

Hayes, Lawrence, Herbert, Peter, Sculthorpe, Nicholas and Grace, Fergal M. (2017) Exercise training improves free testosterone in lifelong sedentary aging men. *Endocrine Connections*, 6 (5). pp. 306-310.

Downloaded from: <http://insight.cumbria.ac.uk/id/eprint/2948/>

***Usage of any items from the University of Cumbria's institutional repository 'Insight' must conform to the following fair usage guidelines.***

Any item and its associated metadata held in the University of Cumbria's institutional repository Insight (unless stated otherwise on the metadata record) may be copied, displayed or performed, and stored in line with the JISC fair dealing guidelines (available [here](#)) for educational and not-for-profit activities

**provided that**

- the authors, title and full bibliographic details of the item are cited clearly when any part of the work is referred to verbally or in the written form
  - a hyperlink/URL to the original Insight record of that item is included in any citations of the work
- the content is not changed in any way
- all files required for usage of the item are kept together with the main item file.

**You may not**

- sell any part of an item
- refer to any part of an item without citation
- amend any item or contextualise it in a way that will impugn the creator's reputation
- remove or alter the copyright statement on an item.

The full policy can be found [here](#).

Alternatively contact the University of Cumbria Repository Editor by emailing [insight@cumbria.ac.uk](mailto:insight@cumbria.ac.uk).

1 ORIGINAL ARTICLE

2

3

4 **Exercise training improves free testosterone in lifelong sedentary aging men**

5

6 Lawrence D Hayes<sup>1\*</sup>, Peter Herbert<sup>2</sup>, Nicholas F Sculthorpe<sup>3</sup>, and Fergal M Grace<sup>4</sup>

7

8

9 *<sup>1</sup>Active Ageing Research Group, Department of Medical and Sport Sciences, University of*  
10 *Cumbria, UK; <sup>2</sup>School of Sport, Health and Outdoor Education, Trinity Saint David,*  
11 *University of Wales, UK; <sup>3</sup>Institute of Clinical Exercise and Health Science, University of the*  
12 *West of Scotland, UK; <sup>4</sup>Faculty of Health, Federation University, Victoria, Australia.*

13

14 \*L. D. Hayes

15 Active Ageing Research group,

16 Department of Medical and Sport Sciences,

17 University of Cumbria,

18 Bowerham Road, Lancaster, LA1 3JD, UK

19 E-mail: [Lawrence.Hayes@Cumbria.ac.uk](mailto:Lawrence.Hayes@Cumbria.ac.uk)

20 Twitter: @DrLawrenceHayes

21 ORCID ID: 0000-0002-6654-0072

22

23 **WORD COUNT: 1626 excluding abstract and reference list.**

24

1

25 **Abstract**

26 As the impact of high intensity interval training (HIIT) on systemic hormones in  
27 aging men is unstudied to date, we investigated whether total testosterone (TT), sex hormone  
28 binding globulin (SHBG), free testosterone (free-T), and cortisol (all in serum) were altered  
29 following HIIT in a cohort of 22 lifelong sedentary ( $62 \pm 2$  years) older men.

30 As HIIT requires preconditioning exercise in sedentary cohorts, participants were  
31 tested at three phases, **each separated by six weeks' training**; baseline (phase A), following  
32 conditioning exercise (phase B), and post-HIIT (phase C). Each measurement phase used  
33 identical methods. TT was significantly increased following HIIT ( $\sim 17\%$ ;  $P < 0.001$ ) with  
34 most increase occurring during preconditioning ( $\sim 10\%$ ;  $P = 0.007$ ). Free-T was unaffected by  
35 conditioning exercise ( $P = 0.102$ ) but was significantly higher following HIIT compared to  
36 baseline ( $\sim 4.5\%$ ;  $P = 0.023$ ). Cortisol remained unchanged from A to C ( $P = 0.138$ ).

37 The present data indicate a combination of preconditioning and HIIT increases TT  
38 and SHBG in sedentary older males, with the HIIT stimulus accounting for a small but  
39 statistically significant increase in free-T. Further study is required to determine the  
40 biological importance of small improvements in free-T in aging men.

41

42 **Key words:** Exercise · HIIT · SHBG · Steroid · Testosterone

43

44

45

46

47 **Introduction**

48 Testosterone is a sex steroid hormone with profound influence on various tissue (1-3).  
49 The precipitous decline in systemic testosterone with age is well described (4). Additionally,  
50 sex hormone binding globulin (SHBG) is positively correlated with age, thereby attenuating  
51 the unbound fraction of testosterone, which is available for androgen receptor interactions  
52 (4,5). With the age-associated reduction in anabolic hormone production, reductions in  
53 cardiorespiratory fitness (6), muscle strength (7), and muscle power (8) are also observed.  
54 Furthermore, significant correlations between testosterone and measures of physical  
55 performance in older adults have been observed (9).

56 Whilst improvements in fitness can be achieved with exercise training in older adults  
57 (10,11) the potential of aging men to increase systemic testosterone through exercise is  
58 poorly understood. Whilst some authors have reported elevated total testosterone (TT) in  
59 highly trained older males compared to controls (12), this is not always the case (13). For  
60 example, experimental data from our laboratory suggest masters athletes exhibit improved  
61 peak oxygen uptake, body composition, and endothelial function compared with age-matched  
62 lifelong sedentary aging men, without any difference in TT (14-17). Yet, we demonstrated  
63 that a six-week intervention of moderate aerobic exercise increased TT in said group of  
64 sedentary older males (11). However, sex hormone binding globulin (SHBG) was increased  
65 which rendered bioavailable testosterone (bio-T) and free testosterone (free-T) unaltered  
66 compared to pre-training.

67 High intensity interval training (HIIT) uses small volumes of exercise to bring about  
68 disproportionate increases in cardiometabolic health (18). Whilst we have reported lifelong  
69 exercise has no influence on basal TT, yet moderate aerobic exercise increases TT in  
70 sedentary older males, there is a paucity of data concerning the influence of short-term HIIT

71 on TT and free-T in older males. Therefore, the purpose of the present investigation was to  
72 examine the influence of HIIT, following moderate aerobic conditioning, on androgen status  
73 in previously sedentary older males. We hypothesized *a priori* that testosterone would  
74 increase following HIIT.

75

## 76 **Materials and Methods**

### 77 *Subjects*

78 Following familiarization with experimental procedures and approval to exercise by  
79 their general practitioner, participants were enrolled to the study which was approved by the  
80 University of the West of Scotland Ethics Committee. Twenty-two sedentary, but otherwise  
81 healthy, males ( $62 \pm 2$  years, with a stature of  $175 \pm 6$  cm, and body mass of  $91 \pm 16$  kg)  
82 participated. Subjects did not participate in any organized exercise program and had not done  
83 for  $>30$  years prior to the period of moderate aerobic conditioning. To account for the  
84 contribution of conditioning exercise and HIIT, participants were tested at three phases;  
85 baseline (phase A), following conditioning exercise (phase B), and post-HIIT (phase C) using  
86 identical methods.

87

### 88 *Exercise Training*

89 Participants undertook a six-week period of pre-conditioning, consisting of  $150$   
90  $\text{min} \cdot \text{wk}^{-1}$  moderate intensity aerobic exercise, in line with the ACSM guidelines for exercise  
91 for older adults (19), followed by six weeks of supervised HIIT as previously described (14).  
92 Because aging men take longer to recover from a single HIIT session (20), sessions were

93 performed every five days, for six weeks (nine sessions in total). Each session consisted of 6  
94 x 30 s sprints at 40% peak power output (PPO) interspersed with 3 min active recovery on a  
95 cycle ergometer (Wattbike Ltd., Nottingham, UK). Sessions were conducted in groups of  
96 between four and six participants and were the sole exercise performed during this time. To  
97 allow for comparison with other literature, training intensities were compared with power  
98 achieved at  $VO_{2peak}$ . Training intensity was  $141 \pm 27\%$  of power at  $VO_{2peak}$ .

99

### 100 *Body Composition*

101 Stature was measured to the nearest 0.1 cm using a stadiometer (Seca, Birmingham,  
102 UK), and body mass and body composition was determined by a multi frequency  
103 bioelectrical impedance analyzer (BIA [Tanita MC-180MA Body Composition Analyzer,  
104 Tanita UK Ltd.]). GMON software (v1.7.0, Tanita UK Ltd.) was used to determine absolute  
105 and relative body fat. Fat free mass (FFM) was calculated by subtracting fat mass from total  
106 body mass.

107

### 108 *Blood Draws and Analysis*

109 Blood samples were collected 07:00-09:00 h, 48-72 hours following the last exercise  
110 session as previously described (21). Serum concentrations of TT, SHBG, and cortisol were  
111 measured by electrochemiluminescent immunoassay on the E601 module of the Roche Cobas  
112 6000 (Burgess Hill, West Sussex, U.K.). Inter-assay coefficients of variation (CV) over a six-  
113 month period were 4.5%, 2.4%, and 4.2% for TT, SHBG, and cortisol respectively. Free-T  
114 was calculated using the Vermueulen equation (22).

115

116 *Data Analysis*

117           Following confirmation of parametricity by a Shapiro-Wilk test of normality and  
118 Levene's test for homogeneity of variance, a one way repeated measures analysis of variance  
119 (ANOVA) with *post hoc* Bonferroni correction was used to identify differences between time  
120 points. Alpha level was set *a priori* at  $P < 0.05$ , and effect size (Cohen's  $d$ ) was calculated.  
121 Data are presented as mean  $\pm$  standard deviation (SD).

122

123 **Results**

124           TT, free-T, and cortisol pre- and post-HIIT are displayed in figure 1. TT increased  
125 from A to B ( $13.2 \pm 5.5$  to  $14.6 \pm 6.1$   $\text{nmol}\cdot\text{l}^{-1}$  respectively [ $P=0.007$ , Cohen's  $d=0.24$ ]) and  
126 remained elevated at C compared to A ( $15.4 \pm 6.6$   $\text{nmol}\cdot\text{l}^{-1}$  at phase C [ $P < 0.001$ , Cohen's  
127  $d=0.36$ ]). SHBG increased following preconditioning ( $P=0.016$ , Cohen's  $d=0.10$  [ $42.6 \pm 22.0$   
128 and  $45.0 \pm 23.9$   $\text{nmol}\cdot\text{l}^{-1}$  at A and B respectively]) and again following HIIT ( $P=0.003$ ,  
129 Cohen's  $d=0.43$  vs. A [ $45.9 \pm 24.6$   $\text{nmol}\cdot\text{l}^{-1}$  at phase C]). Free-T was unchanged after  
130 preconditioning ( $P=0.102$ , Cohen's  $d=0.22$  [ $6.6 \pm 1.9$  and  $7.0 \pm 1.8$   $\text{ng}\cdot\text{dl}^{-1}$  at A and B  
131 respectively]), with a small increase following HIIT ( $7.3 \pm 2.1$   $\text{ng}\cdot\text{dl}^{-1}$  at phase C [ $P=0.023$ ,  
132 Cohen's  $d=0.36$  vs. A]). There was no difference between free-T at phase B and C ( $P=0.185$ ,  
133 Cohen's  $d=0.16$ ). Cortisol was unchanged from A to B ( $302 \pm 114$  and  $297 \pm 107$   $\text{nmol}\cdot\text{l}^{-1}$   
134 respectively [ $P=0.849$ , Cohen's  $d=0.05$ ]), and from A to C ( $256 \pm 86$   $\text{nmol}\cdot\text{l}^{-1}$  at phase C  
135 [ $P=0.138$ , Cohen's  $d=0.46$ ]).

136           At phase A, body fat percentage was  $24.4 \pm 11.6\%$ . Body fat percentage decreased  
137  $\sim 1.1\%$  following preconditioning ( $P=0.006$ , Cohen's  $d=0.10$ ) and a further  $\sim 2.2\%$  following  
138 HIIT ( $P=0.008$ , Cohen's  $d=0.16$ ) which meant body fat percentage was  $\sim 3.3\%$  lower at phase

139 C than at A ( $P < 0.001$ , Cohen's  $d = 0.28$ ). FFM was  $66.7 \pm 7.1$  kg at baseline and was  
140 unchanged following preconditioning ( $P = 0.336$ , Cohen's  $d = 0.06$ ). This was followed by a  
141  $\sim 3.0\%$  increase post-HIIT ( $P = 0.005$ , Cohen's  $d = 0.26$ ), which was  $\sim 3.6\%$  greater than at  
142 baseline ( $P = 0.001$ , Cohen's  $d = 0.32$ ).

143

144 **\*\*INSERT FIGURE 1 NEAR HERE \*\***

145 **Figure 1:** Cortisol (upper panel), total testosterone (middle panel), and free testosterone  
146 (lower panel) in a group of lifelong sedentary aging males at baseline (A), following  
147 conditioning exercise (phase B), and post-high intensity interval training (phase C). \*Denotes  
148 significantly different from A ( $P < 0.05$ ). Data are displayed as individual samples and mean  $\pm$   
149 SD.

150

## 151 **Discussion**

152 The main finding of this study is that preconditioning exercise and HIIT improves TT  
153 by  $\sim 17\%$  in previously sedentary older males, which was maintained post-intervention  
154 despite the training volume reduction from  $\sim 150 \text{ min} \cdot \text{wk}^{-1}$  to  $\sim 3\text{-}6 \text{ min} \cdot \text{wk}^{-1}$  during the final  
155 training phase. In addition, progressive increases at each time point ensured free-T was  
156 elevated post-intervention, compared to pre-training. A such, HITT may be a time-efficient  
157 non-pharmacological strategy in older males to maintain or increase endogenous testosterone  
158 concentrations.

159 We previously hypothesized that increased TT and SHBG were transient  
160 physiological responses to initiation of exercise training, and basal testosterone may return to



161 baseline following prolonged training (11). However, the present study indicates HIIT  
162 confers a prolonged elevation in TT compared to pre-training (~17%).

163         Previously, we observed no increase in free-T following six weeks' moderate aerobic  
164 training in sedentary older males (11). However, the addition of HIIT stimulated a significant  
165 increase in the unbound hormone fraction, compared to moderate aerobic training. This  
166 occurred because of the ~5% increase in TT, compared to the ~2% increase in SHBG from  
167 phase A to C. As such, it is plausible that testosterone available for androgen receptor  
168 interaction was increased post-HIIT, which may partly explain increased FFM.

169         Khoo et al. (23) indicated increased TT (~17%) following 24 weeks' moderate-  
170 intensity aerobic exercise in middle-aged (~44 years) obese men. Whilst the present study  
171 and Khoo et al. (23) both reported increased TT and SHBG, Lovell et al. (24) reported no  
172 change to TT, SHBG, or free-T in an older cohort (~74 years) following resistance or aerobic  
173 training. Importantly, participants were moderately active rather than sedentary as was the  
174 case in the present study and that of Khoo and colleagues (23). Taken together, the small  
175 body of comparable literature indicates that exercise training induces statistically significant,  
176 if not biologically or clinically relevant, increases in steroid hormones in sedentary middle to  
177 older aged men.

178         That previously sedentary aging males can increase TT following moderate exercise  
179 training, and free-T following HIIT, is an encouraging finding. Low testosterone is associated  
180 with diminished cognitive function, depression, osteoporosis, and deterioration of muscle  
181 function (25). Therefore, the confirmation that exercise can increase serum testosterone is  
182 important for medical practitioners because exercise has been proposed as an initial treatment  
183 for low testosterone (26).

184           A limitation to the present investigation is that we utilized a single-arm observational  
185 design, rather than a randomized control trial. As such it is difficult to conclude whether  
186 changes observed at phase C were the result of HIIT, or merely prolonged exercise  
187 intervention (of any modality). Moreover, since participants experienced beneficial  
188 alterations to body composition, it is feasible that the indirect effect of lower body fat may  
189 have resulted in increased free-T, rather than being purely the result of HIIT.

190           In conclusion, because preconditioning exercise increased both TT and SHBG, only a  
191 small increase in free-T was observed, which did not reach significance. However, the  
192 combination of preconditioning and HIIT appears a sufficient stimulus to improve free-T in  
193 lifelong sedentary aging men. Further study is required to confirm these findings and  
194 establish the biological significance of small improvements in free-T in aging men.

195

#### 196 **Declaration of Interest**

197 Authors declare they have no declaration of interest.

198

#### 199 **Funding**

200 Authors declare they have no funding sources.

201

#### 202 **Acknowledgements**

203 Authors declare they have no acknowledgements.

204

205 **References**

- 206 1. Arazi H, Damirchi A & Asadi A. Age-related hormonal adaptations, muscle  
207 circumference and strength development with 8 weeks' moderate intensity resistance  
208 training. *Annales d'endocrinologie* 2013 **74** 30-35.
- 209 2. Capllonch-Amer G, Llado I, Proenza AM, Garcia-Palmer FJ & Gianotti M. Opposite  
210 effects of 17-beta estradiol and testosterone on mitochondrial biogenesis and  
211 adiponectin synthesis in white adipocytes. *Journal of Molecular Endocrinology* 2014  
212 **52** 203-214.
- 213 3. Dubois V, Laurent MR, Jardi F, Antonio L, Lemaire K, Goyvaerts L, Deldicque L,  
214 Carmeliet G, Decallonne B, Vanderschueren D & Claessens F. Androgen deficiency  
215 exacerbates high fat diet-induced metabolic alterations in male mice. *Endocrinology*  
216 2015 **157** 648-665.
- 217 4. Harman SM, Metter EJ, Tobin JD, Pearson J & Blackman MR. Longitudinal effects  
218 of aging on serum total and free testosterone levels in healthy men. *Journal of*  
219 *Clinical Endocrinology and Metabolism* 2001 **86** 724-731.
- 220 5. Bjerner J, Biernat D, Fossa SD & Bjoro T. Reference intervals for serum testosterone,  
221 SHBG, LH and FSH in males from the NORIP project. *Scandinavian Journal of*  
222 *Clinical and Laboratory Investigation* 2009 **69** 873-879 e1-11.
- 223 6. Grey TM, Spencer MD, Belfry GR, Kowalchuk JM, Paterson DH & Murias JM.  
224 Effects of age and long-term endurance training on VO2 kinetics. *Medicine and*  
225 *Science in Sports and Exercise* 2015 **47** 289-298.
- 226 7. Martin JA, Ramsay J, Hughes C, Peters DM & Edwards MG. Age and grip strength  
227 predict hand dexterity in adults. *PloS one* 2015 **10** e0117598.

- 228 8. Metter EJ, Conwit R, Tobin J & Fozard JL. Age-associated loss of power and strength  
229 in the upper extremities in women and men. *The Journals of Gerontology. Series A,*  
230 *Biological Sciences and Medical Sciences* 1997 **52** B267-276.
- 231 9. Aguirre LE, Jan IZ, Fowler K, Waters DL, Villareal DT & Armamento-Villareal R.  
232 Testosterone and adipokines are determinants of physical performance, strength,  
233 and aerobic fitness in frail, obese, older adults. *International Journal of*  
234 *Endocrinology* 2014 507395.
- 235 10. Hayes LD, Grace FM, Sculthorpe N, Herbert P, Ratcliffe JW, Kilduff LP & Baker JS.  
236 The effects of a formal exercise training programme on salivary hormone  
237 concentrations and body composition in previously sedentary aging men.  
238 *SpringerPlus* 2013 **2** 18.
- 239 11. Hayes LD, Sculthorpe N, Herbert P, Baker JS, Spagna R & Grace FM. Six weeks of  
240 conditioning exercise increases total, but not free testosterone in lifelong sedentary  
241 aging men. *Aging Male* 2015 **18** 195-200.
- 242 12. Ari Z, Kutlu N, Uyanik BS, Taneli F & Tavli T. Serum testosterone, growth hormone,  
243 and insulin-like growth factor-1 levels, mental reaction time, and maximal aerobic  
244 exercise in sedentary and long-term physically trained elderly males. *International*  
245 *Journal of Neuroscience* 2004 **114** 623-637.
- 246 13. Hayes LD, Sculthorpe N, Herbert P, Baker JS, Hullin DA, Kilduff LP & Grace FM.  
247 Resting steroid hormone concentrations in lifetime exercisers and lifetime sedentary  
248 males. *Aging Male* 2015 **18** 22-26.
- 249 14. Grace FM, Herbert P, Ratcliffe JW, New KJ, Baker JS & Sculthorpe NF. Age related  
250 vascular endothelial function following lifelong sedentariness: positive impact of  
251 cardiovascular conditioning without further improvement following low frequency  
252 high intensity interval training. *Physiological Reports* 2015 **3** pii: e12234.

- 253 15. Hayes LD, Grace FM, Sculthorpe N, Herbert P, Kilduff LP & Baker JS. Does chronic  
254 exercise attenuate age-related physiological decline in males? *Research in Sports*  
255 *Medicine* 2013 **21** 343-354.
- 256 16. Hayes LD, Sculthorpe N, Herbert P, Baker JS, Hullin DA, Kilduff LP & Grace FM.  
257 Poor levels of agreement between serum and saliva testosterone measurement  
258 following exercise training in ageing men. *Aging Male* 2015 **18** 67-70.
- 259 17. Knowles AM, Herbert P, Easton C, Sculthorpe N & Grace FM. Impact of low-  
260 volume, high-intensity interval training on maximal aerobic capacity, health-related  
261 quality of life and motivation to exercise in ageing men. *Age (Dordr)* 2015 **37** 25.
- 262 18. Weston KS, Wisloff U & Coombes JS. High-intensity interval training in patients  
263 with lifestyle-induced cardiometabolic disease: a systematic review and meta-  
264 analysis. *British Journal of Sports Medicine* 2014 **48** 1227-1234.
- 265 19. Riebe D, Franklin BA, Thompson PD, Garber CE, Whitfield GP, Magal M &  
266 Pescatello LS Updating ACSM's recommendations for exercise participation health  
267 screening. *Medicine and Science in Sports and Exercise* 2015 **47** 2473-2479.
- 268 20. Herbert P, Grace FM & Sculthorpe NF. Exercising caution: prolonged recovery from  
269 a single session of high-intensity interval training in older men. *Journal of the*  
270 *American Geriatrics Society* 2015 **63** 817-818.
- 271 21. Hayes LD, Sculthorpe N, Herbert P, Baker JS, Hullin DA, Kilduff LP, Reed D,  
272 Spagna R & Grace FM. Salivary testosterone measurement does not identify  
273 biochemical hypogonadism in aging men: a ROC analysis. *Endocrine* 2015 **50** 256-  
274 259.
- 275 22. Vermeulen A, Verdonck L & Kaufman JM. A critical evaluation of simple methods  
276 for the estimation of free testosterone in serum. *Journal of Clinical Endocrinology*  
277 *and Metabolism* 1999 **84** 3666-3672.

- 278 23. Khoo J, Tian HH, Tan B, Chew K, Ng CS, Leong D, Teo RC & Chen RY. Comparing  
279 effects of low- and high-volume moderate-intensity exercise on sexual function and  
280 testosterone in obese men. *Journal of Sexual Medicine* 2013 **10** 1823-1832.
- 281 24. Lovell DI, Cuneo R, Wallace J & McLellan C. The hormonal response of older men  
282 to sub-maximum aerobic exercise: The effect of training and detraining. *Steroids* 2012  
283 **77** 413-8.
- 284 25. Petak SM, Nankin HR, Spark RF, Swerdloff RS & Rodriguez-Rigau LJA. American  
285 Association of Clinical Endocrinologists Medical Guidelines for clinical practice for  
286 the evaluation and treatment of hypogonadism in adult male patients--2002 update.  
287 *Endocrine Practice* 2002 **8** 440-456.
- 288 26. Swerdloff R & Anawalt BD. Clinical decisions. Testosterone-replacement therapy.  
289 *New England Journal of Medicine*, 2014 **371** 2032-2034.

290

291

292

293

294

295

296

297

298

299

300

301

302

303

304

**305 Figure Legends**

306 **Figure 1:** Cortisol (upper panel), total testosterone (middle panel), and free testosterone  
307 (lower panel) in a group of lifelong sedentary aging males at baseline (A), following  
308 conditioning exercise (phase B), and post-high intensity interval training (phase C). \*Denotes  
309 significantly different from A ( $P < 0.05$ ). Data are displayed as individual samples and mean  $\pm$   
310 SD.

