

Cardiorespiratory Reference Data in Older Adults: The Generation 100 Study

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ABSTRACT

STENSVOLD, D., S. BUCHER SANDBAKK, H. VIKEN, N. ZISKO, L. S. REITLO, J. NAUMAN, S. E. GAUSTAD, E. HASSEL, M. MOUFACK, E. BRØNSTAD, N. P. ASPVIK, V. MALMO, S. L. STEINSHAMN, A. STØYLEN, S. A. ANDERSSSEN, J. L. HELBOSTAD, Ø. ROGNMO, and U. WISLØFF. Cardiorespiratory Reference Data in Older Adults: The Generation 100 Study. *Med. Sci. Sports Exerc.*, Vol. 49, No. 11, pp. 2206–2215, 2017. **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 (CVD). **Methods:** In total, 1537 (769 women) participants age 70 to 77 yr underwent clinical examinations and cardiopulmonary exercise tests. Peak oxygen uptake ($\dot{V}O_{2peak}$), ventilation (\dot{V}_{Epeak}), expiration of carbon dioxide ($\dot{V}CO_{2peak}$), breathing frequency (BF_{peak}), tidal volume (V_{Tpeak}), oxygen pulse (O_2 pulse_{peak}), ventilatory efficiency ($Eq\dot{V}O_{2peak}$ and $Eq\dot{V}CO_{2peak}$), and 1-min HR recovery were assessed. **Results:** Men compared with women had higher $\dot{V}O_{2peak}$ (31.3 ± 6.7 vs 26.2 ± 5.0 mL·min⁻¹·kg⁻¹), BF_{peak} (41.8 ± 8.0 vs 39.7 ± 7.1 breaths per minute), V_{Tpeak} (2.3 ± 0.5 vs 1.6 ± 0.3), O_2 pulse_{peak} (16.4 ± 3.2 vs 11.3 ± 2.0), $\dot{V}CO_{2peak}$ (2.9 ± 0.2 and 1.9 ± 0.1 L·min⁻¹), \dot{V}_{Epeak} (96.2 ± 21.7 vs 61.1 ± 21.6 L·min⁻¹), $Eq\dot{V}O_{2peak}$ (38.0 ± 6.9 vs 35.1 ± 5.6), and $Eq\dot{V}CO_{2peak}$ (33.5 ± 5.7 vs 31.9 ± 4.5). Women and men with CVD had lower $\dot{V}O_{2peak}$ (14% and 19%), peak HR (5% and 6%), \dot{V}_{Epeak} (8% and 10%), V_{Tpeak} (7% and 4%), and lower $Eq\dot{V}CO_{2peak}$ (4% and 6%) compared with their healthy counterparts, respectively. Compared with healthy women and men, 1-min HR recovery was 12% and 16% lower for women and men with CVD. **Conclusions:** This study represents the largest reference material on directly measured CRF and cardiorespiratory function in older men and women, with and without CVD. This novel information will help researchers and clinicians to interpret data from cardiopulmonary testing in older adults. **Key Words:** CARDIORESPIRATORY FITNESS, CARDIORESPIRATORY FUNCTION, CARDIOPULMONARY EXERCISE TESTING, AGEING

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Although cardiorespiratory fitness (CRF), measured as peak oxygen uptake ($\dot{V}O_{2peak}$) during cardiopulmonary exercise testing (CPET), has been shown to be the single best predictor for future cardiovascular disease (CVD) 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 because 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).

Because 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 January 1, 1936, and December 31, 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 5 yr 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 [SBP] >220 and diastolic blood pressure [DBP] >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 mm Hg despite an increase in workload, SBP >250 mm Hg (>200 mm Hg for those with aortic aneurism), or DBP >110 mm Hg. In addition, the following ECG abnormalities were used as exclusion criteria: ST depression >2 mm, 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-h fast, and a blood sample was obtained from an arm vein. Serum and EDTA-treated plasma were centrifuged at 3000 rpm for 10 min at 20°C. Serum triglycerides (TG), glucose, high-density lipoprotein (HDL), total cholesterol, C-reactive protein (CRP), glycosylated hemoglobin (HbA_{1c}), and high sensitive CRP (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 HR. After resting in a chair for 5 min, blood pressure and resting HR (HR_{rest}) were measured automatically with a Philips IntelliVue MP50 (Philips Medizin Systeme, Boeblingen, Germany). Blood pressure was measured twice with 1-min break between in the right arm. A third measurement was taken if SBP differed ≥ 10 mm Hg and/or DBP differed ≥ 6 mm Hg. The mean of the last two measurements was used to report the SBP and DBP. 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 Sormedics Vmax22 Encore (CareFusion, San Diego, CA) in accordance with the American Thoracic Society/European Respiratory Society criteria (27,29), as previously described by Hassel et al. (17).

Steps per day. The ActiGraph GT3X+ accelerometer (ActiGraph LLC, Pensacola, FL) 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 d of at least 600 min·d⁻¹ recorded.

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 manufacturer's instruction. Thereafter, volume calibration was performed before every test, while gas calibration was performed before every fourth test, or if ambient air measurements were rejected by the analyzer before any test. A HR monitor was used to test HR 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 because they were unable to walk on the treadmill due to reduced functionality or leg pain. After a brief customization to the treadmill, a 10-min 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 HR, and 3) feedback from the participant regarding the perceived intensity. A facemask (Hans Rudolph, 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 3 min. 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 2 min. After submaximal work, load was increased gradually by 1 km·h⁻¹ or 2% inclination, (or 10 W every 30 s if cycling) approximately every one and a half minute, or when oxygen uptake became stable. This procedure was maintained until exhaustion ($\dot{V}O_{2peak}$), or until maximal oxygen uptake ($\dot{V}O_{2max}$) was reached. Combined with a RER 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⁻¹·min⁻¹ between two 30-s epochs (i.e., a leveling-off of $\dot{V}O_2$ despite increased workload). Blood pressure was obtained with an automated monitor specifically designed for stress and exercise testing (Tango+; SunTech Medical Instruments, Morrisville, NC), 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. $\dot{V}O_{2peak}$ was the average of the three highest consecutive values, and peak expiration of carbon dioxide ($\dot{V}CO_{2peak}$) and peak RER_{peak} were the highest value among the corresponding three highest values. Peak ventilation (\dot{V}_{Epeak}) and peak breathing frequency (BF_{peak}) were calculated from the average of the three ventilation values corresponding to the three highest $\dot{V}O_2$ values, and these two values were used to calculate peak tidal volume (V_{Tpeak}). Breathing reserve was calculated as the difference between maximum voluntary ventilation (FEV1×40) and peak ventilation, and presented as percentage of maximum voluntary ventilation (3). Peak HR (HR_{peak}) was recorded as the highest observed HR during the

test. HR recovery (HR-recovery) was recorded 1 min after the completion of the CPET. HR reserve (HRR) was calculated as the difference between HR_{peak} and HR_{rest}. The participants reported their subjective RPE on a Borg scale ranging from 6 to 20 (7) at the two submaximal levels, and immediately after the test. Peak O₂ pulse (O₂ pulse_{peak}) was calculated by dividing $\dot{V}O_{2peak}$ (mL·min⁻¹) by HR_{peak}, and expressed in milliliters per beat. Peak ventilatory efficiency was calculated as Eq $\dot{V}O_2$ ($\dot{V}_{Epeak}/\dot{V}O_{2peak}$) and Eq $\dot{V}CO_2$ ($\dot{V}_{Epeak}/\dot{V}CO_{2peak}$).

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 $\dot{V}O_2$, Eq $\dot{V}O_2$, $\dot{V}CO_2$, Eq $\dot{V}CO_2$, \dot{V}_E , 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 ± 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 % $\dot{V}O_{2peak}$. The statistical analyses were performed using SPSS 22 (Predictive Analytics Software, version 20, Statistical Package for Social Science, Chicago, IL), 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%), TG (9%), DBP (5%), FVC (39%), FEV1 (45%), and D_{LCO} (34%) compared to women, while women had higher total cholesterol (12%), HDL (16%), low-density lipoprotein (LDL) (11%), and

TABLE 1. Descriptive table of the participants.

	Women			Men		
	All	With CVD	Healthy	All	With CVD	Healthy
No. 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·m ⁻²)	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*
hs-CRP (mg·L ⁻¹)	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 ⁻¹)	13.8 ± 0.9	13.7 ± 0.9	13.9 ± 0.9	15.0 ± 1.1**	14.9 ± 1.1	15.1 ± 0.9*
HbA _{1c} (%)	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 ⁻¹)	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)	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 ⁻¹)	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)	1.1 ± 0.5	1.1 ± 0.4	1.1 ± 0.5	1.2 ± 0.6**	1.2 ± 0.6	1.1 ± 0.5
HR rest (bpm)	67 ± 10	66 ± 11	65 ± 9	63 ± 11	62 ± 11	62 ± 11
SBP _{rest} (mm Hg)	135 ± 18	136 ± 20	135 ± 19	134 ± 17	133 ± 18	136 ± 18
DBP _{rest} (mm Hg)	73 ± 9	70 ± 11	73 ± 9*	77 ± 9**	81 ± 11	84 ± 10
SBP _{ortho} (mm Hg)	137 ± 19	136 ± 20	136 ± 20	136 ± 19	133 ± 20	136 ± 18
DBP _{ortho} (mm Hg)	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*	4.3 ± 0.7**	4.3 ± 0.8	4.5 ± 0.7*
FEV1, (L·min ⁻¹)	2.2 ± 0.4	2.2 ± 0.4	2.4 ± 0.4*	3.2**	3.0 ± 0.7	3.3 ± 0.6*
D _{LCO} (mmol·min ⁻¹ ·kPa ⁻¹)	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 ± SD and categorical variables as percentages.

*Significantly different from individuals (within the same sex) with CVD ($P < 0.05$).

**Significantly different from women ($P < 0.05$).

BMI, body mass index; HB, hemoglobin; SBP_{rest}, resting SBP; DBP_{rest}, resting DBP; SBP_{ortho}, orthostatic SBP; DBP_{ortho}, orthostatic DBP; FVC, forced vital capacity; FEV1, forced expired volume at 1 s; D_{LCO}, diffusing capacity of lung for carbon monoxide.

HR_{rest} (6%) compared to men. Men with CVD had higher BMI (5%), waist circumference (3%), and HbA_{1c} (3%) compared to the healthy men, but lower HB (1%), total cholesterol (21%), LDL (33%), FVC (5%), FEV1 (10%), and D_{LCO} (9%). Women with CVD also had higher BMI (5%), waist circumference (4%), and HbA_{1c} (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.

CPET. 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 $\dot{V}O_{2max}$. In women, 60% of the CVD participants and 63% of the healthy participants reached $\dot{V}O_{2max}$. Corresponding numbers for men were 65% and 72%. Men had higher $\dot{V}O_{2peak}$ (20%), O₂ pulse_{peak} (45%), $\dot{V}CO_{2peak}$ (50%), BF_{peak} (5.3%), \dot{V}_{Epeak} (57%), VT (44%), and EqCO_{2peak} (5%) compared to women. Women had 4% higher peak DBP compared with men, no sex differences were found in peak SBP. The healthy men had higher $\dot{V}O_{2peak}$ (19%), $\dot{V}CO_{2peak}$ (19%), BF_{peak} (6%), \dot{V}_{Epeak} (10%), V_{Tpeak} (4%), and peak O₂ pulse (5%) compared with men with CVD. The healthy women had higher $\dot{V}O_{2peak}$ (14%), $\dot{V}CO_{2peak}$ (13%), \dot{V}_{Epeak} (8%), and V_{Tpeak} (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 Eq $\dot{V}CO_{2peak}$, and 6% and 5% lower HR_{peak} compared with 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).

VAT and RCP. VAT was observed at approximately the same % $\dot{V}O_{2peak}$ 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% $\dot{V}O_{2peak}$ for men and women, respectively (Table 3). Both VAT and RCP were observed at a higher RER in men compared with women ($P < 0.01$). Men had significantly higher Eq $\dot{V}O_2$ at VAT and RCP compared to women. VAT was observed at approximately the same % $\dot{V}O_{2peak}$ 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 % $\dot{V}O_{2peak}$ 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 HR and oxygen uptake. Figure 1 shows the correlation between % $\dot{V}O_{2peak}$ and %HR_{peak}, measured during CPET in women and men. The healthy women and men had the highest correlations between %HR_{peak} and % $\dot{V}O_{2peak}$ ($R^2 = 0.860$ and $R^2 = 0.878$, for

TABLE 2. Cardiorespiratory responses during CPET in older men and women.

	Women			Men		
	All	With CVD	Healthy	All	With CVD	Healthy
No. subjects	769	93	150	768	205	160
Speed _{peak} (km·h ⁻¹)	5.2 ± 0.9	5.1 ± 0.7	5.5 ± 0.9*	6.0 ± 1.3**	5.7 ± 0.9	6.5 ± 1.3*
5th/95th percentile	4.0/6.8	3.9/6.0	4.0/7.5	4.0/9.0	4.0/7.0	5.0/9.5
Inclination _{peak} (%)	11.8 ± 3.0	12.0 ± 3.4	11.9 ± 3.3	12.4 ± 4.1**	13.5 ± 4.0	12.4 ± 4.5*
5th/95th percentile	6.0/17.0	5.6/17.0	6.0/17.5	6.0/20.0	7.0/20.0	5.0/20.0
Borg _{peak}	17 ± 2	17 ± 2	17 ± 2	17 ± 1	17 ± 1	17 ± 1
5th/95th percentile	15/19	15/20	15/19	15/19	15/19	15/19
RER _{peak}	1.10 ± 0.09	1.09 ± 0.09	1.12 ± 0.07*	1.14 ± 0.09**	1.11 ± 0.09	1.16 ± 0.08*
5th/95th percentile	0.96/1.25	0.94/1.24	1.00/1.24	0.99/1.29	0.98/1.26	1.04/1.30
HR _{peak} (bpm)	157 ± 16	150 ± 17	158 ± 13*	157 ± 18	152 ± 21	161 ± 14*
5th/95th percentile	128/180	123/176	134/178	122/181	111/181	140/183
VO _{2peak} (L·min ⁻¹)	1.76 ± 0.30	1.65 ± 0.28	1.82 ± 0.31*	2.56 ± 0.51**	2.46 ± 0.57	2.74 ± 0.48*
5th/95th percentile	1.23/2.23	1.14/2.12	1.30/2.34	1.74/3.46	1.52/3.40	2.00/3.61
VO _{2peak} (mL·min ⁻¹ ·kg ⁻¹)	26.2 ± 5.0	24.4 ± 4.1	27.8 ± 5.5*	31.3 ± 6.7**	29.3 ± 6.9	35.0 ± 6.6*
5th/95th percentile	18.9/35.2	17.4/31.9	19.8/37.3	20.8/43.2	17.7/42.1	23.5/46.1
VC _{O2peak} (L·min ⁻¹)	1.94 ± 0.39	1.80 ± 0.36	2.04 ± 0.38*	2.91 ± 0.64**	2.72 ± 0.67	3.16 ± 0.58*
5th/95th percentile	1.28/2.57	1.11/2.39	1.39/2.66	1.87/4.00	1.58/3.89	2.24/4.11
BF _{peak} (breaths per minute)	39.7 ± 7.1	39.9 ± 8.8	39.8 ± 6.6	41.8 ± 8.0**	40.9 ± 8.5	43.3 ± 8.7*
5th/95th percentile	30/52	30/52	30.0/52.4	31/55	30.5/55.5	31.8/59.0
V _{Epeak} (L·min ⁻¹)	61 ± 13	60 ± 14	64 ± 13*	96 ± 22**	93 ± 24	101 ± 20*
5th/95th percentile	41/82	36/78	41/88	61/133	55/134	72/138
Breathing reserve (%)	30.9 ± 13.5	30.8 ± 13.3	31.0 ± 13.7	21.7 ± 16.6	22.1 ± 16.7	20.9 ± 14.7
5th/95th percentile	9.2/53.8	10.1/54.3	6.6/55.7	-3.9/43.3	-6.5/46.1	-2.7/42.9
V _{Ipeak} (V _E /BF)	1.6 ± 0.3	1.5 ± 0.3	1.6 ± 0.3*	2.3 ± 0.5**	2.3 ± 0.5	2.4 ± 0.4*
5th/95th percentile	1.1/2.0	0.9/2.0	1.2/2.1	1.6/3.1	1.4/3.2	1.7/3.1
O ₂ pulse _{peak} (mL per beat)	11.3 ± 2.0	11.1 ± 1.9	11.5 ± 2.0	16.4 ± 3.2**	16.3 ± 3.5	17.1 ± 3.0*
95% CI upper-lower	8.1/14.7	7.5/14.6	8.3/15.0	11.2/22.0	10.8/23.0	12.7/22.2
EqV _{O2peak} (V _{Epeak} /VO _{2peak})	35.1 ± 5.6	36.1 ± 6.5	35.7 ± 5.2	38.0 ± 6.9**	38.6 ± 8.1	37.7 ± 5.7
95% CI upper-lower	26.8/44.7	26.8/46.4	27.0/44.6	29.3/48.3	29.8/51.2	29.6/47.8
EqVC _{O2peak} (V _{Epeak} /VC _{O2peak})	31.9 ± 4.5	33.2 ± 5.1	31.8 ± 4.1*	33.5 ± 5.7**	34.7 ± 6.9	32.6 ± 4.4*
5th/95th percentile	25.5/39.1	26.6/41.5	26.3/38.3	26.4/41.6	26.8/44.8	26.6/38.7
SBP _{peak} (mm Hg)	195 ± 29	189 ± 28	197 ± 27	95 ± 26	188 ± 29	202 ± 21*
95% CI upper-lower	134-231	138-232	136-233	149-229	137-234	160-229
DBP _{peak} (mm Hg)	83 ± 17	85 ± 17	82 ± 19	80 ± 16**	83 ± 14	81 ± 18
5th/95th percentile	55-114	57-119	50-120	53-108	60-109	51-115
HR-recovery (bpm)	26 ± 10	25 ± 10	28 ± 10*	27 ± 11	27 ± 12	31 ± 13*
5th/95th percentile	10-43	10-45	13-43	10-46	9-47	15-54

Values are means ± SD, and 5th and 95th percentile.

*Significantly different from individuals (within the same sex) with CVD (*P* < 0.05).

**Significantly different from women (*P* < 0.05).

HR recovery, HR recovery 1-min after peak cardiopulmonary test.

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_{peak} and %VO_{2peak}) when they reported a subjective effort between 6 to 9 (*P* < 0.05) and 10 to 12 (*P* < 0.01) on the Borg scale compared with women (Table 5). No significant sex differences were observed at the higher intensities of the Borg scale (13–20). Men with CVD worked at a higher %VO_{2peak} at Borg scale 13 to 15 compared with 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

CRF. 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 United States by Kaminsky et al. (20). Interestingly, the

registry data from the United States show that for each age group, Norwegian men and women have higher CRF than those in the United States (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. (11) has presented reference values of CRF in Norwegian adults age 20 to 85 yr. However, people older than 50 yr 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 yr). The procedure for peak oxygen uptake testing in our study is the same as that used in HUNT3 study (2). Men ≥70 yr old in HUNT3 had higher VO_{2peak} (34 mL·kg⁻¹·min⁻¹) compared with 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 with our study. The healthy men and women in our study (free from CVD) had a somewhat higher VO_{2peak} compared with 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

TABLE 3. Respiratory variables at ventilatory anaerobic threshold (VAT) and at respiratory compensation point (RCP).

	Women			Men		
	All	With CVD	Healthy	All	With CVD	Healthy
VAT						
No. subjects	446	42	103	500	127	104
% $\dot{V}O_{2peak}$	76.6 ± 9.9	76.3 ± 8.0	76.9 ± 9.2	75.7 ± 9.2	75.4 ± 9.1	76.0 ± 8.8
5th/95th percentile	57.6/90.7	60.6/88.0	53.6/89.1	59.7/89.0	61.3/89.8	61.7/90.1
$\dot{V}O_2$ (L·min ⁻¹)	1.4 ± 0.3	1.3 ± 0.2	1.4 ± 0.3*	2.0 ± 0.4**	1.9 ± 0.4	2.1 ± 0.4*
5th/95th percentile	0.9/1.9	0.9/1.6	0.9/1.8	1.3/2.7	1.2/2.7	1.5/2.8
Eq $\dot{V}O_2$ ($\dot{V}_E/\dot{V}O_2$)	29.1 ± 3.3	29.4 ± 3.2	29.4 ± 3.1	30.1 ± 3.9**	29.7 ± 4.2	30.3 ± 3.8
5th/95th percentile	23.7/34.5	23.4/35.3	24.8/36.0	24.5/36.8	23.3/37.5	24.5/37.4
$\dot{V}CO_2$ (L·min ⁻¹)	1.3 ± 0.3	1.2 ± 0.2	1.3 ± 0.3*	1.9 ± 0.5**	1.8 ± 0.5	2.0 ± 0.4*
5th/95th percentile	0.7/1.8	0.8/1.6	0.7/1.8	1.1/2.7	1.1/2.7	1.4/2.8
Eq $\dot{V}CO_2$ ($\dot{V}_E/\dot{V}CO_2$)	31.9 ± 3.6	32.2 ± 3.5	32.0 ± 4.0	31.9 ± 4.1	32.4 ± 5.3	31.8 ± 4.8
5th/95th percentile	27.0/38.5	27.1/38.6	27.3/40.2	26.6/38.4	26.3/40.7	26.6/37.5
\dot{V}_E (L·min ⁻¹)	39.9 ± 9.1	38.3 ± 7.0	41.2 ± 8.7*	59.4 ± 14.3**	57.0 ± 14.7	63.8 ± 14.3*
5th/95th percentile	25.4/54.4	26.9/52.4	26.9/55.3	38.0/86.1	35.5/86.2	44.8/89.6
BF (breaths per minute)	29.4 ± 5.5	28.6 ± 4.9	29.4 ± 5.1	29.1 ± 5.6	27.7 ± 5.2	31.0 ± 6.6*
5th/95th percentile	21.4/37.6	21.5/37.2	22.1/38.8	21.4/39.0	19.1/36.0	21.6/42.5
RER	0.91 ± 0.07	0.91 ± 0.06	0.92 ± 0.07	0.94 ± 0.06**	0.93 ± 0.07	0.96 ± 0.5*
5th/95th percentile	0.78/1.02	0.82/1.00	0.78/1.02	0.83/1.04	0.82/1.03	0.86/1.07
RCP						
No. subjects	361	35	86	432	117	94
% $\dot{V}O_{2peak}$	87.7 ± 7.8	87.8 ± 5.9	88.1 ± 7.0	86.9 ± 7.9	86.3 ± 8.2	87.6 ± 7.4
5th/95th percentile	74.3/98.3	78.5/97.5	75.2/98	72.1/98.7	71.2/98.7	74.5/98.9
$\dot{V}O_2$ (L·min ⁻¹)	1.6 ± 0.3	1.5 ± 0.3	1.6 ± 0.3	2.3 ± 0.4**	2.2 ± 0.5	2.4 ± 0.4*
5th/95th percentile	1.1/2.1	1.1/2.0	1.1/2.1	1.5/3.0	1.5/3.0	1.7/3.2
Eq $\dot{V}O_2$ ($\dot{V}_E/\dot{V}O_2$)	32.2 ± 4.4	32.3 ± 4.1	32.6 ± 4.1	32.9 ± 4.7**	32.4 ± 5.3	33.0 ± 4.1
5th/95th percentile	25.7/39.9	25.4/40.3	26.3/41.2	26.3/41.0	24.9/41.1	25.7/40.6
$\dot{V}CO_2$ (L·min ⁻¹)	1.6 ± 0.4	1.5 ± 0.3	1.7 ± 0.4*	2.4 ± 0.5**	2.3 ± 0.5	2.5 ± 0.5*
5th/95th percentile	1.1/2.2	1.1/2.2	1.1/2.4	1.5/3.3	1.4/3.2	1.8/3.4
Eq $\dot{V}CO_2$ ($\dot{V}_E/\dot{V}CO_2$)	31.5 ± 3.5	32.0 ± 3.8	31.7 ± 3.8	31.6 ± 4.9	31.7 ± 5.0	31.3 ± 3.1
5th/95th percentile	25.8/38.0	26.0/40.0	26.6/41.3	26.0/38.0	25.4/39.0	26.2/36/5
\dot{V}_E (L·min ⁻¹)	50.4 ± 11.2	48.6 ± 10.0	52.5 ± 10.6	74.2 ± 17.2**	70.7 ± 17.3	79.7 ± 17.5*
5th/95th percentile	33.2/69.5	34.3/69.1	35.4/69.0	47.8/104.2	41.4/100.3	52.8/110.3
BF (breaths per minute)	33.0 ± 6.3	32.2 ± 6.4	33.2 ± 6.2	32.4 ± 6.3	31.4 ± 6.2	33.9 ± 7.2*
5th/95th percentile	23.1/44.5	24.4/48.9	22.4/45.0	23.8/43.6	22.9/43.0	23.5/47.3
RER	1.02 ± 0.09	1.02 ± 0.07	1.03 ± 0.09	1.04 ± 0.08**	1.03 ± 0.07	1.06 ± 0.08*
5th/95th percentile	0.89/1.17	0.87/1.14	0.91/1.15	0.91/1.17	0.90/1.14	0.93/1.18

Values are means ± SD, and 5th and 95th percentile.

*Significantly different from individuals (within the same sex) with CVD ($P < 0.05$).

**Significantly different from women ($P < 0.05$).

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, because it gives a comprehensive picture of the responses during CPET in a large number of older adults, including individuals with CVD.

Cardiorespiratory function. The results from the present study confirm that women and men with CVD respond differently physiologically during CPET compared with their healthy counterparts. In line with studies on people with heart failure (34), we observed that elderly people with CVD had lower HR_{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 HR (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 HR 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 (based upon the individual physiological response) used in our study may be preferable over more standard protocols (increasing workload at standardized time points) 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 bpm previously reported to be associated with increased risk of premature death (10). This indicates that the individuals with CVD in our population in general do not have a delayed decrease in HR after graded exercise, as often seen in people with heart failure (10,18). Clinical recommendation for CPET states that normal SBP_{peak} for men is approximately 210 mm Hg and for women approximately 190 mm Hg (16). The healthy women in this study had an average SBP_{peak} of 197 mm Hg, indicating that the normal value for SPB_{peak} during CPET for older women should be increased. As 37% of the healthy women had SPB_{peak} ≥ 210, we recommend that normal SBP_{peak} for women should be set to 210 mm Hg as for men. In our population, people with CVD had a normal rise in SBP, but men with CVD had lower SBP_{peak} than their healthy counterparts (SBP_{peak} were 188 mm Hg vs 202 mm Hg, respectively). The reason for slightly lower peak SBP 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 $\dot{V}O_{2max}$ compared with the healthy men. Previously, O_2 pulse has been listed as an important variable in exercise

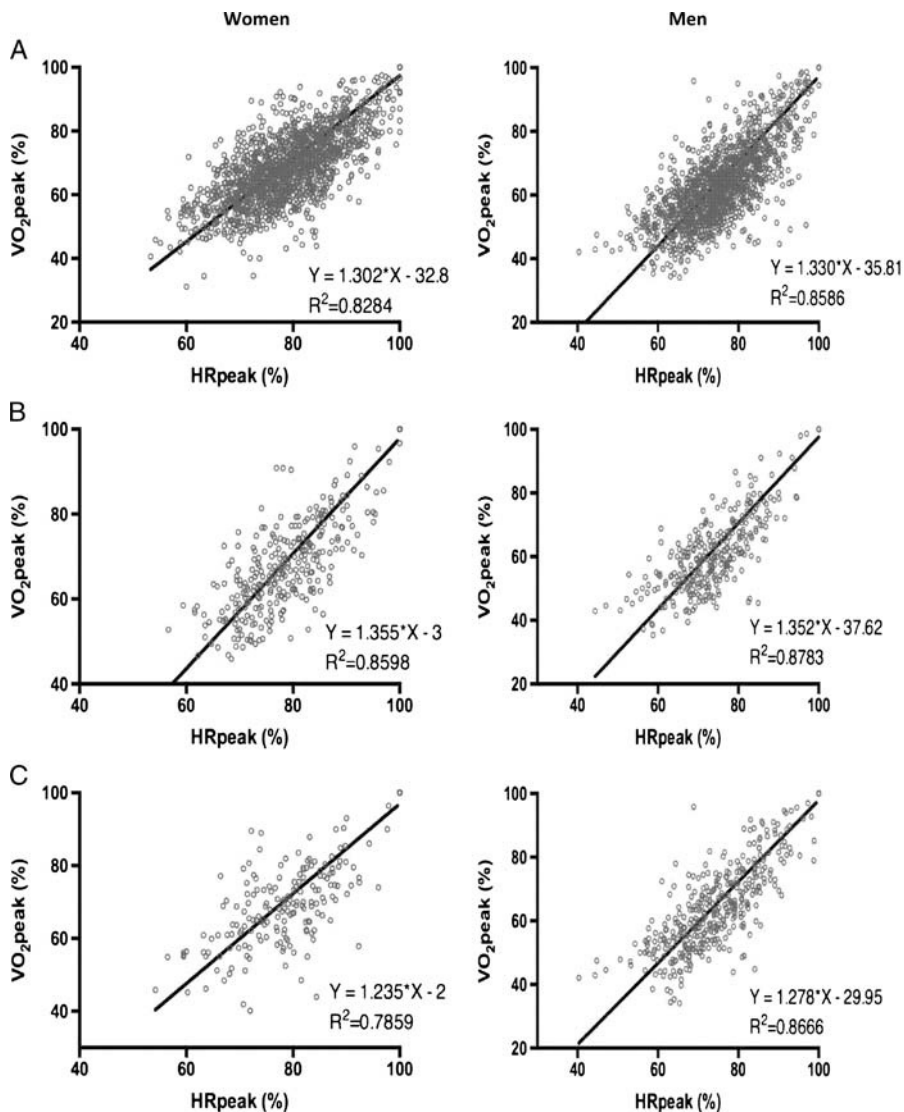


FIGURE 1—Correlation between percentage of HR_{peak} and percentage of peak oxygen uptake (% $\dot{V}O_{2peak}$) in women and men. A, all; B, healthy; C, with CVD.

testing because it reflects stroke volume response to exercise (16). Although it has been shown that the O₂ pulse flattening duration during CPET improves the diagnostic accuracy to identify exercise-induced myocardial ischemia (6), the prognostic value of O₂ pulse_{peak} has been questioned (23). The healthy men in our study had higher O₂ pulse_{peak} compared with men with CVD. Interestingly, O₂ 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

TABLE 4. The relationship between %HR_{peak}, %HRR, and % $\dot{V}O_{2peak}$ for older women and men.

	Women						Men					
	All		With CVD		Healthy		All		With CVD		Healthy	
%HR _{peak}	%HRR	% $\dot{V}O_{2peak}$	%HRR	% $\dot{V}O_{2peak}$	%HRR	% $\dot{V}O_{2peak}$	%HRR	% $\dot{V}O_{2peak}$	%HRR	% $\dot{V}O_{2peak}$	%HRR	% $\dot{V}O_{2peak}$
<57	29 ± 6	48 ± 6	28 ± 11	50 ± 6	No cases	53 ± 0	31 ± 5	48 ± 5	28 ± 6	47 ± 3	31 ± 5	46 ± 5
57–63	38 ± 4	53 ± 7	36 ± 4	53 ± 5	37 ± 4	55 ± 4	38 ± 9	52 ± 7	36 ± 10	51 ± 7	38 ± 10	51 ± 8
64–76	52 ± 7	62 ± 8	50 ± 7	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	71 ± 8*	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	100 ± 1	100 ± 3	95 ± 3	100 ± 2	93 ± 2	100 ± 0

Values are means ± SD.

*Significantly different from individuals (within the same sex) with CVD ($P < 0.05$).

**Significantly different from women ($P < 0.05$).

TABLE 5. Relationship between perceived exhaustion, oxygen uptake and HR in older women and men.

Borg Scale	Women						Men					
	All		With CVD		Healthy		All		With CVD		Healthy	
	%HR _{peak}	% $\dot{V}O_{2peak}$	%HR _{peak}	% $\dot{V}O_{2peak}$	%HR _{peak}	% $\dot{V}O_{2peak}$	%HR _{peak}	% $\dot{V}O_{2peak}$	%HR _{peak}	% $\dot{V}O_{2peak}$	%HR _{peak}	% $\dot{V}O_{2peak}$
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 ± 8	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 ± SD. % $\dot{V}O_{2peak}$: percent of peak oxygen uptake.

*Significantly different from women ($P < 0.05$).

**Significantly different from individuals (within the same sex) with CVD ($P < 0.05$).

with CVD had lower pulmonary parameters at rest, but higher ventilatory cost (Eq $\dot{V}CO_2$), compared with 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 (Eq $\dot{V}O_{2peak}$ and Eq $\dot{V}CO_{2peak}$) were higher in men compared with 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 be examined further in future studies. It has previously been suggested that the normative value for Eq $\dot{V}O_{2peak}$ should be ≤ 40 (16). Interestingly, the Eq $\dot{V}O_{2peak}$ for both men and women with CVD was below this threshold in our study, indicating that the normal values for Eq $\dot{V}O_{2peak}$ might be lower in older adults. Traditionally, $\dot{V}_E/\dot{V}CO_2$ slope is calculated using all exercising data (16), and the prognostic value of Eq $\dot{V}CO_2$ at peak ($\dot{V}_{Epeak}/\dot{V}CO_{2peak}$) is not clear. However, the equation previously presented by Sun et al. (38) indicates that the $\dot{V}_E/\dot{V}CO_2$ at submaximal level (Eq $\dot{V}CO_2$ at VAT) should be < 30 in our population. In line with Loe et al. (26), Eq $\dot{V}CO_2$ at VAT in our study was > 30 for all groups, indicating that for older adults, the normal value for submaximal Eq $\dot{V}CO_2$ should be higher than previously suggested (38).

VAT and RCP. As shown previously, men and women reached VAT and RCP at the same % $\dot{V}O_{2peak}$ (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 with men with CVD, indicating a more effective ventilation for the healthy men.

Correlation between HR and oxygen uptake. The correlation between %HR_{peak}, %HRR, and % $\dot{V}O_{2peak}$ 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 to 64 of %HR_{peak} in our study corresponds to a higher % $\dot{V}O_{2peak}$ compared with American College of Sports Medicine guidelines (13). As previously shown, men worked at a slightly lower % $\dot{V}O_{2peak}$ compared with women at moderate to vigorous intensities (%HR_{peak} 64–95) (25). Both men and women with CVD worked at lower % $\dot{V}O_{2peak}$ and higher %HRR at %HR_{peak} compared with 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 $\dot{V}O_{2peak}/HR_{peak}$ at lower intensities (25,32). Both men and women in our study worked at a significantly higher % $\dot{V}O_{2peak}$ and %HR_{peak} compared with 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 yr).

Strength and Limitations

The main strength of our study is that it includes a large, well-described sample of men and women 70 to 77 yr 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 article showed that the included participants reported somewhat better health and higher education compared with the nonparticipant group (37). However, our sample of older adults appears to be fairly representative with regard to prevalence of CVD compared with 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 \dot{V}_{Epeak} .

CONCLUSIONS

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 and help them to interpret data from CPET in older adults in the future.

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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.

Clinical trial: ClinicalTrials.gov NCT01666340 clinicaltrials.gov/ct2/show/NCT01666340.

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