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**Running title:** Cardiorespiratory data in older adults
ABSTRACT

Purpose: Cardiorespiratory fitness (CRF) is regarded a clinical vital sign, and accurate reference values for all age groups are essential. Little data exist on CRF and cardiorespiratory function in older adults. The aim of this study was to provide normative values for CRF and cardiorespiratory function in older adults, including people with history of cardiovascular diseases.

Methods: In total, 1537 (769 women) participants aged 70-77 underwent clinical examinations and cardiopulmonary exercise tests. Peak oxygen uptake (VO_{2peak}), ventilation (VE_{peak}), expiration of carbon dioxide (VCO_{2peak}), breathing frequency (BF_{peak}), tidal volume (VT_{peak}), oxygen pulse (O_{2}-pulse_{peak}), ventilatory efficiency (EqVO_{2peak} and EqVCO_{2peak}), and 1-minute heart rate recovery were assessed.

Results: Men compared to women had higher VO_{2peak} (31.3± 6.7 versus 26.2±5.0 mL/min/kg), BF_{peak} (41.8±8.0 versus 39.7±7.1 breath/min), VT_{peak} (2.3±0.5 versus 1.6±0.3), O_{2}-pulse_{peak} (16.4±3.2 versus 11.3±2.0), VCO_{2peak} (2.9±0.2 and 1.9±0.1 L/min), VE_{peak} (96.2±21.7 versus 61.1±21.6 L/min), EqVO_{2peak} (38.0±6.9 versus 35.1±5.6), and EqVCO_{2peak} (33.5±5.7 versus 31.9±4.5). Women and men with CVD had lower VO_{2peak} (14% and 19%), HR_{peak} (5% and 6 %), VE_{peak} (8% and 10%), VT_{peak} (7% and 4 %), and lower EqVCO_{2peak} (4% and 6%) compared to their healthy counterparts, respectively. Compared to healthy women and men, 1-minute heart rate recovery was 12% and 16% lower for women and men with CVD.
Conclusion: This study represents the largest reference material on directly measured CRF and cardiorespiratory function in older men and women, with and without CVD. Novel information will help researchers and clinicians to interpret data form cardiopulmonary testing in older adults.

Keywords: Cardiorespiratory fitness, cardiorespiratory function, cardiopulmonary exercise testing, ageing

Clinical trial: ClinicalTrial.gov NCT01666340 clinicaltrials.gov/ct2/show/NCT01666340
BACKGROUND

Although cardiorespiratory fitness (CRF), measured as peak oxygen uptake (VO$_{2peak}$) during cardiopulmonary exercise testing (CPET), has been shown to be the single best predictor for future cardiovascular disease and mortality (21, 24, 31, 42), it is often ignored in health risk assessment (20). In 2013, The American Heart Association (AHA) called for a national databank for establishing valid normative values for CRF (19), and a fitness registry (FRIEND) has now been established in the United States (20). AHA also suggests in a 2017 statement that CRF should be regarded as a clinical vital sign (35). Both the FRIEND-registry committee and the AHA 2017 statement (35) highlights that being able to compare an individual’s CRF to their peers is critical for optimal risk assessment, and will provide important information for physical activity guidelines (19, 20). In addition to CRF, the physiological responses during CPET can be used as a prognostic and diagnostic tool as it may identify underlying pathophysiological mechanisms for several diseases (9, 15, 33). For instance, it has been shown that CPET improves the diagnostic accuracy of standard ECG stress testing in identifying patients with coronary artery disease (6).

As aging often is characterized by profound physiological changes (4, 39), it is a major limitation that the existing reference values for CRF and cardiorespiratory function are based on studies that include few older adults (2, 22, 36, 41). Further, individuals with CVD are typically excluded in studies aiming to present normative values for CRF (2, 11), despite CVD being highly prevalent in older adults (30). Thus, available data on CRF and cardiorespiratory function in older adults are based on a very selected population, and valid reference data in the general elderly population is lacking. The aim of this study was to provide reference values for CRF and cardiorespiratory function in a large diverse group of elderly people.
METHODS

Participants

All men and women born between the 1st of January in 1936 and 31st of December 1942, with a permanent address in the municipality of Trondheim, Norway (n=6966), were invited to participate in the Generation 100 Study, a randomized controlled trial with primary aim to determine the effect of five years of exercise training on mortality and morbidity in elderly people (37). The exclusion criteria were; Illness or disabilities that preclude exercise, uncontrolled hypertension (untreated systolic blood pressure >220 and diastolic blood pressure >110), symptomatic valvular disease, hypertrophic cardiomyopathy, unstable angina pectoris (chest pain at rest), primary pulmonary hypertension, heart failure, severe arrhythmia, diagnosed dementia, cancer that made participation impossible or exercise contraindicated (considered individually, in consultation with physician), chronic communicable infectious diseases, or participation in other exercise training studies. In addition, persons with CVD who fulfilled any of the following criteria during the CPET were excluded: chest pain, intermittent claudication, extreme fatigue, dizziness, blood pressure drop >10 mmHg despite an increase in workload, systolic blood pressure >250mmHg (>200mmHG for those with aortic aneurism), or diastolic blood pressure >110 mmHg. In addition, the following ECG abnormalities were used as exclusion criteria: ST depression >2mm, ST elevation >1 mm, supraventricular tachycardia (including atrial fibrillation not present in the beginning of the test), ventricular tachycardia, and increasing ventricular extra systoles. In total, 1537 (769 women) participants completed baseline examinations and provided complete data on directly measured CRF and cardiorespiratory function. The study was approved by the Regional Committee for Medical Research Ethics.
(REK 2012/381 B), and was registered in the ClinicalTrials.gov registry (NCT01666340). The participants gave informed, written consent to participate in the study. The baseline-data from Generation 100 are used as basis for the present study (37).

Examinations

**Height:** The participants stood with their feet placed against the wall, shoulder-width apart, and height (Seca 222, Hamburg, Germany) was measured to the nearest millimeter.

**Waist circumference:** All clothing and accessories were removed from the abdominal region. The participants stood with feet shoulder-width apart and with their arms crossed over their chest. A measuring tape was placed in a horizontal line from the uppermost border of the iliac crest around the abdomen. The participants were asked to relax and breathe normally. After the third expiration, waist circumference was measured to the nearest millimeter.

**Blood:** The participants arrived at the laboratory after 12-hour fast, and a blood sample was obtained from an arm vein. Serum and EDTA-treated plasma were centrifuged at 3000 rpm for 10 minutes at 20°C. Serum triglycerides (TG), glucose, HDL-, total cholesterol, C-reactive protein (CRP), glycosylated hemoglobin (HbA₁c), and high sensitive C-reactive protein (hs-CRP) were measured immediately using standard procedures at St. Olavs University Hospital, Trondheim. The laboratory at the hospital is under *Lab quality’s quality system* program and quality assurances were thereby performed frequently.

**Blood pressure and resting heart rate:** After resting in a chair for 5 minutes, blood pressure and resting heart rate \((HR_{rest})\) were measured automatically with a Philips IntelliVue MP50 (Philips medizin systeme, Boeblingen, Germany). Blood pressure was measured twice with one-minute break between in the right arm. A third measurement was taken if systolic blood pressure (SBP)
differed ≥10 mmHg and/or diastolic blood pressure (DBP) differed ≥ 6mmHg. The mean of the last two measurements was used to report the systolic- and diastolic blood pressure. The device was under the quality control system at St. Olavs University Hospital, Trondheim, and controls were thereby performed frequently.

**Pulmonary function:** Resting spirometry and single-breath determination of carbon monoxide uptake in the lung were performed with the Sensormedics Vmax22 Encore (CareFusion, San Diego, CA, USA) in accordance with the American Thoracic Society/European Respiratory Society (ATS/ERS) criteria (27, 29), as previously described by Hassel et al. (17).

**Steps per day:** The ActiGraph GT3X+ accelerometer (ActiGraph LLC, Pensacola, FL, USA) was used to obtain steps per day. The monitor was placed on the participants the day they came in for clinical testing, and the participants were told to wear it for 7 consecutive days (including both day and night). Data were considered valid if the subject had at least 4 days of at least 600 min·d⁻¹ recorded.

**Cardiopulmonary exercise testing (CPET):** Due to logistical reasons, two systems for ergospirometry testing were used in this study, Oxycon Pro (Erich Jaeger, Hoechberg, Germany, n=72), and Cortex MetaMax II (Leipzig, Germany, n=1483). Before testing, the ergospirometry systems were calibrated against a standardized motorized mechanical lung (Motorized Syringe with Metabolic Calibration Kit; VacuMed, Canada). At the start of every test day volume and gas calibration were undertaken according to manufacturers instruction. Thereafter, volume calibration was performed before every test, while gas calibration was performed before every 4th test, or if ambient air measurements were rejected by the analyzer before any test. A heart
rate monitor was used to test heart rate during the test (RS100, Polar Electro Oy, Kempele, Finland). Participants with heart diseases (205 men and 93 women) were tested under 12-lead ECG monitoring, and the American College of Cardiology/American Heart Association-guidelines for exercise testing of patients with known CVD were followed (14). Forty-five participants performed the CPET on a bicycle as they were unable to walk on the treadmill due to reduced functionality or leg pain. After a brief customization to the treadmill, a ten-minute warm-up period was performed at an individually adjusted submaximal level (moderate intensity). Workload was selected on the basis of: 1) self-reported physical activity level, 2) monitoring of the heart rate, and 3) feedback from the participant regarding the perceived intensity. A facemask (Hans Rudholph, Germany) connected to the gas-analyzer was then attached to the participants. Step 1 was initiated from the treadmill inclination and speed derived from the last part of the warm-up period, and was a steady state measurement that lasted for three minutes. After Step 1, the treadmill inclination was increased by 2%. Pilot tests showed that the measured parameters stabilize more quickly at Step 2, thus this steady state measurement lasted for two minutes. After submaximal work, load was increased gradually by 1 km/h or 2% inclination, (or 10 Watt every 30 sec. if cycling) approximately every one and a half minute, or when oxygen uptake became stable. This procedure was maintained until exhaustion (VO_{2peak}), or until maximal oxygen uptake (VO_{2max}) was reached. Combined with a respiratory exchange ratio of 1.05 or higher, a maximal test was considered achieved when the participant continued until exhaustion and oxygen uptake did not increase more than 2 mL/kg/min between two 30 second epochs (i.e. a leveling-off of VO_{2} despite increased workload). Blood pressure was obtained with an automated monitor specifically designed for stress and exercise testing (Tango+, SunTech Medical Instruments, Morrisville, North Carolina, USA), and measured at the
two submaximal levels (step 1 and step 2), and at peak when the participants reached a RER-value of 1.05. $\text{VO}_2\text{peak}$ was the average of the three highest consecutive values, and peak expiration of carbon dioxide ($\text{VCO}_2\text{peak}$) and peak respiratory exchange ratio ($\text{RER}_\text{peak}$) were the highest value among the corresponding three highest values. Peak ventilation ($\text{VE}_\text{peak}$) and peak breathing frequency ($\text{BF}_\text{peak}$) were calculated from the average of the three ventilation values corresponding to the three highest $\text{VO}_2$ values, and these two values were used to calculate peak tidal volume ($\text{VT}_\text{peak}$). Breathing reserve was calculated as the difference between maximum voluntary ventilation ($\text{FEV}_{1\times40}$) and peak ventilation, and presented as percentage of maximum voluntary ventilation (3). Peak heart rate ($\text{HR}_\text{peak}$) was recorded as the highest observed heart rate during the test. Heart rate recovery (HR-recovery) was recorded 1 minute after the completion of the CPET. Heart rate reserve (HRR) was calculated as the difference between $\text{HR}_\text{peak}$ and $\text{HR}_{\text{rest}}$.

The participants reported their subjective rating of perceived exertion (RPE) on a Borg scale ranging from 6 to 20 (7) at the two submaximal levels, and immediately after the test. Peak O$_2$-pulse ($\text{O}_2\text{-pulse}_\text{peak}$) was calculated by dividing $\text{VO}_2\text{peak}$ (mL/min) by $\text{HR}_\text{peak}$, and expressed in milliliters per beat. Peak ventilatory efficiency was calculated as $\text{EqVO}_2$ ($\text{VE}_\text{peak}/\text{VO}_2\text{peak}$) and $\text{EqVCO}_2$ ($\text{VE}_\text{peak}/\text{VCO}_2\text{peak}$).

Ventilatory anaerobic threshold and respiratory compensation point: The V-slope method (5) was used to establish ventilatory anaerobic threshold (VAT) and respiratory compensation point (RCP), and $\text{VO}_2$, $\text{EqVO}_2$, $\text{VCO}_2$, $\text{EqVCO}_2$, $\text{VE}$, $\text{BF}$ and RER were reported at VAT and RCP.

History of CVD and medications: A questionnaire containing 21 health-related topics was presented to the participants (37). The questionnaire addressed the participants’ education (college or University vs. primary school/trade school/high school), smoking habits (current smoker vs. previous), usage of antihypertensive medication (yes/no), and use of prescribed
medication (number). People with a self-reported history of heart disease (myocardial infarction, angina pectoris, atrial fibrillation and/or stroke/brain hemorrhage) were classified as having CVD. Apparently healthy participants who reported not to take any prescribed medication were categorized as healthy.

**Statistics**

The results are presented as mean ± standard deviations (SD). In addition, lower (5th percentile) and upper (95th percentiles) limit of normal were reported for the CPET-data. For normally distributed variables (assessed with the Q-Q plot), independent sample t-tests were used to evaluate if there was a differences between the sexes, and between the healthy participants and those with CVD within the same sex. All included variables presented were normally distributed, except for hs-CRP, where a non-parametric test (two independent samples test) was used to evaluate the difference between sexes at baseline. Linear regression analyses were used to examine the correlation between %HR_{peak}, %HRR, and %VO_{2peak}. The statistical analyses were performed using SPSS 22 (Predictive Analytics Software, version 20, Statistical Package for Social Science, Chicago, IL, USA), and P <0.05 was used as the cutoff for statistical significance.

**RESULTS**

**Descriptive data**

Descriptive characteristics of study participants are presented in Table 1. Men had significantly higher BMI (4%), waist circumference (9%), Hb (9%), triglycerides (9%), DBP (5%), FVC (39%), FEV1 (45%), and D_{LCO} (34%) compared to women, while women had higher total
cholesterol (12%), HDL (16%), LDL (11%), and HR_{rest} (6%) compared to men. Men with CVD had higher BMI (5%), waist circumference (3%), and HBA1c (3%) compared the healthy men, but lower HB (1%), total cholesterol (21%), LDL (33%), FVC (5%), FEV1 (10%) and D_{LCO} (9%). Women with CVD had also higher BMI (5%), waist circumference (4%), and HBA1c (2%), compared to the healthy women, but lower total cholesterol (19%), HDL (11%), LDL (30%), DBP (4%), FVC (7%), FEV1 (9%) and D_{LCO} (6%). The prevalence of myocardial infarction, angina pectoris, atrial fibrillation and stroke in men were 8.5%, 4.7%, 9.0%, and 5.9%, respectively. In women, the corresponding prevalence values were 2.0%, 0.9% 2.7%, and 3.9%. Additionally, 3.4% of the men and 1.8% of the women, reported to have other kind of heart disease.

*Cardiopulmonary exercise testing*

CRF values during cardiopulmonary testing (CPET) for women and men are presented in Table 2. In total, 65% of the men and 56% of the women reached VO_{2,max}. In women, 60% of the CVD participants and 63% of the healthy participants reached VO_{2,max}. Corresponding numbers for men were 65% and 72%. Men had higher VO_{2,peak} (20%), O_2-pulse_{peak} (45%), VCO_{2,peak} (50%), BF_{peak} (5.3%), VE_{peak} (57%), VT (44%), and EqCO_{2,peak} (5%) compared to women. Women had 4% higher peak DBP compared to men, no sex differences were found in peak SBP. The healthy men had higher VO_{2,peak} (19%), VCO_{2,peak} (19%), BF_{peak} (6%), VE_{peak} (10%), VT_{peak} (4%), and peak O2- pulse (5%) compared to men with CVD. The healthy women had higher VO_{2,peak} (14%), VCO_{2,peak} (13%), VE_{peak} (8%), and VT_{peak} (7%) compared to those with CVD. There were no differences in peak DBP between the healthy and the CVD- participants. However, men with CVD had significantly lower peak SBP (7%) compared to the healthy men. Men and women
with CVD had a 6% and 4% higher EqVCO$_{2peak}$, and 6% and 5% lower HR$_{peak}$ compared to the healthy men and women, respectively. In addition, HR-recovery was 12% lower in women and 19% lower in men with CVD compared to the healthy women and men. No clear relationship was found between the CPET variables and age in this population (data not presented).

Ventilatory anaerobic threshold (VAT) and respiratory compensation point (RCP)

VAT was observed at approximately the same %VO$_{2peak}$ for men (75.7±9.2%) and women (76.6±9.9%) (Table 3). No difference was observed in the RCP between the sexes (86.9 ± 7.9 and 87.7 ± 7.8 %VO$_{2peak}$ for men and women, respectively (Table 3). Both VAT and RCP were observed at a higher RER in men compared to women (P<0.01). Men had significantly higher EqVO$_{2}$ at VAT and RCP compared to women. VAT was observed at approximately the same %VO$_{2peak}$ for men (75.4±9.1) and women (76.3±8.0) with CVD compared to the healthy men (76.0± 8.8) and women (76.9± 9.2) (Table 3). Also RCP was observed at approximately the same %VO$_{2peak}$ for men and women with CVD (86.3±8.2 and 87.8±5.9, respectively) and healthy men and women (87.6±7.4 and 88.1±7.0, respectively) (Table 3). The healthy men reached VAT and RCP at a higher RER compared to men with CVD (P<0.01).

Correlation between heart rate and oxygen uptake

Figure 1 shows the correlation between %VO$_{2peak}$ and %HR$_{peak}$, measured during CPET in women and men, respectively. The healthy women and men had the highest correlations between %HR$_{peak}$ and %VO$_{2peak}$ (R$^2$=0.860 and R$^2$=0.878, for women and men, respectively). The relation between %HRR and %VO$_{2peak}$ at different %HR$_{peak}$ are presented in Table 4.
Rated perceived exertion using the Borg-scale

Men exercised at a lower relative intensity (both expressed as %HR\(_{\text{peak}}\) and %VO\(_{2\text{peak}}\)) when they reported a subjective effort between 6-9 (P<0.05), and 10-12 (P<0.01) on the Borg scale compared to women (Table 5). No significant sex differences were observed at the higher intensities of the Borg scale (13-15, 16-18, and 19-20). Men with CVD worked at a higher %VO\(_{2\text{peak}}\) at Borg scale 13-15 compared to the healthy men (P<0.05). No other differences were observed within the different Borg-scale categories between the healthy men and women compared to those with CVD.

DISCUSSION

Cardiorespiratory fitness

The Generation 100 study currently provides the largest material for directly measured CRF and cardiorespiratory function in a general population of older adults worldwide. The CRF values reported in the present study are higher compared those previously reported in older adults in the US by Kaminsky et al. (20). Interestingly, the registry data from the US shows that for each age group, Norwegian men and women, have higher CRF than those in the US (20). Although the number of older adults is low in the US -population (137 men, and 98 women), our data reinforce the statement that region and country specific reference values for CRF are warranted (20). Previously, Edvardsen et al. has presented reference values of CRF in Norwegian adults aged 20-85 years old (11). However, people over 50 years of age were excluded if they had more than one traditional cardiovascular risk factor, and the study only included 41 women and 24 men in the oldest age group (70-85 years old). The procedure for peak oxygen uptake testing in our study is the same as that used in HUNT3-study (2). Men ≥70 years old in HUNT3 had higher
VO$_{2\text{peak}}$ (34 mL·kg$^{-1}$·min$^{-1}$) compared to the men in our study (31.1 mL·kg$^{-1}$·min$^{-1}$). The difference are likely due to a smaller (n=269) and more selected sample size (excluded people with CVD) in HUNT3 compared to our study. The healthy men and women in our study (free from cardiovascular disease) had a somewhat higher VO$_{2\text{peak}}$ compared to the HUNT3 participants. However, the healthy men and women in our study were those reporting to take no perceived medications, and are therefore most likely healthier than the participants in the HUNT3. In total, our study gives a more precise picture of CRF and cardiorespiratory function in the general population of older adults. Our study is unique, as it gives a comprehensive picture of the responses during CPET in a large number of older adults, including women and individuals with CVD.

Cardiorespiratory function

The results from the present study confirm that women and men with CVD respond differently physiologically to CPET compared to their healthy counterparts. In line with studies on people with heart failure (34) we observed that elderly people with CVD had lower HR$_{\text{peak}}$ and HR-recovery compared to the healthy participants. In contrast with studies demonstrating that people with CVD have an impaired ability to increase their heart rate (chronotropic incompetence) with increased activity or physical demand (8), we observed that both men and women with CVD showed a relatively normal response, with a gradual increase in heart rate until peak effort during CPET. The reasons for these discrepancies are not known but may be due to different test protocols used, and reflect that the individualized test protocol used in our study may be preferable over more standard protocols (increasing workload at standardized time points rather than based upon the individual physiological response) when testing CVD patients. In addition, different types of medications, age and variety of CVD may have influenced the results, and
further similar studies are warranted in older adults with CVD. The mean HR-recovery in both healthy and CVD individuals were larger than the critical 12 beats per minute previously reported to be associated with increased risk of premature death (10). This indicates that the individuals with CVD in our population in general don’t have a delayed decrease in heart rate after graded exercise, as often seen in people with heart failure (10, 18). Clinical recommendation for CPET states that normal SBP\textsubscript{peak} for men is \textasciitilde 210 mmHg and for women \textasciitilde 190 mmHg (16). The healthy women in this study had an average SBP\textsubscript{peak} of 197 mmHg, indicating that the normal value for SPB\textsubscript{peak} during CPET for older women should be increased. As 37\% of the healthy women had SPB\textsubscript{peak} \geq 210, we recommend that normal SBP\textsubscript{peak} for women should be set to 210 mmHG as for men. In our population, people with CVD had a normal rise in systolic blood pressure, but men with CVD had lower SBP\textsubscript{peak} than their healthy counterparts (SBP\textsubscript{peak} were 188 mmHg versus 202 mmHg, respectively). The reason for slightly lower peak systolic blood pressure in men with CVD is not known, but may have been influence by the medication use in the CVD participants, or reflect that a lower percentage reached the true VO\textsubscript{2max} compared to the healthy men. Previously, O\textsubscript{2}-pulse has been listed as an important variable in exercise testing as it reflects stroke volume response to exercise (16). Although it has been shown that the O\textsubscript{2}-pulse flattening duration during CPET improves the diagnostic accuracy to identify exercise induced myocardial ischemia (6), the prognostic value of O\textsubscript{2}-pulse\textsubscript{peak} has been questioned (23). The healthy men in our study had higher O\textsubscript{2}-pulse\textsubscript{peak} compared to men with CVD. Interestingly, O\textsubscript{2}-pulse in men with CVD in our study was relatively high compared to previously reported in people with heart failure (43) and coronary heart disease (23), again indicating that our CVD patients were somewhat healthier than in previous studies. On the other side, previous studies are small, and it may be that our data are more representative. Several large studies are warranted to
elucidate this. In line with the previous literature, our study shows that there are sex differences in pulmonary function, both at rest and during exercise (26, 28). Men and women with CVD had lower pulmonary parameters at rest, but higher ventilatory cost (EqVCO2), compared to the healthy participants. Importantly, many of the risk factors associated with CVD (such as smoking and dyslipidemia) also affect the pulmonary system (40). Contrary to previous findings, ventilatory equivalents (EqVO2peak and EqVCO2peak) were higher in men compared to women in our study (26), indicating that there was a higher ventilatory cost for oxygen uptake and expired carbon dioxide for men. The reason for this is not known and should examined further in future studies. It has previously been suggested that the normative value for EqVO2peak should be \( \leq 40 \) (16). Interestingly, the EqVO2peak for both men and women with CVD were below this threshold in our study, indicating that the normal values for EqVO2peak might be a lower in older adults.

Traditionally, VE/VCO2-slope is calculated using all exercising data (16), and the prognostic value of EqCO2 at peak (VEpeak/VCO2peak) are not clear. However, the equation previously presented by Sun et al., indicate that the VE/VCO2 at submaximal level (EqVCO2 at VAT) should be <30 in our population (38). In line with Loe et al. (26), EqVCO2 at VAT in our study was >30 for all groups, indicating that for older adults, the normal value for submaximal EqVCO2 should be higher than previously suggested (38).

**Ventilatory anaerobic threshold (VAT) and respiratory compensation point (RCP)**

As shown previously, men and women reached VAT and RCP at the same \%VO2peak (26), and no differences were seen between the healthy people and people with CVD. However, the healthy men reached VAT and RCP at a higher RER compared to men with CVD, indicating a more effective ventilation for the healthy men.
Correlation between heart rate and oxygen uptake

The correlation between $%\text{HR}_{\text{peak}}$, $%\text{HRR}$, and $%\text{VO}_2\text{peak}$ in our study differs from the classification given by the American college of sports medicine (13). The differences are pronounced at lower intensities, where an exercise intensity at 57-64 of $%\text{HR}_{\text{peak}}$ in our study corresponds to a higher $%\text{VO}_2\text{peak}$ compared to ACSM guidelines (13). As previously shown, men worked at a slightly lower $%\text{VO}_2\text{peak}$ compared to women at moderate to vigorous intensities ($%\text{HR}_{\text{peak}}$ 64-95) (25). Both men and women with CVD worked at lower $%\text{VO}_2\text{peak}$ and higher $%\text{HRR}$ at $%\text{HR}_{\text{peak}}$ compared to their healthy counterparts, indicating that it is a greater physiological cost to work at higher intensities for people with CVD.

Rated perceived exertion using the Borg-scale

Our findings support previous studies in showing that there is a sex difference related to subjectively rated effort using Borg scale and relative $\text{VO}_2\text{peak}/\text{HR}_{\text{peak}}$ at lower intensities (25, 32). Both men and women in our study worked at a significantly higher $%\text{VO}_2\text{peak}$ and $%\text{HR}_{\text{peak}}$ compared to what has been reported previously (1, 7). However, our data are close to what Loe et al. found in the general Norwegian population (46.7±13.1 yrs).

Strength and limitations

The main strength of our study is that it includes a large, well-described sample of men and women 70-77 years of age. A major strength of this study is that all tests were performed at the same laboratory, and by the same eight trained technicians, who could discuss the unexpected challenges on a daily basis. Selection bias may limit generalizability in the present study. A previously published paper showed that the included participants reported somewhat better
health and higher education compared to the non-participant group (37). However, our sample of older adults appears to be fairly representative with regards to prevalence of CVD compared to registry data of the general older adult population in Norway (12). Our sample had a wide range of health and disease status, and although potentially selection bias may have occurred, this allows for a larger degree of generalizability to older adults, at least in Norway. The existing data on key cardiorespiratory variables in people with CVD are derived from specific patient groups (myocardial infarction, heart failure, and angina) with few women included. Overall, our study provides the largest data material on cardiorespiratory responses in an older population worldwide, and is the first to present normative values for a general CVD-population, including women. Maximal voluntary ventilation was estimated, and not directly measured. The negative lower limit of normal for breathing reserve in men, is likely a result of maximal voluntary ventilation being estimated, and that some individuals measured to low FEV1 and/or too high VEpeak.

**Conclusion**

The study represents the largest data material on directly measured CRF and cardiorespiratory function in the general population of older men and women, including people with CVD. Data from the present study will provide important information for researchers and clinicians to interpret data from cardiopulmonary testing in older adults in the future.
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Conflict of interest

There are no conflicts of interest. The results of the present study do not constitute endorsement by ACSM. The results of the study are presented clearly, honestly, and without fabrication, falsification, or inappropriate data manipulation.
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Figure 1. Correlation between percentage of peak heart rate (\%HR_{peak}) and percentage of peak oxygen uptake (\%VO_{2peak}) in women and men. A; all, B; healthy, C; with cardiovascular disease (CVD).
|                         | **Women**       | **Men**       | **Healthy** | **All** | **With CVD** | **Healthy** |
|-------------------------|-----------------|---------------|-------------|---------|--------------|-------------|
| **Number of subjects**  | 769             | 93            | 150         | 768     | 205          | 160         |
| **Age (yr)**            | 72.9±2.1        | 73.0±2.2      | 72.8±2.1    | 72.7±2.1| 72.9±2.1     | 72.7±2.1    |
| **Height (cm)**         | 163.3±5.2       | 162.5±5.0     | 164.1±5.6†  | 176.9±5.9*| 176.9±6.1    | 177.1±5.6   |
| **Body mass (kg)**      | 68.2±10.7       | 68.7±10.2     | 66.2±9.7    | 82.9±11.6*| 84.6±12.8    | 80.0±11.3†  |
| **BMI (kg/m²)**         | 25.5±3.7        | 26.1±3.8      | 24.7±3.5†   | 26.4±3.3* | 26.9±3.5     | 25.5±3.3†   |
| **Waist circumference (cm)** | 90.0±10.8  | 91.3±10.4     | 87.5±10.1†  | 98.4±9.6*| 99.2±9.7     | 95.9±9.8†   |
| **hsCRP (mg/L)**        | 2.1±3.0         | 2.2±3.2       | 1.8±2.0     | 2.6±4.9  | 2.4±4.3      | 2.1±2.7     |
| **Hb (g/dL)**           | 13.8±0.9        | 13.7±0.9      | 13.9±0.9    | 15.0±1.1*| 14.9±1.1     | 15.1±0.9†   |
| **HbA1c (%)**           | 5.7±0.4         | 5.7±0.5       | 5.6±0.5*    | 5.7±0.5  | 5.8±0.6      | 5.6±0.3†    |
| **Total cholesterol (mmol/L)** | 6.0±1.1   | 5.3±1.2       | 6.3±1.0†    | 5.3±1.1* | 4.7±1.1      | 5.7±0.9†    |
| **HDL (mmol/L)**        | 1.9±0.5         | 1.8±0.5       | 2.0±0.5†    | 1.6±0.4* | 1.5±0.5      | 1.6±0.4     |
| **LDL (mmol/L)**        | 3.6±1.0         | 3.0±1.1       | 3.9±0.9†    | 3.2±1.0* | 2.7±1.0      | 3.6±0.8†    |
| **TG (mmol/L)**         | 1.1±0.5         | 1.1±0.4       | 1.1±0.5     | 1.2±0.6* | 1.2±0.6      | 1.1±0.5     |
| **Heart rate rest (beat/min)** | 67±10       | 66±11         | 65±9        | 63±11    | 62±11        | 62±11       |
| **SBP rest (mmHg)**     | 135±18          | 136±20        | 135±19      | 134±17   | 133±18       | 136±18      |
| **DBP rest (mmHg)**     | 73±9            | 70±11         | 73±9†       | 77±9**   | 81±11        | 84±10       |
| **SBP ortho (mmHg)**    | 137±19          | 136±20        | 136±20      | 136±19   | 133±20       | 136±18      |
| **DBP ortho (mmHg)**    | 80±11           | 78±12         | 80±10       | 82±10    | 81±11        | 83±10       |
| **FVC, (L)**            | 3.1±0.5         | 3.0±0.5       | 3.2±0.4†    | 3.4±0.7* | 4.3±0.8      | 4.5±0.7†    |
| **FEV1, (L/min)**       | 2.2±0.4         | 2.2±0.4       | 2.4±0.4†    | 3.2*     | 3.0±0.7      | 3.3±0.6†    |
| **DlCO (mmol/min/kPa)** | 6.7±1.1         | 6.5±1.9       | 6.9±1.1†    | 9.0±1.7* | 8.6±1.8      | 9.4±1.6†    |
| **Current smoker (%)**  | 8.5             | 12            | 9           | 8.5      | 7            | 8           |
| **College/university (%)** | 44          | 41            | 48          | 58*      | 60           | 66          |
| **Heart disease (%)**   | 11              | 100           | 0           | 26       | 100          | 0           |
| **BP medication (%)**   | 31              | 53            | 0           | 36**     | 51           | 0           |
| **Steps per day**       | 6042±2880       | 5709±2520     | 6064±3076   | 6175±2868| 5809±2891    | 6792±2903   |
Continuous variables are presented as mean±standard deviation and categorical variables as percentages. CVD; cardiovascular diseases, BMI; body mass index, hsCRP; high sensitive C-reactive protein, HB; hemoglobin, HbA1c; glycated hemoglobin, HDL; high-density lipoprotein, LD; low-density lipoprotein, TG; triglycerides. SBP<sub>rest</sub>; resting systolic blood pressure, DBP<sub>rest</sub>; diastolic blood pressure, HR<sub>rest</sub>; resting heart rate, SBP<sub>ortho</sub>; orthostatic systolic blood pressure, DBP<sub>ortho</sub>; orthostatic diastolic blood pressure, FVC; forced vital capacity, FEV1; forced expired volume at 1 second, D<sub>LCO</sub>; Diffusing capacity of lung for carbon monoxide, *Significantly different from women (P<0.05). †Significantly different from individuals (within the same sex) with CVD (P<0.05).
**Table 2.** Cardiorespiratory responses during cardiopulmonary testing in older men and women

|                          | Women                        | Men                        | Healthy                   | Men                        | Healthy                   |
|--------------------------|------------------------------|----------------------------|---------------------------|----------------------------|---------------------------|
|                          | All                          | With CVD                   | All                       | With CVD                   | All                       |
| Number of subjects       | 769                          | 93                         | 150                       | 768                        | 205                       | 160                       |
| Speed\(_{\text{peak}}\) (km/h) 5th/95th percentile | 5.2±0.9                      | 4.0/6.8                    | 5.1±0.7                   | 3.9/6.0                    | 5.5±0.9                   | 4.0/7.5                   | 6.0±1.3*                  | 4.0/9.0                    | 5.7±0.9                   | 4.0/7.0                    | 6.5±1.3†                  | 5.0/9.5                    |
| Inclination\(_{\text{peak}}\) (%) 5th/95th percentile | 11.8±3.0                     | 6.0/17.0                   | 12.0±3.4                  | 5.6/17.0                   | 11.9±3.3                  | 6.0/17.5                   | 12.4±4.1*                 | 6.0/20.0                   | 13.5±4.0                  | 7.0/20.0                   | 12.4±4.5†                 | 5.0/20.0                   |
| Borg\(_{\text{peak}}\) 5th/95th percentile | 17±2                         | 15/20                      | 17±2                      | 15/19                      | 17±1                      | 15/19                      | 17±1                      | 15/19                      | 17±1                      | 15/19                      |
| RER\(_{\text{peak}}\) 5th/95th percentile | 1.10±0.09                    | 0.96/1.25                  | 1.10±0.09                 | 0.94/1.24                  | 1.12±0.07†                | 1.00/1.24                  | 1.14±0.09*                | 1.09/1.24                  | 1.11±0.09†                | 1.09/1.24                  | 1.16±0.08†                | 1.04/1.30                  |
| HR\(_{\text{peak}}\) (beats/min) 5th/95th percentile | 157±16                       | 128/180                    | 150±17                    | 123/176                    | 158±13†                   | 134/178                    | 157±18                   | 122/181                    | 152±21                   | 111/181                    | 161±14†                   | 140/183                    |
| VO\(_{2}\)\(_{\text{peak}}\) (L/min) 5th/95th percentile | 1.76±0.30                    | 1.23/2.23                  | 1.65±0.28                 | 1.14/2.12                  | 1.82±0.31†                | 1.30/2.34                  | 2.56±0.51†                | 1.74/3.46                  | 2.46±0.57†                | 1.52/3.40                  | 2.74±0.48†                | 2.00/3.61                  |
| VO\(_{2}\)\(_{\text{peak}}\) (ml/min/kg) 5th/95th percentile | 26.2±5.0                     | 18.9/35.2                  | 24.4±4.1                  | 17.4/31.9                  | 27.8±5.5†                 | 19.8/37.3                  | 31.3±6.7†                 | 20.8/43.2                  | 29.3±6.9                  | 17.7/42.1                  | 35.0±6.6†                 | 23.5/46.1                  |
| VCO\(_{2}\)\(_{\text{peak}}\) (L/min) 5th/95th percentile | 1.94±0.39                    | 1.28/2.57                  | 1.80±0.36                 | 1.11/2.39                  | 2.04±0.38†                | 1.39/2.66                  | 2.91±0.64†                | 1.87/4.00                  | 2.72±0.67                 | 1.58/3.89                  | 3.16±0.58†                | 2.24/4.11                  |
| BF\(_{\text{peak}}\) (b/min) 5th/95th percentile | 39.7±7.1                     | 30/52                      | 39.9±8.8                  | 30/52                      | 39.8±6.6                  | 30.0/52.4                  | 41.8±8.0†                 | 31/55                      | 40.9±8.5                  | 30.5/55.5                  | 43.3±8.7†                 | 31.8/59.0                  |
| VE\(_{\text{peak}}\) (L/min) 5th/95th percentile | 61±13                        | 41/82                      | 60±14                     | 36/78                      | 64±13†                    | 41/88                      | 96±22†                   | 61/133                     | 93±24                    | 55/134                     | 101±20†                   | 72/138                     |
| Breathing Reserve (%) 5th/95th percentile | 30.9±13.5                    | 9.2/53.8                   | 30.8±13.3                 | 10.1/54.3                  | 31.0±13.7                 | 6.6/55.7                   | 21.7±16.6                 | -3.9/43.3                  | 22.1±16.7                 | -6.5/46.1                  | 20.9±14.7                 | -2.7/42.9                  |
| VT\(_{\text{peak}}\) (VE/BF) 5th/95th percentile | 1.6±0.3                      | 1.1/2.0                    | 1.5±0.3                   | 0.9/2.0                    | 1.6±0.3†                  | 1.2/2.1                    | 2.3±0.5†                 | 1.6/3.1                    | 2.3±0.5                   | 1.4/3.2                    | 2.4±0.4†                  | 1.7/3.1                    |
| O\(_{2}\) pulse\(_{\text{peak}}\) (ml/beat) 95% CI Upper-lower | 11.3±2.0                     | 8.1/14.7                   | 11.1±1.9                  | 7.5/14.6                   | 11.5±2.0                  | 8.3/15.0                   | 16.4±3.2†                | 11.2/22.0                  | 16.3±3.5                  | 10.8/23.0                  | 17.1±3.0†                 | 12.7/22.2                  |
| EqVO\(_{2}\)\(_{\text{peak}}\) (VE\(_{\text{peak}}\)/VO\(_{2}\)\(_{\text{peak}}\)) 95% CI Upper-lower | 35.1±5.6                     | 26.8/44.7                  | 36.1±6.5                  | 26.8/46.4                  | 35.7±5.2                  | 27.0/44.6                  | 38.0±6.9†                | 29.3/48.3                  | 38.6±8.1                  | 29.8/51.2                  | 37.7±5.7                  | 29.6/47.8                  |
| EqVCO\(_{2}\)\(_{\text{peak}}\) (VE\(_{\text{peak}}\)/VCO\(_{2}\)\(_{\text{peak}}\)) 5th/95th percentile | 31.9±4.5                     | 25.5/39.1                  | 33.2±5.1                  | 26.6/41.5                  | 31.8±4.1†                 | 26.3/38.3                  | 33.5±5.7†                | 26.4/41.6                  | 34.7±6.9                  | 26.8/44.8                  | 32.6±4.4†                 | 26.6/38.7                  |
| SBP\(_{\text{peak}}\) (mmHg) 95% CI Upper-lower | 195±29                       | 134/231                    | 189±28                    | 138/232                    | 197±27                    | 136/233                    | 195±26                   | 149/229                    | 188±29                    | 137/234                    | 202±21†                   | 160/229                    |
| DBP\(_{\text{peak}}\) (mmHg) 5th/95th percentile | 83±17                        | 55/114                     | 85±17                     | 57/119                     | 82±19                     | 50/120                     | 80±16*                   | 53/108                     | 83±14                     | 60/109                     | 81±18                     | 51-115                     |
| HR-recovery (beats/min) 5th/95th percentile | 26±10                        | 10/43                      | 25±10                     | 10/45                      | 28±10†                    | 13/43                      | 27±11                    | 10/46                      | 27±12                     | 9/47                       | 31±13†                    | 15-54                      |
Values are means±standard deviation, and 5th and 95th percentile. CVD; cardiovascular diseases, HR; heart rate, VO₂; oxygen uptake, VCO₂; expired carbon dioxide, BF; breathing frequency, VE; ventilation, VT; tidal volume, RER; respiratory exchange ratio, EqVO₂/EqVCO₂; ventilatory equivalence of oxygen/carbon dioxide, SBP; systolic blood pressure, DBP; diastolic blood pressure, HR-recovery; heart rate recovery 1-minute after peak cardiopulmonary test. *Significantly different from women (P<0.05). †Significantly different from individuals (within the same sex) with CVD (P<0.05).
|                      | Women | Men |
|----------------------|-------|-----|
|                      | All   | With CVD | Healthy | All   | With CVD | Healthy |
| **VAT**              |       |       |         |       |       |         |
| Number of subjects   | 446   | 42    | 103     | 500   | 127    | 104     |
| %VO_{peak} 5th/95th percentile | 76.6±9.9 | 76.3±8.0 | 53.6±89.1 | 75.7±9.2 | 61.3±89.8 | 61.7±90.1 |
| VO_{2peak} 5th/95th percentile | 1.4±0.3 | 1.3±0.2 | 1.4±0.3 | 2.0±0.4* | 1.9±0.4 | 2.1±0.4* |
| EqVO_{2} (VE/VO_{2}) 5th/95th percentile | 29.1±3.3 | 29.4±3.2 | 29.4±3.1 | 30.1±3.9* | 29.7±4.2 | 30.3±3.8 |
| VCO_{2} (L/min) 5th/95th percentile | 1.3±0.3 | 1.2±0.2 | 1.3±0.3 | 1.9±0.5* | 1.8±0.5 | 2.0±0.4* |
| EqVCO_{2} (VE/VCO_{2}) 5th/95th percentile | 31.9±3.6 | 32.2±3.5 | 32.0±4.0 | 31.9±4.1 | 32.4±5.3 | 31.8±4.8 |
| VE (L/min) 5th/95th percentile | 39.9±9.1 | 38.3±7.0 | 41.2±8.7* | 59.4±14.3* | 57.0±14.7 | 63.8±14.3* |
| BF (breaths/min) 5th/95th percentile | 29.4±5.5 | 28.6±4.9 | 29.4±5.1 | 29.1±5.6 | 27.7±5.2 | 31.0±6.6* |
| RER 5th/95th percentile | 0.91±0.07 | 0.91±0.06 | 0.92±0.07 | 0.94±0.06* | 0.93±0.07 | 0.96±0.05* |
| **RCP**             |       |       |         |       |       |         |
| Number of subjects   | 361   | 35    | 86      | 432   | 117    | 94      |
| %VO_{peak} 5th/95th percentile | 87.7±7.8 | 87.8±5.9 | 88.1±7.0 | 86.9±7.9 | 86.3±8.2 | 87.6±7.4 |
| VO_{2} (L/min) 5th/95th percentile | 1.6±0.3 | 1.5±0.3 | 1.6±0.3 | 2.3±0.4* | 2.2±0.5 | 2.4±0.4* |
| EqVO_{2} (VE/VO_{2}) 5th/95th percentile | 32.2±4.4 | 32.3±4.1 | 32.6±4.1 | 32.9±4.7* | 32.4±5.3 | 33.0±4.1 |
| VCO_{2} (L/min) 5th/95th percentile | 1.6±0.4 | 1.5±0.3 | 1.7±0.4* | 2.4±0.5* | 2.3±0.5 | 2.5±0.5* |
| EqVCO_{2} (VE/VCO_{2}) 5th/95th percentile | 31.5±3.5 | 32.0±3.8 | 31.7±3.8 | 31.6±4.9 | 31.7±5.0 | 31.3±3.1 |
| VE (L/min) 5th/95th percentile | 50.4±11.2 | 48.6±10.0 | 52.5±10.6 | 74.2±17.2* | 70.7±17.3 | 79.7±17.5* |

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Table 3. Respiratory variables at ventilatory anaerobic threshold (VAT) and at respiratory.

Values are means±standard deviation, and 5th and 95th percentile. VAT: ventilatory anaerobic threshold, RCP: respiratory compensation point, CVD: cardiovascular disease, VO₂peak: Peak oxygen uptake, VO₂: Oxygen uptake, VCO₂: Expired carbon dioxide, EqVO₂/ EqVCO₂: ventilatory equivalence of oxygen/carbon dioxide, VE: ventilation, BF: breathing frequency, RER: respiratory exchange ratio. *Significantly different from women (P<0.05). †Significantly different from individuals (within the same sex) with CVD (P<0.05).
Table 4. The relationship between %HR<sub>peak</sub>, %HRR, and %VO<sub>2peak</sub> for older men and women

| %HR<sub>peak</sub> | Women |  |  |  | Men |  |  |  |  |
|-------------------|-------|---|---|---|------|---|---|---|---|
|                   | All   | With CVD | Healthy | All   | With CVD | Healthy | All   | With CVD | Healthy |
| <57               | 29±6  | 48±6 | 50±6 | No cases | 53±0 | 31±5 | 48±5 | 28±6 | 47±3 | 31±5 | 46±5 |
| 57-63             | 38±4  | 53±7 | 53±5 | 37±4 | 55±4 | 38±9 | 52±7 | 36±10 | 51±7 | 38±10 | 51±8 |
| 64-76             | 52±7  | 62±8 | 65±10 | 53±6† | 61±8† | 52±7 | 58±8* | 50±9 | 59±9 | 53±6 † | 57±8 |
| 77-95             | 70±9  | 72±9 | 68±9 | 71±9 | 72±9 | 70±9 | 70±10* | 70±9 | 73±11 | 71±8 | 69±10† |
| ≥96               | 100±2 | 100±3 | 100±1 | 100±3 | 100±1 | 100±2 | 95±3 | 100±2 | 93±2 | 100±0 |

Values are means±standard deviation. HR<sub>peak</sub>; peak heart rate, HRR; heart rate reserve, VO<sub>2peak</sub>; peak oxygen uptake, *Significantly different from women (P<0.05). †Significantly different from individuals (within the same sex) with CVD (P<0.05).
Table 5. Relationship between perceived exhaustion, oxygen uptake and heart rate in older women and men

| Borg Scale | Women |           |           | Men |           |           |
|------------|-------|-----------|-----------|-----|-----------|-----------|
|            | All   | With CVD  | Healthy   | All | With CVD  | Healthy   |
|            | %HR_{peak} | %VO_{2peak} | %HR_{peak} | %VO_{2peak} | %HR_{peak} | %VO_{2peak} | %HR_{peak} | %VO_{2peak} | %HR_{peak} | %VO_{2peak} |
| 6-9        | 72±7  | 60±10     | 73±4     | 62±7 | 74±8     | 63±10     | 68±8* | 55±9* | 66±8     | 52±10     | 67±11     | 55±10     |
| 10-12      | 76±8  | 65±10     | 75±8     | 63±10 | 75±6     | 64±9      | 73±8* | 59±10* | 71±9     | 59±11     | 71±8      | 57±9      |
| 13-15      | 83±10 | 74±14     | 81±9     | 73±12 | 82±9     | 72±12     | 80±11 | 70±15 | 79±12    | 72±15     | 80±10     | 68±15†    |
| 16-18      | 99±5  | 98±8      | 98±5     | 97±7 | 99±3     | 98±6      | 99±5  | 98±5  | 99±5     | 98±6      | 99±5      | 99±6      |
| 19-20      | 100±1 | 100±2     | 100±0    | 100±0 | 100±0    | 100±0     | 100±2 | 100±3 | 100±0    | 100±0     | 99±4      | 99±7      |

Values are means±standard deviation. CVD; cardiovascular diseases, %HR_{peak}; percent of peak heart rate, %VO_{2peak}; percent of peak oxygen uptake. *Significantly different from women (P<0.05). †Significantly different from individuals (within the same sex) with CVD (P<0.05).