

# Reference Standards for Cardiorespiratory Fitness Measured With Cardiopulmonary Exercise Testing: Data From the Fitness Registry and the Importance of Exercise National Database

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## Abstract

**Objective:** To develop standards for cardiorespiratory fitness by establishing reference values derived from cardiopulmonary exercise testing (CPX) in the United States.

**Patients and Methods:** Eight laboratories in the US experienced in CPX administration with established quality control procedures contributed data from January 1, 2014, through February 1, 2015, from 7783 maximal (respiratory exchange ratio,  $\geq 1.0$ ) treadmill tests from men and women (aged 20-79 years) without cardiovascular disease (CVD) to the Fitness Registry and the Importance of Exercise: A National Data Base (FRIEND). Percentiles of maximal oxygen consumption ( $\dot{V}O_{2\max}$ ) for men and women were determined for each decade from 20 years of age through 79 years of age. Comparisons of  $\dot{V}O_{2\max}$  were made to reference data established with CPX data from Norway and to US reference data established without CPX measurements.

**Results:** There were significant differences between sex and age groups for  $\dot{V}O_{2\max}$ . In FRIEND, the 50th percentile  $\dot{V}O_{2\max}$  of men and women aged 20 to 29 years decreased from 48.0 and 37.6  $\text{mLO}_2 \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$  to 24.4 and 18.3  $\text{mLO}_2 \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$  for ages 70 to 79 years, respectively. The rate of decline in this cohort during a 5-decade period was approximately 10% per decade.

**Conclusion:** These are the first cardiorespiratory fitness reference data using measures obtained from CPX in the United States. FRIEND can be used to provide a more accurate interpretation of measured  $\dot{V}O_{2\max}$  from maximal exercise tests for the US population compared with previous standards on the basis of workload-derived estimations.

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An increasing body of data have revealed that cardiorespiratory fitness (CRF) powerfully predicts outcomes across the spectrum of health and disease.<sup>1-4</sup> CRF can be directly measured as maximal oxygen consumption ( $\dot{V}O_{2\max}$ ) from a cardiopulmonary exercise testing (CPX) or is often estimated as the exercise capacity (maximal work rate) from an exercise test. Indeed, during the last 2 decades, many epidemiologic studies have reported that CRF is a more powerful predictor of risk for adverse outcomes than traditional risk factors, including hypertension, lipid abnormalities, smoking, physical inactivity, obesity, and diabetes mellitus.<sup>2,5,6</sup> Low CRF, typically defined

as the lowest quartile or quintile on an exercise test, is associated with 2- to 5-fold increases in CVD or all-cause mortality, independent of other CVD risk factors.<sup>4-7</sup> Importantly, relatively small improvements in CRF (such as 1 metabolic equivalent [MET]) have been associated with considerable reductions in mortality (10% to 25%).<sup>1,3-8</sup> These findings have led health authorities to recommend, and some US health systems to mandate, physical activity assessment and counseling as part of clinical encounters.<sup>9</sup> However, despite the fact that low CRF is one of the most important determinants of health outcomes, it is often neglected in the risk paradigm in favor of risk markers more familiar to most



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TABLE 1. Descriptive Characteristics of the FRIEND Cohort<sup>a,b</sup>

Characteristic	Age group (y)					
	20-29 (n = 513 men and 410 women)	30-39 (n = 963 men and 608 women)	40-49 (n = 1327 men and 843 women)	50-59 (n = 1078 men and 805 women)	60-69 (n = 593 men and 408 women)	70-79 (n = 137 men and 98 women)
<b>Men</b>						
Age, y	24.6±2.7	34.9±2.8	44.4±2.8	54.0±2.7	63.7±2.7	72.7±2.4
Height (cm)	179.6±7.4	178.8±6.9	178.8±6.6	178.1±8.9	177.3±6.9	175.5±6.9
Weight (kg)	82.6±16.6	82.6±16.3	86.3±16.1	88.1±17.2	87.1±16.4	83.9±15.0
<b>Women</b>						
Age, (y)	24.8±2.6	34.9±2.8	44.6±2.9	54.2±2.8	63.6±2.6	73.1±2.2
Height (cm)	166.1±7.1	165.4±6.4	164.3±6.6	163.4±6.6	162.6±6.1	162.1±5.8
Weight (kg)	66.3±15.4	71.4±19.0	74.0±19.6	76.9±18.4	77.2±16.2	74.8±15.9

<sup>a</sup>FRIEND = Fitness Registry and the Importance of Exercise National Database.

<sup>b</sup>Data are presented as mean ± SD.

clinicians who are likely to focus on conditions treatable with drugs or invasive procedures.<sup>9-12</sup>

Given the importance of CRF in estimating health risk, it is essential to have accurate reference values to know what constitutes a “normal” value. When reviewing results of an exercise test, an individual’s CRF should initially be considered in terms of what is normal for a given individual if he or she were healthy. This is critical because CRF decreases with age, and higher values are generally observed in men. Thus, a given CRF level for a 40-year-old man has a significantly different meaning than the same CRF for an elderly woman. Knowing an individual’s exercise capacity relative to their peers will not only help to optimize risk stratification but also can facilitate discussions between health care professionals and patients regarding health risks, provide a baseline for improving CRF, and provide support for physical activity counseling. Currently, the only widely cited reference data in the United States are derived from the Cooper Clinic, which uses estimated CRF values that are calculated from treadmill speed and grade.<sup>13</sup>

The 2003 Statement on CPX by the American Thoracic Society and the American College of Chest Physicians recognized that having normal reference values “is critical to any interpretative scheme.”<sup>14</sup> However, they recognized that at the time, no clear set of standards existed from CPX. Paap and Takken<sup>15</sup> performed a systematic review of the literature on reference values for CPX and noted that most studies had small sample sizes and used cycling for the mode. They reported that only 4 studies met their criterion for

high quality, with only 2 of these using treadmill testing. Both the American Thoracic Society/American College of Chest Physicians statement and the Paap and Takken review provide summaries of attempts to derive normative CRF regression equations from the criterion standard measurement, CPX, to predict CRF on the basis of age, sex, and, in some cases, body mass. The primary limitation of currently available US equations using this approach is the relatively small cohorts assessed with limited diversity. In addition, all are specific to the population from which they were drawn. For example, equations published by Hansen, Sue, and Wasserman are the most widely used standards for directly measuring  $\dot{V}O_{2max}$ ; however, they were derived from a small group (n=77) of men who underwent cycle testing combined with a sample of 295 women and men who performed treadmill tests from a previous study.<sup>16,17</sup> Recently, 2 studies provided some reference values using CPX in Norwegian cohorts.<sup>18,19</sup> The latter analysis is considered a significant advance in the field given that a much larger cohort was analyzed (n=3816) across the lifespan. Nevertheless, applicability of the Norwegian CRF reference values to individuals in the United States is uncertain.

The clear need for developing reference standards for CRF in the United States was recognized in a policy statement by the American Heart Association.<sup>20</sup> An independent group was formed with preliminary funding to establish a CRF registry office and advisory board (members listed in [Acknowledgments](#)).

TABLE 2. CPX Responses at Maximal Effort for Men and Women<sup>a,b</sup>

Variable	Age group (y)							All (n= 4611 men and 3172 women)
	20-29 (n= 513 men and 410 women)	30-39 (n= 963 men and 608 women)	40-49 (n= 1327 men and 843 women)	50-59 (n= 1078 men and 805 women)	60-69 (n= 593 men and 408 women)	70-79 (n= 137 men and 98 women)		
<b>Men</b>								
$\dot{V}O_{2max}$ (mL $O_2$ ·kg <sup>-1</sup> ·min <sup>-1</sup> )	47.6±11.3	43.0±9.9	38.8±9.6	33.8±9.1	29.4±7.9	25.8±7.1	37.9±11.1	
HR <sub>max</sub> (/min)	190±11	185±11	176±14	168±14	158±17	147±20	174±17	
RER	1.20±0.10	1.18±0.10	1.18±0.10	1.16±0.09	1.15±0.09	1.16±0.10	1.17±0.10	
<b>Women</b>								
$\dot{V}O_{2max}$ (mL $O_2$ ·kg <sup>-1</sup> ·min <sup>-1</sup> )	37.6±10.2	30.9±8.0	27.9±7.7	24.2±6.1	20.7±5.0	18.3±3.6	27.6±9.1	
HR <sub>max</sub> (/min)	189±12	184±11	176±14	167±15	157±17	147±21	172±18	
RER	1.17±0.10	1.18±0.10	1.17±0.10	1.16±0.10	1.13±0.09	1.13±0.08	1.16±0.10	

<sup>a</sup>CPX = cardiopulmonary exercise testing; HR<sub>max</sub> = maximum heart rate; RER = respiratory exchange ratio;  $\dot{V}O_{2max}$  = maximal oxygen uptake.

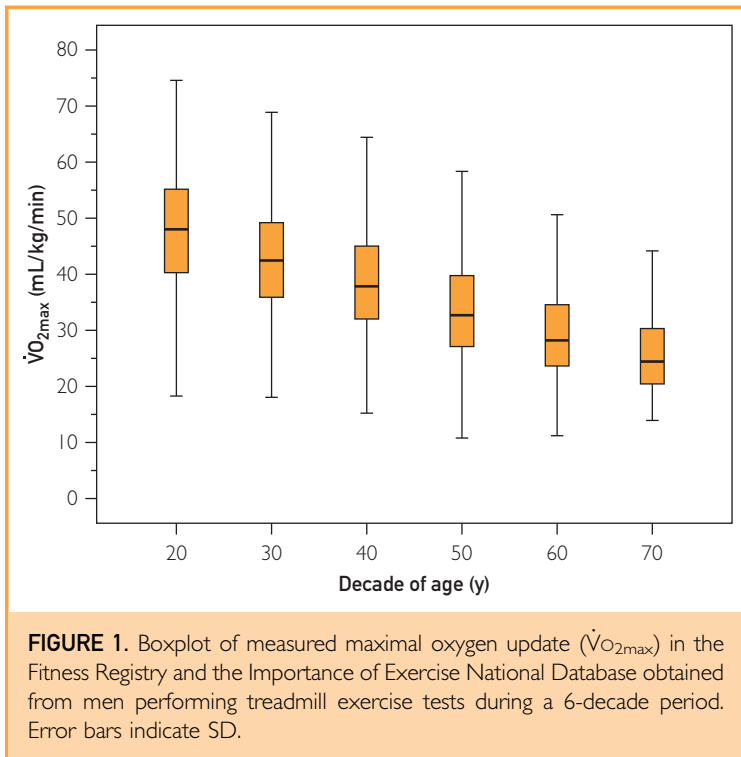
<sup>b</sup>Data are presented as mean ± SD. All statistical comparisons of differences in  $\dot{V}O_{2max}$  were significant (P<.001, men greater than women, both for sex main effect and at each decade).

The overarching purpose of the registry was to develop a US database to enhance the value of CRF across environments, including the clinical setting and the workplace, as well as the general public, to better inform national policy efforts on physical activity, fitness, and health. The first phase of this project involved determining a list of variables to be included in the registry and establishing a process to acquire CPX data that met objectively verified criteria for maximal effort from diverse sites across the United States. The purpose of this report was to improve on previous efforts to develop normal standards for exercise capacity by establishing CRF reference values derived from CPX in the United States. This first report will focus on standards from treadmill testing.

**METHODS**

In 2014, a multi-institutional initiative, the Fitness Registry and the Importance of Exercise: A National Data Base (FRIEND) was established by the CRF advisory board with the primary charge of establishing normative CRF values in the United States across the adult lifespan.<sup>20</sup> Briefly, laboratories from within the United States that were experienced in CPX administration and had access to data collected with rigorous methods were invited to be considered for inclusion in FRIEND. The CPX laboratories contributing data to FRIEND were all determined by the CRF advisory board to be well established, indicating valid and

reliable calibration and testing procedures and using experienced personnel qualified to conduct exercise tests. Although there were some variations in laboratory equipment, protocols, and procedures, the characteristics of all participating CPX laboratories are consistent with recommendations provided in recently published guidelines.<sup>21,22</sup>  $\dot{V}O_{2max}$  was defined according to the specific laboratory procedure, but all used some form of averaging readings during the final 30 to 60 seconds of the CPX. These CPX laboratories were provided a core guidance document and standardized spreadsheet to be used to contribute their data to FRIEND from January 1, 2014, through February 1, 2015. The guidance document contained an established glossary of terms and a data dictionary. This document enabled participating sites to prepare data in a manner consistent with the established goals of the national registry project.<sup>20</sup> Through this process, data entry errors were also minimized. Contact information for the FRIEND core CPX laboratory (ie, email and telephone) was also provided to participating sites in the event questions arose while preparing their data set for submission. Participating CPX laboratories were responsible for obtaining local institutional review board approval for inclusion in FRIEND, providing documentation that they were authorized to submit deidentified, coded data to the coordinating center at Ball State University, which then forwarded these data to the



core CPX laboratory housed at the University of Illinois, Chicago. Institutional review board approval for the core CPX laboratory was also obtained at the University of Illinois, Chicago. The FRIEND advisory board reviewed the data from each CPX laboratory for uniformity before inclusion in the registry. Databases from each participating site included key baseline characteristics and CPX measures. The University of Illinois, Chicago, core CPX laboratory performed a preliminary analysis of each laboratory's submitted data to ensure data points were within expected normal ranges. In the event errors were identified or data points were outside the normal expected range, the CPX laboratory submitting the data in question was contacted for any needed correction of data entry errors. Once each laboratory's data were verified, it was merged into FRIEND.

### Cohort

The current analysis includes 7783 tests from the 8 participating CPX laboratories (see [Acknowledgments](#)) with geographic representation from Connecticut, Indiana, Illinois,

Louisiana, Maryland, North Carolina, Tennessee, and Texas. The indication for the exercise tests for this cohort was determination of CRF before entry into an exercise program or research study. Participant screening was specific to each laboratory's procedures to rule out contraindications for exercise testing and for risk stratification. For this cohort, laboratories provided data on individuals who at the time of the test were without known CVD (coronary artery disease, peripheral artery disease, or heart failure) or chronic obstructive pulmonary disease. Inclusion criteria were (1) age of 20 years or older, (2) maximal exercise test performed on a treadmill, and (3) peak respiratory exchange ratio (RER) of 1.00 or higher. Exclusion criteria were any tests that were terminated for abnormal clinical findings before achieving voluntary maximal effort.

### Statistical Analyses

Continuous data are reported as mean (SD), whereas categorical data are reported as frequencies (percentages). Analysis of variance was used to compare differences in  $\dot{V}O_{2max}$  values between sex and across age groups. When significant differences were detected by analysis of variance, the Tukey test was used for the post hoc analysis. SPSS statistical software, version 22.0 (SPSS Inc), was used for all analyses. All tests with a  $P < .05$  were considered statistically significant.

### RESULTS

The FRIEND cohort included 4611 tests on men and 3172 on women, with ages ranging from 20 to 79 years. Descriptive characteristics of the cohort, by sex and in 10-year age groups, are listed in [Table 1](#).

Peak responses during CPX are presented in [Table 2](#), including RERs providing objective indications of adequate effort. There were significant differences between sex and age groups for  $\dot{V}O_{2max}$ . The overall mean difference in  $\dot{V}O_{2max}$  between men and women was 27% with the absolute difference narrowing from approximately 3 METs (ie,  $10 \text{ mL}O_2 \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ ) in patients in their 20s to approximately 2 METs (ie,  $7.5 \text{ mL}O_2 \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ ) in patients in their 70s. The decrease in mean  $\dot{V}O_{2max}$  with each decade of age is shown in [Figure 1](#) for men and [Figure 2](#) for women.

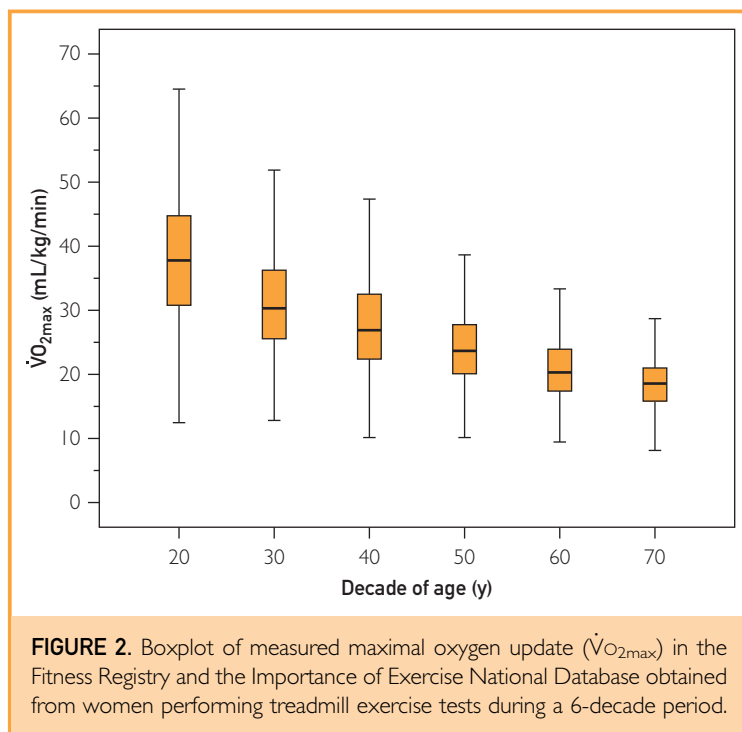
For both men and women, the percentile values for each age group from FRIEND and

previously published data from the Cooper Clinic are given in Table 3.<sup>13</sup> No formal statistical comparisons could be performed due to unavailability of the individual participant data from the Cooper Clinic cohort; therefore, the data presented in Table 3 are for observation only. Compared with Cooper Clinic data, the 50th percentile scores for men in FRIEND were higher for the 20-year-old age group, similar for the 30-year-old age group, and lower for all age groups beginning with the 40s. For women, the 50th percentile scores in FRIEND were similar for the 20-year-old age group but were lower for all other age groups compared with Cooper Clinic values.

## DISCUSSION

The current analysis represents the first reference data for CRF using measures obtained from CPX in the United States. The only other known reference values for CRF measures using CPX data are derived from 2 separate data sets in Norway.<sup>18,19</sup>

Comparisons of means by sex and age group among these 3 data sets are given in Table 4. No formal statistical comparisons could be performed because of unavailability of the individual participant data from the Norwegian cohorts; therefore, the data presented in Table 4 are for observation only. For each age group, both Norwegian men and women had notably higher CRF than those in the United States. In addition, the US men and women had a greater mean annual decrease from their 20s to their 70s ( $0.44 \text{ mL O}_2 \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$  and  $0.38 \text{ mL O}_2 \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$  per year, respectively) compared with the patients in the studies by Loe et al ( $0.38 \text{ mL O}_2 \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$  and  $0.29 \text{ mL O}_2 \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$  per year, respectively) and Evardsen et al ( $0.38 \text{ mL O}_2 \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$  and  $0.34 \text{ mL O}_2 \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$  per year, respectively). In all 3 data sets, the annual amount of decrease is greater in men, which results in a smaller absolute difference between men and women in their 70s ( $7.5$ ,  $7.0$ , and  $6.6 \text{ mL O}_2 \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ ; for FRIEND, the study by Loe et al, and the study by Evardsen et al, respectively) compared with their 20s ( $10$ ,  $11.4$ , and  $8.6 \text{ mL O}_2 \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$  for FRIEND, the study by Loe et al, and the study by Evardsen et al, respectively). An excellent literature review on the rate of decrease in  $\dot{V}_{O_{2\max}}$  with age noted that there are reports of lower rates of decrease in individuals who perform high-intensity training



**FIGURE 2.** Boxplot of measured maximal oxygen uptake ( $\dot{V}_{O_{2\max}}$ ) in the Fitness Registry and the Importance of Exercise National Database obtained from women performing treadmill exercise tests during a 6-decade period.

programs compared with sedentary individuals.<sup>23</sup> However, they concluded that the typical rate of decrease per decade is approximately 10% regardless of activity level. The FRIEND data revealed a similar rate of decrease during a 50-year age range of 9.2% and 10.3% per decade for men and women, respectively (Figures 1 and 2). Both Norwegian studies had lower rates for men and women: 7.0% and 6.9%, respectively, in the study by Loe et al and 8.3% and 7.2%, respectively, in the study by Evardsen et al. Collectively, the findings of the current analysis in conjunction with previous studies indicate a decrease in CRF across the lifespan irrespective of sex. Even so, the sex-based differences in CRF seem to be greater earlier in life and begin to narrow in elderly individuals. This has obvious implications for interpreting the exercise test; specifically, an individual's sex and age have primary bearing on what defines a normal CRF response. In addition, the limited available data clearly indicate that differences in CRF reference values may exist among countries. Interestingly, these preliminary comparisons revealing a higher CRF across the lifespan for Norwegians vs Americans do not entirely correspond to reports of moderate and high physical activity habits between these countries (34% and 40% in Norway vs 22% and 62% in

**TABLE 3. Sex-Specific Percentiles for CRF From Treadmill Exercise Tests With Measured  $\dot{V}O_{2max}$  Obtained From FRIEND and Predicted  $\dot{V}O_{2max}$  ( $mL O_2 \cdot kg^{-1} \cdot min^{-1}$ ) Reported by the Cooper Clinic<sup>13,a,b</sup>**

Age group (y)	Percentile						
	5th	10th	25th	50th	75th	90th	95th
<b>Men from FRIEND<sup>c</sup></b>							
20-29	29.0	32.1	40.1	48.0	55.2	61.8	66.3
30-39	27.2	30.2	35.9	42.4	49.2	56.5	59.8
40-49	24.2	26.8	31.9	37.8	45.0	52.1	55.6
50-59	20.9	22.8	27.1	32.6	39.7	45.6	50.7
60-69	17.4	19.8	23.7	28.2	34.5	40.3	43.0
70-79	16.3	17.1	20.4	24.4	30.4	36.6	39.7
<b>Men from Cooper Clinic<sup>d</sup></b>							
20-29	31.8	34.7	39.0	43.9	48.5	54.0	55.5
30-39	31.2	33.8	37.8	42.4	47.0	51.7	54.1
40-49	29.4	32.3	35.9	40.1	44.9	49.6	52.5
50-59	26.9	29.4	32.8	37.1	41.8	46.8	49.0
60-69	23.6	25.6	29.5	33.8	38.3	42.7	45.7
70-79	20.8	23.0	26.9	30.9	35.2	39.5	43.9
<b>Women from FRIEND<sup>c</sup></b>							
20-29	21.7	23.9	30.5	37.6	44.7	51.3	56.0
30-39	19.0	20.9	25.3	30.2	36.1	41.4	45.8
40-49	17.0	18.8	22.1	26.7	32.4	38.4	41.7
50-59	16.0	17.3	19.9	23.4	27.6	32.0	35.9
60-69	13.4	14.6	17.2	20.0	23.8	27.0	29.4
70-79	13.1	13.6	15.6	18.3	20.8	23.1	24.1
<b>Women from Cooper Clinic<sup>d</sup></b>							
20-29	27.6	29.5	33.0	37.8	42.4	46.8	49.6
30-39	25.9	28.0	32.0	36.7	41.0	45.3	47.4
40-49	25.1	26.6	30.2	34.5	38.6	43.1	45.3
50-59	23.0	24.6	28.0	31.4	35.2	38.8	41.0
60-69	21.8	23.0	25.1	28.8	32.3	35.9	37.8
70-79	19.6	21.5	24.2	27.6	29.8	32.5	37.2

<sup>a</sup>CRF = cardiorespiratory fitness; CPX = cardiopulmonary exercise testing; FRIEND = Fitness Registry and the Importance of Exercise National Database;  $\dot{V}O_{2max}$  = maximal oxygen uptake.  
<sup>b</sup>All patients are considered free of known cardiovascular disease.  
<sup>c</sup>The FRIEND CRF data were measured with CPX.  
<sup>d</sup>The Cooper Clinic data reported were predicted from Balke test time or work rate.

the United States, respectively).<sup>24</sup> Although these discordant findings may be due to known limitations with self-reported physical activity measurements and possible sampling differences between FRIEND and the Norwegian studies, our findings indicate normative CRF values are region and country specific. Thus, given the clear importance of CRF as it relates to health trajectory and prognosis, efforts should be undertaken to quantify reference values on a global scale to provide a region- and county-specific data.

The most widely used CRF reference data in the United States are from the Cooper Clinic; however, the values used for  $\dot{V}O_{2max}$  were predicted from maximal exercise test workload or

test time on the Balke protocol.<sup>13</sup> As indicated in Table 3, the percentile scores by age group and sex for FRIEND were either similar or higher for the 20- to 40-year-old age groups (differences by sex) but lower for all other age groups than those from the Cooper Clinic reference data. The exact reasons for the observed differences between the current findings and the Cooper clinic data are difficult to elucidate; however, there are some factors that could serve as plausible hypotheses for observed differences. One is that the fixed speed (3.3 mph) of the Balke protocol requires individuals with higher CRF to perform at very high treadmill grades (>20%), which can cause local fatigue of calf muscles and potentially an early test

**TABLE 4. Mean Reference Values for CRF With Measured  $\dot{V}O_{2max}$  Obtained From Treadmill CPX Tests From FRIEND Compared With Previously Published Values<sup>a,b</sup>**

Sex	Age group (y)					
	20-29	30-39	40-49	50-59	60-69	70-79
<b>Male</b>						
FRIEND	47.6±11.3 (n=513)	43.0±9.9 (n=963)	38.8±9.6 (n=1327)	33.8±9.1 (n=1078)	29.4±7.9 (n=593)	25.8±7.1 (n=137)
Loe et al <sup>19</sup>	54.4±8.4 (n=199)	49.1±7.5 (n=324)	47.2±7.7 (n=536)	42.6±7.4 (n=466)	39.2±6.7 (n=300)	35.3±6.5 (n=76)
Evardsen et al <sup>18</sup>	48.9±9.6 (n=38)	46.2±8.5 (n=73)	42.7±9.3 (n=91)	36.8±6.6 (n=88)	32.4±6.4 (n=81)	30.1±4.8 (n=23)
<b>Female</b>						
FRIEND	37.6±10.2 (n=410)	30.9±8.0 (n=608)	27.9±7.7 (n=843)	24.2±6.1 (n=805)	20.7±5.0 (n=408)	18.3±3.6 (n=98)
Loe et al <sup>19</sup>	43.0±7.7 (n=215)	40.0±6.8 (n=359)	38.4±6.9 (n=493)	34.4±5.7 (n=428)	31.1±5.1 (n=240)	28.3±5.2 (n=53)
Evardsen et al <sup>18</sup>	40.3±7.1 (n=37)	37.6±7.5 (n=63)	33.0±6.4 (n=86)	30.4±5.1 (n=79)	28.7±6.6 (n=59)	23.5±4.1 (n=41)

<sup>a</sup>CRF = cardiorespiratory fitness; CPX = cardiopulmonary exercise testing; FRIEND = Fitness Registry and the Importance of Exercise National Database;  $\dot{V}O_{2max}$  = maximal oxygen uptake.

<sup>b</sup>Data are expressed as means ± SD with sample sizes for each age range. All patients were considered free of known cardiovascular disease.

termination. This would result in a lower predicted  $\dot{V}O_{2max}$ . Another is that the equations used to estimate  $\dot{V}O_{2max}$  from treadmill speed and grade were only validated for submaximal steady-state exercise; thus, these equations are known to overpredict  $\dot{V}O_2$  at higher levels of exercise.<sup>25</sup> In addition, although handrail use is discouraged, if not well regulated it will result in the ability to tolerate higher work rates on a treadmill exercise test at a lower oxygen cost, which could lead to overestimation of  $\dot{V}O_{2max}$ . Regardless of the reason for these differences, it is clear that the reference CRF values derived from CPX results in notably different values compared with those derived from an estimation of CRF from treadmill speed and grade. It is noteworthy to point out that the age-related decrease during the same 50-year time frame is much lower in the predicted Cooper Clinic reference data for men and women (5.9% and 5.4% per decade, respectively) than for those mentioned above using CPX data.

The strengths of this study are that it provides the first reference data for  $\dot{V}O_{2max}$  measured from CPX using treadmill testing for the US population. All laboratories contributing data were experienced in CPX administration, and the test effort was objectively determined by RER. The sample size was relatively large, with a good age distribution for both men and women, and provides improved geographic distribution of the United States because it included data from 8 different states. It is important to recognize the differences that exist between  $\dot{V}O_{2max}$  measured from CPX and those estimated from exercise test data. As with any estimation

procedure, there is a need to consider the error of measurement. Predictions of  $\dot{V}O_{2max}$  from either maximal treadmill test time or maximal speed and grade have reported estimation errors of ±3.4 and ±4.4 mL $O_2$ ·kg<sup>-1</sup>·min<sup>-1</sup>, respectively.<sup>26,27</sup> Thus, this study provides more appropriate reference values for laboratories that include CPX as part of the maximal exercise test measurements.

Common to studies using retrospective data there are some limitations that should be considered. Patients with previously diagnosed CVD were excluded from this data set. However, the term *apparently healthy* would not be appropriate for the entire study population because some had diseases (eg, diabetes, obesity), musculoskeletal concerns (eg, back pain, osteoarthritis), and cardiovascular risk factors. Although all tests were performed for functional capacity measurement, the individual referral for the tests varied (clinical assessment, fitness screening, and research evaluation), and the choice of treadmill protocols, measurement equipment, and data collection procedures, although consistent with recommendations provided in recently published guidelines, was specific to each contributing laboratory.<sup>21,22</sup> In addition, the geographic distribution of 8 states is good, although not truly representative of the entire United States. The geographic distribution of FRIEND will improve with continued recruitment efforts. Finally, the sample size varies among the age groups, with the most representation between the decades of the 30s through the 60s and the least in those older than 70 years (approximately 3% of total sample). Although this is similar to

the other published data sets compared, it suggests that future reports should seek more representation in the younger and older age groups. Finally, because we had no access to the individual subject data from the other published cohorts, no statistical tests were performed, thus limiting us to only be able to make observational comparisons.

## CONCLUSION

FRIEND was created in response to a need to develop CRF reference values derived from CPX in the United States. These values should provide for a more accurate interpretation of measured  $\dot{V}O_{2\max}$  from treadmill tests for the US population compared with previous standards on the basis of workload-derived estimations of  $\dot{V}O_{2\max}$ . The development of the FRIEND data is ongoing because additional data are being added. Subsequent reports will be released providing more reference values for a variety of measures obtained from CPX with expansion planned to include data from clinical populations and children, as well as data from countries outside the United States.

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