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ORIGINAL RESEARCH

Reference Standards for Cardiorespiratory Fitness by Cardiovascular Disease Category and Testing Modality: Data From FRIEND

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BACKGROUND: The importance of cardiorespiratory fitness for stratifying risk and guiding clinical decisions in patients with cardiovascular disease is well-established. To optimize the clinical value of cardiorespiratory fitness, normative reference standards are essential. The purpose of this report is to extend previous cardiorespiratory fitness normative standards by providing updated cardiorespiratory fitness reference standards according to cardiovascular disease category and testing modality.

METHODS AND RESULTS: The analysis included 15 045 tests (8079 treadmill, 6966 cycle) from FRIEND (Fitness Registry and the Importance of Exercise National Database). Using data from tests conducted January 1, 1974, through March 1, 2021, percentiles of directly measured peak oxygen consumption (VO_{2peak}) were determined for each decade from 30 through 89 years of age for men and women with a diagnosis of coronary artery bypass surgery, myocardial infarction, percutaneous coronary intervention, or heart failure. There were significant differences between sex and age groups for VO_{2peak} ($P<0.001$). The mean VO_{2peak} was 23% higher for men compared with women and VO_{2peak} decreased by a mean of 7% per decade for both sexes. Among each decade, the mean VO_{2peak} from treadmill tests was 21% higher than the VO_{2peak} from cycle tests. Differences in VO_{2peak} were observed among the age groups in both sexes according to cardiovascular disease category.

CONCLUSIONS: This report provides normative reference standards by cardiovascular disease category for both men and women performing cardiopulmonary exercise testing on a treadmill or cycle ergometer. These updated and enhanced reference standards can assist with patient risk stratification and guide clinical care.

Key Words: cardiopulmonary exercise testing ■ health ■ peak oxygen consumption ■ risk factors ■ well-being

Cardiorespiratory fitness (CRF), defined as peak oxygen consumption (VO_{2peak}), reflects the interplay between the pulmonary, cardiovascular, and muscular systems in transporting oxygen from the atmosphere to the working muscles.[1] As such, CRF is a singular measure of whole-body physiological function that is associated with health and quality of life for a variety of populations. In patients with cardiovascular disease (CVD), lower CRF is associated with greater risk for early mortality, future CVD events, and higher healthcare costs.[2–7] CRF is also a stronger predictor of mortality and CVD risk compared with traditional risk factors such as obesity, diabetes, and dyslipidemia.[8–10] This convincing body of evidence resulted in recommendations that CRF should be regularly assessed alongside other established CVD risk factors to stratify patient risk and guide clinical care.[11–16]

Normative reference standards are essential for CRF to be effectively applied, particularly in a clinical setting. Because of the well-established differences in CRF caused by factors such as age and sex, interpreting CRF should initially be considered in terms of what constitutes a "normal" value for that individual. Therefore, a number of CRF reference standards have been published.[17–25] However, the majority of these previously published reference standards were developed using data from

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CLINICAL PERSPECTIVE

What Is New?

- This report provides normative reference standards for cardiorespiratory fitness by cardiovascular disease category for both men and women performing testing on a treadmill or cycle ergometer, which can optimize the clinical value of cardiorespiratory fitness assessments.
- There were significant differences in directly measured peak oxygen consumption between sex, age, and test modality groups with additional differences observed between cardiovascular disease categories.

What Are the Clinical Implications?

- The substantial differences in cardiorespiratory fitness between sex, age, and test modality groups highlight the importance of utilizing the appropriate normative reference standards in clinical settings.
- Considering that differences in cardiorespiratory fitness were observed between cardiovascular disease categories, these enhanced reference standards can improve patient risk stratification and guide clinical care.

Nonstandard Abbreviations and Acronyms

CPX	cardiopulmonary exercise testing
CRF	cardiorespiratory fitness
FRIEND	Fitness Registry and the Importance of Exercise National Database
RER	respiratory exchange ratio
VO_{2peak}	peak oxygen consumption

apparently healthy individuals.[17–24] One study created reference standards using data from patients with CVD entering a cardiac rehabilitation program,[25] demonstrating a lower CRF compared with age- and sex-matched apparently healthy individuals. These CRF reference standards for patients with CVD, however, were derived only from tests conducted on a treadmill at 2 centers and covered the time period of 1996 to 2004. Reference standards are also needed for cycle ergometer tests as this exercise mode is commonly used in clinical settings[26] and elicits lower values compared with exercise on a treadmill.[12] Additionally, while the CRF reference standards for patients with CVD was a pioneering publication, updated reference standards derived from a larger number of tests from multiple testing sites are needed.

Established following a policy statement from the American Heart Association,[27] the FRIEND (Fitness Registry and the Importance of Exercise National Database) is a database containing directly measured CRF from cardiopulmonary exercise testing (CPX). The data within FRIEND has previously been used to create CRF reference standards for apparently healthy individuals[17–19] yet the registry also includes data on a substantial number of patients with CVD. Thus, the purpose of this report is to improve on previous CRF normative reference standards in the CVD population by providing CRF reference standards for men and women performing CPX on either a treadmill or cycle ergometer.

METHODS

The procedures detailing data collection and management of FRIEND have been previously reported.[17] Briefly, FRIEND is composed of data from high-quality laboratories performing CPX administered by experienced personnel. While laboratories varied in terms of equipment, protocols, and definitions of CRF (eg, VO_{2peak} determined from time averages between 15 and 60 seconds), all laboratories conducted testing in accordance with published guidelines.[28] Each contributing laboratory obtained local research ethics board approval (or waiver of consent) prior to submitting deidentified, coded data to the data coordinating center and core laboratory at Ball State University, which has institutional review board approval for maintaining the database. Data from each contributing laboratory were reviewed by both the coordinating center and core laboratory to ensure CRF values were within expected normal ranges before the data were added to FRIEND. The data that support the findings of this study are available from the corresponding author upon reasonable request.

Cohort

The present analysis includes 15 045 tests (8079 treadmill, 6966 cycle ergometer) from 12 participating laboratories (see Acknowledgments) that were performed from January 1, 1974, through March 1, 2021. Geographical representation was limited to North America (Canada and the United States) as FRIEND currently contains limited data on patients with CVD from outside of this area and global differences in CRF[19] could influence the results. Inclusion criteria used to create the present cohort were: (1) current or previous occurrence of coronary artery bypass graft (CABG), myocardial infarction (MI), percutaneous coronary intervention (PCI), or heart failure (HF); (2) CPX performed on a treadmill or cycle ergometer; (3) age 30 to 89 years; and (4) peak respiratory exchange ratio (RER) ≥1.0 to indicate a sufficient effort.

Statistical Analysis

Analyses were performed in R version 3.6.1 (R Core Team). General CVD patient reference standards for CRF in men and women were created with all CVD categories combined (CABG, MI, PCI, and HF). To describe the CRF of patients with CVD compared with apparently healthy individuals, age- and sex-specific fitness percentiles were determined using the appropriate treadmill/cycle FRIEND reference standards for apparently healthy individuals.[17,18] Reference standards for peak workload during cycle CPX were also created, although peak workload was missing for some cycle tests.

Next, CRF reference standards for the individual CVD categories were created for those aged 40 to 89 years; reference standards were not created for the 30- to 39-year age group because of small sample sizes within the individual cardiac categories. The CVD categories were defined in agreement with previous research[29] (Figure 1). The CABG category included those who also reported MI but did not include those who reported PCI or HF. The PCI category excluded individuals who also reported CABG, MI, or HF. For the MI category, individuals who also reported CABG or HF were excluded. Last, the HF category did not exclude those who reported any occurrence of the other CVD categories.

For the overall CVD reference standards, 2-way ANOVA was used to compare differences in CRF values between sex and among age groups. One-way ANOVA was used to compare differences in CRF among age groups in the individual CVD category reference standards. Only general differences and trends were examined, therefore no post hoc analyses were performed. Additionally, box plots were created to compare changes in CRF among age deciles. Statistical significance was designated at the $P<0.05$ level. Continuous data are presented throughout the article as mean±SD, while categorical data are reported as frequencies (percentages).

RESULTS

The FRIEND CVD cohort included 12 262 tests in men (6487 from treadmill; 5775 from cycle ergometer) and 2783 tests in women (1592 from treadmill; 1191 from cycle ergometer). Descriptive characteristics of the cohort, by sex and in 10-year age groups, are provided in Table 1. For all CVD categories combined, peak responses during CPX, including RER for objective indications of sufficient effort, are provided in Table 2 for treadmill CPX and Table 3 for cycle ergometer CPX. When using CRF reference standards for apparently healthy individuals, the mean CRF percentile of the patients with CVD was 23% for treadmill CPX and 25% for cycle CPX. Observationally, compared with the CRF values previously reported by Ades et al, CRF values in the present study were consistently higher

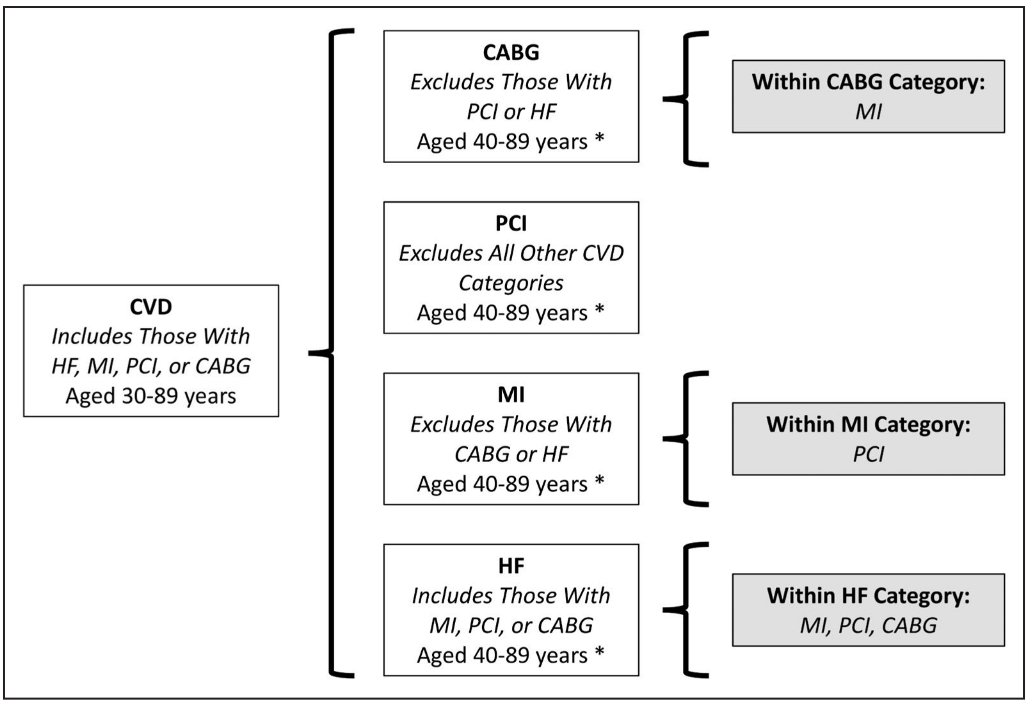

Figure 1. Overview of how the cardiovascular disease (CVD) categories were created.
*Cardiorespiratory fitness reference standards for the individual CVD categories were created for only those aged 40 to 89 years because of small sample sizes within the 30- to 39- year age group. CABG indicates coronary artery bypass graft; HF, heart failure; MI, myocardial infarction; and PCI, percutaneous coronary intervention.

among all age groups, averaging 13% higher in men and 21% higher in women.

There were significant differences between sex and age groups for CRF determined from either treadmill or cycling CPX ($P<0.001$). Further, there was a significant interaction between sex and age group for CRF determined from treadmill or cycling CPX ($P<0.001$). On average, men had a 4.2-mL·kg^{-1}·min^{-1} (23%) greater VO_{2peak} than women for treadmill CPX and a 3.3-mL·kg^{-1}·min^{-1} (22%) greater VO_{2peak} than women for cycling CPX. The change in CRF with each decade of age is illustrated in Figure 2 for treadmill CPX and Figure 3 for cycling CPX. For all CVD categories among both men and women, percentiles (including quartiles) by age group for CRF are presented in Table 4.

Peak responses during CPX for each of the 4 CVD categories are presented in Table 5 for treadmill CPX and Table 6 for cycling ergometer CPX. Percentiles (including quartiles) by age group for CRF are presented for each CVD category in Table 7 for treadmill CPX and Table 8 for cycling CPX. One-way ANOVA indicated significant group differences between age groups for each CVD category ($P<0.001$), with the exception of the HF category in women ($P=0.17$). The changes in CRF with each decade of age for each specific CVD category are illustrated in Figure 4 for treadmill CPX and Figure 5 for cycling CPX.

DISCUSSION

This analysis provides practical and current CRF normative reference standards for patients with CVD that can be used for interpreting results from either treadmill or cycle ergometer CPX. Similar to findings in apparently healthy individuals,[17–24] CRF was significantly lower in the older age groups, as well as for women compared with men. Previous research has reported declines in the CRF of healthy individuals ranging from 7% to 10% per decade whether using treadmill or cycle ergometer CPX.[17,18,21,22] Although not always consistent from decade to decade, the mean decline in CRF in the FRIEND CVD cohort was 7% (9% for treadmill CPX and 5% for cycle ergometer CPX). Differences in CRF between men and women with CVD were also similar to those observed in their apparently healthy peers. The present study found a difference of 23%, while others have reported differences between 26% and 30%.[17–19,30]

Table 1. Descriptive Characteristics of the FRIEND CVD Cohort for the Treadmill and Cycling Ergometer Analysis

	Age group, y					
	30–39	40–49	50–59	60–69	70–79	80–89
Treadmill						
Men	(n=250)	(n=857)	(n=1858)	(n=2104)	(n=1141)	(n=277)
Age, y	35.7±2.8	45.6±2.8	54.9±2.8	64.3±2.8	73.7±2.8	82.8±2.3
Height, cm	177.9±9.1	176.2±7.5	175.3±7.5	174.4±7.4	173.5±7.4	170.7±7.4
Weight, kg	94.4±23.5	92.1±19.2	90.0±17.9	86.7±16.2	83.5±14.6	77.5±11.6
BMI, kg·m^{-2}	29.7±6.8	29.6±5.6	29.3±5.3	28.5±5.1	27.7±4.3	26.6±3.7
Women	(n=123)	(n=208)	(n=424)	(n=472)	(n=297)	(n=68)
Age, y	35.1±2.8	44.9±2.8	54.9±3.0	64.4±2.8	73.7±2.8	82.8±2.3
Height, cm	165.4±7.6	163.1±7.3	161.8±7.6	160.4±6.9	159.1±8.0	157.0±6.6
Weight, kg	77.1±20.7	79.1±18.8	78.4±18.0	73.9±17.8	68.6±14.1	62.0±10.6
BMI, kg·m^{-2}	28.1±7.1	29.8±7.1	30.1±7.6	28.7±6.6	27.1±5.3	25.2±4.1
Cycle ergometer						
Men	(n=130)	(n=645)	(n=1626)	(n=1856)	(n=1205)	(n=313)
Age, y	36.0±2.7	45.6±2.7	55.0±2.8	64.3±2.9	74.0±2.8	83.0±2.5
Height, cm	175.2±9.6	174.9±12.3	173.4±7.6	172.8±7.5	170.9±8.5	170.3±7.8
Weight, kg	90.2±21.5	88.7±18.5	85.8±17.4	84.3±15.7	81.1±14.5	76.4±12.7
BMI, kg·m^{-2}	29.4±7.2	29.1±5.9	28.5±5.1	28.2±4.9	27.8±5.3	26.4±4.3
Women	(n=48)	(n=112)	(n=297)	(n=362)	(n=295)	(n=77)
Age, y	36.0±2.7	45.8±2.6	54.8±2.8	64.5±2.9	74.2±2.9	82.9±2.1
Height, cm	164.1±7.2	162.5±7.9	161.1±6.6	160.1±7.4	158.5±6.1	156.7±5.7
Weight, kg	74.2±20.0	76.7±19.3	75.3±17.4	74.4±15.8	68.9±14.4	64.9±12.2
BMI, kg·m^{-2}	27.6±7.4	29.0±6.7	29.0±6.2	29.0±5.8	27.4±5.4	26.4±4.7

Values are presented as mean±SD.
BMI indicates body mass index; CVD, cardiovascular disease; and FRIEND, Fitness Registry and the Importance of Exercise National Database.

Table 2. Treadmill CPX Responses at Peak Effort for Men and Women With CVD

	Age group, y					
	30–39	40–49	50–59	60–69	70–79	80–89
Men	(n=250)	(n=857)	(n=1858)	(n=2104)	(n=1141)	(n=277)
VO_{2peak}, mL·kg^{-1}·min^{-1}	27.3±9.7	25.5±8.2	23.6±7.4	21.5±6.3	18.7±5.1	16.4±4.3
FRIEND CRF percentile	14.2±19.2	15.1±18.5	19.3±20.9	22.8±21.5	22.0±21.1	…
Peak HR, beat·min^{-1}	150.7±23.5	140.8±22.1	132.7±21.9	125.4±21.0	117.7±20.9	111.2±20.2
Peak RER	1.15±0.10	1.16±0.28	1.15±0.09	1.14±0.10	1.13±0.09	1.13±0.16
Women	(n=123)	(n=208)	(n=424)	(n=472)	(n=297)	(n=68)
VO_{2peak}, mL·kg^{-1}·min^{-1}	22.0±8.0	19.2±6.6	18.0±5.5	17.9±5.2	16.4±4.4	14.2±3.8
FRIEND CRF percentile	20.8±23.9	19.4±23.5	21.9±24.1	35.0±29.9	35.2±30.6	…
Peak HR, beat·min^{-1}	149.3±20.9	139.8±23.3	129.5±20.9	125.3±20.8	116.0±20.5	108.5±19.7
Peak RER	1.14±0.11	1.15±0.10	1.13±0.09	1.11±0.08	1.10±0.08	1.09±0.08

Values are presented as mean±SD.

CRF indicates cardiorespiratory fitness; CVD, cardiovascular disease; FRIEND CRF percentile, peak oxygen consumption (VO_{2peak}) percentile ranking from the Fitness Registry and the Importance of Exercise National Database reference standards for apparently healthy individuals performing treadmill cardiopulmonary exercise testing (CPX)[17] (publication does not include reference values for those aged 80–89 years); HR, heart rate; and RER, respiratory exchange ratio.

Furthermore, while not examined statistically, there were observable differences between CRF determined from treadmill compared with cycle ergometer CPX. On average, the CRF from treadmill CPX was 21% higher than that from cycling CPX, similar to what has previously been reported for healthy individuals.[18]

In addition to similarities, expected differences were observed between patients with CVD and apparently healthy individuals. Principally, the mean CRF percentile of the patients with CVD was 23% for treadmill and 25% for cycle CPX when using the CRF reference standards for healthy individuals.[17,18] For treadmill CPX, men with CVD had a mean CRF that was 31% lower compared with healthy peers, while a difference of 22% was observed in women. With cycle ergometer CPX, CRF differences between patients with CVD and healthy peers were 26% for men and 27% for women. These substantial differences in CRF highlight the importance of utilizing the appropriate normative reference standards in clinical settings.

Table 3. Cycle Ergometer CPX Responses at Peak Effort for Men and Women With CVD

	Age group, y					
	30–39	40–49	50–59	60–69	70–79	80–89
Men	(n=130)	(n=645)	(n=1626)	(n=1856)	(n=1205)	(n=313)
VO_{2peak}, mL·kg^{-1}·min^{-1}	19.8±6.2	20.7±5.8	19.6±5.2	18.0±4.7	16.1±4.1	14.8±3.6
FRIEND CRF percentile	13.6±17.0	20.7±22.7	20.0±23.6	22.6±24.4	24.2±25.6	…
VO_{2peak}, L·min^{-1}	1.75±0.60	1.81±0.53	1.66±0.49	1.50±0.42	1.29±0.36	1.12±0.30
Peak workload, W	125.5±42.3 *(n=117)*	125.0±38.8 *(n=625)*	116.1±35.6 *(n=1602)*	104.4±31.8 *(n=1835)*	88.0±27.1 *(n=1190)*	71.8±25.3 *(n=308)*
Peak HR, beat·min^{-1}	133.3±24.5	127.8±20.3	122.7±19.1	115.1±19.6	107.5±19.3	101.0±17.6
Peak RER	1.16±0.09	1.17±0.10	1.18±0.09	1.18±0.25	1.16±0.09	1.14±0.09
Women	(n=48)	(n=112)	(n=297)	(n=362)	(n=295)	(n=77)
VO_{2peak}, mL·kg^{-1}·min^{-1}	17.4±5.6	16.3±4.3	15.2±4.3	14.5±3.8	13.2±2.8	12.7±2.8
FRIEND CRF percentile	27.5±30.0	28.1±25.7	30.6±28.7	34.2±31.9	31.2±28.1	…
VO_{2peak}, L·min^{-1}	1.25±0.41	1.23±0.40	1.13±0.35	1.06±0.30	0.89±0.22	0.82±0.23
Peak workload, W	89.1±37.4 *(n=38)*	82.3±31.5 *(n=104)*	77.9±28.9 *(n=283)*	70.6±24.5 *(n=359)*	55.4±20.8 *(n=292)*	46.1±20.9 *(n=76)*
Peak HR, beat·min^{-1}	135.5±26.6	124.3±20.6	119.3±21.0	113.1±18.5	106.6±18.4	100.0±16.6
Peak RER	1.14±0.07	1.18±0.10	1.18±0.10	1.17±0.12	1.14±0.10	1.11±0.08

Values are presented as mean±SD.

CRF indicates cardiorespiratory fitness; CVD, cardiovascular disease; FRIEND CRF percentile, peak oxygen consumption (VO_{2peak}) percentile ranking from the Fitness Registry and the Importance of Exercise National Database reference standards for apparently healthy individuals performing cycle ergometer cardiopulmonary exercise testing (CPX)[18] (publication does not include reference values for those aged 80–89 years); HR, heart rate; and RER, respiratory exchange ratio.

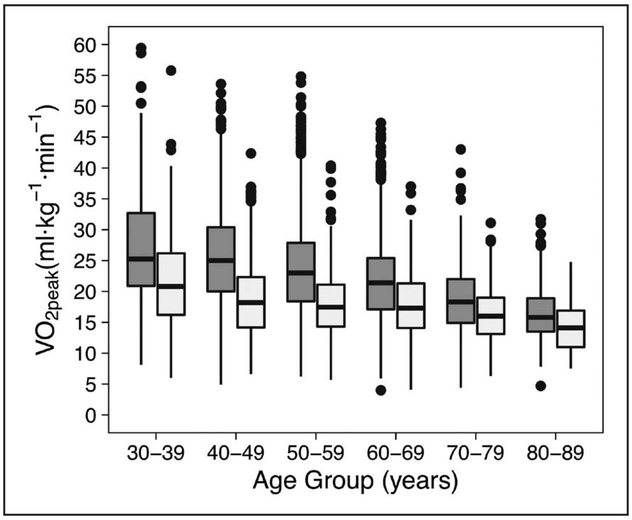

Figure 2. Box plots illustrating the median, interquartile range, and outliers for measured peak oxygen uptake (VO_{2peak}) from all cardiovascular disease categories determined from treadmill cardiopulmonary exercise testing for men (dark gray) and women (light gray).

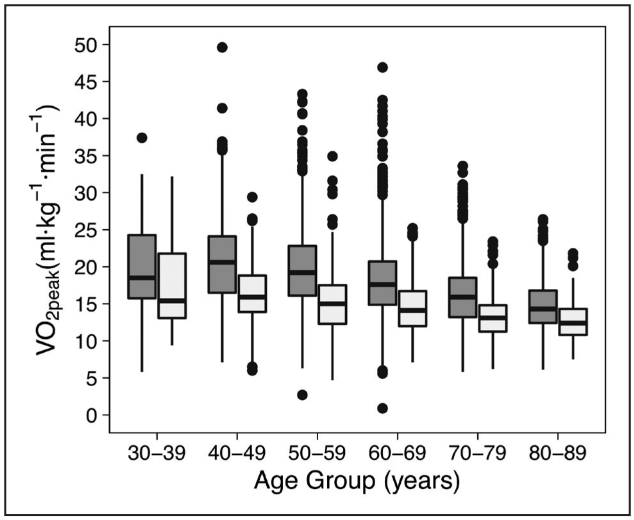

Figure 3. Box plots illustrating the median, interquartile range, and outliers for measured peak oxygen uptake (VO_{2peak}) from all cardiovascular disease categories determined from cycling ergometer cardiopulmonary exercise testing for men (dark gray) and women (light gray).

The only other known CRF reference values for patients with CVD were developed using data from 2 centers with a treadmill as the testing activity mode.[25] When comparing treadmill-derived CRF standards, the present study found 13% to 21% higher CRF values among the age groups compared with the previous reference standards. Of note, a portion of the data used to create the previous reference standards are also included in the FRIEND CVD cohort. These previous reference standards were developed using CPX data from patients entering a cardiac rehabilitation program relatively soon after experiencing a CVD event (mean of ≈40 days). Although the mean length of time between the CVD event and testing is not known in the FRIEND data set, tests from different points in the cardiac rehabilitation program are included. Tests performed later in cardiac rehabilitation would allow for greater myocardial recovery and the inclusion of individuals further removed from a CVD event may explain the higher values observed in the present study.

The cycling-derived CRF values of the FRIEND CVD cohort are similar to those reported in previous studies that also used cycle ergometer CPX with CVD populations. The CRF of age-matched men, expressed as absolute VO_{2peak}, was similar to those reported by Kavanagh et al[5] (1.6±0.4 $L\cdot min^{-1}$, aged 54.7±9.6 years) and Vanhees et al[4] (1.70±0.46 $L\cdot min^{-1}$, aged 53.0±7.8 years). For men, CRF expressed as relative VO_{2peak} was also similar to those reported by Kavanagh et al[5] (20.2±5.1 $mL\cdot kg^{-1}\cdot min^{-1}$), yet lower than that reported by Vanhees et al[4] (22.3±6.0 $mL\cdot kg^{-1}\cdot min^{-1}$). The Vanhees et al study was published in 1994 and there has been a general trend of increased body weight since that time.[31] Indeed, the mean body weight in the Vanhees et al cohort was ≈12kg lower than that of the present FRIEND CVD cohort, which may partly explain much of the differences in relative VO_{2peak}. For women, the mean CRF in the present study is comparable to the CRF reported as relative VO_{2peak} by Kavanagh et al[6] (15.1±3.9 $mL\cdot kg^{-1}\cdot min^{-1}$, aged 59.7±9.5 years). Some of the similarities between the present study and the Kavanagh reports may be attributable to the inclusion of data from the same geographical testing location and center as the Kavanagh cohorts. Nonetheless, the similarities indicate the cohort of individuals with CVD used to develop the FRIEND CRF reference standards are representative of those found in clinical settings.

The present report also provides current CRF normative reference standards within specific CVD categories. Differences were observed among the CVD categories similar to the findings of previous research examining CABG, MI, and PCI.[25] The highest CRF was observed in the PCI group, while the lowest CRF was observed in the patients with HF in the FRIEND cohort. These differences are likely attributable to the degree of myocardial injury within each group, as well as muscle limitations and therefore exercise capacity. Also of note, the mean CRF of the cohort is comparable to previous research. For men, Kavanagh et al[5] report similar cycling-derived CRF values expressed as relative VO_{2peak} for both CABG (19.2±4.5 $mL\cdot kg^{-1}\cdot min^{-1}$, aged 57.1±9.4 years) and MI (20.5±5.2 $mL\cdot kg^{-1}\cdot min^{-1}$, aged 53.5±9.5 years), while Guazzi et al[32] reported a mean cycling-derived relative

Table 4. CRF Percentiles for the FRIEND CVD Cohort by Age Group for Treadmill and Cycling Ergometer CPX With Directly Measured VO_{2peak} ($mL \cdot kg^{-1} \cdot min^{-1}$)

Percentile	Age group, y											
	Men						Women					
	30–39	40–49	50–59	60–69	70–79	80–89	30–39	40–49	50–59	60–69	70–79	80–89
Treadmill												
	(n=250)	(n=857)	(n=1858)	(n=2104)	(n=1141)	(n=277)	(n=123)	(n=208)	(n=424)	(n=472)	(n=297)	(n=68)
10	15.0	15.1	14.4	13.5	12.5	11.6	12.7	11.9	11.6	11.8	11.3	9.7
25	20.9	20.0	18.4	17.1	14.9	13.5	16.2	14.2	14.3	14.1	13.1	11.0
50	25.2	25.0	23.0	21.4	18.3	15.8	20.8	18.2	17.5	17.3	16.0	14.1
75	32.7	30.4	27.9	25.4	22.0	18.9	26.2	22.3	21.1	21.3	19.0	16.9
90	40.3	35.8	33.1	29.6	25.9	22.4	31.5	28.5	25.1	25.1	22.7	18.8
Cycling												
	(n=130)	(n=645)	(n=1626)	(n=1856)	(n=1205)	(n=313)	(n=48)	(n=112)	(n=297)	(n=362)	(n=295)	(n=77)
10	12.2	13.9	13.5	12.7	11.1	10.5	10.9	11.2	9.7	9.7	9.7	9.4
25	15.7	16.5	16.1	14.9	13.2	12.4	13.1	13.9	12.3	12.0	11.2	10.8
50	18.5	20.6	19.2	17.6	15.9	14.3	15.4	15.9	15.0	14.1	13.1	12.4
75	24.3	24.1	22.8	20.7	18.5	16.8	21.8	18.8	17.5	16.7	14.8	14.3
90	27.7	28.0	26.3	23.7	21.6	20.1	26.7	21.7	20.3	20.0	16.5	15.8

CRF indicates cardiorespiratory fitness; CPX, cardiopulmonary exercise testing; CVD, cardiovascular disease; and FRIEND, Fitness Registry and the Importance of Exercise National Database.

Table 5. Treadmill CPX Responses at Peak Effort According to CVD Category

	Age group, y									
	Men					Women				
	40–49	50–59	60–69	70–79	80–89	40–49	50–59	60–69	70–79	80–89
CABG	(n=121)	(n=423)	(n=585)	(n=327)	(n=66)	(n=10)	(n=47)	(n=80)	(n=72)	(n=11)
VO_{2peak}, mL·kg^{-1}·min^{-1}	23.2±5.6	21.5±5.3	20.1±5.2	17.7±4.4	15.4±3.1	14.9±3.2	17.3±4.0	16.6±4.6	14.7±2.9	11.9±2.1
FRIEND CRF percentile	8.5±10.1	11.9±13.0	16.6±17.0	17.2±17.3	…	5.2±4.0	16.3±18.5	28.4±25.6	22.1±20.8	…
Peak HR, beat·min^{-1}	141.0±19.1	129.0±19.3	122.8±20.3	116.1±20.6	110.3±21.5	122.3±14.7	125.0±20.0	122.0±19.4	114.5±20.7	105.0±17.5
Peak RER	1.15±0.09	1.15±0.09	1.14±0.09	1.13±0.09	1.12±0.08	1.15±0.08	1.12±0.09	1.11±0.08	1.09±0.07	1.09±0.08
MI	(n=333)	(n=564)	(n=537)	(n=262)	(n=64)	(n=51)	(n=128)	(n=136)	(n=79)	(n=25)
VO_{2peak}, mL·kg^{-1}·min^{-1}	27.9±7.2	26.2±6.8	23.6±5.7	20.4±5.3	17.8±4.6	20.4±5.0	20.0±5.4	19.5±5.3	17.2±4.8	14.9±4.2
FRIEND CRF percentile	18.3±18.9	25.5±22.1	28.9±21.6	28.4±23.3	…	20.9±20.2	29.7±26.4	43.5±32.0	42.6±34.5	…
Peak HR, beat·min^{-1}	140.3±19.0	135.1±19.5	127.0±18.6	118.8±19.9	108.7±16.6	139.2±17.6	130.8±19.2	125.2±19.8	114.1±19.0	104.2±19.9
Peak RER	1.18±0.43	1.14±0.08	1.14±0.11	1.12±0.08	1.11±0.08	1.14±0.09	1.13±0.08	1.10±0.07	1.10±0.08	1.09±0.07
PCI	(n=117)	(n=351)	(n=443)	(n=238)	(n=57)	(n=18)	(n=60)	(n=115)	(n=86)	(n=16)
VO_{2peak}, mL·kg^{-1}·min^{-1}	28.9±7.2	26.9±6.9	24.1±6.1	20.5±4.8	17.2±3.9	21.1±6.4	19.6±5.0	19.6±5.0	17.5±4.5	15.9±3.9
FRIEND CRF percentile	20.4±20.5	27.9±23.1	31.5±23.5	28.9±21.5	…	27.0±23.2	27.8±24.6	44.5±29.4	43.3±31.0	…
Peak HR, beat·min^{-1}	147.8±21.1	138.9±20.2	130.9±20.7	119.2±21.1	109.5±18.8	144.3±22.6	131.2±21.8	128.6±19.8	118.2±20.7	120.8±21.3
Peak RER	1.14±0.08	1.14±0.08	1.14±0.08	1.12±0.07	1.13±0.09	1.14±0.09	1.13±0.08	1.12±0.08	1.10±0.08	1.10±0.08
HF	(n=284)	(n=493)	(n=477)	(n=290)	(n=85)	(n=127)	(n=183)	(n=138)	(n=57)	(n=11)
VO_{2peak}, mL·kg^{-1}·min^{-1}	22.3±9.2	20.0±7.9	18.7±6.7	16.9±5.3	15.7±4.9	18.7±7.3	16.2±5.4	15.7±4.6	15.7±4.3	12.6±3.3
FRIEND CRF percentile	12.0±18.7	12.7±19.1	15.7±20.1	15.6±19.1	…	19.0±25.4	15.6±21.5	22.4±24.6	29.9±28.5	…
Peak HR, beat·min^{-1}	138.5±26.3	128.8±26.3	122.5±23.7	117.4±22.3	115.3±22.4	140.9±25.4	129.2±22.1	124.6±23.1	117.3±22.2	106.5±16.9
Peak RER	1.16±0.11	1.16±0.11	1.14±0.11	1.15±0.12	1.15±0.27	1.15±0.10	1.14±0.10	1.11±0.08	1.11±0.09	1.10±0.09

Values are presented as mean±SD.

CABG indicates coronary artery bypass graft; CRF, cardiorespiratory fitness; CVD, cardiovascular disease; FRIEND CRF percentile, peak oxygen consumption (VO_{2peak}) percentile ranking from the Fitness Registry and the Importance of Exercise National Database reference standards for apparently healthy individuals performing treadmill cardiopulmonary exercise testing (CPX)[17] (publication does not include reference values for those aged 80–89 years); HF, heart failure; HR, heart rate; MI, myocardial infarction; PCI, percutaneous coronary intervention; and RER, respiratory exchange ratio.

Table 6. Cycle Ergometer CPX Responses at Peak Effort According to CVD Category

	Age group, y									
	Men					Women				
	40–49	50–59	60–69	70–79	80–89	40–49	50–59	60–69	70–79	80–89
CABG	(n=108)	(n=374)	(n=644)	(n=452)	(n=92)	(n=15)	(n=47)	(n=70)	(n=72)	(n=13)
VO_{2peak}, mL·kg^{-1}·min^{-1}	19.2±4.5	18.4±4.1	17.3±3.9	15.8±3.7	14.6±2.7	16.4±4.3	14.9±3.9	14.6±3.9	12.9±2.4	12.1±3.9
FRIEND CRF percentile	13.6±17.1	13.7±17.8	18.0±20.5	21.6±23.9	…	26.7±28.8	27.4±25.5	34.4±32.4	27.6±25.4	…
VO_{2peak}, L·min^{-1}	1.6±0.4	1.5±0.4	1.4±0.4	1.2±0.3	1.1±0.3	1.3±0.4	1.1±0.3	1.0±0.3	0.8±0.2	0.8±0.2
Peak workload, W	110.3±28.4	104.2±27.3	99.2±26.0	84.5±23.4	72.7±24.9	78.2±30.7	74.9±23.1	70.0±24.7	51.5±18.3	37.4±18.3
Peak HR, beat·min^{-1}	126.7±19.6	122.0±18.5	114.8±19.4	106.5±19.4	102.4±19.1	116.7±17.2	116.9±19.6	113.8±18.5	105.5±17.3	89.5±10.6
Peak RER	1.20±0.10	1.20±0.10	1.20±0.34	1.18±0.10	1.15±0.09	1.16±0.09	1.21±0.11	1.19±0.15	1.16±0.11	1.09±0.06
MI	(n=317)	(n=710)	(n=569)	(n=314)	(n=98)	(n=50)	(n=116)	(n=137)	(n=103)	(n=23)
VO_{2peak}, mL·kg^{-1}·min^{-1}	22.3±5.3	20.9±5.0	19.3±4.8	17.5±4.2	15.7±4.0	17.9±3.4	15.9±3.8	14.8±3.8	13.3±3.1	13.8±3.3
FRIEND CRF percentile	25.9±24.0	24.3±25.1	28.5±26.3	32.0±28.2	…	36.1±24.7	34.5±28.1	35.8±31.9	33.5±29.2	…
VO_{2peak}, L·min^{-1}	1.9±0.5	1.8±0.5	1.6±0.4	1.4±0.4	1.2±0.3	1.4±0.4	1.2±0.3	1.1±0.3	0.9±0.2	0.9±0.2
Peak workload, W	134.1±34.4	124.4±34.4	112.6±32.0	95.1±28.9	77.0±26.4	95.1±24.4	81.4±23.7	72.0±25.3	54.8±20.7	50.6±20.0
Peak HR, beat·min^{-1}	128.7±19.0	122.9±18.2	115.4±18.5	109.2±17.9	102.2±15.4	127.4±19.7	120.0±18.7	111.2±16.3	104.4±19.2	103.5±15.1
Peak RER	1.17±0.09	1.18±0.09	1.16±0.09	1.16±0.08	1.16±0.09	1.21±0.11	1.18±0.10	1.17±0.11	1.12±0.10	1.14±0.07
PCI	(n=84)	(n=271)	(n=323)	(n=202)	(n=54)	(n=8)	(n=53)	(n=85)	(n=61)	(n=18)
VO_{2peak}, mL·kg^{-1}·min^{-1}	22.9±5.4	21.4±5.3	19.6±4.9	17.5±4.1	16.1±3.7	18.9±4.5	17.2±4.3	15.5±3.7	14.0±2.9	13.3±2.0
FRIEND CRF percentile	26.7±25.1	26.7±27.2	30.7±27.4	31.5±27.1	…	43.6±31.7	43.7±31.4	42.7±32.4	39.1±30.3	…
VO_{2peak}, L·min^{-1}	2.03±0.55	1.87±0.48	1.65±0.43	1.46±0.37	1.23±0.28	1.42±0.40	1.33±0.35	1.12±0.27	0.98±0.20	0.93±0.19
Peak workload, W	139.9±36.2	127.7±33.2	114.0±31.3	98.1±25.9	77.8±23.6	91.9±28.9	95.2±28.2	72.6±20.1	62.9±20.9	52.7±21.6
Peak HR, beat·min^{-1}	133.6±19.0	126.1±19.2	119.8±19.8	110.2±18.7	101.0±17.8	127.8±20.5	123.3±19.7	114.3±18.6	111.4±18.0	103.1±13.8
Peak RER	1.16±0.09	1.17±0.09	1.18±0.34	1.15±0.09	1.13±0.09	1.15±0.10	1.18±0.09	1.17±0.10	1.16±0.10	1.09±0.09
HF	(n=108)	(n=200)	(n=219)	(n=176)	(n=56)	(n=39)	(n=73)	(n=62)	(n=57)	(n=21)
VO_{2peak}, mL·kg^{-1}·min^{-1}	16.2±5.8	15.5±4.8	14.6±4.5	13.1±3.6	12.4±3.0	13.7±4.0	12.8±4.2	12.9±3.7	12.3±2.6	11.3±1.4
FRIEND CRF percentile	8.8±14.7	8.4±15.3	10.2±16.5	10.8±16.2	…	15.2±18.7	18.4±25.0	21.7±28.0	23.2±25.2	…
VO_{2peak}, L·min^{-1}	1.53±0.56	1.41±0.50	1.28±0.44	1.11±0.36	0.97±0.24	0.99±0.33	0.95±0.33	1.00±0.32	0.88±0.24	0.72±0.19
Peak workload, W	99.0±48.8 (n=88)	93.1±41.1 (n=176)	82.9±37.4 (n=199)	72.2±26.6 (n=161)	53.9±20.3 (n=52)	61.0±32.1 (n=31)	60.8±32.6 (n=59)	66.0±28.7 *(n=59)*	52.5±22.1 *(n=54)*	41.7±21.6 *(n=20)*
Peak HR, beat·min^{-1}	122.4±24.1	119.6±22.6	109.5±20.9	104.1±21.9	96.1±18.7	122.6±22.5	116.7±25.6	116.8±22.7	107.2±18.2	100.1±21.0
Peak RER	1.15±0.10	1.16±0.10	1.15±0.09	1.14±0.09	1.12±0.08	1.17±0.09	1.15±0.11	1.15±0.10	1.12±0.09	1.12±0.08

Values are presented as mean±SD.

CABG indicates coronary artery bypass graft; CRF, cardiorespiratory fitness; CVD, cardiovascular disease; FRIEND CRF percentile, peak oxygen consumption (VO_{2peak}) percentile ranking from the Fitness Registry and the Importance of Exercise National Database reference standards for apparently healthy individuals performing cycle ergometer cardiopulmonary exercise testing (CPX)[18] (publication does not include reference values for those aged 80–89 years); HF, heart failure; HR, heart rate; MI, myocardial infarction; PCI, percutaneous coronary intervention; and RER, respiratory exchange ratio.

Table 7. CRF Percentiles According to CVD Category for Treadmill CPX With Directly Measured VO_{2peak} ($mL \cdot kg^{-1} \cdot min^{-1}$)

Percentile	Age group, y									
	Men					Women				
	40–49	50–59	60–69	70–79	80–89	40–49	50–59	60–69	70–79	80–89
CABG	(n=121)	(n=423)	(n=585)	(n=327)	(n=66)	(n=10)	(n=47)	(n=80)	(n=72)	(n=11)
10	16.5	14.9	13.6	12.4	11.9	12.1	13.2	11.1	10.9	9.7
25	19.3	17.6	16.6	14.5	13.6	12.9	14.8	13.3	12.7	10.2
50	22.6	21.5	19.7	17.3	14.6	14.6	16.5	16.8	14.7	11.6
75	26.6	25.0	23.1	20.6	17.2	17.0	19.7	18.9	16.3	13.4
90	30.3	27.9	26.7	23.2	20.1	19.2	22.5	22.6	18.5	13.8
MI	(n=333)	(n=564)	(n=537)	(n=262)	(n=64)	(n=51)	(n=128)	(n=136)	(n=79)	(n=25)
10	18.7	18.3	16.6	13.9	12.6	14.4	14.0	13.2	10.8	9.7
25	22.9	21.8	19.9	16.7	14.5	17.1	16.5	15.5	13.1	10.7
50	27.8	25.8	23.6	20.0	17.1	20.0	19.6	19.1	17.1	15.6
75	31.7	29.8	26.8	23.6	20.5	22.8	22.7	23.2	20.5	17.7
90	37.0	34.9	30.2	27.1	23.9	26.3	27.7	26.4	23.5	20.3
PCI	(n=117)	(n=351)	(n=443)	(n=238)	(n=57)	(n=18)	(n=60)	(n=115)	(n=86)	(n=16)
10	21.4	18.5	15.8	14.3	12.7	12.0	13.9	14.0	12.4	11.8
25	23.9	21.9	20.1	17.1	14.6	18.2	16.2	16.1	14.7	14.3
50	27.5	26.3	24.1	20.4	16.6	21.3	19.4	19.2	17.1	15.5
75	33.4	31.1	28.2	23.9	19.2	26.2	22.2	22.9	20.0	17.1
90	38.5	35.2	31.6	26.7	22.2	28.9	26.4	26.3	23.0	20.1
HF	(n=284)	(n=493)	(n=477)	(n=290)	(n=85)	(n=127)	(n=183)	(n=138)	(n=57)	(n=11)
10	12.1	11.8	11.2	10.6	10.4	11.2	10.1	10.8	11.3	9.0
25	15.5	14.4	13.6	13.6	11.9	13.6	12.7	12.7	13.0	10.6
50	20.9	18.7	17.7	16.4	14.8	16.9	15.2	14.8	15.4	11.7
75	27.1	24.3	22.6	19.5	18.6	22.2	19.1	18.5	16.9	14.6
90	35.7	30.7	27.8	23.3	21.6	28.7	23.5	20.6	20.8	17.2

CABG indicates coronary artery bypass graft; CRF, cardiorespiratory fitness; CPX, cardiopulmonary exercise testing; CVD, cardiovascular disease; HF, heart failure; MI, myocardial infarction; PCI, percutaneous coronary intervention; and VO_{2peak}, peak oxygen consumption.

VO_{2peak} of ≈16 to 17 $mL \cdot kg^{-1} \cdot min^{-1}$ for HF (mean age, ≈53 years). Women had lower CRF values compared with men in agreement with findings from a cardiac rehabilitation program.[30] For women, similarities are found between the present study and Kavanagh et al[5] who reported cycling-derived relative VO_{2peak} values for both CABG (14.0±3.3 $mL \cdot kg^{-1} \cdot min^{-1}$, aged 61.3±8.9 years) and MI (15.4±4.0 $mL \cdot kg^{-1} \cdot min^{-1}$, aged 58.5±9.8 years).

As expected, there were overall age-related decreases in CRF within each CVD category. For men, the decreases ranged between 6% and 12%, with greater decreases observed for treadmill (8%–12%) compared with cycle ergometer CPX (6%–8%). For women, the mean age-related decrease was 7%, although decreases among age groups were not consistently observed and may be related to the smaller sample sizes. For each CVD category, differences were also observed between CRF derived from treadmill compared with cycle ergometer CPX. Among both sexes, the CRF from treadmill CPX was 7% to 30% higher than cycle ergometer CPX. The largest difference in testing mode was again observed for patients with HF. Thus, it is of particular importance to consider testing mode when using CRF cut points for clinical decisions (such as cardiac transplantation[11]), as values are not interchangeable between treadmill and cycle ergometer CPX. Furthermore, the CRF normative reference standards created from the whole FRIEND CVD cohort are appropriate for use in patients with CVD yet the CRF standards for specific CVD categories may improve clinical interpretations and treatment. For example, CRF normative reference standards can be used for patient education by providing patients with information regarding their CRF status compared with those in the same CVD category and provide targets for improvement in cardiac rehabilitation programs.

Of note, there were markedly fewer women compared with men included in the FRIEND CVD cohort.

Table 8. CRF Percentiles According to CVD Category for Cycle Ergometer CPX With Directly Measured VO_{2peak} ($mL \cdot kg^{-1} \cdot min^{-1}$)

	Age group, y									
	Men					Women				
Percentile	40–49	50–59	60–69	70–79	80–89	40–49	50–59	60–69	70–79	80–89
CABG	(n=108)	(n=374)	(n=644)	(n=452)	(n=92)	(n=15)	(n=47)	(n=70)	(n=72)	(n=13)
10	14.1	13.5	12.7	11.4	11.2	12.4	10.8	9.8	10.0	8.4
25	15.3	15.6	14.7	13.3	12.6	13.6	11.9	11.8	11.5	8.9
50	18.5	18.1	16.9	15.4	14.3	14.4	14.8	14.1	12.9	11.8
75	22.5	21.0	19.7	18.0	16.6	18.9	17.1	16.9	14.3	14.1
90	25.0	23.8	22.5	20.6	18.0	21.4	18.0	19.5	15.7	16.0
MI	(n=317)	(n=710)	(n=569)	(n=314)	(n=98)	(n=50)	(n=116)	(n=137)	(n=103)	(n=23)
10	15.6	15.1	13.8	12.3	10.7	14.4	11.9	10.0	9.6	9.8
25	18.1	17.5	16.1	14.7	13.2	15.6	13.6	12.7	11.0	11.9
50	22.0	20.6	18.9	16.8	15.4	17.1	15.7	14.5	13.4	12.9
75	25.5	23.8	22.0	20.0	18.0	19.4	17.8	16.7	15.2	15.1
90	30.2	27.4	24.8	23.1	21.0	22.5	20.2	20.2	16.7	18.0
PCI	(n=84)	(n=271)	(n=323)	(n=202)	(n=54)	(n=8)	(n=53)	(n=85)	(n=61)	(n=18)
10	16.9	15.2	13.8	12.7	11.7	13.9	12.6	10.8	10.6	10.9
25	19.0	17.9	16.1	14.8	13.4	14.6	14.3	13.1	12.3	11.6
50	22.0	20.5	19.2	17.1	15.3	19.9	16.6	15.5	13.8	13.8
75	25.1	24.2	22.2	19.7	19.1	20.7	19.6	17.7	15.3	15.0
90	31.2	28.2	25.4	22.7	20.6	23.3	22.5	20.6	17.9	15.6
HF	(n=108)	(n=200)	(n=219)	(n=176)	(n=56)	(n=39)	(n=73)	(n=62)	(n=57)	(n=21)
10	9.7	10.4	9.5	9.2	9.3	8.8	7.7	8.3	9.1	9.9
25	12.8	12.1	11.7	10.5	10.5	11.0	9.5	10.3	10.9	10.5
50	15.4	14.9	14.4	12.8	12.3	13.9	12.5	12.7	12.2	11.2
75	18.6	18.0	16.6	15.4	13.6	16.4	15.2	14.5	13.9	12.4
90	22.9	21.2	19.9	17.8	15.5	17.9	18.1	17.8	15.5	12.8

CABG indicates coronary artery bypass graft; CPX, cardiopulmonary exercise testing; CRF, cardiorespiratory fitness; CVD, cardiovascular disease; HF, heart failure; MI, myocardial infarction; PCI, percutaneous coronary intervention; and VO_{2peak}, peak oxygen consumption.

One reason for the fewer number of women is that they are significantly less likely to be referred in exercise-based cardiac rehabilitation programs than men,[29,33] resulting in fewer women performing CPX. Additionally, women were less likely to meet the inclusion criteria of RER ≥1.0. Differences in treatment and in the assessment of CRF, such as not pushing women to exercise to the higher intensities that elicit high RER values, are concerning. It is well established that CRF is related to health outcomes in patients with CVD,[2–7] thus accurately assessing this vital sign in women is critical for improving clinical care and patient outcomes.

The strengths of the present study are the determination of normative CRF reference standards for patients with CVD utilizing a large sample size of patients from different testing laboratories. Further, the standards are derived from CPX, the gold-standard assessment of exercise capacity. There were, however, some limitations that should be addressed. The sample sizes used in developing the reference standards for some age groups and activity modes were relatively small, particularly for women. Moreover, participants may not have achieved a true maximal effort despite reaching an RER ≥1.0, which could result in an underestimation of CRF in this population. The reference standards also do not account for other comorbidities that could influence CRF, such as hypertension, diabetes, lung disease, and orthopedic conditions. Further, the same individuals did not perform both a treadmill CPX and cycle ergometer CPX. It is possible that unknown comorbidities may explain some of the differences in CRF observed between testing modes. Additionally, laboratories are not required to include race and ethnicity data when submitting to FRIEND and race and ethnicity are only known for 23% of the cohort used in the present study, of which 91% of patients were reported as White. The time between an individual's CVD event and their CPX is also not known in the FRIEND cohort. Last, although all data were from experienced

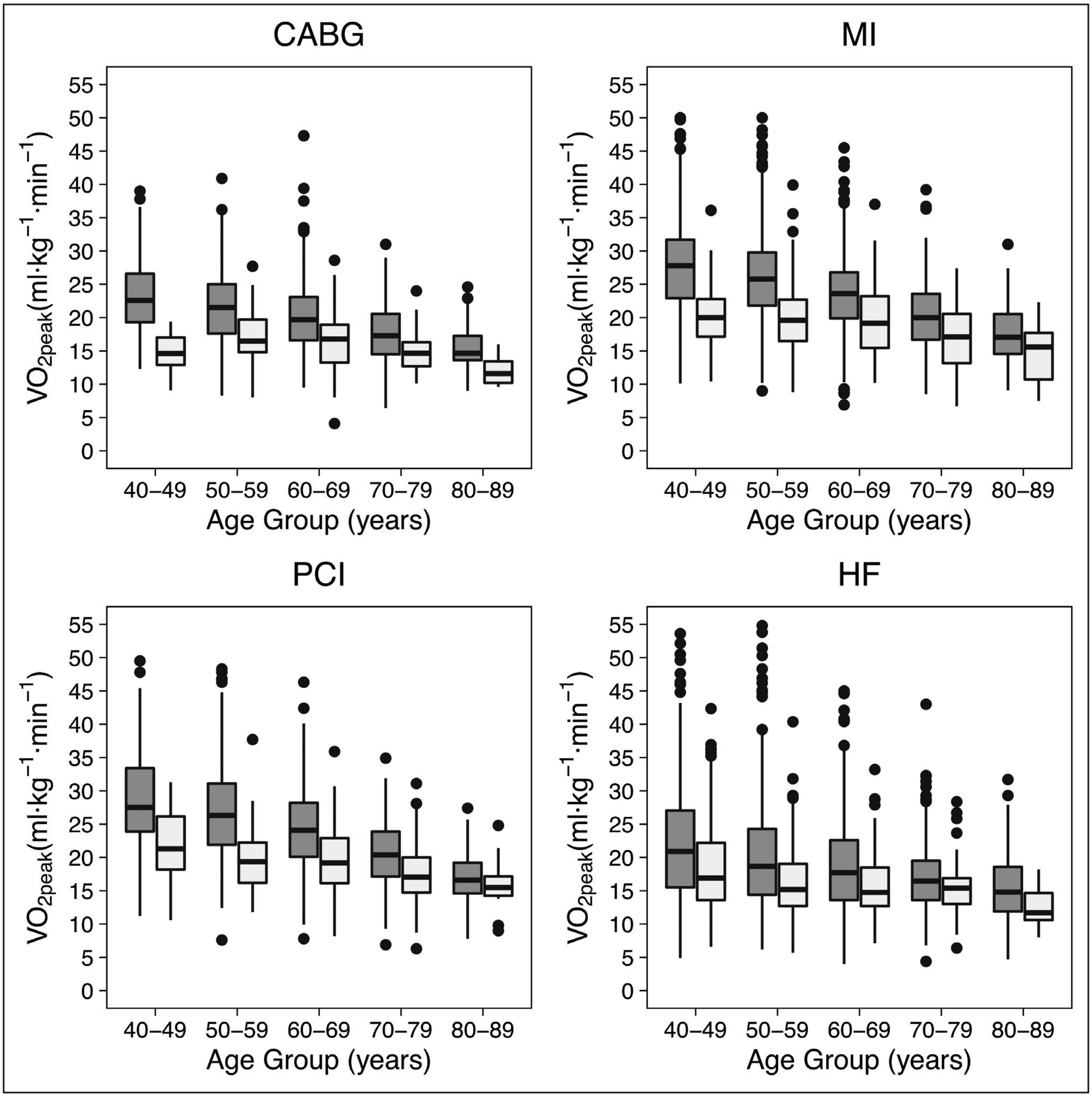

Figure 4. Box plots illustrating the median, interquartile range, and outliers for measured peak oxygen uptake (VO_{2peak}) for the cardiovascular disease categories determined from treadmill cardiopulmonary exercise testing.
Men are presented in dark gray and women are presented in light gray. CABG indicates coronary artery bypass graft; HF, heart failure; MI, myocardial infarction; and PCI, percutaneous coronary intervention.

laboratories and test effort was objectively determined, differing testing protocols, equipment, and definitions of test effort could have impacted the determination of CRF.

In conclusion, patients with CVD have a lower CRF compared with their age- and sex-matched apparently healthy peers. Thus, utilizing the appropriate normative reference standards for patients with CVD is essential to ensure accurate interpretation and guiding treatment. This report provides normative reference standards for both men and women performing CPX on a treadmill or cycle ergometer. Similar to reference standards for apparently healthy individuals, CRF is lower with increasing age, lower in women compared with men, and higher when a treadmill is used as the activity mode during CPX. Further differences are observed within specific CVD categories and suggest the need for continued development of CPX-derived

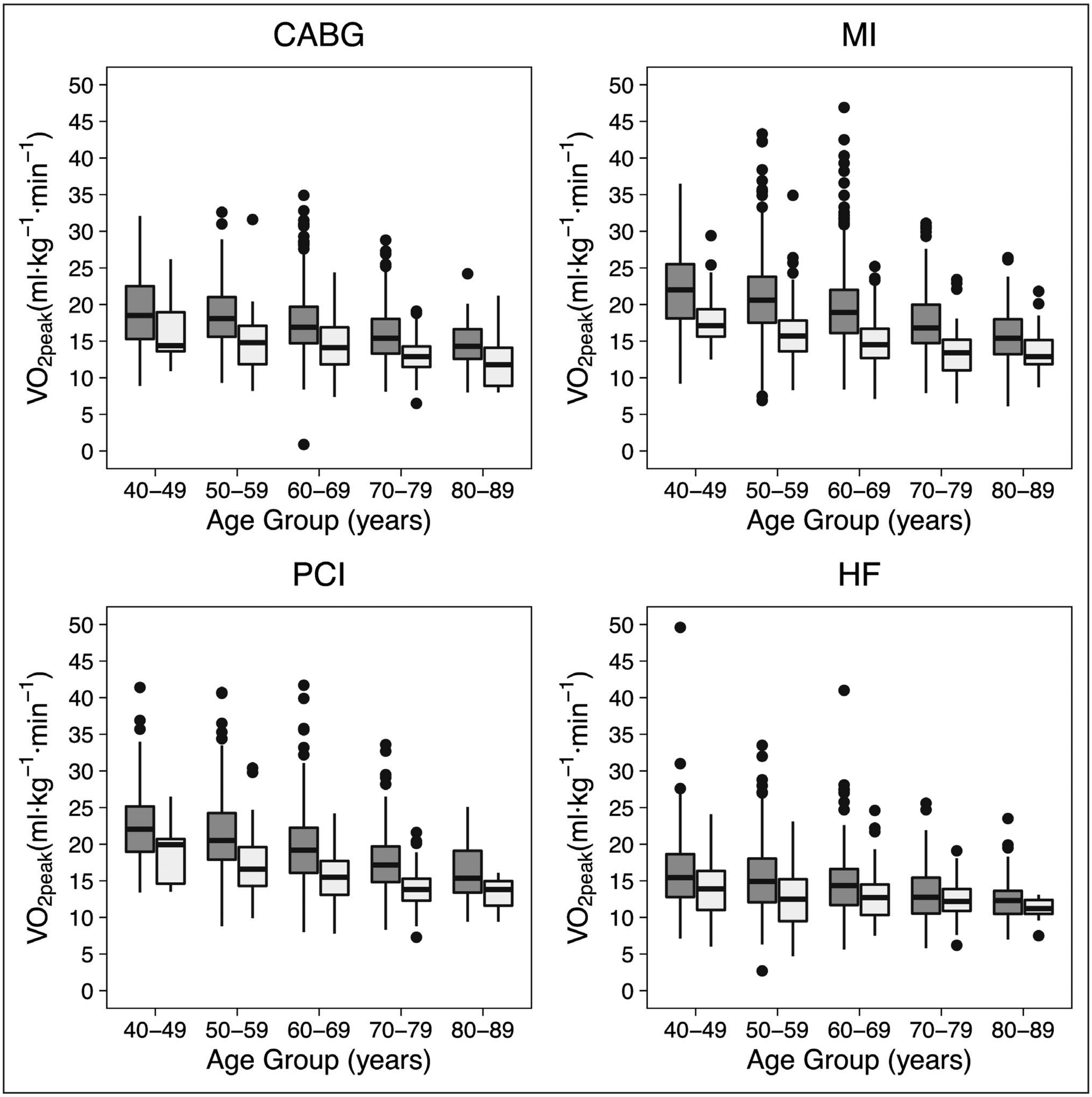

Figure 5. Box plots illustrating the median, interquartile range, and outliers for measured peak oxygen uptake (VO_{2peak}) for the cardiovascular disease categories determined from cycle ergometer cardiopulmonary exercise testing.

Men are presented in dark gray and women are presented in light gray. CABG indicates coronary artery bypass graft; HF, heart failure; MI, myocardial infarction; and PCI, percutaneous coronary intervention.

CRF reference standards to improve patient care in the clinical setting.

ARTICLE INFORMATION

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