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2 Prediction of physiological responses and performance at altitude using the 6MWT in normoxia and  
3 hypoxia  
4

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6 Treadmill & Outdoor 6MWT in Normoxia & Hypoxia  
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11 **Authors:**  
12 Oliver R Gibson, MSc, University of Brighton.  
13 Neil S Maxwell, PhD, University of Brighton.  
14 Alan J Richardson PhD, University of Brighton.  
15 Mark Hayes, PhD, University of Brighton.  
16 Ben Duncan, BSc, University of Brighton.  
17

18 **Author Affiliations**  
19 Centre for Sport and Exercise Science and Medicine. University of Brighton, UK.  
20

21 **Corresponding Author Contact Information**  
22 School of Sport and Service Management, Welkin Laboratories, University of Brighton, Eastbourne, BN20  
23 7SR. [o.r.gibson@brighton.ac.uk](mailto:o.r.gibson@brighton.ac.uk)  
24

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43

44 **Abstract**

45 **Objective.** The six minute walk test (6MWT) is a reliable and valid tool for determining an individual's  
46 functional capacity, and has been used to predict summit success. The primary aim of the study was to  
47 evaluate whether a 6MWT in normobaric hypoxia could predict physiological responses and exercise  
48 performance at altitude. The secondary aim was to determine construct validity of the 6MWT for  
49 monitoring acclimatization to 3,400m (Cuzco, Peru).

50 **Methods.** Twenty nine participants performed six 6MWTs in four conditions; Normoxic Overground (NO),  
51 Normoxic Treadmill (NT), Hypoxic Treadmill (HT) all once, and Hypoxic Overground three times, 42 hours  
52 (HO1), 138 hours (HO2) and 210 hours (HO3) following arrival at Cuzco.

53 **Results.** One-way ANOVA observed no difference ( $p > 0.05$ ) between NO and HO1 for 6MWT distance. HT  
54 and HO protocols were comparable for the measurement of  $\Delta$ heart rate (HR) and post-test peripheral  
55 oxygen saturation (%SpO<sub>2</sub>) ( $p > 0.05$ ). Acclimatization was evidenced by reductions ( $p < 0.05$ ) in resting  
56 HR and respiratory rate (RR) between HO1, HO2 and HO3, and preservation of SpO<sub>2</sub> between HO1 and  
57 HO2. Post exercise HR, and RR, were not different ( $p > 0.05$ ) with acclimatization. The duration to ascend  
58 to 4,215m on a trek was moderately correlated ( $p < 0.05$ ) to HR during the trek and the 6MWT distance  
59 during HT, no other physiological markers predicted performance.

60 **Conclusions.** The 6MWT is a simple, time efficient tool for predicting physiological responses to  
61 simulated and actual altitude, which are comparable. The 6MWT is effective at monitoring elements of  
62 acclimatization to moderate altitude.

63

64

65

66 **Introduction**

67 Acute altitude exposure can lead to acute mountain sickness (AMS), with 48-51% of travellers to Cuzco,  
68 Peru reporting symptoms<sup>1,2</sup>. Prolonged exposures at elevations >1,500 m are sufficient to induce AMS  
69 which is on the high altitude illness (HAI) spectrum with potential to progress to high altitude pulmonary  
70 oedema (HAPE) and high altitude cerebral oedema (HACE) if untreated<sup>3,4</sup>. Physical exertion increases AMS  
71 with increased physiological strain placed upon cardiac, pulmonary, vascular and muscular systems. The  
72 development of a simple and efficient test for monitoring changes in physiological responses, and  
73 symptoms of AMS prior to travel and at altitude<sup>5</sup> would be beneficial in aiding the identification of  
74 individuals at risk of altitude illness.

75  
76 The 6MWT has been widely used in clinical and research settings to determine and monitor exercise  
77 capacity. Performance can be linked to rates of ascent and physiological responses to exercise at altitude  
78 determined<sup>5,6</sup>. Previously, a peripheral oxygen saturation (SpO<sub>2</sub>) >75% following a 6 minute walk test  
79 (6MWT) at a 4365m basecamp was demonstrated to be a useful screening test for predicting the outcome  
80 of successfully reaching the summit of Aconcagua (6962m)<sup>5</sup>. More recently however, Daniels<sup>6</sup> concluded  
81 SpO<sub>2</sub> and 6MWT performance were unlikely to be effective in predicting summit success on Kilimanjaro  
82 (5895m). If data demonstrates a good relationship between performances in the 6MWT and physiological  
83 responses to altitude and summit success, then the 6MWT may be a useful test.

84  
85 The primary aim of the study was to evaluate whether a 6MWT in normobaric hypoxia could predict  
86 physiological responses and exercise performance at altitude. Secondly, we aimed to determine construct  
87 validity of the 6MWT for monitoring acclimatization to 3,400m (Cuzco, Peru).

88 **Method**

89 Twenty nine (14 female) healthy participants (Age 22.2 ± 5.4 years; No prior history of AMS, No exposure  
90 to simulated or actual altitude for 8 weeks prior to commencement of study. For day of test descriptive  
91 data, see table 1) volunteered to participate in an 18 day project in Eastbourne, UK and Cuzco, Peru.  
92 Following full description of experimental procedures the protocol was approved by the University of  
93 Brighton ethics committee. All participants completed medical questionnaires and provided written  
94 informed consent following the principles outlined by the Declaration of Helsinki of 1975, as revised in  
95 2008.

96  
97 *Preliminary Testing*

98 Anthropometric data were collected for height (cm; Detecto Physicians Scales; Cranlea & Co., Birmingham,  
99 UK), body mass (kg; ADAM GFK 150, USA) and percentage body fat obtained following multi-frequency  
100 bioelectrical impedance analysis (Xitron 4000, San Diego, CA) after 20 min of supine rest. Hydration status  
101 was confirmed in accordance with established guidelines to reduce the potential for fluid dependent  
102 changes in AMS<sup>7,8</sup>.

103  
104 *6-minute walk testing*

105 Each participant completed testing on six occasions where a first familiarisation, and then experimental  
106 6MWT were performed to permit habituation to the method and environment, and ensure reliability on  
107 each day<sup>9</sup>. Ten minutes seated rest was provided between familiarisation and experimental trials. Only  
108 data from the experimental 6MWT were analysed. Participants performed a normoxic treadmill (NT) test,  
109 normoxic outdoor (NO) test, and a hypoxic treadmill test (HT) within a 7 day period (all sea level,  
110 760mmHg) separated with 24 hours of rest. After arrival in Cuzco, Peru (altitude ~3,400m, 460mmHg),  
111 three additional hypoxic outdoor tests were performed at 42 (HO1), 138 (HO2), and 210 (HO3) hours post  
112 arrival. Participants performed all 6MWTs in identical athletic attire between 09.00 and 12.00; data were  
113 collected during the month of April. Environmental conditions are presented in table 1. Standardised  
114 instructions were provided before each test as follows: "walk as far as possible in 6 minutes without  
115 running or jogging", and every 60s duration was communicated until the final 60 s where 30 s remaining  
116 was also communicated. During the treadmill familiarisation trials, participants were asked to self-select a  
117 treadmill start speed they could maintain for 6 minutes. Participants began each experimental trial at 50%  
118 of their self-selected start speed, which was doubled within 5s and then obscured from the view of the  
119 participant. Participants signalled to increase speed, decrease speed, or stop the treadmill as needed.

120

121 The NT 6MWT was performed on a treadmill (Woodway, ELG2, Germany) in temperate (20°C, 40%  
122 relative humidity (RH)) laboratory conditions ( $FiO_2 = 0.2093$ ). The HT 6MWT was performed on treadmill  
123 (Woodway PPS 55sport, Germany) in a purpose built hypoxic chamber (The Altitude Centre, UK) set at  
124  $FiO_2 = 0.137$ ; ~3,400m and 20°C to simulate field-testing location (Cuzco, Peru). The NO 6MWT was  
125 performed outside on level concrete tennis courts and the HO 6MWT was performed in Cuzco, Peru on a  
126 stadium tartan athletic track, for each trial a measured distance of 40 m, with 5m intervals was  
127 demarcated. Temperature and humidity were monitored by a portable heat stress meter (Extech HT30,  
128 USA) and wind speed via a wind anemometer (Technoline EA3010, USA) for both outdoor trials  
129 (environmental data are presented in table 1). Prior to all trials, a Lake Louise Score (LLS) was self-  
130 reported as an indicator of AMS. During all trials, heart rate (HR) and peripheral arterial saturation ( $SpO_2$ )  
131 were measured before and immediately after the test in a seated position using a pulse oximeter (Nonin  
132 2500, Nonin Medical Inc, USA) affixed to the right index finger. Respiratory rate (RR) was counted over a  
133 30s period commencing upon sitting.

134

135 In addition to 6MWTs in Cuzco, participants also performed a 4 day trek carrying day packs and dressed  
136 in typical trekking attire commencing 24 hours after HO3. Prior to departure LLS was recorded to  
137 determine AMS symptoms. The duration taken to reach the summit (Dead Woman's Pass, Peru - 4,215m,  
138 48hr after HO3) from the camp (3,459m) was recorded for each participant with HR and  $SpO_2$  taken  
139 immediately upon reaching the pass.

140

#### 141 *Statistical Analysis*

142 All statistical calculations were performed using PASW software version 20.0 (SPSS, Chicago, IL, US). All  
143 outcome variables were assessed for normality of distribution and sphericity prior to further analysis and  
144 met these criteria in all instances unless otherwise stated. Data are reported as mean (95% CI), with two

145 tailed significance accepted at  $p < 0.05$ . One-way Analysis of Variance (ANOVA) with repeated measures  
146 was used to compare NT, NO, HT, HO1, HO2 and HO3 data. Bonferroni pairwise comparisons compared  
147 between trials to determine the differences between tests. Pearson's correlations ( $r$ ) were used to  
148 examine the relationships between dependent variables in HT and HO1, and for comparisons of the trek  
149 data with HT, HO1 and HO3.

150

## 151 **Results**

152 Twenty-four of the twenty-nine participants completed all tests. One participant was unable to complete  
153 the NO trial due to an acute musculoskeletal injury. Three people were excluded from the HO2 dataset for  
154 as a result of diarrhoea and vomiting ( $n=2$ ) and severe AMS symptoms ( $n=1$ ). Two different individuals  
155 were excluded from the HO3 data set as a result of diarrhoea and vomiting. Each of the ill participant's  
156 data were within the mean  $\pm$  SD for six minute walk distance (6MWD) and post-trial physiological  
157 responses during HO1 and are therefore considered unremarkable.

158

### 159 *Hypoxic Treadmill 6MWT vs. Hypoxic Outdoor 6MWT*

160 A difference ( $p < 0.05$ ) was observed between HT and HO1 (Table 2) for 6MWD, LLS, HR<sub>pre</sub>, HR<sub>post</sub>, SpO<sub>2pre</sub>,  
161 change in ( $\Delta$ ) SpO<sub>2</sub>, RR<sub>pre</sub>, RR<sub>post</sub> and  $\Delta$ RR. No correlation ( $p > 0.05$ ) was observed for SpO<sub>2pre</sub>,  $\Delta$ SpO<sub>2</sub>, RR<sub>pre</sub>,  
162 RR<sub>post</sub> or  $\Delta$ RR (figure 1). No difference ( $p > 0.05$ ) was observed between HT and HO1 for  $\Delta$ HR and SpO<sub>2post</sub>  
163 with significant ( $p < 0.05$ ) relationships observed between HT and HO1 trials for HR<sub>pre</sub>, ( $r = 0.753$ ), HR<sub>post</sub>  
164 ( $r = 0.721$ ),  $\Delta$ HR ( $r = 0.538$ ), SpO<sub>2post</sub> ( $r = 0.545$ ) and 6MWD ( $r = 0.614$ ).

165

### 166 *Normoxic Treadmill 6MWT vs. Normoxic Outdoor 6MWT*

167 No differences ( $p > 0.05$ ) were observed between NT and NO for 6MWD, LLS HR<sub>pre</sub>, HR<sub>post</sub>,  $\Delta$ HR, SpO<sub>2pre</sub>,  
168 SpO<sub>2post</sub>,  $\Delta$ SpO<sub>2</sub>, RR<sub>pre</sub>, RR<sub>post</sub> and  $\Delta$ RR (table 2).

169

### 170 *Normoxic Outdoor 6MWT vs. Hypoxic Outdoor 6MWT*

171 Differences ( $p < 0.05$ ) were observed between NO and HO1 for LLS, HR<sub>pre</sub>, HR<sub>post</sub>,  $\Delta$ HR, SpO<sub>2pre</sub>, SpO<sub>2post</sub>,  
172  $\Delta$ SpO<sub>2</sub>, RR<sub>pre</sub>, RR<sub>post</sub> and  $\Delta$ RR. No difference ( $p > 0.05$ ) was observed between NO and HO1 for 6MWD.

173

### 174 *Hypobaric Hypoxic comparisons - The effect of acclimatisation*

175 Performance and physiological variables 6MWD, LLS, HR<sub>pre</sub>, HR<sub>post</sub>,  $\Delta$ HR, SpO<sub>2pre</sub>, SpO<sub>2post</sub>,  $\Delta$ SpO<sub>2</sub>, RR<sub>pre</sub>,  
176 RR<sub>post</sub>,  $\Delta$ RR reported differences ( $p < 0.05$ ) between NO, HT, HO1, HO2 and HO3; post hoc analysis is  
177 detailed in Table 2.

178

### 179 *Trek Data*

180 Time taken to complete the ascent to Dead Woman's Pass (157 min; CI 144 - 171) was weakly correlated  
181 with HR ( $r = 0.420$ ,  $p < 0.05$ ) and the HT 6MWD ( $r = 0.407$ ,  $p < 0.05$ ). Additionally, SpO<sub>2</sub> following the  
182 ascent (78.2 % CI 76.4 - 79.9) was weakly correlated with the  $\Delta$ RR during HO3 ( $r = 0.391$ ,  $p < 0.05$ ) (Table  
183 3); no relationships were observed for the LLS (0.9 CI 0.4 - 1.31) prior to the ascent.

184

185 **Discussion**

186 Our data demonstrate that  $\Delta$ HR and post-test %SpO<sub>2</sub> were correlated between hypoxic treadmill and  
187 overground 6MWT protocols. Other physiological or performance markers are not correlated. In  
188 accordance with our primary aim, these variables are therefore appropriate for use to determine  
189 physiological responses to simulated altitude prior to travel and upon immediate arrival at altitude. AMS  
190 symptoms were not clinically relevant or related to performance of any 6MWT.

191  
192 In comparison to the normoxic outdoor baseline trial, no differences were observed in the distance  
193 walked during hypoxic outdoor trials. Acclimatization was evidenced by reductions in resting HR and RR,  
194 although post exercise HR, SpO<sub>2</sub> and RR, and the change in variables were not different with  
195 acclimatization. This might suggest that the physiological challenge of exercising in hypoxia in comparison  
196 to normoxia is too great to overcome, or the sensitivity / construct validity of the test is inadequate. Our  
197 hypoxic outdoor trial data suggests participants were able to walk a greater distance, and consequently,  
198 elicited more favourable physiological responses (increased HR, decreased RR and preserved SpO<sub>2</sub> post-  
199 test) at 3,400m in Cuzco, in comparison to a similar study performed at 4,365m<sup>5</sup>. This is unsurprising due  
200 to the differences in PO<sub>2</sub> at these locations.

201  
202 The duration taken to reach the peak ascent (Dead Woman's Pass), a field based performance indicator,  
203 was moderately related to the 6MWD in the HT trial suggesting that the exercise capacity of an individual  
204 is important in governing the speed of ascent. The relationship between ascent time and the HR during the  
205 ascent also provides a useful performance indicator. The lack of relationship between the duration taken  
206 to ascend, and any other physiological or AMS marker suggest that SpO<sub>2</sub> and 6MWD are unlikely to be  
207 effective tools for predicting successful ascent<sup>6</sup>. It has been suggested that with AMS symptoms likely  
208 amongst climbers, psychological factors would more likely dictate peak or summit success<sup>6</sup>. The success of  
209 reaching a pass or summit of a peak is dependent upon a number of variables including acclimatization,  
210 psychological factors, weather, impaired sleep, inflammation, fluid shifts, and haematopoiesis thus  
211 success, cannot be fully elucidated with vital signs in a small group alone.

212  
213 *Limitations*

214 The severity of AMS symptoms peak between days 1 and 3 of arrival at altitude<sup>10</sup>, and acclimatization  
215 tends to occur during the first week. Therefore, the identification of no differences between H02 and H03  
216 is unsurprising, and future studies should implement earlier and more frequent analysis. The authors  
217 acknowledge that differences in participant approach to overland and treadmill walking e.g. pacing may  
218 have affected findings. Further, deceleration and acceleration associated with turning during overland  
219 walking may have reduced strain. Finally, the rate of ascent, and physiological data may have been  
220 affected by pacing e.g. additional rest breaks or faster walking at the end of the ascent, continuous  
221 monitoring of HR and O<sub>2</sub>, and walking velocity, via GPS would be more beneficial.

222

223 **Conclusion**

224 The 6MWT is a useful and simple tool for determining performance and physiological responses to self-  
225 paced exercise in hypoxia that can be administered using a treadmill and over level ground. The  
226 implementation of the 6MWT warrants further investigation as a means for predicting for responses to  
227 acute exposures, and altitude acclimatization, via the post exercise changes in physiological responses to,  
228 but not performance during the 6MWT. Preliminary data suggests the 6MWT may be useful to determine  
229 acclimatization to altitude as attenuation of physiological responses (change in HR and post-test SpO<sub>2</sub>)  
230 from baseline tests.

231

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