

# 1                   **High-intensity Interval Training: A Potential Exercise** 2                   **Countermeasure During Human Spaceflight?**

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**36 ABSTRACT**

37

38 High-intensity interval training (HIT) is an effective approach for improving a range of  
39 physiological markers associated with physical fitness. A considerable body of work has  
40 demonstrated substantial improvements in cardiorespiratory fitness following short-term training  
41 programmes, while emerging evidence suggests HIT can positively impact aspects of  
42 neuromuscular fitness. Given the detrimental consequences of prolonged exposure to microgravity  
43 on both of these physiological systems, and the potential for HIT to impact multiple components  
44 of fitness simultaneously, HIT is an appealing exercise countermeasure during human spaceflight.  
45 As such, the primary aim of this mini-review is to synthesise current terrestrial knowledge relating  
46 to the effectiveness of HIT for inducing improvements in cardiorespiratory and neuromuscular  
47 fitness. As exercise-induced fitness changes are typically influenced by the specific exercise  
48 protocol employed, we will consider the effect of manipulating programming variables, including  
49 exercise volume and intensity, when prescribing HIT. In addition, as the maintenance of HIT-  
50 induced fitness gains and the choice of exercise mode are important considerations for effective  
51 training prescription, these issues are also discussed. We conclude by evaluating the potential  
52 integration of HIT into future human spaceflight operations as a strategy to counteract the effects  
53 of microgravity.

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**58 INTRODUCTION**

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60 The prolonged exposure to microgravity ( $\mu\text{G}$ ) and the space environment associated with human  
61 spaceflight necessitates effective countermeasures to manage the multi-system adaptation that  
62 occurs. These adaptations are both short-term, including headache, drowsiness, nausea, vomiting,  
63 and dizziness, collectively referred to as ‘space motion sickness’ (Ortega and Harm, 2008), and  
64 longer-term, including fluid redistribution and reductions in maximal oxygen uptake ( $\text{VO}_{2\text{max}}$ ),  
65 muscle size and strength, and bone mineral density (BMD) (Demontis et al., 2017).

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67 Exercise training is a fundamental strategy for managing adaptation to spaceflight; however, the  
68 potential physical (size and internal dimensions of vehicle/habitats), logistical (supply of food and  
69 water, and device maintenance/repair) and operational (time for exercise, interference with other  
70 crewmembers’ work) constraints of future space exploration missions highlight a need for alternate  
71 approaches to counteracting  $\mu\text{G}$  induced changes (Scott et al., 2019). High-intensity interval  
72 training (HIT), involving repeated bouts of intense exercise, interspersed with periods of rest or  
73 lower intensity active recovery, is a widely used training approach with demonstrated efficacy for  
74 inducing physiological adaptation across a range of outcomes. As an exercise countermeasure, HIT  
75 may offer several operational advantages including: 1) Substantial physiological stimulus possible  
76 in a short time period; 2) Potential to impact multiple components of fitness simultaneously; 3)  
77 Typically performed using a single exercise mode; 4) Ability to target upper- and lower-body  
78 function. This review aims to highlight the potential for HIT as an exercise countermeasure during  
79 human spaceflight by summarising the terrestrial evidence base relating to its effectiveness and  
80 considering exercise programming variables in the context of spaceflight.

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**83 HIGH-INTENSITY INTERVAL TRAINING**

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85 Despite intensifying scientific enquiry over the last 15-20 years, HIT is not a new approach to  
86 exercise training (Billat, 2001). Although terminology varies, HIT can be: High-intensity interval  
87 training (HIT), performed at ‘near maximal’ or ‘submaximal’ intensity ( $\geq 80\%$  maximal heart rate);  
88 or Sprint interval training (SIT), often described as low-volume HIT, characterised by efforts  
89 performed at ‘all out’ or ‘supramaximal’ intensity ( $\geq 100\% \text{VO}_{2\text{max}}$ ) (MacInnis and Gibala, 2017;  
90 Weston et al., 2014a). Despite broad protocol dichotomisation, HIT exists on a continuum,  
91 encompassing a wide spectrum of exercise intensities, with longer duration HIT intervals (e.g.

92 Wisloff et al., 2007) at the lower end and SIT (e.g. (Gibala et al., 2006)) the upper end. As exercise  
93 intensity is a key mediator of training adaptation (Shephard, 1968), it may be the intense stimulus  
94 induced by HIT is a potent catalyst for physiological remodelling (MacInnis and Gibala, 2017).  
95 Despite a predominant focus on  $VO_{2max}$  improvement, the intensity of HIT places considerable  
96 demands on both the aerobic and anaerobic energy systems, and the neuromuscular system  
97 (Buchheit and Laursen, 2013a; 2013b), suggesting potential for adaptation across multiple  
98 physiological systems.

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## 101 **EFFECTIVENESS OF HIGH-INTENSITY INTERVAL TRAINING**

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### 103 **Cardiorespiratory fitness**

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105 Numerous interventions [e.g. (Astorino et al., 2017; Burgomaster et al., 2008; Helgerud et al., 2007;  
106 Matsuo et al., 2014)] demonstrated HIT as a potent strategy for improving  $VO_{2max}$ . These  
107 experimental findings have been corroborated in several meta-analyses in healthy (Bacon et al.,  
108 2013; Milanovic et al., 2015; Sloth et al., 2013; Weston et al., 2014b) and clinical populations (Liou  
109 et al., 2016; Weston et al., 2014a). Compared with moderate intensity continuous training (MICT),  
110 HIT may elicit adaptations of a similar (Burgomaster et al., 2008; Gibala et al., 2006; Scribbans et  
111 al., 2014) or even greater magnitude (Daussin et al., 2008; Helgerud et al., 2007; Matsuo et al.,  
112 2014), despite a substantially reduced time commitment. Previous work has reported large  
113 improvements in  $VO_{2max}$  following HIT (Mean  $\pm$  SD;  $22.5 \pm 12.2\%$ ) and SIT ( $16.7 \pm 11.6\%$ ),  
114 compared with a moderate improvement ( $10.0 \pm 8.9\%$ ) following continuous training (Matsuo et  
115 al., 2014), while a recent meta-analysis demonstrated a possibly small beneficial effect for HIT on  
116  $VO_{2max}$  ( $1.2 \text{ mL}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ ; 95% confidence limits  $\pm 0.9 \text{ mL}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ ) when compared with  
117 continuous endurance training (Milanovic et al., 2015). It may be that the underlying physiological  
118 mechanisms differ between HIT and MICT (Daussin et al., 2008), although this remains to be fully  
119 determined.

120 Exercise at both ends of the intensity continuum, and that representing the middle ground (e.g.  
121 (Little et al., 2010)), can induce substantial (e.g., 10-15%) improvements in  $VO_{2max}$  following short-  
122 term training programmes (MacPherson et al., 2011; Matsuo et al., 2014; Metcalfe et al., 2012).  
123 Nevertheless, participant-related factors (e.g. baseline fitness (Weston et al., 2014b)) and protocol-  
124 related factors (e.g. repetition duration (Bacon et al., 2013)) moderate responses, suggesting  
125 effective manipulation of programming variables is necessary to maximise physiological adaptation

126 (Buchheit and Laursen, 2013a). While mechanisms responsible for HIT induced improvements in  
127 cardiorespiratory fitness remain elusive, both peripheral (e.g. increased mitochondrial content and  
128 function) and central adaptations (e.g. increased cardiac output) may contribute to increased  $VO_{2max}$   
129 (Astorino et al., 2017; Burgomaster et al., 2008; Daussin et al., 2007; Jacobs et al., 2013).

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### 132 **Neuromuscular fitness**

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134 The intensity of HIT induces a substantial acute neuromuscular load (Buchheit and Laursen, 2013a)  
135 and induces high levels of muscle fibre recruitment (Sale, 1987); therefore, providing a stimulus  
136 for neuromuscular adaptation (Creer et al., 2004; Martinez-Valdes et al., 2017). Although resistance  
137 training represents the primary strategy for improving muscle morphology, previous investigations  
138 demonstrated HIT-induced increases in lean or fat free mass (Gillen et al., 2013; Robinson et al.,  
139 2017; Sculthorpe et al., 2017) and muscle cross-sectional area (Osawa et al., 2014). Increases in  
140 protein synthesis (Bell et al., 2015) and satellite cell activity (Nederveen et al., 2015) may contribute  
141 to these observed changes. These findings are not universal however (Nybo et al., 2010), and the  
142 potential for HIT to increase muscle mass remains largely unknown.

143

144 Substantial improvements in mean and peak power output (PPO) of ~5-20% have been observed  
145 following SIT (Astorino et al., 2011; Burgomaster et al., 2005; Sculthorpe et al., 2017; Zelt et al.,  
146 2014) (Burgomaster et al., 2006), potentially mediated by changes in anaerobic enzyme activity  
147 (MacDougall et al., 1998; Rodas et al., 2000). However, power output determined during short-  
148 duration cycling bouts (e.g., Wingate test) may primarily represent metabolic not neuromuscular  
149 power. Nonetheless, emerging evidence suggests HIT increases explosive muscular power,  
150 assessed via leg extension (Hurst et al., 2018) and broad jump (Buckley et al., 2015). Improvements  
151 in muscle strength following HIT also exist (Buckley et al., 2015; Martinez-Valdes et al., 2017;  
152 McRae et al., 2012) with small–moderate increases (~7%) in knee extensor strength following 6  
153 sessions of cycle-based HIT performed at 100% PPO (Martinez-Valdes et al., 2017). These findings  
154 reaffirm the potential for HIT as a training strategy capable of improving cardiorespiratory and  
155 neuromuscular fitness simultaneously.

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## 158 **PROGRAMMING CONSIDERATIONS FOR HIGH-INTENSITY INTERVAL TRAINING** 159 **DURING SPACEFLIGHT**

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161 While HIT can simultaneously improve cardiorespiratory and neuromuscular fitness, acute training  
162 responses and subsequent adaptations are determined by the interaction of several programming  
163 variables (Buchheit and Laursen, 2013a; 2013b; MacInnis and Gibala, 2017). The following section  
164 discusses programming considerations relevant to the operational use and potential advantages of  
165 HIT during spaceflight.

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### 168 **Exercise Volume**

169

170 Low-volume HIT, typically involving 4 to 6 repetitions of 30–60 s exercise performed at ‘all-out’  
171 intensity, induces substantial improvements in cardiorespiratory fitness (Sloth et al., 2013; Weston  
172 et al., 2014b) and may offer the potential for rapid fitness gains in a short time period. However,  
173 despite the potent effects of this training stimulus, the intensive nature of this exercise protocol  
174 necessitates substantial recovery periods between intervals (~ 4 min), meaning that session duration  
175 is often ~30 minutes. Reducing the volume of exercise does not necessarily lessen the magnitude  
176 of adaptation following SIT, and improvements in  $VO_{2max}$  can be enhanced with fewer repetitions  
177 (Vollaard et al., 2017). For example, a protocol of 3 x 20 s all out cycle sprints performed 3 times  
178 per week for 6 weeks (Gillen et al., 2014) or 12 weeks (Gillen et al., 2016) increased peak oxygen  
179 uptake ( $VO_{2peak}$ ) by 12% and 19%, respectively. Reducing exercise volume further, improvements  
180 of 10-15% in  $VO_{2peak}$  can occur following six weeks of three sessions per week involving only 2 x  
181 20 s all out sprints (Metcalf et al., 2012; 2016). Importantly, a reduced exercise volume does not  
182 appear to have a detrimental effect on anaerobic, as well as aerobic performance, given that  
183 improvements in PPO were not different following 2-4 weeks of SIT intervals of either 15 or 30 s  
184 (Zelt et al., 2014) or 10 or 30 s (Hazell et al., 2010) duration. Even with a reduced exercise volume,  
185 HIT maintains the potential to induce rapid fitness gains.

186

187 Exercise training programmes typically involve a combination of resistance and endurance training  
188 and are termed ‘concurrent’ (Fyfe et al., 2014) or ‘combined’ training (Hurst et al., 2019). Although  
189 resistance and endurance training represent effective strategies for improving muscular and  
190 cardiorespiratory fitness respectively, concurrent training may induce an ‘interference effect’  
191 whereby improvements in muscular fitness are attenuated compared with performing resistance  
192 training alone (Fyfe et al., 2014). Incorporating SIT into a concurrent training programme may help  
193 to mitigate any observed interference effects (Cantrell et al., 2014) as these may largely be exercise  
194 volume rather than intensity dependent (Fyfe et al., 2016).

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**197 Differentiation of HIT**

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199 As HIT incorporates a broad spectrum of intensities, performing exercise across this range is an  
200 effective strategy to induce a differential adaptive response (Barnes et al., 2013; Rønnestad et al.,  
201 2015). Exercise bout duration represents a key programming variable because of the inverse  
202 relationship between duration and intensity (i.e. shorter intervals typically involve higher intensity  
203 exercise). Therefore, manipulating exercise duration alters energy system contribution (Gastin,  
204 2001) as well as the degree of neuromuscular loading (Buchheit and Laursen, 2013b). Shorter (30-  
205 s) compared with long duration cycle-based intervals (300-s) have been demonstrated to result in a  
206 higher training intensity ( $363 \pm 32$  W vs.  $324 \pm 42$  W) and lead to significant increases in  $VO_{2max}$   
207 ( $8.7 \pm 5.0\%$ ) and PPO ( $8.5 \pm 5.2\%$ ) (Rønnestad et al., 2015). Furthermore, following uphill running-  
208 based HIT, improvements in aerobic fitness and performance variables are optimal around the  
209 middle intensity (100% velocity at  $VO_{2max}$ ; 10% gradient; 1:2 work:rest ratio) with increases in  
210 neuromuscular measures (e.g. peak power, maximum rate of force development) greatest at the  
211 highest intensity (Barnes et al., 2013). Repeated-sprint training (RST), typically defined as a series  
212 of short sprints (3 to 7 s in duration), separated by recovery periods of less than 60 s (Buchheit and  
213 Laursen, 2013a), is another HIT derivative at the highest end of the intensity spectrum. As with  
214 SIT, RST induces considerable acute metabolic and neuromuscular demands (Buchheit and  
215 Laursen, 2013b), thereby highlighting potential as a multicomponent training tool. This supposition  
216 was supported in a recent meta-analysis that reported clear beneficial effects of RST on measures  
217 of countermovement jump height, sprint times, repeated sprint ability and high-intensity running  
218 performance (Taylor et al., 2015). Manipulating HIT exercise intensity therefore promotes a  
219 differential training response, with these findings further demonstrating potential for HIT as a  
220 combined training tool for inducing adaptation across multiple physiological systems. Ultimately,  
221 varied HIT prescription within a training programme [e.g. (Wright et al., 2016)] is necessary to  
222 maximise metabolic and neuromuscular adaptations (Buchheit and Laursen, 2013a; 2013b).

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**225 Maintenance of HIT induced gains**

226

227 Although short-term fitness gains are well documented following HIT, maintaining fitness over an  
228 extended time period represents another challenge. To date however, only a limited number of  
229 studies evaluated the effects of manipulating session frequency on the maintenance of HIT induced

230 fitness improvements. Following a 2-week SIT intervention which increased  $VO_{2max}$  (3%) and  
231 high-intensity intermittent running performance (17%), participants completed a single weekly SIT  
232 session for 5 weeks (Macpherson and Weston, 2015). Interestingly, this maintenance phase induced  
233 a 4.2% improvement in  $VO_{2max}$ , indicating that reduced training frequency can be an effective  
234 strategy to maintain SIT induced fitness improvements (Macpherson and Weston, 2015). In another  
235 investigation, performing 24 HIT sessions at either moderate frequency (MF; 3 sessions per week)  
236 or high frequency (HF; 8 sessions per week), led to a 10.7% increase in  $VO_{2max}$  in the MF group  
237 with no statistically significant improvement (3.0%) in the HF group (Hatle et al., 2014). Following  
238 the intervention, participants completed a 9-week detraining period involving no training with both  
239 groups demonstrating increased  $VO_{2max}$  at 12 days post-intervention and a return to baseline 4  
240 weeks after highest measurement (Hatle et al., 2014). These data support the idea that lower  
241 frequency training may be as effective as higher frequency training for maintaining fitness,  
242 although there remains only limited evidence to support this assertion, particularly in well-trained  
243 individuals.

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#### 246 **Exercise Mode**

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248 Traditionally, HIT has been delivered using a single exercise mode with treadmill walking/running  
249 and cycle ergometry the most commonly used approaches. However, despite the logistical  
250 advantages of this approach, these exercise modes deliver a predominantly lower-body training  
251 stimulus. In the context of spaceflight, this is likely to be suboptimal because the performance  
252 profile of astronauts necessitates a synergy of upper- and lower-body fitness. Recently however,  
253 there has been an increased desire to move beyond the exercise modes typically associated with  
254 HIT. Alternative exercise modes for performing HIT included body-weight resistance exercise  
255 (McRae et al., 2012), non-weight bearing all-extremity ergometers (Hwang et al., 2016), hydraulic  
256 resistance machines (Hurst et al., 2018), a combination of strength and endurance exercises  
257 (Buckley et al., 2015) and high-intensity circuit-type training (Sperlich et al., 2017). These modes  
258 provide a whole-body training stimulus, inducing substantial improvements in  $VO_{2peak}$  (~8%),  
259 lower-body muscle power (6-15%), upper- and lower-body 1RM strength (27%) and muscular  
260 endurance (40-280%) (Buckley et al., 2015; McRae et al., 2012), following short-term training  
261 programmes.

262

263 As well as the need for upper- and lower-body fitness, exercise interventions delivered using a  
264 single exercise mode are desirable because of physical constraints during spaceflight. Performing



265 combined upper- and lower body HIT using a hydraulic resistance machine for 12-weeks improves  
266 explosive leg power (~10%) and predicted  $VO_{2max}$  (8.4%) (Hurst et al., 2018), while 8-weeks of  
267 HIT performed using a non-weight-bearing ergometer improves aerobic fitness (11%) and cardiac  
268 systolic function (Hwang et al., 2016). While these findings are encouraging, it should be noted  
269 that both of these studies involved older adults with relatively low baseline fitness who typically  
270 demonstrate greater training induced improvements. Collectively however, these data highlight  
271 potential for innovative approaches to training delivery and should encourage researchers to explore  
272 alternative exercise modes.

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## 275 **INTEGRATION INTO CURRENT AND/OR FUTURE HUMAN SPACEFLIGHT** 276 **OPERATIONS**

277

278 Interval exercise during spaceflight is not new, having been previously used during Shuttle missions  
279 and on the Mir Space Station. More recently, several interval-type protocols have been routinely  
280 used on the International Space Station (ISS) since Expedition 1 (Loehr et al., 2015). The intensity  
281 of these treadmill-based protocols was initially limited by technological constraints (*e.g.* maximal  
282 belt speed); however, the availability of the 'T2' treadmill and cycle ergometry protocols from  
283 Expeditions 20-25 onwards enabled exercise at higher intensities (Loehr et al., 2015). The  
284 maximum intensity of cycle-based protocols is currently 90%  $VO_{2max}$  - characterising them as HIT  
285 rather than SIT. However, the interval intensity of within-session varies (60 to 90%  $VO_{2max}$ ),  
286 thereby differing from typical experimental HIT protocols where prescribed intensity within a  
287 session remains constant. Despite the routine use of interval exercise during spaceflight, NASA's  
288 SPRINT study (National Aeronautics and Space Administration [NASA], 2018) is the only  
289 controlled investigation involving HIT in  $\mu G$  to date. Notwithstanding positive initial findings, the  
290 experimental design and limited available data from this study (Goetchius et al., 2019) makes it  
291 impractical to draw definitive conclusions about the effectiveness of this training approach.

292

293 Maximal intensity exercise, in the form of maximal oxygen uptake ( $VO_{2max}$ ) assessment, was first  
294 incorporated during Shuttle Missions (Levine et al., 1996; Moore et al., 2001) with tests performed  
295 on ISS since 2009 (Moore et al., 2014) and used operationally without incident since 2016. This  
296 could provide a framework for the use of HIT at intensities up to 100%  $VO_{2max}$  during flight, which  
297 have been delivered with low risk across a range of healthy and clinical terrestrial populations  
298 (Rognmo et al., 2012). While SIT protocols ( $\geq 100\%$   $VO_{2max}$ ) may represent low risk in terrestrial

299 populations, the physiology of astronauts is altered (although not apparently compromised; *e.g.*  
300 maximum heart rate (Moore et al., 2014)) in microgravity and therefore the use of SIT for  
301 countermeasure exercise requires additional consideration.

302

303 Although HIT session duration is often  $\geq 30$  minutes, this is consistent with current continuous and  
304 interval-type protocols used on ISS and would fit within the current time allowance for aerobic  
305 exercise (60-min) (Loehr et al., 2015). However, as HIT achieves significant benefits when interval  
306 duration and/or number are reduced, time savings may well be realised. Moreover, if HIT can  
307 induce neuromuscular changes this reduces current and future reliance on resistance training,  
308 potentially achieving further time savings. In addition to potential time savings, lower energy  
309 expenditure and elevations in metabolism from HIT compared with continuous protocols (Matsuo  
310 et al., 2012) offers significant operational benefits over the course of a long mission. Specifically,  
311 reduced energy requirements (*i.e.* provision of food, which represents additional mass) and reduced  
312 burden on the environmental management systems (*i.e.* removal of CO<sub>2</sub>, moisture, heat). The  
313 effectiveness of short-term low-volume HIT programmes might also facilitate the intermittent use  
314 of countermeasure exercise to achieve further savings in resources and by-product management. In  
315 this approach, informed by systematic tests of function (*e.g.* VO<sub>2max</sub>), a degree of adaptation could  
316 be allowed with periods of HIT interspersed to manage the magnitude of change.

317

318 Finally, the potential effectiveness of HIT across different exercise modes offers an advantage for  
319 exploration. Vehicle/mission constraints make it likely that only one exercise device will be  
320 available to crew and current concepts do not include treadmill running (Danish Aerospace  
321 Company, 2018; NASA, 2017). However, they do envisage multiple modes of exercise, including  
322 cycling, rowing and upper- and lower-body resistance-type exercise, all of which could  
323 accommodate HIT/SIT protocols.

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## 328 CONCLUSION

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330 Collective evidence suggests HIT could offer a range of operational and physiological benefits  
331 during spaceflight making it a viable tool within the exercise countermeasure programme.  
332 Substantial terrestrial findings support the efficacy of HIT as a time-efficient tool for  
333 cardiorespiratory fitness improvement with emerging data indicating potential beneficial effects on

334 the neuromuscular system. The potential for HIT to impact other physiological markers affected by  
335  $\mu\text{G}$  (e.g. BMD) remains largely unknown however and further investigation is warranted.  
336 Furthermore, despite encouraging terrestrial evidence, there remains no rigorous evaluation of HIT  
337 in  $\mu\text{G}$  and the efficacy of HIT during spaceflight is still unknown. Finally, consideration of  
338 astronaut specific physiology (e.g.  $\mu\text{G}$ -induced fluid shifts) and well as logistical constraints (e.g.  
339 provision of appropriate exercise devices) and exercise programming variables is needed to  
340 maximise the potential application of HIT.

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344 to the work and approved it for publication.

345

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349

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