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A ten year follow-up of key gas exchange exercise parameters in a general population – Results of the Study of Health in Pomerania

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Abstract

Background:

Cardiopulmonary exercise testing (CPET) is a frequently used method for the evaluation of the cardiorespiratory system. The prognostic relevance of the measured parameters is commonly known. Longitudinal data on cardiorespiratory fitness in a large sample of well characterised healthy volunteers are rare in literature.

Methods:

CPET data of 615 healthy individuals who voluntarily took part in the Study of Health in Pomerania (SHIP) at three times were analysed. The median observation time was 10.5 years. The age range was 25 to 85 years.

Results: Over the observed timeframe and with rising age a decline in maximum power, oxygen uptake and oxygen uptake at the anaerobic threshold was detectable. This decline was aggravated with rising age. For the VÉ/VCO_2 slope an increase in individuals older than 50 years was measured only.

Conclusion:

The present study affirms the decrease in aerobic capacity with increasing age in a selected, well characterised, healthy study sample, that seems to be less pronounced in women.

Introduction

Cardiopulmonary exercise testing (CPET) is used in clinical practice to measure pulmonary, cardiac and musculoskeletal function to assess the severity of an existing disorder. Several parameters of cardiorespiratory fitness assessed by CPET (e.g. VO_2peak, VO_2@AT, O_2-pulse, VÉ/VCO_2 slope) are known to have prognostic relevance. Hence, they are used for risk stratification in patients with cardiorespiratory diseases (1).

In addition to its clinical application, CPET is used in epidemiological studies. For example, high levels of cardiorespiratory fitness are related to a lower risk of mortality (2-4) and cardiovascular diseases (5, 6). The Norwegian HUNT study demonstrated a cross-sectional association between objectively measured VO_2peak and levels of conventional cardiovascular risk factors in 20- to 90-year-old volunteers (2,368 men and 2,263 women) (7). Further cross-sectional studies confirmed age and sex as important determinants of cardiorespiratory fitness (8-10) and consistently confirmed higher age to be related to lower levels of aerobic fitness. Another study in 751 men and women aged 20-85 reported a linear decrease (8% per decade) in VO_2peak for both sexes, starting from the age of 30 (11). Likewise, a linear decrease in aerobic capacity (VO_2peak and VO_2@AT) was seen in 298 men and woman aged 55-86 (12). In a much larger study that analysed data of 4,494 volunteers, a decline in VO_2peak of almost 50% has been found for both sexes in a younger age group (20-29 years) compared to an older age group (70-79 years), this is a decline of 10% per decade (13). Finally, in a meta-analysis of 17 cross-sectional studies the decline in aerobic capacity of 10% per decade was confirmed (14). Another meta-analysis of 242 studies with 13,828 male subjects (15) showed no significant difference in the decrease of VO_2peak over time depending on age or physical activity. In contrast, a meta-analysis of 109 studies with 4,484 female subjects found a greater decrease in aerobic capacity with age in physically active women (16). The decrease in VO_2peak and O_2 pulse with higher age was also confirmed in a further meta-analysis (17).

Smaller longitudinal studies confirmed the finding of a decrease in aerobic capacity with increasing age [overview in (14)]. For example, in one study that initially included 441 volunteers aged 55-85 only 115 were examined after 10 years, and only data of 62 were included into the analyses. Among this very selected study sample, however, VO_2peak decreased by 14% in men compared to only 7% in women (18). Furthermore, three population-based longitudinal studies (375 women, 435 men; age 21-87 years, median observation 7.9 years, (19); 339 women, 253 men, age 53-87 years, median observation 6.3 years, (20); 579 men, age 42-60 years, median observation 11 years, (21), demonstrated a decrease of VO_2peak of about 10% per decade for both sexes.

In summary, it can be concluded that in both cross-sectional and longitudinal studies an age-related decrease in aerobic capacity has been consistently observed for both sexes. However, available data from longitudinal studies in volunteers were often limited by small sample sizes (n mostly < 100). Up to now, only two population based longitudinal larger studies with multiple measurement times are available (19, 20). Only the data by Fleg et al. (19) report data of a wide age range (21-87 years). These data were raised between 1978-98 as part of the “Baltimore Longitudinal Study of Aging“.

The aim of our study was to analyse the course of aerobic capacity in a large sample of the population-based Study of Health in Pomerania (SHIP) between 2002 and 2019, under consideration of a wide age range and at three different measurement times.

Methods

1. Description of the samples

SHIP (Study of Health in Pomerania) is a population-based study, conducted in a region in north-eastern Germany (West Pomerania) with about 213,000 inhabitants. The methodological approaches have already been described previously in detail (22, 23). In brief, the first examination (SHIP-0) included 4,308 subjects (response rate 68.8%) around the cities of Greifswald and Stralsund and was carried out between 1997 and 2001. Between 2002-2006 still living participants were invited to the first follow-up examination (SHIP-1) and 3,300 (corresponding to a response rate 83.6%) could be examined. At this time point, both pulmonary function test and CPET were offered for the first time on a voluntary basis. A total of 1,703 (51.6 %) subjects participated in CPET. The second follow-up examination (SHIP-2) was conducted between 2008-2012, with 2,333 subjects (i.e. 67.4% response rate) being included. Among those a total of 1,442 (61.8 %) subjects volunteered to participate in CPET. During the third follow-up examination (SHIP-3) a total of 1,718 subjects (response rate 39,9%) were examined between 2014-2019, 1,066 (62.0 %) of whom received CPET (see flow chart below).

For our analyses data of 615 subjects (317 men and 298 women) who participated in CPET at all three examination points were available. The median observation time was 10.5 years.

The study conformed to the principles of the Declaration of Helsinki as reflected by the approval by the Ethics Committee of the University of Greifswald.

2. Cardiopulmonary exercise testing

The method used in SHIP for CPET has been described in detail previously (24, 25). In brief, symptom-limited CPET was performed according to a modified Jones protocol using a calibrated electromagnetically braked cycle ergometer (Ergoselect 100, Ergoline, Germany). Gas exchanges were measured breath-by-breath using an Oxycon Pro with a Rudolf's mask (JÄGER/VIASYS Healthcare System, Hoechberg, Germany).

In SHIP-1 and SHIP-2, the assessment of VO_2peak, VO_2@AT, O_2 pulse and VÉ/VCO_2 slope was based on the printout, while in SHIP-3 these parameters were assessed using a computer-aided algorithm. Therefore, a "correction formula" had to be applied. Here, which has been developed based on a random sample of SHIP-1 (n=446) and SHIP-2 (n=606) by comparing the values derived by the original printout-based method with those calculated by a double determination using the computer-assisted method. Differences for VO_2@AT and VÉ/VCO_2 slope and the following were calculated by linear regression and applied to the data for correction: VO_2@AT: SHIP-1: 149.04 + 0.83*VO_2@AT, SHIP-2: 104.67 + 0.93*VO_2@AT; VÉ/VCO_2 slope: SHIP-1: 5.11 + 0.78*VÉ/VCO_2 slope, SHIP-2: -0.29 + 0.93*VÉ/VCO_2 slope.

Statistical analyses

To describe differences between participants and non-participants at the follow-up examinations, we compared these two groups by median, 25th, and 75th percentiles for continuous baseline data and by absolute numbers and percentages for categorical baseline data. The progression of continuous variables over the three time points (SHIP-1, 2, 3) is described by box plots and the progression of categorical variables is given by bar plots. Differences in continuous variables between SHIP-1 and SHIP-3 were evaluated by t-tests for paired data (continuous data) or by McNemar tests (categorical data). Stratified by sex we associated age with 5-year and 10-year changes of maximal power, VO_2peak, VO_2@AT, VÉ/VCO_2 slope, and O_2 pulse by linear regression models. For VO_2peak we furthermore calculated expected values at the 5-year and 10-year follow-up using the median formulas described by Gläser et al. (25). The expected VO_2 peak values were calculated by dividing the coefficient for age from the reported formulas multiplied with the respective individual follow-up time from the VO_2 peak value observed in SHIP-1, e.g. in men the formula for median VO_2 peak from Gläser et al. was "254.761 – 22.6925 * age + 17.2463 * height + 4.4114 * weight" assuming that in males the VO2 peak decreases by 22.6925 ml/min per year. For calculation of the predicted value we took the VO_2 peak value at baseline and subtracted 22.6925 ml/min per year of follow-up. The observed values in SHIP-2 and SHIP-3 were associated respectively with the expected values in SHIP2 and SHIP-3 and the R^2 were calculated. These calculations were conducted in the total population as well as sex-stratified. In all calculation a $p < 0.05$ was considered as statistically significant. Analyses were done with Stata 16.1 (Stata Corporation, College Station, TX, USA).

Results

In Table 1 we compare the baseline characteristics of the 615 individuals who participated at all three time points with the baseline characteristics of the 1087 individuals who did not participate at all three time points. Individuals participating at all three time points were slightly younger, were more often males but less often smokers, had a lower body mass index (BMI), and had less often type 2 diabetes mellitus, hypertension, stroke, and myocardial infarction than individuals not available at all three time points. Baseline markers of lung function and CPET were in tendency better in individuals attending CPET examinations at all three time points.

Of the 615 individuals available at all three time points, 141 individuals were at baseline between 25 to 39 years old, 328 individuals between 40 and 59 years old, and 146 individuals between 60 and 85 years old. The amount of current smokers decreased from 20.5% at baseline to 14.8% and 13.4% at the follow-up's (Figure 1). The decrease from baseline to the first follow-up was significant ($p<0.001$) but not the decrease from the first to the second follow-up ($p=0.108$). The median BMI increased from 25.9 kg/m^2 to 27.0 kg/m^2 and 27.3 kg/m^2 at the follow-up's (Figure 1). Increases from baseline to the first follow-up and between the first and the second follow-up were statistically significant ($p<0.001$). The prevalence of type 2 diabetes increased from 5.0% at baseline to 7.6% ($p<0.001$) and 9.1% ($p=0.035$) at the follow-up's. Likewise, prevalence of arterial hypertension increased from 39.2% to 50.2% ($p<0.001$) at the five-year-follow-up and to 63.1% ($p<0.001$) at the second-follow-up. Prevalence of myocardial infarction (baseline 1.6%; 5-year-FU 2.4% [p=0.063]; 10-year-FU 3.4% [p=0.109]) and stroke (baseline 0.8%; 5-year-FU 1.6% [p=0.063]; 10-year-FU 3.3% [p=0.007]) increased moderately during follow-up.

While in individuals younger than 60 years no decrease in maximum power until the second follow-up was observed, there was a significant decrease in individuals older than 60 years (Figure 2, Tables 2 & 3). Overall, the mean maximum power decreased until the first follow-up from 165 W to 160 W and afterwards increased again to 165 W during the second follow-up. The mean peak oxygen uptake decreased significantly in the group of individuals older than 40 years over the whole study period, whereas in younger individuals only a slight decrease was observed (Figure 3, Tables 2 & 3). In males the mean peak oxygen uptake decreased from 2507 ml/min at baseline to 2339 ml/min and 2263 ml/min at the follow-ups corresponding to a mean decrease of 8.5% over the 10 years of follow-up. In females the mean peak oxygen uptake decreased from 1678 ml/min at baseline to 1573 ml/min at the first follow-up and afterwards slightly increased to 1614 ml/min during the second time period. Over the ten years of follow-up the mean peak oxygen uptake decreased by 3.1% in women. The mean oxygen uptake at the anaerobic threshold decreased in all age- and sex-groups over the whole study period except for women older than 65 years (Figure 4). Significant decreases were only observed in men older than 60 years and women younger than 40 years (Table 2). Overall, there was a decrease in mean oxygen uptake at the anaerobic threshold in the first time period, while in the second time period mean values slightly increased in men and women (Table 3). For the VÉ/VCO_2 slope mean values increased significantly only in individuals older than 50 years (Figure 5, Tables 2 & 3). While there was an increase of mean VÉ/VCO_2 slope during the first follow-up, mean VÉ/VCO_2 slope values decreased between the first and second follow-up in men and women (Figure 5). The mean maximum oxygen pulse decreased significantly in individuals older than 40 years over whole study period, while in the group of individuals younger than 40 years only a slight decrease was observed (Figure 6, Table 2 & 3). In males the mean maximum oxygen pulse decreased in both time periods, whereas in women an increase was observed over the second time period (Figure 6).

The expected peak oxygen uptake levels for the first follow-up as determined from the formula by Gläser et al. (25) showed a good correlation with the observed peak oxygen uptake levels at the first follow-up (R^2=0.73, Figure 7). This correlation was slightly higher in males (R^2=0.58) than in females (R^2=0.50). The correlation of the expected versus the observed peak oxygen levels for the second follow-up was 0.60 (Figure 8) and comparable between males and females (both R^2=0.45). In tendency lower peak oxygen uptake levels (values between 1000-2000 ml/min) were underestimated, while higher peak oxygen uptake levels [values of 2500 ml/min (men) or 1500 ml/min (women)] were overestimated.

Discussion

At three different measurement points 615 individuals (317 men, 298 women), age range 25-85 years, were examined with CPET as part of the epidemiologic study “Study of Health in Pomerania”. The median observation time was 10.5 years. In summary, males showed a decrease in cardiorespiratory fitness (presented as VO_2peak) of -8.5 % over 10 years. Females showed also a decrease in aerobic capacity, but only of -3.1% over 10 years. For the first time the decrease in cardiopulmonary performance with age was proven in a large population based, European study.

This phenomenon (the age-dependent loss of aerobic capacity) was demonstrated also in current cross-sectional (26) as well as longitudinal studies (21) with CPET. Studies with other functional methods [age-specific tests in 1,288 persons, (27)] and survey data [study on adult health in Germany 2008-2011,(28)] can also be used to prove this.

However, this trend is not only evident in older volunteers, but can also be observed in younger ones (29-31). The data on the age-dependent loss of aerobic capacity were mainly obtained from cross-sectional investigations using linear models. However, longitudinal surveys show a disproportionate decrease in aerobic capacity with increasing age (19). It was between 8-18 % for the first 10 years and 15-34% for the following 10 years depending on the amount of training. Our study shows over 10 years for both men and women a lower decrease of VO_2peak in younger age groups (men: 20-39 years decline -1.6%; 40-59 years decline -8.1%; over 60 years decline -14.9%; women: 20-39 years increase +0.3%; 40-59 years decline -2.2%; over 60 years decline -10.3%). Data from previous work already indicate that the VO_2peak for women is less waste than for men in old age (12, 32).

In agreement with other authors, we were able to show statistical significance when comparing calculated and measured values for the VO_2peak. The prediction of VO_2peak values for 5 and 10 years based on our data shows a clinically acceptable correlation (r=0.6-0.7 in the whole group). For both sexes, however, higher values of VO_2peak overestimate future results. This aspect should be considered in the evaluation, especially in the context of clinical decisions.

A variety of factors are cited to explain this reduction, including chronic disease, the presence of cardiovascular risk factors and lack of physical activity. Physiological factors influencing aerobic capacity (decrease of maximum heart rate, reduced stroke volume, reduction of peripheral arteriovenous exhaustion, reduction of oxidative capacity of working muscles, etc.) also change with increasing age (33-37). Recently, the age-related factors influencing aerobic capacity were summarised again (38). Among other things, it was shown that lung-functional parameters are involved in the decline of performance over time. This fact could be proven by 3,332 persons aged 18-35 years when the study was repeated after 20 years (2,735 participants) (39). It was found that a greater decrease in fitness was documented in individuals with a greater decrease in lung function (FEV_1 or FVC).

VO2 peak does not drop in the same way between age groups and between women and men. Possible reasons for gender specific differences may be weight gain, activity, hormones (40, 41), alcohol consumption (42) as well as cardiovascular risk factors and socioeconomic factors (43). The number of included participants with cardiovascular diseases (myocardial infarction, stroke), except for arterial hypertension, is negligible and therefore not influencing the results.

Conclusion

In summary, it can be concluded that in cross-sectional and longitudinal studies a decrease in aerobic capacity is concordantly observed with increasing age. In the literature, an exponential decrease is observed in the course of age (3-6% per decade for 20 and 30 year olds and about 20% per decade for 70 year olds and older). These data can be confirmed by our longitudinal study over 10 years (considering the selected age groups). As already shown in previous studies, the age-related decrease seems to be somewhat less pronounced in women.

Limitations

Small deviations of the values are to be assumed by the retrospective introduction of a correction factor with different data collection. In contrast to the compilation of normative values, we included all test persons in the current analysis, so that those with ventilation disorders, chronic lung or heart diseases known from anamnesis and chronic medication (ATC codes C01, 07, 08 and R03) were also included.

We have tested all subjects with CPET after a modified JONES protocol on the bicycle, with no differences in the decrease of aerobic capacity with increasing age in the literature [bicycle vs. treadmill, meta-analysis by Wilson et al. (15)].

Cardiorespiratory fitness shows a high association with the socioeconomic status of the subjects (43), which we did not consider in our analyses.

The measurement of the AT shows an interobserver variability in asymptomatic volunteers (44). This has to be considered when interpreting the results.

The non-linear models used in the literature to describe the course of the CPET data were not used due to the short measurement times. In both older analyses (32) and more recent studies (10), they seem to be an alternative to linear models in the representation of age-dependent VO_2peak progressions from cross-sectional studies.

Figure legend
Figure 1. Sex-specific developments of smoking status and BMI over the 3 time points (left males; right females).
Figure 2. Age- and sex-specific changes in maximum power over the 3 time points (left males; right females). Decline of the mean maximum power over 5 and 10 years for both sexes.
Figure 3. Age- and sex-specific changes in peak oxygen uptake over the 3 time points (left males; right females). Decline of the peak oxygen uptake over 5 and 10 years for both sexes.
Figure 4. Age- and sex-specific changes in oxygen uptake at the anaerobic threshold (AT) over the 3 time points (left males; right females). Change of the oxygen uptake at the anaerobic threshold over 5 and 10 years for both sexes.
Figure 5. Age- and sex-specific changes in VE/VC02 Slope over the 3 time points (left males; right females). Change of the breathing efficiency at the anaerobic threshold over 5 and 10 years for both sexes.
Figure 6. Age- and sex-specific changes in oxygen pulse at peak over the 3 time points (left males; right females). Decline of peak oxygen pulse over 5 and 10 years for both sexes.
Figure 7. Correlation between expected and observed peak oxygen uptake values at the first follow-up in the total (black), male (blue) and female (red) population.
Figure 8. Correlation between expected and observed peak oxygen uptake values at the second follow-up in the total (black), male (blue) and female (red) population.

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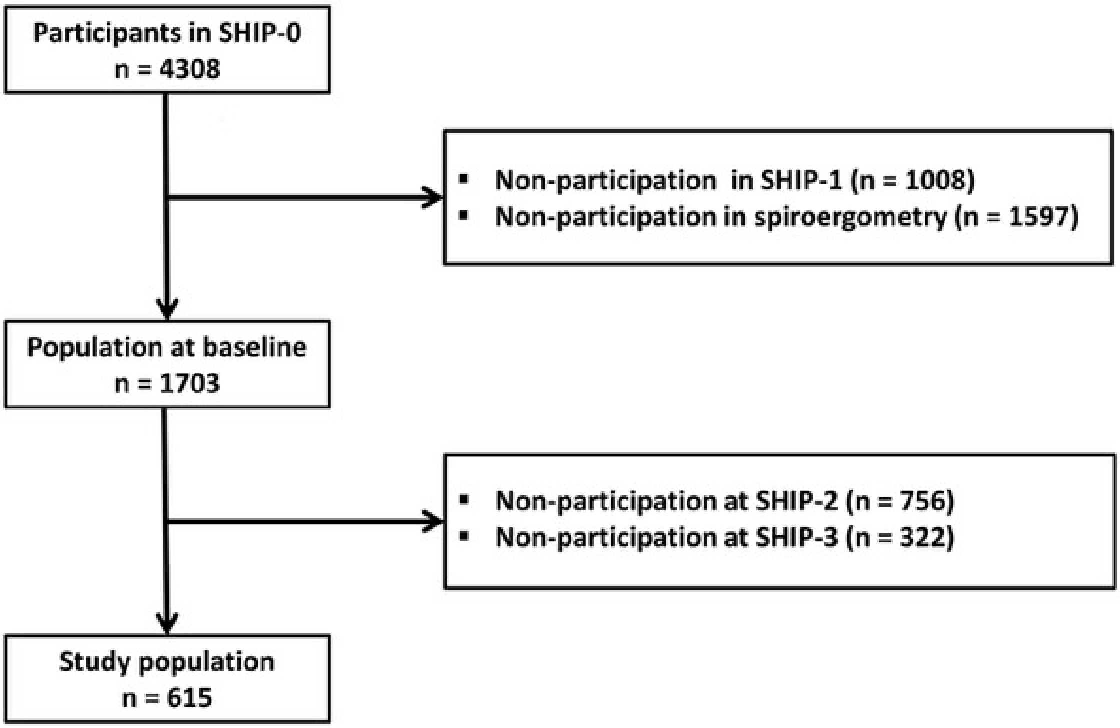
Statement of interest:

The authors do not report any conflicts of interest.

Flow-Chart SHIP



Abbreviation list

CPET	Cardiopulmonary exercise testing
SHIP	Study of Health in Pomerania
VÉ/VCO_2 slope	breathing efficiency
VO_2peak	peak oxygen uptake
VO_2@AT	oxygen uptake at anaerobic threshold
O_2-pulse	oxygen pulse
BMI	body mass index
FU	follow-up
W	Watt
FEV_1	forced expiratory volume in one second
FVC	forced vital capacity
ATC code	anatomical-therapeutic-chemical code

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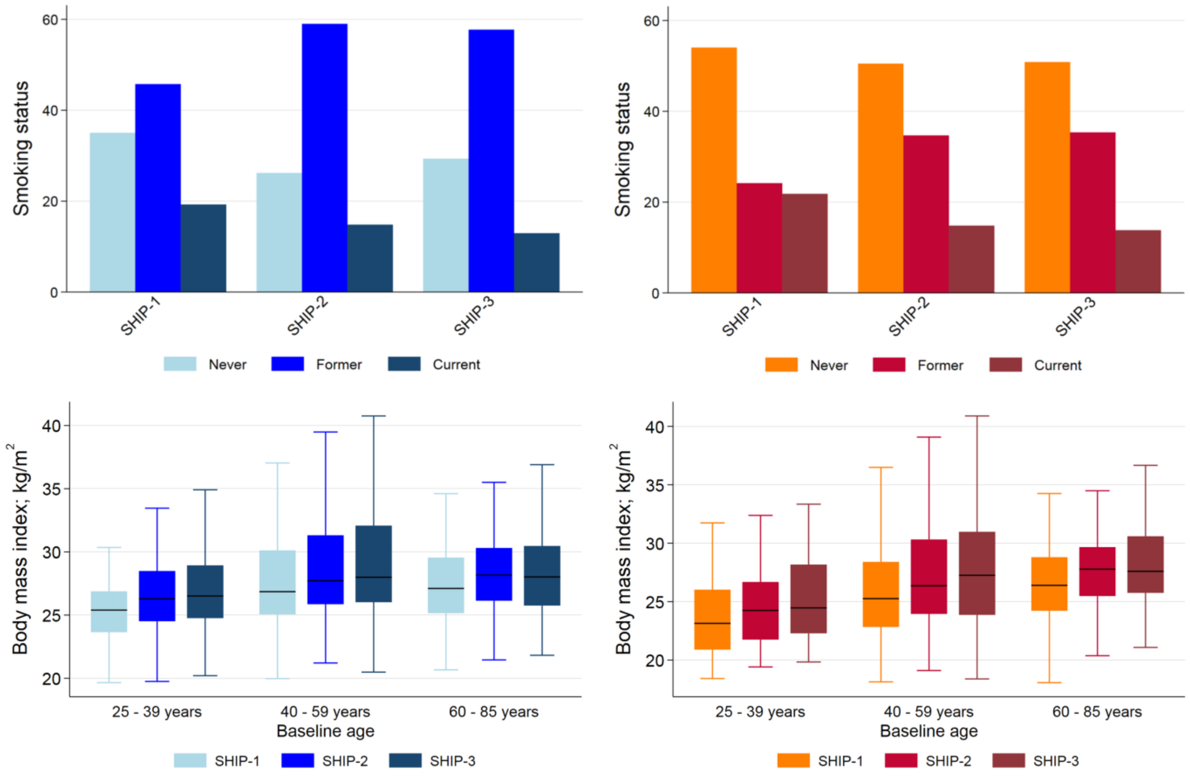
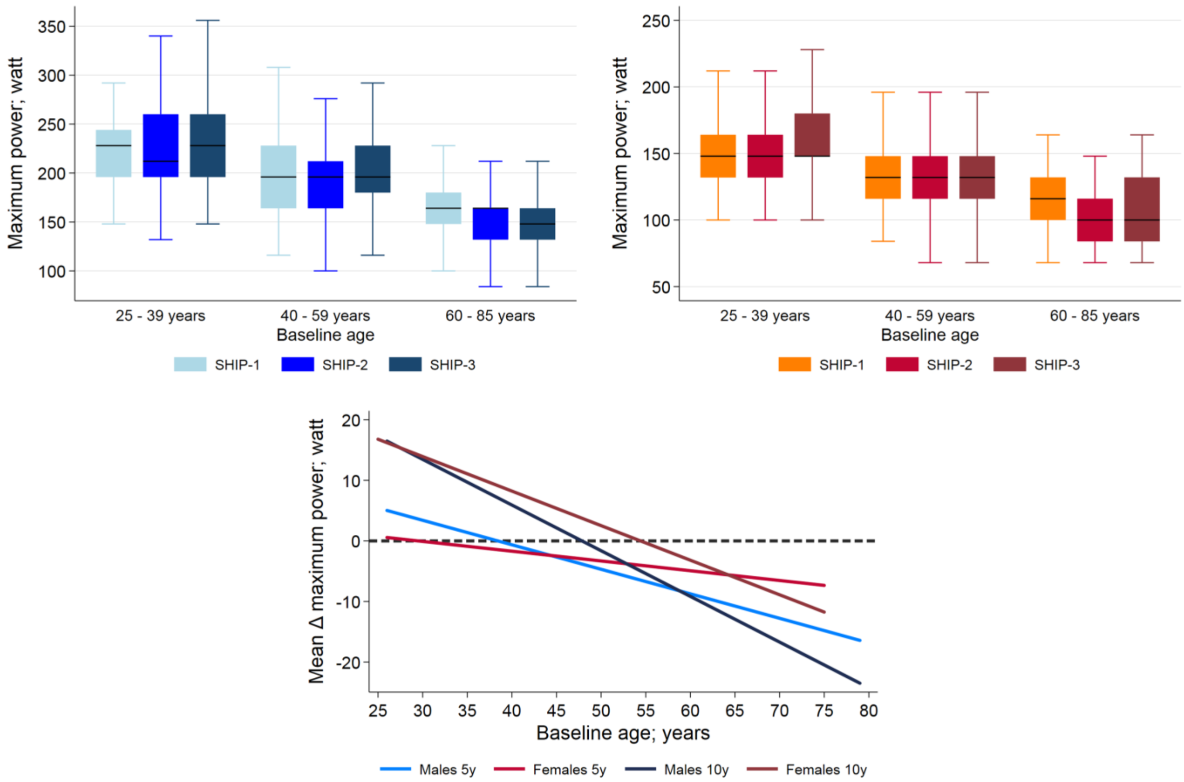
Figure 1



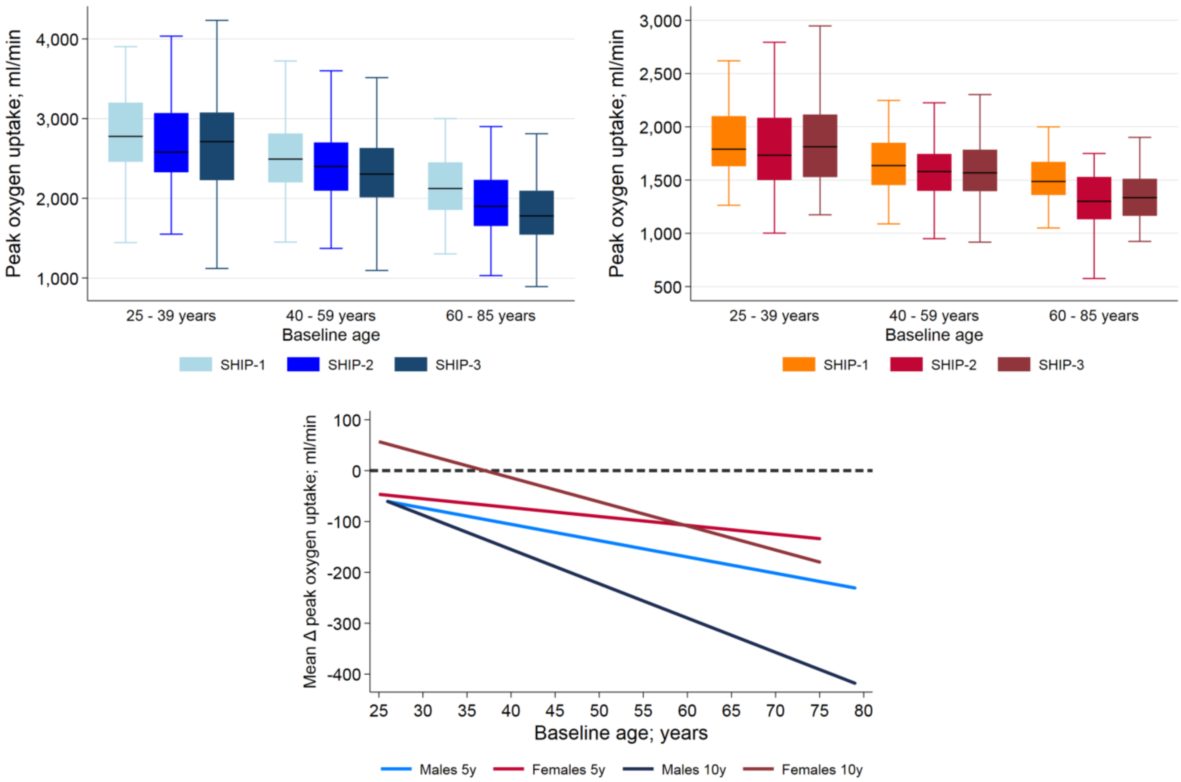
Smoking status
60
40
20
0
SHIP-1
SHIP-2
SHIP-3
Never
Former
Current
Smoking status
60
40
20
0
SHIP-1
SHIP-2
SHIP-3
Never
Former
Current
Body mass index; kg/m2
40
35
30
25
20
25 - 39 years
40 - 59 years
60 - 85 years
Baseline age
SHIP-1
SHIP-2
SHIP-3
Body mass index; kg/m2
40
35
30
25
20
25 - 39 years
40 - 59 years
60 - 85 years
Baseline age
SHIP-1
SHIP-2
SHIP-3

Figure 2



Maximum power; watt
350
300
250
200
150
100
25 - 39 years
40 - 59 years
60 - 85 years
Baseline age
SHIP-1
SHIP-2
SHIP-3
Maximum power; watt
250
200
150
100
50
25 - 39 years
40 - 59 years
60 - 85 years
Baseline age
SHIP-1
SHIP-2
SHIP-3
Mean Δ maximum power; watt
20
10
0
-10
-20
25
30
35
40
45
50
55
60
65
70
75
80
Baseline age; years
Males 5y
Females 5y
Males 10y
Females 10y

Figure 3



Peak oxygen uptake; ml/min
4,000
3,000
2,000
1,000
25 - 39 years
40 - 59 years
60 - 85 years
Baseline age
SHIP-1
SHIP-2
SHIP-3
Peak oxygen uptake; ml/min
3,000
2,500
2,000
1,500
1,000
500
25 - 39 years
40 - 59 years
60 - 85 years
Baseline age
SHIP-1
SHIP-2
SHIP-3
Mean Δ peak oxygen uptake; ml/min
100
0
-100
-200
-300
-400
25
30
35
40
45
50
55
60
65
70
75
80
Baseline age; years
Males 5y
Females 5y
Males 10y
Females 10y

Figure 4

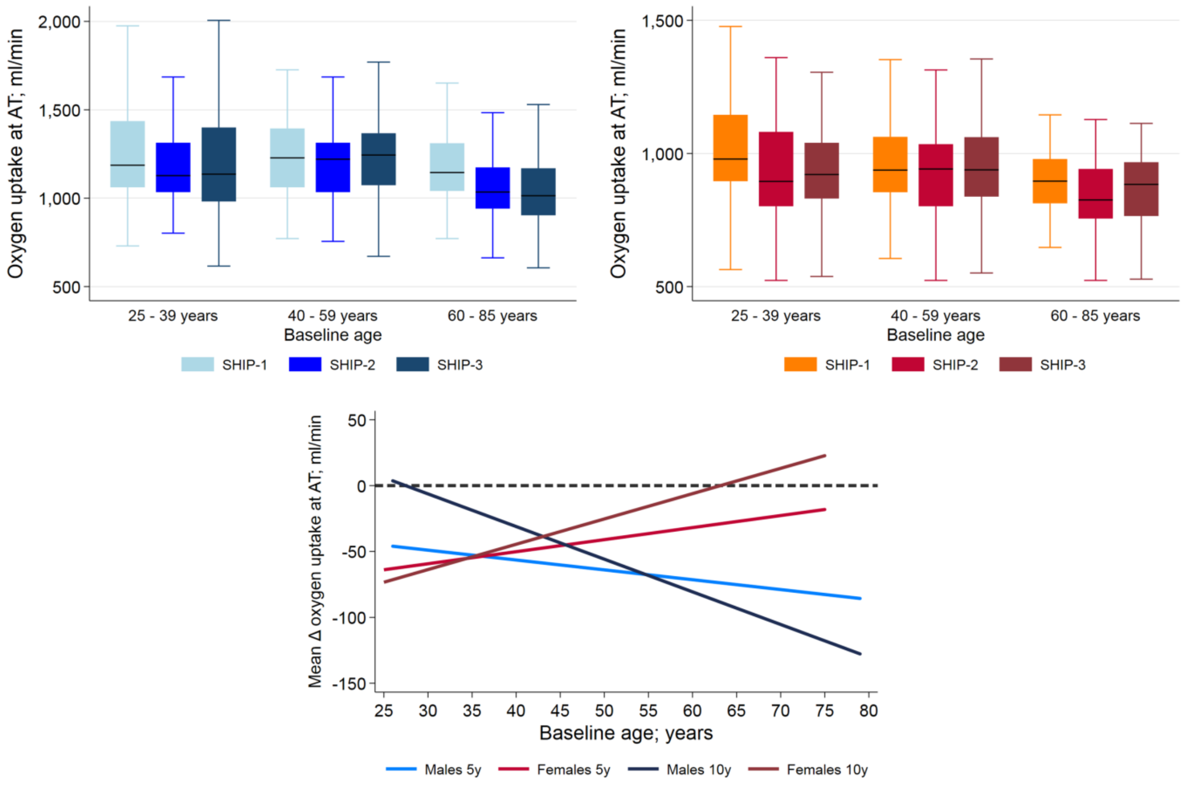

Oxygen uptake at AT; ml/min
2,000
1,500
1,000
500
25 - 39 years
40 - 59 years
60 - 85 years
Baseline age
SHIP-1
SHIP-2
SHIP-3
Oxygen uptake at AT; ml/min
1,500
1,000
500
25 - 39 years
40 - 59 years
60 - 85 years
Baseline age
SHIP-1
SHIP-2
SHIP-3
Mean Δ oxygen uptake at AT; ml/min
50
0
-50
-100
-150
25 30 35 40 45 50 55 60 65 70 75 80
Baseline age; years
Males 5y
Females 5y
Males 10y
Females 10y

Figure 5

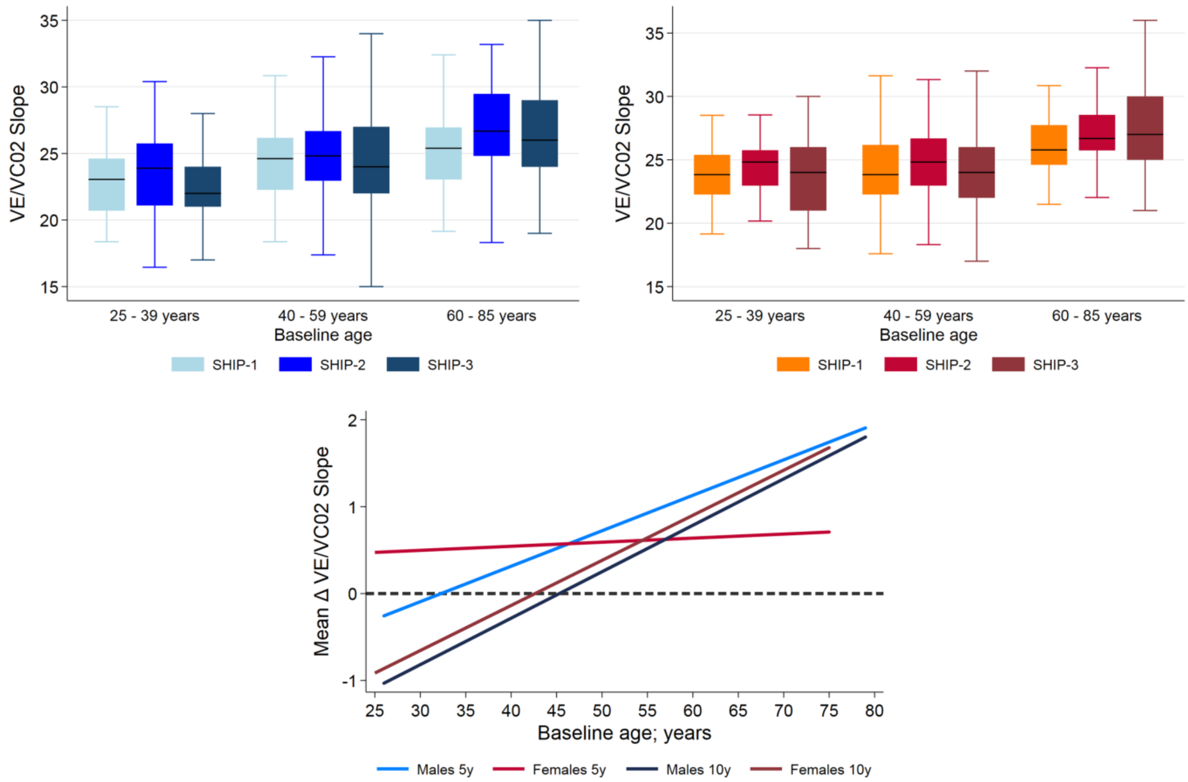
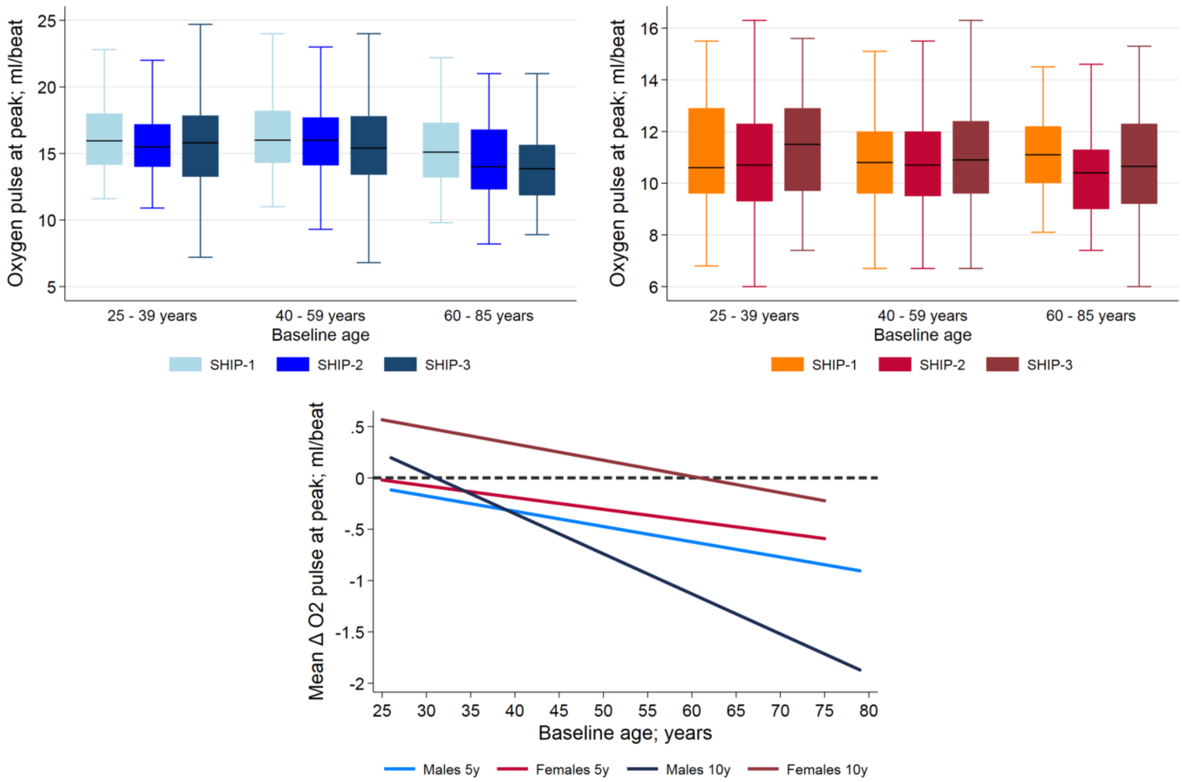

VE/VC02 Slope
35
30
25
20
15
25 - 39 years
40 - 59 years
60 - 85 years
Baseline age
SHIP-1
SHIP-2
SHIP-3
Mean Δ VE/VC02 Slope
2
1
0
-1
25 30 35 40 45 50 55 60 65 70 75 80
Baseline age; years
Males 5y
Females 5y
Males 10y
Females 10y

Figure 6



Oxygen pulse at peak; ml/beat
25 - 39 years
40 - 59 years
60 - 85 years
Baseline age
SHIP-1
SHIP-2
SHIP-3
Mean Δ O2 pulse at peak; ml/beat
Baseline age; years
Males 5y
Females 5y
Males 10y
Females 10y

Figure 7

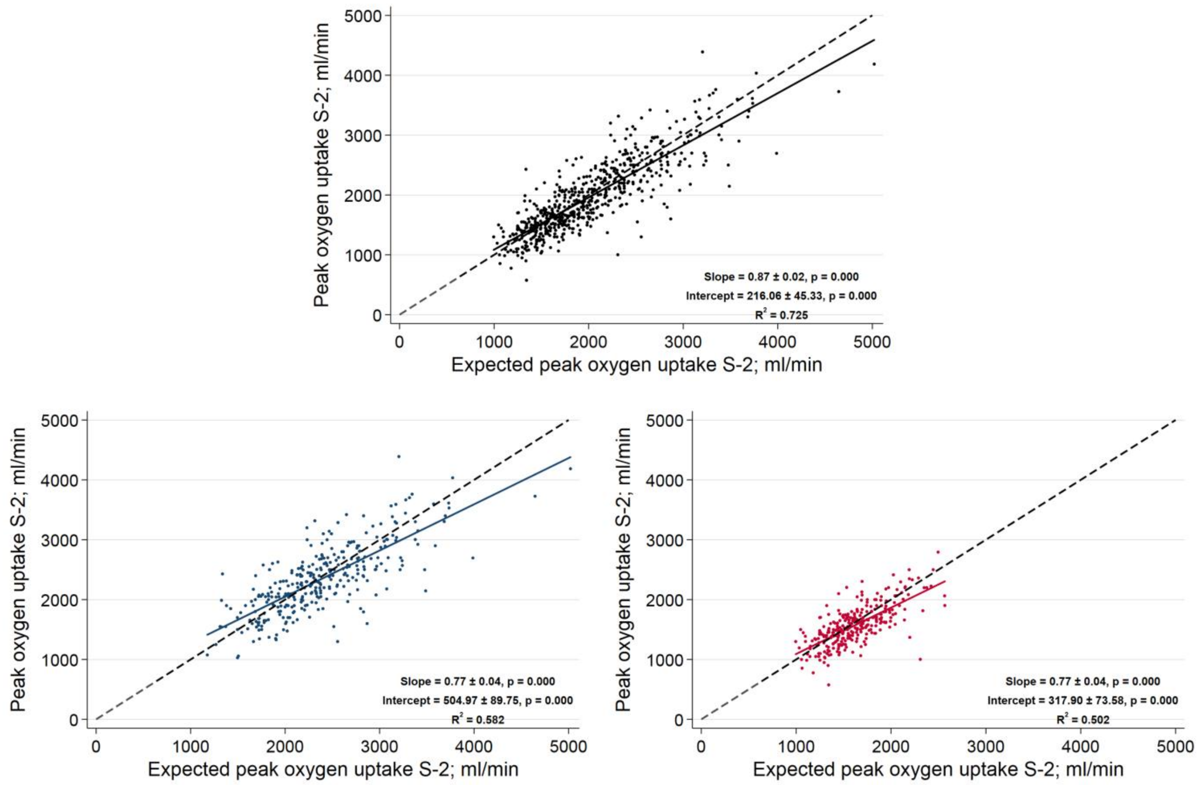

Peak oxygen uptake S-2; ml/min
Expected peak oxygen uptake S-2; ml/min
Slope = 0.87 ± 0.02, p = 0.000
Intercept = 216.06 ± 45.33, p = 0.000
R² = 0.725
Peak oxygen uptake S-2; ml/min
Expected peak oxygen uptake S-2; ml/min
Slope = 0.77 ± 0.04, p = 0.000
Intercept = 504.97 ± 89.75, p = 0.000
R² = 0.582
Peak oxygen uptake S-2; ml/min
Expected peak oxygen uptake S-2; ml/min
Slope = 0.77 ± 0.04, p = 0.000
Intercept = 317.90 ± 73.58, p = 0.000
R² = 0.502

Figure 8

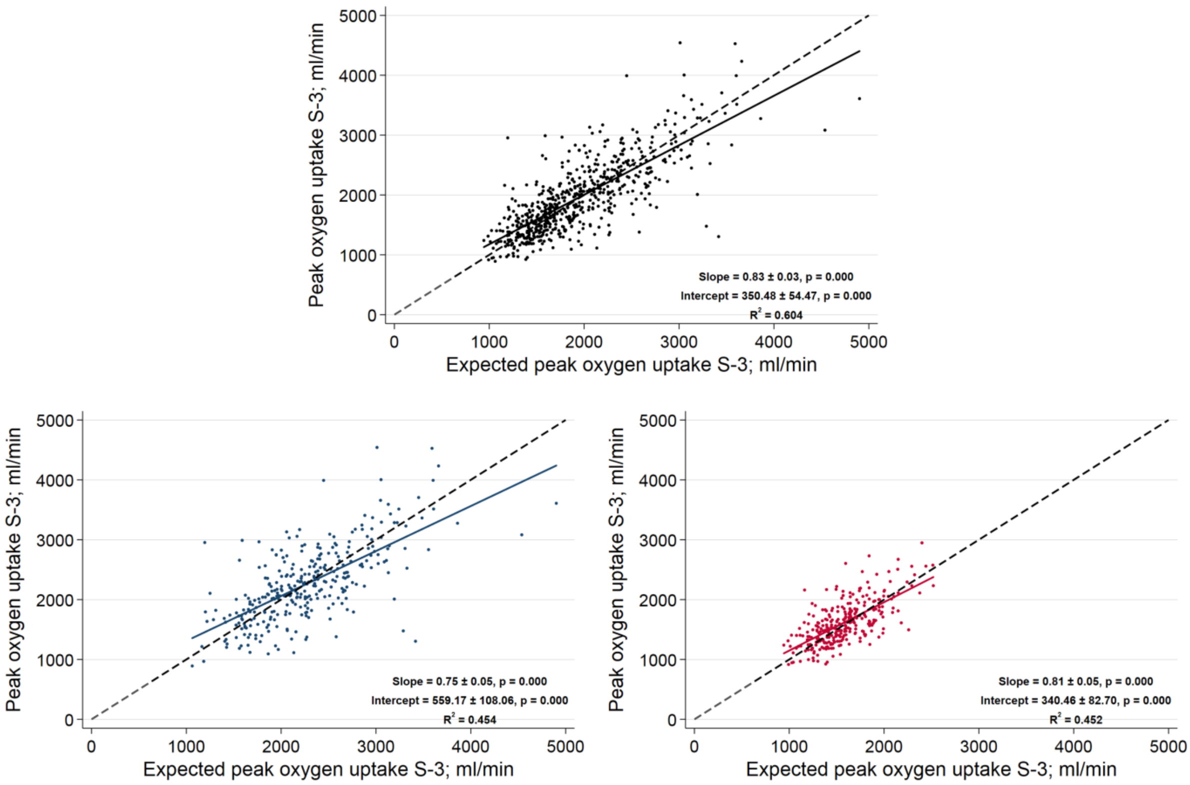

Peak oxygen uptake S-3; ml/min
Expected peak oxygen uptake S-3; ml/min
Slope = 0.83 ± 0.03, p = 0.000
Intercept = 350.48 ± 54.47, p = 0.000
R² = 0.604
Peak oxygen uptake S-3; ml/min
Expected peak oxygen uptake S-3; ml/min
Slope = 0.75 ± 0.05, p = 0.000
Intercept = 559.17 ± 108.06, p = 0.000
R² = 0.454
Peak oxygen uptake S-3; ml/min
Expected peak oxygen uptake S-3; ml/min
Slope = 0.81 ± 0.05, p = 0.000
Intercept = 340.46 ± 82.70, p = 0.000
R² = 0.452

Table 1. Baseline characteristics stratified by participation at follow-up.

	Participants (n = 615)	Non-participants (n = 1087)
Age; years	51 (41; 60)	53 (42; 65)
Males	317 (51.5%)	513 (47.2%)
Smoking status		
Never	272 (44.2%)	473 (43.5%)
Former	217 (35.3%)	333 (30.6%)
Current	126 (20.5%)	281 (25.9%)
Body mass index; kg/m^2	25.9 (23.7; 28.7)	27.2 (24.2; 30.8%)
Type 2 diabetes mellitus	31 (5.0%)	102 (9.4%)
Hypertension	241 (39.2%)	556 (51.2%)
Myocardial infarction	10 (1.6%)	33 (3.0%)
Stroke	5 (0.8%)	20 (1.8%)
FEV_1; % expected	100.1 (92.2; 108.1)	97.2 (86.9; 105.6)
Maximum power; % expected	99.3 (88.2; 111.5)	90.8 (79.0; 104.0)
VO_2peak; % expected	99.9 (89.7; 111.0)	92.2 (82.6; 104.8)
VO_2@AT; % expected	96.6 (85.1; 107.6)	92.5 (82.8; 103.1)
VE/VCO_2 slope; % expected	99.2 (92.1; 108.1)	101.4 (93.9; 110.8)
Maximum oxygen pulse; ml/beat	102.8 (92.8; 113.8)	100.0 (90.0; 112.3)

Data are reported as median, 25th and 75th percentile (continuous data) or as absolute numbers and percentages (categorical data).

Table 2. Absolute differences in CPET marker levels between baseline and the second follow-up (10-year-change).

	Males			Females		
Age in years	**20 – 39** (n=76)	**40 – 59** (n=149)	**>60** (n=92)	**20 – 39** (n=65)	**40 – 59** (n=179)	**>60** (n=54)
Maximum power; watt	9.1 (28.1)*	-1.7 (28.0)	-13.9 (24.1)*	9.2 (20.9)*	3.1 (19.2)*	-6.6 (17.9)*
Peak oxygen uptake; ml/min	-86 (572)	-241 (450)*	-335 (308)*	-10 (300)	-49 (251)*	-161 (210)*
Oxygen uptake @ AT; ml/min	-39 (336)	-22 (287)	-136 (210)*	-64 (180)*	-11 (181)	-27 (159)
VE/VCO_2 slope	-0.7 (3.8)	0.2 (3.3)	1.4 (3.2)*	0.1 (2.8)	0.1 (3.1)	1.6 (3.1)*
Maximum oxygen pulse; ml/beat	-0.16 (2.94)	-0.70 (3.22)*	-1.46 (2.94)*	0.27 (1.74)	0.31 (1.83) *	-0.39 (2.61)

Data are expressed as mean difference and standard deviation.
*p<0.05 (derived from a t-Test for paired data**)**

Table 3. Percentual differences in CPET marker levels between baseline and the second follow-up (10-year-change).

	Males			Females		
Age in years	**20 – 39** (n=76)	**40 – 59** (n=149)	**>60** (n=92)	**20 – 39** (n=65)	**40 – 59** (n=179)	**>60** (n=54)
Maximum power; %	5.4 (15.9)	0.5 (15.2)	-7.8 (14.4)	7.0 (14.5)	3.5 (15.8)	-5.1 (16.2)
Peak oxygen uptake; %	-1.6 (22.2)	-8.1 (17.8)	-14.9 (13.4)	0.3 (17.4)	-2.2 (15.0)	-10.3 (13.7)
Oxygen uptake @ AT; %	-0.6 (23.4)	1.9 (29.8)	-10-0 (16.8)	-4.3 (20.6)	0.3 (19.7)	-1.9 (17.7)
VE/VCO_2 slope; %	-1.9 (12.8)	1.2 (13.9)	6.0 (12.7)	1.2 (13.0)	1.0 (12.6)	6.6 (12.2)
Maximum oxygen pulse; %	-0.2 (20.0)	-3.3 (19.5)	-7.8 (17.2)	3.4 (16.2)	3.8 (17.0)	-2.3 (22.2)

Data are expressed as mean percentual difference and standard deviation.