposes</u><sup>1</sup>
- Some examples:

Supplement	Purpose
Caffeine	Enhance physical performance and cognition
Creatine monohydrate	Enhance high-intensity exercise capacity and lean body mass
Sports foods e.g. sports drink, sports gel, whey protein	Practical sources of nutrients when it is impractical to consume everyday foods
Dietary nitrates/beetroot juice	Enhance exercise economy, endurance exercise performance, and skeletal muscle contractile function
Glycerol	Augment fluid retention and hydration

<sup>1</sup> Maughan, R.J., et al. Br J Sports Med 2018, 52, 439–455.



### Background

- Prevalence of any DS or NS use in US soldiers is 61% of males and 73% of females<sup>2</sup>
- Trends in DS and NS use is increasing
- DS and NS market worth US\$ 133 billion in 2016; US\$ 220 billion by 2020<sup>3</sup>
- Some DS and NS can have adverse side effects
- Australian Defence Force legislation / policy prohibits the use of dietary supplements containing substances on the World Anti-Doping Association (WADA) Prohibited List, including<sup>4</sup>:
  - WADA S0, S1, S2, S4, S5, S6, S7, S8 & S8 substances
  - Anabolic agents, peptide hormones, growth factors, beta-2 agonists
  - Related substances and mimetics
  - Diuretics and masking agents

<sup>2</sup> Austin, KG et al 2016. Appl Physiol Nutr Metab, 41, 1217–1224.

<sup>3</sup>Zion Market Research, 2017.

<sup>4</sup> Department of Defence (2011). Defence Instructions (General) Personnel 15-5. Management of the use or involvement with prohibited substances in the Australian Defence Force. Canberra, ACT.



### Aims

- This study aimed to:
  - investigate the prevalence of the regular use (i.e. ≥1 times/week) of any DS or NS among active-duty Australian soldiers
  - 2. determine which demographic and military characteristics predict DS and/or NS use
  - 3. determine the prevalence of adverse side effects resulting from use

4. advance our knowledge of DS and NS use among Active-duty Australian soldiers

### Methods

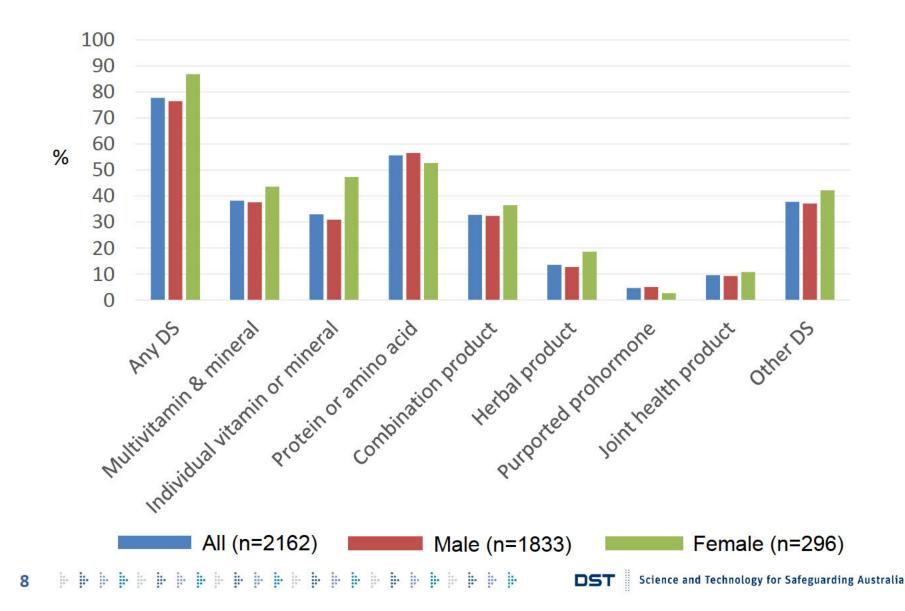
- Cross-sectional survey administered in 2017
  - Demographic and military characteristics
  - Physical activity levels (i.e. cardio and strength training)
  - 70 generic products and 50 brand name products
- E-mail invitations to all regular Army members (approx. 25,000)
- Paper survey distribution to a convenience sample of combat arms, combat support and combat service support soldiers (approx. 500)
- Self reported side-effects e.g. rapid heartbeat, abnormal heartbeat, tremors, stomach pain, dizziness, numbness/tingling
- Prevalence of supplement use was reported as % of users
- Logistic regression was used to test for significant predictors of DS and NS use

DST

Defence FOI 386/22/23

Document 12

### Prevalence of DS use ≥1 times/week

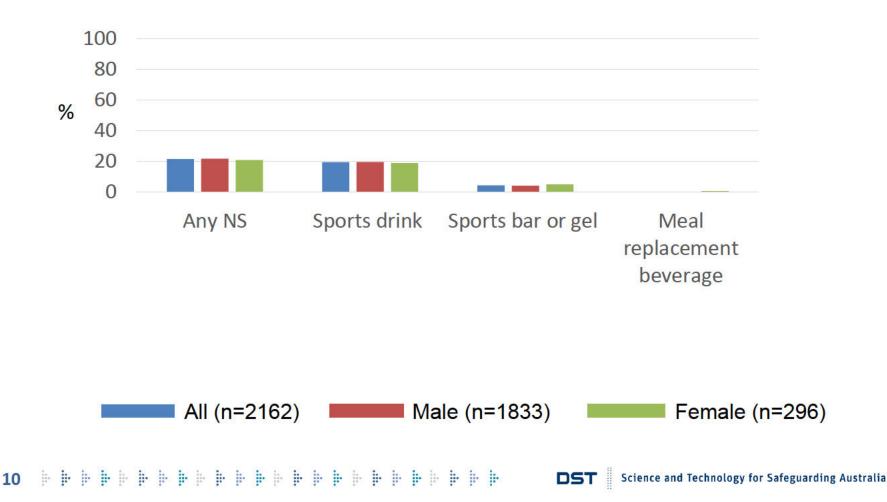


### **Predictors of DS use ≥1 times per week**

Variable	Multi- vitamin / mineral	Individual vitamin / mineral	Protein / amino acid	Combination product	Herbal	Purported pro- hormone	Joint Health	Other DS
Gender	*	**						
Age	**		**	*			**	**
Special Forces	*	**						
BMI range				*		**	*	
Body weight goals	**	**	**	**		**		*
Rank								
Corps area								
Strength training	**	**	**	**	*	**	**	**
Cardio in own time		*	**	**				
Cardio within unit			*	**				
Total cardio								

Notes: significant predictors are marked with \*(P<0.05) and \*\*(P<0.001)

## **Prevalence of NS use ≥1 times/week**



### **Predictors of NS use ≥1 times per week**

Variable	Any	Sports	Sports
	NS	drink	bar/gel
Gender			
Age	**	**	
Special Forces			
BMI range			
Body weight			
goals			
Rank			
Corps area			
Strength			
training			
Cardio in own	**	**	**
time			
Cardio within	**	**	*
unit			
Total cardio	**	**	**

Notes: significant predictors are marked with \*(P<0.05) and \*\*(P<0.001)



# Significant predictors of number of DSs used

Variable	Subgroup	OR (95% CI)	p value
Gender			< 0.001*
	Male	1.00	-
	Female	1 43 (1 23–1 66)	< 0.001*
Age group			< 0.001*
	18–22	1.00	-
	23–27	1.58 (1.30–1.91)	< 0.001*
	28–32	1.56 (1.28–1.90)	< 0.001*
	33–37	1.73 (1.40–2.14)	< 0.001*
	38–42	1.51 (1.20–1.90)	0.001*
bivii range			0.005
	<25	1.00	5
	25–30	1.21 (1.08–1.37)	0.001*
	>30	1.19 (1.00–1.42)	0.045*
Body weight goals			< 0.001*
	Trying to lose weight	1.00	127
	Trying to gain weight	1.08 (0.91–1.29)	0.016*
	Trying to maintain weight	1.17 (1.03–1.34)	0.377
	Not trying anything	0.73 (0.64–0.84)	< 0.001*
Strength training (sessions/week)		1.16 (1.14–1.18)	< 0.001*

12 \*

## Side effects of DS use

- One or more adverse side effects were reported by 15.9% of DS users
- The most commonly reported adverse side effects were:
  - Palpitations (10.6%)
  - Tingling in the face, fingers, arms or legs (5.5%)
  - Tremors or shaking (2.9%)
  - Flushing (2.3%)
  - Headache (2.0%)
  - Abdominal pain (1.6%)
  - Anxiety (1.4%)
  - Dizziness or confusion (0.9%)



### Conclusions

- Use of several categories of DS is widespread among soldiers
- Several demographic and military characteristics significantly predicted a higher prevalence of DS use
- Future behavioural change and educative strategies should focus on promoting the use of DSs and NSs that are evidencebased only where needed and avoiding adverse side effects
- Future research should aim to understand further the motivators for supplement use and the benefits and barriers associated with their use



UNCLASSIFIED – Approved for Public Release



Australian Government

**Department of Defence** Science and Technology Defence FOI 386/22/23 Document 12

# **ANY QUESTIONS**

For further information please contact:

### Thank you for listening

Published article search for DOI: 10.3390/nu11071462

