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REVIEW

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Reference Values for Peak Oxygen Uptake

Referenzwerte für die maximale Sauerstoffaufnahme: Querschnittsanalysen von Fahrrad-Spiroergometrien aus dem Prevention First Register

Summary

- **Objective:** To construct quantile reference values for peak oxygen uptake ($\dot{V}O_2$peak) measured by cycle ergometer-based incremental cardiopulmonary exercise tests.
- **Design:** Cross-sectional study using quantile regressions to fit sex- and age-specific quantile curves. Exercise tests were conducted using cycle ergometry. Maximal effort in the exercise tests was assumed when RER ≥1.1 or lactate ≥8mmol*L^{-1} or maximal heart rate ≥90% of the age-predicted maximal heart rate. This was assessed retrospectively for a random subsample with an a priori calculated sample size of n=252 participants. A network of private outpatient clinics in three German cities recorded the results of cycle ergometer-based cardiopulmonary exercise tests to a central data base ("Prevention First Registry") from 2001 to 2015.
- **Participants:** 10,090 participants (6,462 men, 3,628 women) from more than 100 local companies volunteered in workplace health promotion programs. Participants were aged 46±7 years, were free of acute complaints, and had primarily sedentary working environments.
- **Results:** Peak oxygen uptake was measured as absolute $\dot{V}O_2$peak in L*min^{-1} and relative $\dot{V}O_2$peak in mL*min^{-1}*kg^{-1}. Median relative $\dot{V}O_2$peak was 36 and 30mL*min^{-1}*kg^{-1} at 40 to 49 years, as well as 32 and 26mL*min^{-1}*kg^{-1} at 50 to 59 years for men and women, respectively. An estimated proportion of 97% of the participants performed the exercise test until exertion.
- **Conclusions:** Reference values and nomograms for $\dot{V}O_2$peak were derived from a large cohort of preventive health care examinations of healthy white-collar workers. The presented results can be applied to participants of exercise tests using cycle ergometer who are part of a population that is comparable to this study.

KEY WORDS:
Exercise Test, Physical Fitness, Peak Oxygen Uptake, VO_2peak, Reference Values

Zusammenfassung

- **Hintergrund:** Auf Basis eines Registers präventivmedizinischer Untersuchungen wurden Referenzwerte und Nomogramme für die maximale Sauerstoffaufnahme ($\dot{V}O_2$peak) abgeleitet.
- **Methoden:** Querschnittsstudie zur Ermittlung alters- und geschlechtsspezifischer Referenzwerte für die $\dot{V}O_2$peak mittels Quantil-Regressionen. Die Belastungsuntersuchung wurden auf dem Fahrradergometer durchgeführt. Als Ausbelastungskriterien wurden definiert: RER ≥1,10, Laktat ≥8,0mmol/L oder Herzfrequenz ≥90% der vorhergesagten maximalen Herzfrequenz. Ausbelastungskriterien wurden in einer nachträglichen Auswertung einer a-priori kalkulierten, repräsentativen Stichprobe (n=252) validiert. Die Spiroergometrien auf dem Fahrradergometer erfolgten im Rahmen von Untersuchungen zur betrieblichen Gesundheitsförderung in drei präventivmedizinischen Privatpraxen und wurden in der zentralen Studiendatenbank (Prevention First Register) dokumentiert.
- **Teilnehmer:** 10 090 Personen (6 462 Männer und 3 628 Frauen) nahmen freiwillig am Prevention First-Gesundheits-Check-up im Rahmen der betrieblichen Gesundheitsförderung von mehr als 100 Unternehmen teil. Die Teilnehmer waren durchschnittlich 46±7 Jahre alt, frei von akuten gesundheitlichen Beschwerden und gingen beruflich überwiegend einer sitzenden Tätigkeit nach.
- **Ergebnisse:** Die maximale Sauerstoffaufnahme wurde als absolute $\dot{V}O_2$peak in L*min^{-1} und relative $\dot{V}O_2$peak in mL*min^{-1}*kg^{-1} erfasst. Die Mediane relative $\dot{V}O_2$peak lag jeweils für Männer und Frauen bei 36 und 30mL*min-^{1}*kg^{-1} für 40- bis 49-Jährige sowie bei 32 und 26mL*min^{-1}*kg^{-1} für 50- bis 59-Jährige. Eine maximale Ausbelastung gemäß der definierten Kriterien wurde bei 97% der Teilnehmer erreicht.
- **Schlussfolgerung:** Zwecks Einstufung der kardiopulmonalen Leistungsfähigkeit in der täglichen ärztlichen Praxis wurden aus einem großen Kollektiv gesunder Angestellter mit überwiegend sitzender Tätigkeit Referenzwerte und Nomogramme abgeleitet. Die präsentierten Daten können für spiroergometrische Untersuchungen auf dem Fahrradergometer eingesetzt werden, die an Populationen mit vergleichbarer Zusammensetzung durchgeführt werden.

SCHLÜSSELWÖRTER:
Spiroergometrie, Fitness, Maximale Sauerstoffaufnahme, VO_2max, Referenzwerte

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Introduction

A comprehensive body of evidence shows that a low cardiorespiratory fitness (CRF) is a strong, independent, and modifiable risk factor for a plethora of health threats such as premature death, cardiovascular disease (15, 27), diabetes mellitus (31), and neoplasia. (26) On the other hand, CRF can be improved by physical activity and exercise, which makes it a crucial target for health interventions (16). Hence, the assessment of CRF should be a key component of clinical practice in preventive health care check-ups (24) Despite its high predictive power, CRF has not been included in widely used cardiovascular ›

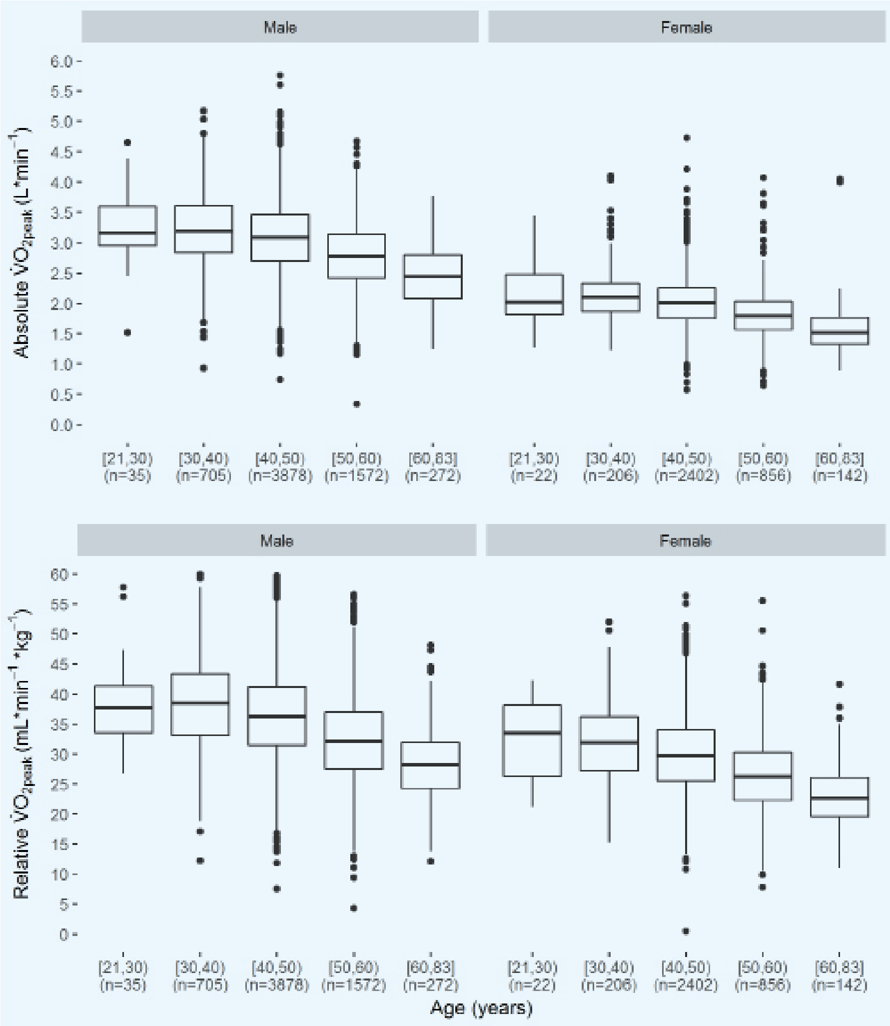

Figure 1

Box plots of absolute and relative VO_2peak by gender and age group.

risk models such as Framingham (5), European SCORE (4) JBS3 (10) or PROCAM (1). Therefore, it is particularly important to incorporate the measurement of CRF in preventive medicine beyond commonly used risk factors such as tobacco smoking or diabetes mellitus.

The gold standard of cardiopulmonary exercise testing is spiroergometry with respiratory gas exchange measurement (20, 22, 24)

The goal of the present analysis was to generate age- and sex-specific reference values for cycle ergometry-based $\dot{V}O_2$peak, based on a sample of more than 10,000 participants from primary preventive health care check-ups in three German cities. We constructed nomograms and created an interactive web application for visualisation.

Methods

Study Design and Participants

A network of private outpatient clinics ("Prevention First") recorded the results of preventive health care check-ups for 21- to 83-year-old participants in three German cities (Rüdesheim, Frankfurt, Munich) from 2001 to 2015. 95% of the participants were acquired in the course of workplace health promotion programs. Overall, the majority of this study population consisted of white-collar workers and employees with office jobs and a primarily sedentary working environment.

Exercise tests were performed according to guidelines (2, 20, 23). All participants were evaluated prior to exercise by an experienced physician. Pre-exercise evaluation included anamnesis, physical examination, resting electrocardiogram, and laboratory tests. If a participant had no contraindications such as hypertensive crisis, acute infections, or orthopaedic impairments (2), the exercise test was performed with the goal of reaching exhaustion.

Pseudonymised data were recorded in a central data base ("Prevention First Registry"). Participants were only included if they provided informed consent to use their data for scientific purposes. For the present cross-sectional analysis, only the first contact of a participant was considered. Follow-up examinations have not been included in the data.

Measurement of Peak Oxygen Uptake

We performed incremental maximal exercise tests to assess $\dot{V}O_2$peak using calibrated, electronically-breaked cycle ergometers. Gas exchange measurement was conducted through breath-by-breath analysis using the Ganshorn PowerCube system (Ganshorn Medizin Electronic GmbH, Niederlauer, Germany). We analysed and recorded the results with Ganshorn LF8 V8.5 and the previous versions of this software. Details of calibration procedures and exercise protocols chosen are described in the original publication (32).

It was aimed to continue every exercise test until exhaustion at the maximal volitional work rate, unless there were medical indications for termination (6). Criteria for maximal effort were recorded in medical records but not in the main study data base. Therefore, a subsequent data acquisition was performed for a random sample of n=252 participants.

Maximal effort of the participant was defined when one of the following criteria was met: i) capillary lactate levels were ≥8mmol*L^{-1} ii) respiratory exchange ratio ≥1.1 iii) maximal heart rate ≥90% of the age-predicted maximal heart rate (19, 25). Age-predicted maximal heart rate was estimated using the equation 208-0.7*age of the participant in years (29).

Statistical Methods

The statistical methods have been described extensively in the original publication (32).

Results

Description of study population

Overall, the results of 10,090 (6,462 males, 3,628 females) healthy participants from preventive health care examinations were eligible for the analysis and provided plausible, non-missing values for age and peak oxygen uptake.

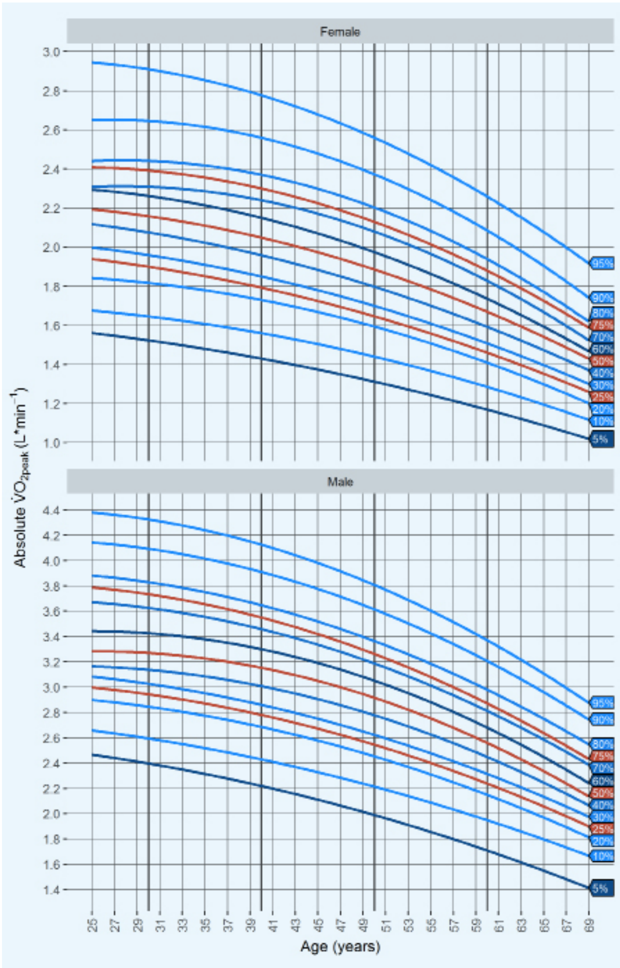

Figure 2

Nomograms of percentile reference values of absolute VO_2peak by gender and age.

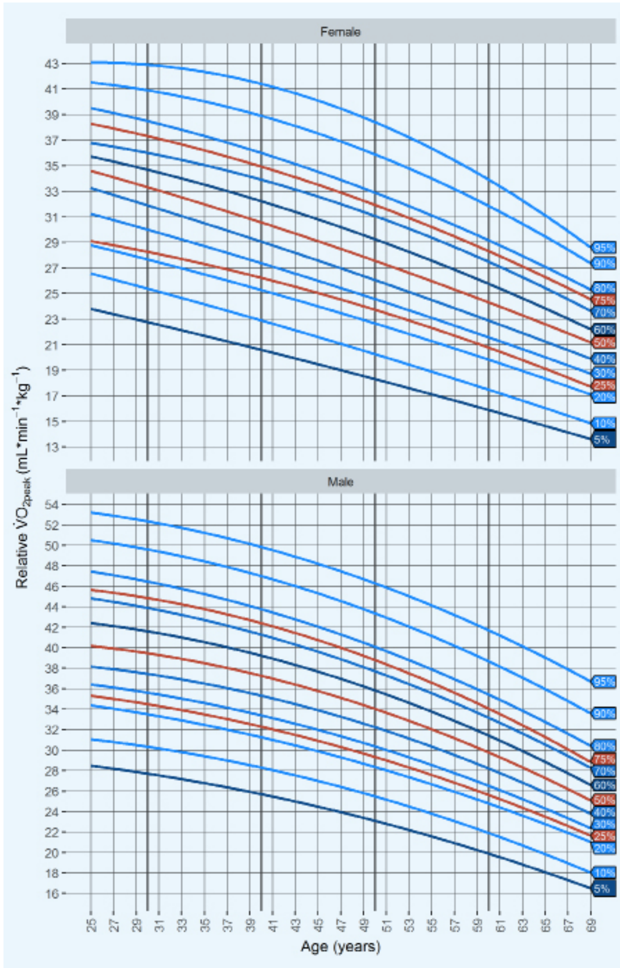

Figure 3

Nomograms of percentile reference values of relative VO_2peak by gender and age.

The mean age was 46 years for both males and females. Peak oxygen uptake was significantly higher in males. Mean relative $\dot{V}O_2$peak was 35 and 29 mL*min^{-1}*kg^{-1} for males and females, respectively (Table 1). Furthermore, a decline in peak oxygen uptake among older participants was observed (Figure 1).

There were also significant differences between our study population and the German population. In males, the proportions of smokers, overweight, and obese participants were significantly lower compared to the DEGS1 study (Table 2). Likewise, in females, the proportions of smokers, overweight, obese, and hypertensive participants were significantly lower compared to the DEGS1 study.

The bivariate distributions of absolute as well as relative $\dot{V}O_2$peak and age class are displayed in Figure 1 and supplementary Tables 1 and 2 (online). Figures 2 and 3 are nomograms including percentile curves. The nomograms can also be accessed as an interactive web application at www.uks.eu/vo2peak.

Validation of Maximal Exhaustion from Random Sample

Within our entire study population, we also drew a random sample of n=252. These participants did not differ significantly from the entire study population for the variables sex, age, peak oxygen uptake, BMI, and smoking status.

Maximal exhaustion was reached in 239/247 (97%, 95% CI 94% to 99%) participants. This proportion was 150/155 (97%, 95% CI 94% to 99%) in males, and 89/92 (97%, 95% CI 93% to 100%) in females. Reasons for termination prior to exhaustion were mainly orthopaedic impairments, anxiety from wearing the mask for gas exchange measurement, or muscular exhaustion due to a low level of fitness.

Discussion

The presented quantile reference values for $\dot{V}O_2$peak were derived from a sample of more than 10,000 participants who volunteered in preventive health care check-ups, primarily in the course of workplace health promotion programs. To our knowledge, this currently constitutes the largest sample for $\dot{V}O_2$peak reference values using cycle ergometer-based exercise tests. Data were acquired in three different German cities.

Other Reference Values

The reference values published by the Cooper Clinic (Dallas, Texas) (23) are among the most commonly used and comprehensive reference values for $\dot{V}O_2$peak. The exercise tests to acquire those reference values were performed using treadmill ergometers and an indirect measurement of $\dot{V}O_2$peak using prediction equations based on the achieved treadmill-time (8). Earlier publications by Hansen, Sue and Wasserman (1984) (7) as well as Jones et al (1985) (11) were based on rather low numbers of observations, which led to imprecise estimations (22). Furthermore, Hansen, Sue, and Wasserman used a sample of shipyard workers, which is a highly-selected population (7). An early systematic review collected and arranged ›

Table 1

Characteristics of maximal exercise test participants. Values are mean (standard deviation) unless stated otherwise. P values were calculated using student's t-test for two independent samples or chi-square test as appropriate.

	MALE N=6,462	FEMALE N=3,628	P VALUE
Age (years)	46.0 (7.09)	46.1 (6.87)	0.620
VO_2peak Relative (mL*min^{-1}*kg^{-1})	35.4 (7.68)	28.9 (6.66)	<0.001
VO_2peak Absolute (L*min^{-1})	3.00 (0.60)	1.96 (0.43)	<0.001
Weight (kg)	85.9 (13.2)	69.1 (13.5)	<0.001
Height (cm)	181 (7.14)	168 (6.87)	<0.001
BMI (kg*m^{-2})	26.2 (3.63)	24.6 (4.67)	<0.001
Body fat (caliper) (%)	23.1 (6.27)	30.8 (7.50)	<0.001
Blood pressure systolic (mmHg)	128 (15.4)	120 (16.6)	<0.001
Blood pressure diastolic (mmHg)	83.1 (8.95)	78.3 (9.28)	<0.001
Blood glucose (mg*dL^{-1})	97.1 (14.5)	92.2 (14.5)	<0.001
HbA1c (%)	5.42 (1.43)	5.41 (1.52)	0.756
Total cholesterol (mg*dL^{-1})	216 (39.1)	211 (38.4)	<0.001
HDL cholesterol (mg*dL^{-1})	54.1 (12.4)	67.6 (15.1)	<0.001
LDL cholesterol (mg*dL^{-1})	136 (35.9)	124 (41.6)	<0.001
Triglycerides (mg*dL^{-1})	135 (88.1)	100 (63.7)	<0.001
No (%) smoker	867 (13.5)	522 (14.5)	0.182
No (%) former smoker	1634 (29.6)	910 (29.7)	0.928

normal standards that were published before 1990 (28). However, those results are now only relevant from a historical perspective (22).

The above-mentioned shortcomings have been raised by the American Thoracic Society (ATS) and by the American College of Chest Physicians (ACCP) in their comprehensive statement on exercise tests in 2003 (2). They emphasised that valid and representative reference values were critical for the interpretation of CRF, but reliable reference values were lacking at that time in the USA. This issue has recently been addressed by an initiative that recorded data from several laboratories in the USA to a registry (FRIEND) (12, 13). Reference quantiles were obtained for treadmill ergometer-based (12) as well as cycle ergometer-based13 exercise tests using the results of 7,783 and 4,494 participants, respectively. The exercise tests that were recorded by the FRIEND study were performed in the course of exercise programs or research studies.

Reference values for a German population were published in 2009 using data from a prospective, population-based study (SHIP-study) (14) A representative sample of 7,008 adults was drawn from a north-eastern region of Germany. Due to non-responders and rigorous exclusion of smokers, obese participants, and other factors, the final sample yielded 534 participants (253 males, 281 females) who were eligible for the exercise tests. Measures of exhaustion were not published in the described study.

Comparison of Reference Values

The exercise tests in our study were performed using cycle ergometers. Cycle and treadmill ergometers were also the most common choices in past studies. However, in order to select appropriate reference values, it has to be considered that the choice of ergometer has a large impact on the obtained reference values. Peak oxygen uptake measured by treadmill ergometers was assumed to be 5 to 10% higher compared to cycle ergometers as a larger muscle mass is involved in treadmill ergometry and cycle ergometry is often terminated due to localised muscle fatigue (2). This effect appears to be even stronger when compared to the results of the FRIEND study. A 35-year-old male showed a median relative $\dot{V}O_2$peak of 42 mL*min^{-1}*kg^{-1} using treadmill ergometer and 30 mL*min^{-1}*kg^{-1} using cycle ergometer (12, 13) Therefore, reference values should only be considered for interpretation if the type of ergometer in the performed exercise test is identical to those used for calculating the reference values.

Exercise test protocols of past studies have been diverse or have not been described (13, 14, 23) However, the choice of exercise test protocol does not seem to have a strong effect on $\dot{V}O_2$peak (9, 30).

Considering the methodological differences, our reference values were slightly higher compared to other cycle ergometer-based studies. The reference values of the SHIP study, the ergometer-based FRIEND study, and our results are compared in Figure 4 and Figure 5.

Generalisability of the Study Sample

Our results were based on a sample of German white-collar workers with a predominantly sedentary working environment. This economic sector describes a large and increasing proportion of the population, not only in Germany, but also in other industrialised countries (3).

However, our study sample had significantly lower proportions of smokers, overweight and obese persons compared to the overall German population. These differences are likely due to our sample including primarily white-collar workers and also due to a selection of participants with a healthier lifestyle than the German population. A selection of healthy

Table 2

Comparing characteristics of present study to results representing German population (DEGS1). Values are percent (95% confidence interval). PF Registry=Prevention First Registry. DEGS1 = Studie zur Gesundheit Erwachsener in Deutschland (17, 18, 21). Results were directly age standardised using German population of 2011 to ascertain comparability. Characteristics have been defined according to DEGS1: Overweight=BMI ≥25kg*m^{-2}, obesity=BMI ≥30kg*m^{-2}, hypertension=systolic blood pressure ≥140mmHg or diastolic blood pressure ≥90mmHg.

	MALES		FEMALES	
	PF REGISTRY	DEGS1	PF REGISTRY	DEGS1
Smoker	14.5 (12.5 to 16.5)	26.1 (24.0 to 28.2)	15.1 (12.6 to 17.9)	21.4 (19.7 to 23.1)
Former smoker	29.3 (26.9 to 31.9)	33.7 (31.9 to 35.5)	26.9 (23.9 to 30.2)	22.8 (21.4 to 24.2)
Overweight	60.5 (57.9 to 63.0)	67.1 (65.0 to 69.2)	37.9 (34.6 to 41.3)	53.0 (50.8 to 55.1)
Obese	13.7 (12.0 to 15.6)	23.3 (21.2 to 25.4)	12.5 (10.3 to 15.0)	23.9 (22.0 to 25.9)
Hypertension	35.7 (33.2 to 38.3)	33.3 (31.1 to 35.6)	20.9 (18.2 to 23.8)	29.9 (28.1 to 31.9)

participants might yield reference values that are higher than in the whole population.

Strengths and Weaknesses of the Study

Strengths of the present study include the high number of observations from three different German cities. Based on this sample, it was possible to obtain reference values with high precision and narrow confidence intervals. Exercise tests were performed by experienced personnel according to guidelines and predefined quality standards which yielded reliable test results. In contrast to earlier studies that commonly used age in 10-year age classes, we used quantile regressions to create nomograms with age in years as an independent variable. Based on that, the exercise test results of an individual at a certain age can be interpreted more precisely and in light of the inter-individual variability. Furthermore, nomograms and an interactive web application may help clinicians and participants of exercise tests to better understand the results.

Conclusions and Implications for Clinicians

The reference values for peak oxygen uptake presented by this study may be used in populations that are comparable to our sample. Laboratories using cycle ergometer-based cardiopulmonary exercise tests can interpret their results precisely and with background information. The reference values have also been embedded into an interactive web application (www.uks.eu/vo2peak) with the goal of facilitating the interpretation of exercise tests in clinical practice and improving the communication of exercise test results to the participant.

Conflict of Interest
The authors have no conflict of interest.

Original Publication

http://bmjopen.bmj.com/content/8/3/e018697

List of Abbreviations

CI: Confidence interval
CRF: Cardiorespiratory fitness
DEGS1: Studie zur Gesundheit Erwachsener in Deutschland
FRIEND: Fitness Registry and the Importance of Exercise National Database
PF Registry: Prevention First Registry
$\dot{V}O_2$peak: Peak oxygen uptake
SHIP: Study of Health in Pomerania

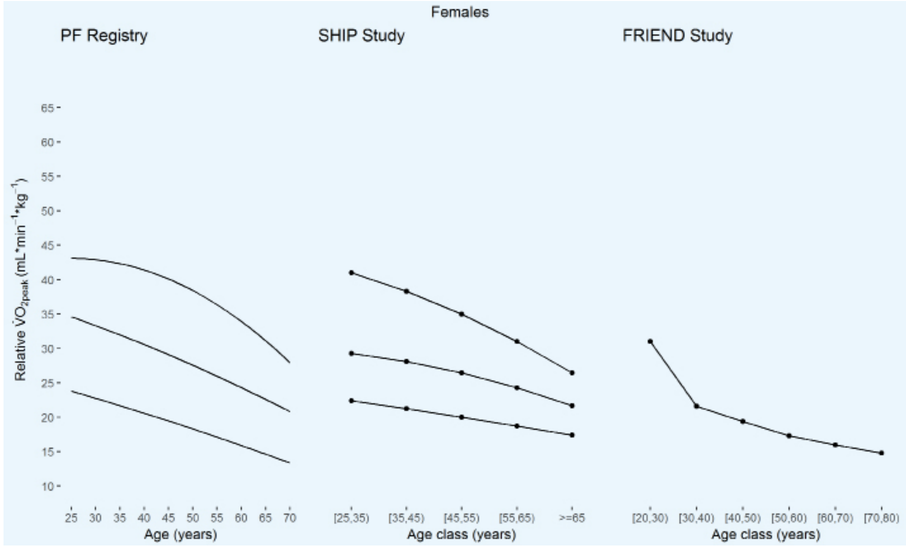

Figure 4

Cycle ergometer-based reference values for relative VO_2peak of females compared between three studies. PF=Prevention First, SHIP Study (14), and FRIEND Study (13) 25th, 50th, and 75th percentiles are plotted. For the FRIEND Study, only the 50th percentile is plotted.

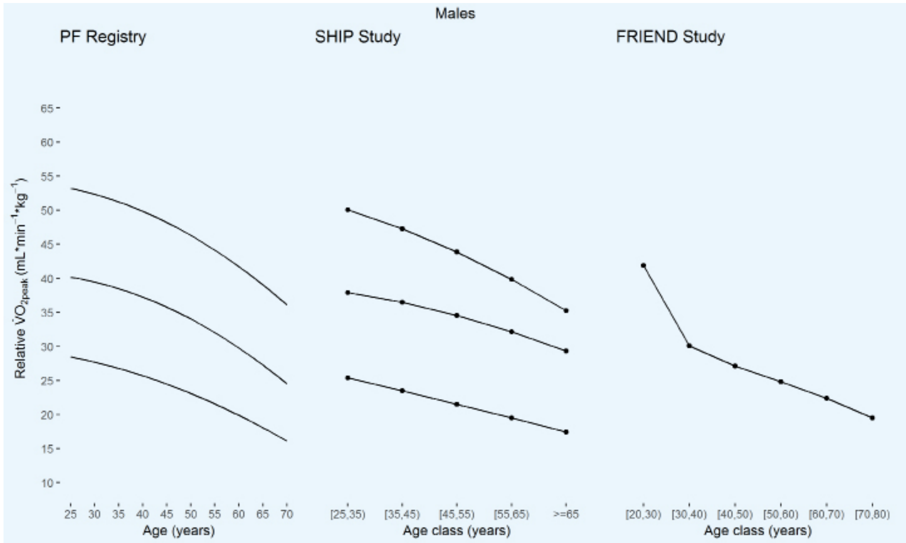

Figure 5

Cycle ergometer-based reference values for relative VO_2peak of males compared between three studies. PF=Prevention First, SHIP Study (14), and FRIEND Study (13). 25th, 50th, and 75th percentiles are plotted. For the FRIEND Study, only the 50th percentile is plotted.

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