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| 1 | ORIGINAL | ARTICLE |
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#### Six weeks of high intensity interval training (HIIT) preserves aerobic capacity in sedentary older males and male masters athletes for four years: A reunion study

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## 1 Abstract

Long-term implications of acutely increased cardiorespiratory fitness following short-term exercise interventions in older adults are unknown. In this study, we examined peak oxygen uptake (VO<sub>2peak</sub>) after four years of 'free-living' after a high intensity interval training (HIIT) intervention. Seventeen lifelong exercisers (LEX) and 17 previously sedentary (SED) males (55-74 years of age in 2012) were tested four years (phase D) after our previous experiment which included 6-weeks of aerobic moderate intensity exercise (phase B), followed by 6-weeks of HIIT (phase C). At all stages, a standard incremental exercise protocol on a cycle ergometer was completed to determine VO<sub>2peak</sub>. SED (P=1.000, Cohen's d=0.01) and LEX (P=1.000, Cohen's d=0.11) VO<sub>2peak</sub> at phase D was not different from phase A (enrolment). SED experienced a large decrease in VO<sub>2peak</sub> from phase C to phase D (32  $\pm$  6 ml·kg·min<sup>-1</sup> to 27  $\pm$ 6 ml·kg·min<sup>-1</sup> [P<0.001, Cohen's d=0.81]). LEX experienced a small decrease in VO<sub>2peak</sub> from phase C to phase D  $(42 \pm 7 \text{ ml} \cdot \text{kg} \cdot \text{min}^{-1} \text{ to } 39 \pm 9 \text{ ml} \cdot \text{kg} \cdot \text{min}^{-1} \text{ [P}<0.001, \text{ Cohen's d}=0.46])$ . At phase D, LEX had greater VO<sub>2peak</sub> than SED (P<0.001, Cohen's d=1.73). The proportion of subjects who reported discontinuing training, maintaining moderate training, and maintaining HIIT differed between groups (P=0.023), with LEX self-reporting more HIIT, and SED selfreporting more discontinuation from exercise. Those who continued exercising experienced a reduction in VO<sub>2peak</sub> over the four years from  $39 \pm 7$  ml·kg·min<sup>-1</sup> to  $36 \pm 9$  ml·kg·min<sup>-1</sup> (N=25, P < 0.001, Cohen's d = 0.37), and those who discontinued exercising also experienced a reduction in VO<sub>2peak</sub> from  $30 \pm 7$  ml·kg·min<sup>-1</sup> to  $25 \pm 9$  ml·kg·min<sup>-1</sup> (N=9, P=0.003, Cohen's d=0.62). Four years after completing a brief period of aerobic exercise and HIIT, older males demonstrated a preservation of VO<sub>2peak</sub>, irrespective of training status (LEX or SED). However, LEX exhibited greater VO<sub>2peak</sub> than SED after 4-years of unsupervised 'free-living'. Finally, those who discontinued exercising experienced a greater reduction in VO<sub>2peak</sub>. These findings infer that to maintain aerobic capacity, 6 weeks of HIIT every four year may be sufficient, but to attenuate the decline, exercise should be maintained. 

# Keywords

Ageing; Exercise; HIIT; Masters athletes; Oxygen uptake; Sedentary

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#### 1 1 Introduction

Biological ageing is characterised by a progressive loss of physical function and increased risk 2 of developing various common diseases, including cardiovascular disease (CVD), type II 3 diabetes, and many cancers (Butler et al., 2008). Indeed, cardiovascular fitness is a powerful 4 predictor of loss of independence (de Oliveira Brito et al., 2014), and risk of morbidity (Blair 5 6 et al., 1989; Seccareccia and Menotti, 1992) and mortality (Imboden et al., 2018). Thus, the decline in physiological function that accompanies advancing age presents a major obstacle to 7 8 achieving increased health span (Beard and Bloom, 2015), the phase of life without disability 9 and free from serious chronic diseases (Seals and Melov, 2014). Lifestyle interventions capable of ameliorating the deleterious changes in physiological system (e.g. muscular, cardiovascular, 10 endocrine, immune, to name but a few) associated with chronological ageing will prolong the 11 heath span (Seals and Melov, 2014), whilst also reducing risk of age-related CVD (Chiao and 12 13 Rabinovitch, 2015). One such strategy is physical activity, with recent meta-analytical work demonstrating running activities were associated with a 30% reduction in cardiovascular 14 mortality (Pedisic et al., 2019). This corroborates the recently published narrative by the United 15 Kingdom government, identifying a curvilinear dose-response relationship between physical 16 activity and health outcomes (UK Chief Medical Officers' report). Furthermore, exercise has 17 18 been proposed as a countermeasure to biological ageing in humans, whereby physically active humans are phenotypically younger than sedentary counterparts, or where individuals display 19 a 'younger' phenotype as a result of exercise training (Beaumont et al., 2019; Campbell et al., 20 21 2019; Elliott et al., 2017; Hayes et al., 2015a, 2015b; Mcleod et al., 2019; Piasecki et al., 2019; 22 Sellami et al., 2019, 2018, 2017; Stenbäck et al., 2019a, 2019b). Moreover, the 'masters athlete' - broadly defined as an individual older than 45 or 50 years of age involved with competitive 23 exercise (D'Andrea et al., 2007; Wilson et al., 2010) - represents a non-pharmacological model 24 to isolate the inexorable from the preventable declines in cardiovascular ageing (Beaumont et 25 26 al., 2018).

27 One characteristic of advancing age is a reduced peak oxygen uptake (VO<sub>2peak</sub>) 28 (Astrand, 1960; Beaumont et al., 2020; Dill et al., 1967; Rogers et al., 1990). This decrease accelerates with age (Hawkins and Wiswell, 2003) such that there is a ~16% decrease across 29 the fifth decade but a ~26% decrease during the seventh decade and above (Fleg et al., 2005). 30 Indeed, lower levels of cardiorespiratory fitness are associated with an increased risk of 31 cardiovascular and all-cause mortality (Imboden et al., 2018; Paffenbarger et al., 1993). 32 33 Although decreased VO<sub>2peak</sub> with increased age occurs irrespective of training status (Pimentel et al., 2003), the rate of decline may be "flattened" through exercise training, as masters athletes 34 35 exhibit less VO<sub>2peak</sub> loss over 8 years than sedentary counterparts (Rogers et al., 1990). This 36 "flattened" decline with regular training becomes important given that small improvements in cardiorespiratory fitness have a disproportionately large impact on health and survival 37 (Kaminsky et al., 2013b; Kodama et al., 2009). Although these studies report improved health 38 and fitness with regular exercise training over the life course, sedentary individuals who take-39 40 up exercise later in life may also achieve considerable health benefits (Knowles et al., 2015).

Despite convincing evidence for improved cardiorespiratory fitness as a consequence of engaging in short term exercise (Esfandiari et al., 2014; Grace et al., 2018; Knowles et al., 2015), long-term implications of these benefits in older adults are unclear. Whilst a supervised exercise intervention is known to improve cardiorespiratory fitness, the longer-term effect of this during subsequent unsupervised years is unknown.

In 2012, we completed a study of adaptation to low-volume high intensity interval training (HIIT) in older lifelong exercising (LEX) masters athletes and age matched longstanding sedentary (SED) men (Grace et al., 2015; Knowles et al., 2015). On completion, participants were provided with a detailed summary of their cardiovascular and metabolic health and returned to the community. Apart from this debrief and an open offer of advice from the lead investigator, there was no formal support. The present study attempted to address the dearth of information regarding legacy effects of training interventions by presenting a followup of our previous work (Knowles et al., 2015). In medicine, a legacy effect, first discussed by Holman et al. (2008) describes the lasting benefit of a treatment long after cessation of said treatment (Coppo, 2013).

Therefore, the aim of the present investigation was to examine the legacy effect of 6weeks of conditioning exercise followed by 6-weeks of supervised HIIT, on cardiorespiratory
fitness after 4 years of 'free-living'. We examined VO<sub>2peak</sub> 4 years later, in a 'reunion' study to
ascertain long-term implications. We hypothesised 1) both groups would experience a decline
in VO<sub>2peak</sub>, 2) LEX would experience less of a decline in VO<sub>2peak</sub>, and 3) VO<sub>2peak</sub> would be
greater in LEX compared to SED at follow up.

#### 13 2 Materials and Methods

## 14 2.1 Participants

In 2012, we recruited 39 participants aged 55-74 years from a random sample of the local 15 community to participate in a HIIT study (participant descriptions in Table 1). To be eligible, 16 participants were required to be healthy and have no medical conditions liable to contraindicate 17 18 the training programme. Following approval to exercise by their general practitioner, participants provided informed written consent prior to the study which was approved by the 19 University of the West of Scotland and the University of Wales ethics committees. The 20 21 investigation adhered to the declaration of Helsinki. A SED and LEX group participated in the 22 study as previously described (Grace et al., 2018; Hayes et al., 2020; Knowles et al., 2015). In 23 2016, participants were invited to participate in a reunion study to identify changes in 24 cardiorespiratory fitness. These participants were not informed of a follow-up study during the original investigation in 2012 and thus, were only invited back a few weeks prior to the 25 26 scheduled testing in 2016. The same inclusion criteria were used as for the 2012 assessments. SED participants had not participated in organised exercise programmes for >30 years prior to 27 28 enrolment in the 2012 study. The LEX group were highly active exercisers and had been so for the previous >30 years. They consisted of current masters athletes in sports including water-29 30 polo, triathlon, track cycling, road cycling, and distance running. Participants arrived in the 31 exercise physiology laboratory between the hours of 07.00-09.00 h, following an overnight 32 fast and having abstained from strenuous exercise for a minimum of 48 h. Participants were 33 reminded to maintain standardised conditions prior to each assessment point which included arriving in a hydrated state having abstained from caffeine and alcohol consumption for 36 h. 34 35

**Table 1:** Participant characteristics at baseline. SED = lifelong sedentary older males. LEX = lifelong exercising older males.  $VO_{2peak}$  = Peak oxygen uptake. \*Different to SED at the P<0.05

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|  | SED (n=22)               | LEX (n=17)               |
|--|--------------------------|--------------------------|
| Age (years)                                    | $62 \pm 2$ (range 55-74) | $60 \pm 5$ (range 53-71) |
| Stature (cm)                                   | $175 \pm 6$              | $173 \pm 6$              |
| Mass (kg)                                      | $91 \pm 16$              | $78 \pm 12^{*}$          |
| BMI (kg·m <sup>2</sup> )                       | $29.5 \pm 4.9$           | $26.0 \pm 2.5^*$         |
| Fat free mass (kg)                             | $67 \pm 7$               | $65 \pm 6$               |
| Body fat percentage (%)                        | $24 \pm 17$              | $16 \pm 6^{*}$           |
| VO <sub>2peak</sub> (ml·kg·min <sup>-1</sup> ) | $28 \pm 6$               | $39 \pm 6^{*}$           |
| Peak power output (W)                          | $699 \pm 173$            | $766 \pm 163*$           |
| Peak power output (W·kg <sup>-1</sup> )        | $7.7 \pm 1.6$            | $9.7 \pm 1.8^{*}$        |

39 40

2.2 Peak oxygen uptake determination

1 Peak oxygen uptake was determined using a Cortex II Metalyser 3B-R2 (Cortex, Biophysik,

2 Leipzig, Germany) utilising methods previously described (Knowles et al., 2015) and a

modified Storer Test (Storer et al., 1990) on an air-braked cycle ergometer (Wattbike Ltd.,
 Nottingham, UK). Coefficient of variation for VO<sub>2peak</sub> determination in our laboratory is <3%,</li>

and the metabolic equipment was serviced and maintained according to manufacturer's

6 recommendations. The same equipment was used at all testing phases. Cycle ergometers were

7 numbered, and each participant used the same ergometer for training and testing at all time

8 points. Manufacturer reliability has been specified as  $\pm 2\%$  across the full power range.

9

#### 10 2.3 Body composition determination

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

16

# 17 2.4 Exercise training

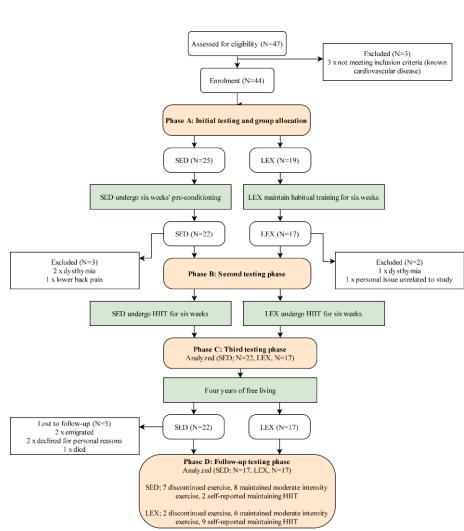
To account for the contribution of aerobic conditioning exercise in SED, participants were 18 initially tested at three phases in 2012 (A, B, and C; Figure 1), which were interspersed with 19 two six week training blocks as previously described (Knowles et al., 2015). Briefly, training 20 block 1 (between phase A and B) consisted of moderate aerobic training amounting to 150 21 22 min·wk<sup>-1</sup> for the SED group, in line with the physical activity guidelines (Garber et al., 2011). During this time, LEX maintained their current training, which allowed us to capture training 23 volumes and intensities. SED completed a minimum of two sessions per week. Participants 24 were given verbal instructions on the use of a Polar FT1 heart rate monitor (Polar, Kempele, 25 26 Finland) and exercise intensities were self-monitored, enabling recording of exercise time, and 27 average and peak heart rate (exercise was unsupervised, but heart rate was checked). The aim was to achieve an average heart rate reserve (HRR [(Karvonen and Vuorimaa, 1988)]) of 28 approximately 55% for the first two weeks of the intervention. This was increased to 60% HRR 29 for the subsequent weeks including 5-10 s of increased intensity (prescribed as 'vigorous' in 30 31 line with the ACSM guidelines (Garber et al., 2011)) every 10 min. The final two weeks included brief periods of exercise which elicited a HRR of 60-65% every 5 min. The mode of 32 training was optional, and included walking, jogging, and cycling. During the six-weeks of 33 preconditioning, SED exercised for  $160 \pm 15 \text{ min} \cdot \text{wk}^{-1}$ . Heart rate was recorded, using %HRR 34 as a determinant of exercise intensity. Exercise training logs, including heart rate data, were 35 submitted to the research team on a weekly basis to ensure participants adhered to instructions. 36 If required, interventions were amended, ensuring intensity and duration were achieved. No 37 38 nonexercise component (e.g. dietary guidance) was provided and no adverse events occurred, 39 according to self-reporting, when questioned at each training session by the lead researcher. Whilst SED underwent preconditioning, LEX maintained their habitual training (unsupervised) 40 which totalled 281  $\pm$  144 min wk<sup>-1</sup> structured training. Exercise type, frequency, intensity 41 42 (recorded by heart rate telemetry), and duration of training was recorded.  $214 \pm 131 \text{ min} \cdot \text{wk}^{-1}$ 43 and  $67 \pm 52 \text{ min} \cdot \text{wk}^{-1}$  was spent at <65% HRR, and >65% HRR respectively.

Both groups underwent HIIT from phase B to C (training block 2). HIIT was performed
on a cycle ergometer (Wattbike Ltd., Nottingham, UK) every five days, for six weeks (nine
sessions in total). Rationale for this frequency comes from our previous work which identified

five days of rest was required for recovery of peak power output (PPO) following HIIT in older 1 males (Herbert et al., 2015a). Sessions consisted of 6 x 30 s sprints at 40% PPO, with a cadence 2 between 75 rpm and 100 rpm, interspersed with 3 min active recovery. Rationale for this 3 intensity comes from our previous work which demonstrated this protocol achieved >90% HRR 4 5 in a similarly aged cohort, and achieved improvements in muscle power (Sculthorpe et al., 2017) which is imperative in ageing cohorts (Manini and Clark, 2012). Sessions were 6 7 conducted in groups of 4-6, supervised by a member of the research team in an exercise 8 physiology laboratory. HIIT was conducted according to participants' availability, but primarily during traditional working hours (i.e. 09.00-17.00 h). No adverse events were 9 reported, and no nonexercised component (i.e. nutritional guidance) was provided. During this 10 11 phase, HIIT was the sole exercise performed by both groups.

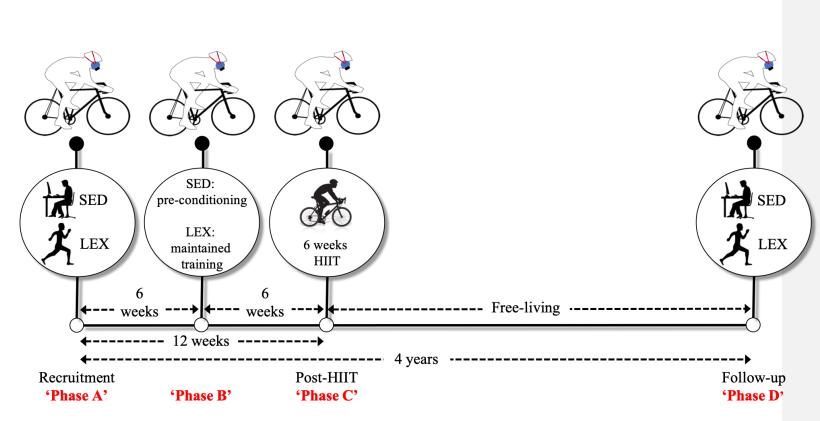
Phase D was completed 4 years later, using identical testing methods but without supervised training in the intervening 4 years (**Figure 2**). At follow-up (phase D), participants provided a current training diary. This included whether they were competing in masters events, the type of training (moderate aerobic conditioning, HIIT, and/or resistance training),

16 and the training volume per week, in minutes.



**Figure 1:** The CONSORT (Consolidated Standards of Reporting Trials) flow chart depicting transition of lifelong sedentary (SED) and lifelong exercising (LEX) participants though the

study. HIIT = high intensity interval training.



**Figure 2:** Peak oxygen uptake (VO<sub>2peak</sub>) was determined at Phases A, B, C and D. Sedentary (SED) vs. lifelong exercisers (LEX) were compared at Phase D in their original groupings determined in Phase A. Phase A-B, 6 week intervention period whereby SED conducted pre-conditioning exercise and LEX maintained normal training; Phase B-C, 6 weeks high-intensity interval training (HIIT) in both LEX and SED; Phase C-D, period of free-living without intervention; Phase A- D, 4-year follow-up period.

#### 2 2.5 Statistical Analysis

1

Data were analysed using Jamovi version 1.6.16. Following a Shapiro-Wilk test of normality 3 and Levene's test for homogeneity of variance, a two-way (group [SED, LEX] x phase [A, B, 4 C, D]) mixed factorial analysis of variance (ANOVA) was conducted to test for differences 5 6 between groups and time points. Subsequently, posterori T-tests with Bonferroni correction were conducted to determine differences between groups and between phases. A chi-square 7 8 tested for differences in training habits between LEX and SED. To establish the effect of 9 continuing or discontinuing exercise, a two-way (exercise habit ['continuer', 'discontinuer'] x phase [A, B, C, D]) mixed factorial ANOVA was conducted. Subsequently, posterori T-tests 10 with Bonferroni correction were conducted to determine differences between groups (unpaired 11 T-tests) and between phases (paired T-tests). Alpha level is reported as exact P values as 12 13 suggested by Hurlbert et al. (2019) and effect size for paired comparisons is reported as Cohen's 14 d whereby the difference in means between two samples was divided by the pooled standard 15 deviation (SD). Thresholds of 0.15, 0.40, and 0.75 for *Cohen's d* were interpreted as small, moderate, and large as these are appropriate in gerontology (Brydges, 2019). The analysis will 16 primarily deal with comparisons between phase A (enrolment) and D (follow up), and phase C 17 18 (post-HIIT) and D, consistent with other reunion studies (Johnson et al., 2019). Data are presented as mean ± standard deviation (SD) in text and figures are presented as grouped dot 19 plots, as recommended by Drummond and Vowler (2012). 20

# 2223 **3 Results**

21

# 24 *3.1 Peak oxygen uptake*

VO<sub>2peak</sub> data have been previously reported for phases A, B, and C of the original study
(Knowles et al., 2015). Briefly, both LEX and SED improved relative and absolute VO<sub>2peak</sub>
following HIIT, and LEX VO<sub>2peak</sub> was greater than SED VO<sub>2peak</sub> at all phases (all P<0.05).</li>

28 There was a main effect of time (P<0.001), and group (P<0.001) on relative VO<sub>2peak</sub>. However, there was no interaction between group and time (P=0.313). SED VO<sub>2peak</sub> was 27  $\pm$ 29 30 6 ml·kg·min<sup>-1</sup> at enrolment (phase A), which increased post-HIIT ( $32 \pm 6 \text{ ml·kg·min}^{-1}$  at phase 31 C; P<0.001, Cohen's d=0.81). Subsequently, SED VO<sub>2peak</sub> decreased to  $27 \pm 6 \text{ ml} \cdot \text{kg} \cdot \text{min}^{-1}$  at 32 phase D (P<0.001, Cohen's d=0.81 compared to C). Importantly, SED VO<sub>2peak</sub> at phase D was 33 not different from phase A (P=1.000, Cohen's d=0.01) or B (P=0.234, Cohen's d=0.23). LEX  $VO_{2peak}$  was 38 ± 6 ml·kg·min<sup>-1</sup> at enrolment (phase A), which was increased post-HIIT (42 ± 34 7 ml·kg·min<sup>-1</sup> at phase C; P<0.001, Cohen's d=0.67). Subsequently, LEX VO<sub>2peak</sub> decreased to 35 36  $39 \pm 9$  ml·kg·min<sup>-1</sup> at phase D (P<0.001, Cohen's d=0.46 compared to C). LEX VO<sub>2peak</sub> at phase D was not different from phase A (P=1.000, Cohen's d=0.11) or B (P=1.000, Cohen's 37 d=0.15). VO<sub>2peak</sub> was lower in SED compared to LEX at phase D (P<0.001, Cohen's d=1.73). 38 In terms of absolute VO<sub>2peak</sub>, results were concomitant with relative VO<sub>2peak</sub> in that there 39 40 was a main effect of time (P<0.001), and group (P<0.001). However, there was no interaction between group and time (P=0.641). SED VO<sub>2peak</sub> was  $2.38 \pm 0.33 \text{ l} \cdot \text{min}^{-1}$  at enrolment (phase 41 A), which increased post-HIIT (2.80  $\pm$  0.47 l·min<sup>-1</sup> at phase C; P<0.001, Cohen's d=1.03). 42 43 Subsequently, SED VO<sub>2peak</sub> decreased to  $2.39 \pm 0.46$  l·min<sup>-1</sup> at phase D (P<0.001, Cohen's d=0.88 compared to C). Importantly, SED VO<sub>2peak</sub> at phase D was not different from phase A 44 (P=1.000, Cohen's d=0.02) or B (P=1.000, Cohen's d=0.28). LEX VO<sub>2peak</sub> was  $3.08 \pm 0.50$ 45  $1 \cdot \text{min}^{-1}$  at enrolment (phase A), which was increased post-HIIT ( $3.43 \pm 0.52 \ 1 \cdot \text{min}^{-1}$  at phase C; 46 P<0.001, Cohen's d=0.69). Subsequently, LEX VO<sub>2peak</sub> decreased to 3.14 ± 0.55 l·min<sup>-1</sup> at 47 48 phase D (P=0.003, Cohen's d=0.54 compared to C). LEX VO<sub>2peak</sub> at phase D was not different from phase A (P=1.000, Cohen's d=0.17) or B (P=1.000, Cohen's d=0.05). Absolute VO<sub>2peak</sub> 49

so was lower in SED compared to LEX at phase D (P<0.001, Cohen's d=1.48).

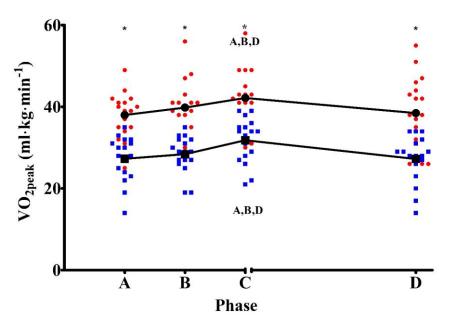


Figure 3: Peak oxygen uptake (VO<sub>2peak</sub>), in a group of sedentary (SED; blue squares) and
lifelong exercising (LEX; red circles) older males. Data are presented as means plus individual
data points. \*Denotes differences between groups at this experimental phase at the P<0.05</li>
level. A = Different from phase A at the P<0.05 level. B = Different from phase B at the P<0.05</li>
level. D = Different from phase D at the P<0.05 level.</li>

The proportion of subjects who reported discontinuing training, maintaining moderate 9 training, and maintaining HIIT differed between groups (P=0.023), with LEX self-reporting 10 more HIIT, and SED self-reporting more discontinuation from exercise. As there were not 11 12 enough SED participants who continued HIIT, and not enough LEX participants who discontinued exercise, we pooled these data into two groups; those who continued to exercise 13 (N=25; 15 LEX), and those who discontinued exercise (N=9; 2 LEX) in the four years of free 14 15 living. When comparing relative  $VO_{2peak}$  at phase C and D, there was an effect of time (P<0.001), and exercise continuation (continued exercising or discontinued exercising; 16 P=0.002), but no interaction between exercise continuation and time [P=0.399]). In pairwise 17 comparisons, those who continued exercising experienced a reduction in VO<sub>2peak</sub> over the four 18 years from  $39 \pm 7 \text{ ml} \cdot \text{kg} \cdot \text{min}^{-1}$  to  $36 \pm 9 \text{ ml} \cdot \text{kg} \cdot \text{min}^{-1}$  (N=25, P<0.001, Cohen's d=0.37), and 19 20 those who discontinued exercising also experienced a reduction in VO<sub>2peak</sub> from 30  $\pm$  7 ml·kg·min<sup>-1</sup> to  $25 \pm 9$  ml·kg·min<sup>-1</sup> (N=9, P=0.003, Cohen's d=0.62). When examining the SED 21 22 cohort only, there was an effect of time (P<0.001), and exercise continuation (continued exercising, discontinued exercising; P=0.008), but no interaction between exercise 23 continuation and time (P=0.755). In posteori Bonferroni corrected comparisons, those who 24 25 continued exercise experienced a reduction in VO<sub>2peak</sub> from  $35 \pm 3$  ml·kg·min<sup>-1</sup> at phase C to  $30 \pm 3 \text{ ml} \cdot \text{kg} \cdot \text{min}^{-1}$  at phase D (N=10, P<0.001, Cohen's d=1.05), and those who discontinued 26 27 exercising experienced a reduction in VO<sub>2peak</sub> from  $28 \pm 6 \text{ ml} \cdot \text{kg} \cdot \text{min}^{-1}$  at phase C to  $23 \pm 6$ 

2

ml·kg·min<sup>-1</sup> at phase D (N=7, P<0.001, Cohen's d=0.83). At phase A, SED 'continuers' VO<sub>2peak</sub> 1 was  $29 \pm 4$  ml·kg·min<sup>-1</sup> and SED 'discontinuers' VO<sub>2peak</sub> was  $25 \pm 7$  ml·kg·min<sup>-1</sup> (two-tailed 2 post hoc Bonferroni corrected T-test P=0.109, Cohen's d=0.84). At phase B, SED 'continuers' 3 VO<sub>2peak</sub> was  $30 \pm 3$  ml·kg·min<sup>-1</sup> and SED 'discontinuers' was  $26 \pm 5$  ml·kg·min<sup>-1</sup> (P=1.000, 4 Cohen's d=1.16). At phase C, SED 'continuers' VO<sub>2peak</sub> was  $35 \pm 3$  ml·kg·min<sup>-1</sup> and SED 5 'discontinuers' was 28 ± 6 ml·kg·min<sup>-1</sup> (P=0.289, Cohen's d=1.42). At phase D, SED 6 'continuers' VO<sub>2peak</sub> was 30 ± 3 ml·kg·min<sup>-1</sup> and SED 'discontinuers' was 23 ± 6 ml·kg·min<sup>-1</sup> 7 8 (P=0.185, Cohen's *d*=1.47).

9 To further investigate the effect of the intervening four years on aerobic capacity, we examined self-reported exercise intensity (n=14 moderate intensity exercise only and n=11 10 self-reported maintaining HIIT) on VO<sub>2peak</sub> from phase C to D. In this context, there was a main 11 effect of time (P<0.001), and intensity group (HIIT or moderate intensity [P<0.001]) on relative 12 13 VO<sub>2peak</sub>. There was an interaction between intensity group and time (P=0.012). HIIT group  $VO_{2peak}$  was 39 ± 5 ml·kg·min<sup>-1</sup> at enrolment (phase A), which increased post-HIIT (44 ± 7 14 ml·kg·min<sup>-1</sup> at phase C; P<0.001, Cohen's d=0.82). Subsequently, HIIT group VO<sub>2peak</sub> was 15 unchanged from C to D  $(43 \pm 7 \text{ml} \cdot \text{kg} \cdot \text{min}^{-1} \text{ at phase D}; P=1.000$ , Cohen's d=0.14 compared to 16 C). In terms of magnitude, the HIIT group VO<sub>2peak</sub> at phase D was moderately increased from 17 18 phase A (P=0.081, Cohen's d=0.66). The moderate intensity group VO<sub>2peak</sub> was  $31 \pm 6$ ml·kg·min<sup>-1</sup> at enrolment (phase A), which was greater post-HIIT ( $36 \pm 5 \text{ ml·kg·min}^{-1}$  at phase 19 C; P<0.001, Cohen's d=0.90). Subsequently, the moderate intensity group VO<sub>2peak</sub> decreased 20 21 to  $30 \pm 7 \text{ ml} \cdot \text{kg} \cdot \text{min}^{-1}$  at phase D (P<0.001, Cohen's d=1.20 compared to C). Moderate intensity 22 group VO<sub>2peak</sub> at phase D was not different from phase A (P=1.000, Cohen's d=0.18) or B 23 (P=0.403, Cohen's d=0.54). VO<sub>2peak</sub> was lower in the moderate intensity group compared to the HIIT at all phases (P $\leq 0.038$ , Cohen's  $d \geq 1.30$ ). 24 25

#### 26 *3.2 Body composition*

Body composition in both groups at all phases is displayed in **table 2**. In brief, there was no main effect of time (P=0.071) or group (P=0.143) on total body mass at the P<0.05 level. However, there was an interaction between group and time (P=0.027). There was no main effect of time (P=0.440), group (P=0.163), or interaction (P=0.689) on lean body mass at the P<0.05 level. There was no main effect of time (P=0.156) on body fat percentage. However, the effect of group (P=0.005), and interaction between group and time (P=0.014) did reach the P<0.05 level.

Table 2: Body composition at phase A, B, C, and D in lifelong sedentary (SED) and lifelong
 exercising (LEX) older males.

|         |                 | LEX (N=17)           | SED (N=17)                 |
|---------|-----------------|----------------------|----------------------------|
|         | Total body mass |                      |                            |
| Phase A |                 | 81.3 ± 12.4 kg       | 90.6 ± 17.8 kg             |
| Phase B |                 | $81.0\pm12.6~kg$     | $89.6 \pm 17.2 \text{ kg}$ |
| Phase C |                 | $81.7\pm12.6~kg$     | $89.8\pm18.1~\mathrm{kg}$  |
| Phase D |                 | $83.5\pm15.7~kg^{B}$ | $89.8\pm18.6~kg$           |
|         | Lean body mass  |                      |                            |
| Phase A |                 | $62.9\pm6.7~kg$      | $63.7\pm7.0\ kg$           |
| Phase B |                 | $62.0\pm6.8~kg$      | $63.4\pm7.5~kg$            |

| Phase C             | $62.2\pm7.1~kg$ | $64.0 \pm 8.3 \text{ kg}$ |
|---------------------|-----------------|---------------------------|
| Phase D             | $62.8\pm7.9~kg$ | $62.8\pm8.1~kg$           |
| Body fat percentage |                 |                           |
| Phase A             | $18.9\pm5.2\%$  | $26.4\pm7.1\%$            |
| Phase B             | $19.5\pm6.1\%$  | $25.5\pm7.6\%$            |
| Phase C             | $19.9\pm6.0\%$  | $24.9\pm7.6\%$            |
| Phase D             | $20.5\pm7.2\%$  | $25.8\pm7.5\%$            |

# 4 Discussion

<sup>B</sup>=different from phase B at the P<0.05 level.

4 In this reunion study, we evaluated changes in cardiorespiratory fitness 4 years after completing 5 the original intervention, relative to assessments at enrolment. Accordingly, the present study represents the intervention-related changes plus those persisting over the intervening 4 years, 6 aptly named the 'legacy effect'. The main findings of this study are; (1) a short-term HIIT 7 intervention which followed six weeks moderate intensity activity preserved VO<sub>2peak</sub> over a 8 four-year timespan, (2) lifelong exercise results in greater aerobic capacity than is achievable 9 10 following a short-term HIIT intervention, (3) a short-term HIIT intervention resulted in half of the original SED group maintaining self-reported exercise adherence for four years, and (4) 11 12 even in a group of highly motivated, life-long exercisers there is a attrition rate in terms of 13 exercise engagement of 12% over 4 years. Taken together these findings indicate that shortterm HIIT interventions can have substantial impacts on aerobic capacity, and by extension 14 cardiovascular risk. 15

The finding that a short-term HIIT intervention can preserve VO<sub>2peak</sub> over a four-year 16 17 period is both novel and important. While the observation that LEX had greater 18 cardiorespiratory fitness than LEX is not new, it is encouraging that irrespective of initial 19 fitness levels, both groups exhibited a similar response pattern following short-term HIIT and then after 4-years of 'free-living'. Few other studies have followed participants over such a 20 21 long-time frame. Moreover, the lack of decline between Phase A and D is impressive given 22 previous work. In the STRRIDE Reunion Study (Johnson et al., 2019), VO<sub>2peak</sub> declined by ~10% from enrolment to 10 years follow-up, although the vigorous intensity training groups 23 experienced only a ~5% decrease from pre-training to follow-up. This appeared primarily due 24 to the 8 months of vigorous intensity training creating the greatest increase in VO<sub>2peak</sub> (~10%, 25 26 like the increase observed in our 12-week study). The obvious differences between the STRRIDE Reunion Study and this investigation was the difference in follow-up time (10 vs. 4 27 years, respectively), the difference in intervention duration (8 months vs 12 weeks, 28 29 respectively), and the type of intervention (aerobic conditioning vs aerobic conditioning and 30 HIIT). However, despite differences, both Johnson et al (2019), and we surmise that a short-31 term exercise intervention has significant legacy effects for cardiorespiratory fitness, which may be intensity dependent. The seminal work of Rogers et al. (1990) reported that in the 32 absence of a training regime, sedentary individuals can expect to lose 10% of their aerobic 33 34 capacity over an 8-year period. The same data would therefore predict a 5% decline in VO<sub>2peak</sub> across the 4 years of our follow-up data which was not the case. One criticism of short-term 35 36 interventions is the tendency to demonstrate large effect sizes over the short term during supervised, laboratory based interventions, which may not be sustained over the longer term, 37 38 or may be reduced once moved out of a controlled laboratory setting, often termed the 'voltage 39 drop' of interventions (Chambers et al., 2013; Kilbourne et al., 2007). The present data supports

this view, since the intervention resulted in initial increases in aerobic capacity, which were
 lost over the 4-years.

Despite the 'free living' nature of the follow up period, most previously sedentary 3 4 participants remained engaged with some form of regular exercise and prevented further declines relative to their original VO<sub>2peak</sub>. Considering cardiorespiratory fitness is an 5 independent predictor of all-cause mortality (Kodama, 2009), and that small increases 6 correspond to large reductions in CVD risk (Kaminsky et al., 2013a) these observations have 7 8 important implications for the role of exercise prescription in managing aerobic capacity and CVD risk in advancing age. Furthermore, although this investigation concerned VO<sub>2peak</sub> 9 exclusively, it would be expected that the maintenance of fitness would likely be associated 10 with improved blood pressure, cholesterol, and other CVD risk factors. Future studies should 11 explore whether the extent of this protection extends beyond 4 years. If we assume the rate of 12 13 decline in the LEX group represents the best possible outcome, it is feasible that the SED group could maintain their level of fitness for a decade or more. In addition, future work should also 14 15 investigate the influence of variations in HIIT protocols.

16 There are additional important findings from this study which also warrant further discussion. Aside from the intervention, our original study provided no additional access to 17 supervised exercise or sport participation. However, the lead investigator did offer to provide 18 19 ongoing advice to any participants who requested it. Considering this, the adherence rate of 59% is substantial given that it was not an aim in the original investigation. The reason for the 20 21 relatively high adherence is unclear. The lead investigator (PH) is a member of the local community from which participants were recruited, and a local advocate for healthy ageing. It 22 may be that being known in the community, combined with regular advice contributed to the 23 higher adherence than anticipated, and future qualitative work will investigate this hypothesis. 24 Conversely, it may be that the early introduction of HIIT, and the increase in aerobic capacity 25 at Phase C resulted in participants feeling more able to take part moderate to high intensity 26 27 exercise and removed their fear of participation. Previous work indicated that HIIT in this age group resulted in reductions in pain and increase in general health (Knowles et al., 2015). 28 29 Others have also reported that sedentary participants find HIIT more enjoyable than moderate intensity exercise (Bartlett et al., 2011; Thum et al., 2017). It is plausible therefore that together, 30 31 these factors may have contributed to the relatively high exercise adherence over the 4-years. Our hypothesis that greater aerobic capacity at phase C as a result of HIIT resulted in greater 32 likelihood of exercise participation in the subsequent four years is supported by comparison 33 34 between 'continuers' and 'discontinuers'. We observed that individuals classified as 'continuers' 35 of exercise in the four years of free living had a greater VO<sub>2peak</sub> at enrolment (phase A) and 36 throughout the experiment. Although this was not at the P<0.05 level, the large effect size and difference of >1 MET (3.5 ml·kg·min<sup>-1</sup>) at all phases suggest this was a clinically meaningful 37 difference. Interestingly, continuers had a greater aerobic capacity than discontinuers, and they 38 39 were more responsive to the HIIT stimulus (i.e. the difference in VO<sub>2peak</sub> between phase A and phase C) was greater in continuers compared to discontinuers (5.3 ml·kg·min<sup>-1</sup> vs. 3.3 40 41 ml·kg·min<sup>-1</sup> respectively), suggesting that absolute fitness, but also adaptation to training, may underpin increased exercise participation. 42

A final unanticipated finding of the present study was that the attrition rate in the LEX group was higher than anticipated at 12% across the 4 years. Given that this group where originally included to act as a positive control, they represent a cohort of individuals who have a strong and persistent drive to exercise and maintain physical fitness and are likely therefore, to represent the greatest degree of adherence possible in this age group. While admittedly in a relatively small cohort, the present data suggests the best adherence realistically achievable in

free-living studies. Thus, the 59% adherence of the SED group in this study, and adherence in
 general in other studies of the same age-range, should be viewed against this best feasible 88%
 (LEX group) outcome, rather than the best theoretical adherence of 100%.

4 There are some strengths and limitations of the current study that should be noted. A 5 specific strength is the number of participants included in the follow up. Thirty-four (87%) of the original cohort agreed to be re-measured, which is comparable to the Johnson et al (2019) 6 7 return success rate for STRRIDE (Studies of Targeted Risk Reduction Interventions through 8 Defined Exercise) reunion study. Moreover, we have follow-up data regarding the reason for not being able to assess the remaining 10 participants, five of whom dropped out before phase 9 10 B of the original study. However, an important limitation is the use of self-reported exercise at phase D rather than an objective assessment. However, given the duration of follow up, 11 objective methods were unfeasible. Moreover, attempts to use objective measures at phase D 12 would likely have suffered from a Hawthorn effect as others have noted (DÖSSEGGER et al., 13 2014). Likewise, self-reported activity of continuation or discontinuation of exercise were only 14 15 recorded on one occasion which may not be reflective of the entire follow-up period. Although, repeated measurement could have violated a true 'free-living' period by altering said 16 17 behaviours. Consequently, we accepted these as limitation as an unavoidable consequence of 18 the duration and nature of follow-up. In addition, the assessed aerobic capacity of participants was broadly commensurate with their reported levels of physical activity. Secondly, non-19 20 exercise control groups from phase A to phase D would have strengthened the conclusions of this study. However, recruiting a SED and LEX group who did not undertake the HIIT 21 22 intervention was not the aim of our initial work (Knowles et al., 2015). Although non-exercise 23 control groups would have provided additional credence to the legacy effects we propose here in, and also to ascertain whether there was a true prevention in a reduction of VO<sub>2peak</sub>, the work 24 25 of Rogers et al. (1990) and Johnson et al. (2019) both detail expected decreases in aerobic capacity, so the lack of  $VO_{2peak}$  loss reported here is noteworthy. While the exercise training in 26 27 Phases A and B were of an aerobic nature, exercise modalities performed during the free-living 28 period may have varied within and between participants. Accordingly, we are unable to 29 ascertain the isolated influence from a dichotomous classification of endurance or resistance exercise types. Although, our intention was to assess cardiorespiratory fitness mediated 30 31 through self-directed exercise during the free-living phase. Nonetheless, the contributions from 32 exercise modality warrants future consideration. Furthermore, while we assessed a single, indirect marker of cardiovascular risk through cardiorespiratory fitness, we were unable to 33 report on other clinical markers related to cardiometabolic health. Future work should consider 34 35 these considering that the longer term implications of cardiorespiratory fitness and cardiometabolic parameters may be intensity dependant Johnson et al. (2019). Thus, extension 36 37 of our work pertaining to low frequency, short term HIIT would be beneficial.

In conclusion, the addition of six weeks of HIIT following six weeks of moderate 38 intensity exercise training increasedVO<sub>2peak</sub> to the extent that it was unchanged four years later 39 in a cohort of LEX and SED older men. Thus, this combination of exercise appears a potent 40 41 stimulus to increase (in the short-term) or maintain (in the long-term) VO<sub>2neak</sub> in older males. 42 The implication of these data is that exercise training concluding with 6 weeks HIIT can be 43 utilised by practitioners and healthcare professionals to increase VO<sub>2peak</sub> over a short period of 44 time, which appears to be a catalyst for maintained cardiorespiratory fitness for years to come. 45 There is an emergent body of evidence that endorses HIIT as an effective alternative to traditional endurance training that can yield enhancements in both cardiorespiratory fitness and 46 47 a variety of health outcomes (Buchheit and Laursen, 2013; Gibala et al., 2012; Sylta et al., 2017, 2016; Yasar et al., 2019) and consequently, improvements in cardiorespiratory fitness 48 49 have a significant impact on health and survival (Kaminsky et al., 2013b; Kodama et al., 2009).

#### 2 Authors contributions statement

Peter Herbert: Conceptualization, methodology, validation, investigation, resources, project
 administration, writing – review & editing. Lawrence Hayes: Formal analysis, writing –
 original draft, review & editing, visualization. Alexander Beaumont: Formal analysis, writing
 original draft, review & editing, visualization. Fergal Grace: Conceptualization,
 methodology, validation, investigation, project administration, supervision. Nicholas
 Sculthorpe: Conceptualization, methodology, validation, investigation, project
 administration, writing – review & editing, supervision.

#### 11 Conflict of interest statement

- 12 The authors have no conflict of interest to declare.
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