

2018

Peak Ventilation Reference Standards from Exercise Testing: From the FRIEND Registry

Leonard A. Kaminsky

Matthew P. Harber

Mary T. Imboden

Ross Arena

Jonathan Myers

Follow this and additional works at: https://digitalcommons.georgefox.edu/hhp_fac



Part of the [Medicine and Health Sciences Commons](#)

Peak Ventilation Reference Standards from Exercise Testing: From the FRIEND Registry

LEONARD A. KAMINSKY¹, MATTHEW P. HARBER², MARY T. IMBODEN², ROSS ARENA³, and JONATHAN MYERS⁴

¹Fisher Institute of Health and Well-Being and Clinical Exercise Physiology Laboratory, Ball State University, Muncie, IN; ²Clinical Exercise Physiology Laboratory, Ball State University, Muncie, IN; ³Department of Physical Therapy and Integrative Physiology Laboratory, College of Applied Science, University of Illinois, Chicago, IL; and ⁴Division of Cardiology, VA Palo Alto Healthcare System, Palo Alto, CA

ABSTRACT

KAMINSKY, L. A., M. P. HARBER, M. T. IMBODEN, R. ARENA, and J. MYERS. Peak Ventilation Reference Standards from Exercise Testing: From the FRIEND Registry. *Med. Sci. Sports Exerc.*, Vol. 50, No. 12, pp. 2603–2608, 2018. **Purpose:** Cardiopulmonary exercise testing (CPX) provides valuable clinical information, including peak ventilation (\dot{V}_{Epeak}), which has been shown to have diagnostic and prognostic value in the assessment of patients with underlying pulmonary disease. This report provides reference standards for \dot{V}_{Epeak} derived from CPX on treadmills in apparently healthy individuals. **Methods:** Nine laboratories in the United States experienced in CPX administration with established quality control procedures contributed to the Fitness Registry and the Importance of Exercise National Database from 2014 to 2017. Data from 5232 maximal exercise tests from men and women without cardiovascular or pulmonary disease were used to create percentiles of \dot{V}_{Epeak} for both men and women by decade between 20 and 79 yr. Additionally, prediction equations were developed for \dot{V}_{Epeak} using descriptive information. **Results:** \dot{V}_{Epeak} was found to be significantly different between men and women and across age groups ($P < 0.05$). The rate of decline in \dot{V}_{Epeak} was 8.0% per decade for both men and women. A stepwise regression model of 70% of the sample revealed that sex, age, and height were significant predictors of \dot{V}_{Epeak} . The equation was cross-validated with data from the remaining 30% of the sample with a final equation developed from the full sample ($r = 0.73$). Additionally, a linear regression model revealed forced expiratory volume in 1 s significantly predicted \dot{V}_{Epeak} ($r = 0.73$). **Conclusions:** Reference standards were developed for \dot{V}_{Epeak} for the United States population. Cardiopulmonary exercise testing laboratories will be able to provide interpretation of \dot{V}_{Epeak} from these age and sex-specific percentile reference values or alternatively can use these nonexercise prediction equations incorporating sex, age, and height or with a single predictor of forced expiratory volume in 1 s. **Key Words:** CARDIOPULMONARY EXERCISE TESTING, PREDICTION EQUATIONS, REFERENCE VALUES, APPARENTLY HEALTHY

Cardiopulmonary exercise testing (CPX) is increasingly being used as a valuable tool in assessing patients with a variety of chronic diseases (1). Peak exercise ventilation (\dot{V}_{Epeak}) is a measure obtained from CPX and is a key component of peak oxygen uptake ($\dot{V}O_{2peak}$) and carbon dioxide production ($\dot{V}CO_{2peak}$). \dot{V}_{Epeak} is also an important component in the assessment of individuals with unexplained exertional dyspnea and patients diagnosed with pulmonary disease. Additionally, \dot{V}_E , $\dot{V}O_2$, and $\dot{V}CO_2$ are further combined and used with other variables such as $\dot{V}_E/\dot{V}CO_2$ slope, exercise oscillatory \dot{V}_E pattern, partial pressure of end-tidal CO_2 , which have been shown to have

both diagnostic and prognostic value in chronic disease populations (2,3).

The importance of cardiorespiratory fitness (CRF) measured as $\dot{V}O_{2peak}$, one of the key variables from CPX, was promoted in a Policy Statement by the American Heart Association (4). The need for a national CRF registry was suggested, because there were no reference standards for interpretation of $\dot{V}O_{2peak}$. This led to the development of the Fitness Registry for the Importance of Exercise National Database (FRIEND) which has provided United States based CRF reference standards for individuals without cardiovascular disease (CVD) or chronic obstructive pulmonary diseases (COPD) (5–7). Recently, the American Heart Association issued a scientific statement suggesting that CRF should be considered a vital sign and thus should be assessed routinely in clinical practice (8). A recent review and a report on worldwide CRF levels provide additional support of the importance of CRF (9,10).

\dot{V}_{Epeak} is an important component of $\dot{V}O_{2peak}$ and may be a limiting factor for exercise capacity for patients with moderate to severe COPD (11). Generally, if interpreted at all, \dot{V}_{Epeak} is compared with maximal voluntary ventilation (MVV) and is typically considered normal if the ratio ranges between 50% and 80% (12). Alternatively, \dot{V}_{Epeak}

is subtracted from MVV to calculate breathing reserve, with values $<15 \text{ L}\cdot\text{min}^{-1}$ considered abnormal, indicating a pulmonary mechanism for abnormally low CRF (13). With the exception of comprehensive pulmonary function testing profiles, MVV is rarely measured but rather it is more typical to predict it from forced expiratory volume in 1 s (FEV_1) (14). Similar to CRF, having reference standards for \dot{V}_{Epeak} are needed and would aid in the interpretation of this important CPX variable. Additionally, having reference values of the $\dot{V}_{\text{Epeak}}/\text{MVV}$ ratio will provide enhanced opportunities for the interpretation of the peak ventilation from a CPX result, when MVV data are available. This will also allow future investigations to evaluate how \dot{V}_{Epeak} may contribute to the diagnosis and/or prognosis of patients with chronic diseases, as well as refine the ability to diagnose a pulmonary limitation to CRF in those with unexplained exertional dyspnea.

Therefore, the purpose of this study was to develop reference standards for \dot{V}_{Epeak} measurements obtained during CPX using data from the FRIEND Registry. Additionally, because \dot{V}_{Epeak} has commonly been interpreted relative to MVV, reference values of the $\dot{V}_{\text{Epeak}}/\text{MVV}$ ratio were also developed. A secondary purpose was to develop simple-regression equations to predict \dot{V}_{Epeak} : 1) from sex, age, and height if pulmonary function test results are not available; and 2) from FEV_1 if pulmonary function test results are available.

METHODS

The procedures used for acquiring and managing the data for FRIEND have been previously reported (5). Briefly, laboratories contributing to FRIEND provided resting and CPX data from maximal treadmill protocols using an average of data during the final 30 to 60 s of the CPX. Local institutional review board approval for participation in the FRIEND Registry was obtained by each participating CPX laboratory to submit deidentified, coded data to the data coordinating center at Ball State University, which then forwarded these data to the core CPX laboratory housed at the University of Illinois at Chicago. Institutional review board approval for the core CPX laboratory was also obtained at the University of Illinois at Chicago.

The current analysis includes 5232 tests from the nine participating CPX laboratories (see acknowledgments) with geographical representation from seven states including California, Connecticut, Indiana, Maryland, Missouri, North Carolina, and Texas. Any subject identified as having a preexisting diagnosis of CVD or COPD was excluded from the current analysis. Inclusion criteria included CPX data for those free from any known CVD and COPD at the time of testing, as well as: 1) age ≥ 20 yr; 2) maximal exercise test performed on a treadmill; 3) peak respiratory exchange ratio value ≥ 1.00 . Of these there were 3434 test records that included a measure of FEV_1 . For all subjects, FEV_1 was also predicted using the Crapo equations for men and women (15), and MVV was predicted as both $\text{FEV}_1 \times 35$ and $\text{FEV}_1 \times 40$ (16,17).

Statistical analysis. Analysis of variance was used to compare differences in \dot{V}_{Epeak} values between sex and across age groups. When significant differences were detected by ANOVA, the Tukey test was used for *post hoc* analysis.

Regression analyses were used to develop equations for predicting \dot{V}_{Epeak} using descriptive data available in the FRIEND data (18). As sex, age, and height have been established as the primary predictors of spirometry values, a stepwise regression model was performed with these three variables in 70% of the sample that was randomly assigned to the validation group (19). This equation was cross-validated with data from the remaining 30% of the sample, with a final equation developed from the full sample (20). Additionally, for circumstances where FEV_1 is available, a linear regression model was performed with FEV_1 as the sole predictor. Pearson product moment correlations were computed for the measured and predicted \dot{V}_{Epeak} . The SPSS 24.0 (IBM, Armonk, NY) statistical software package was used for all analyses. All tests with a *P* value <0.05 were considered statistically significant.

RESULTS

The FRIEND cohort for this report included data on 3043 men and 2189 women (Table 1). Table 2 provides \dot{V}_{Epeak} values, measured during CPX on treadmills, for both men and women in six decades of age groups. \dot{V}_{Epeak} was significantly ($P < 0.05$) higher for men compared with women and for each younger age group in both sexes.

FEV_1 data, obtained from spirometry was available for approximately 65% of this cohort and is shown in Table 3. FEV_1 was also predicted from the descriptive data for this cohort and was used to predict MVV from two commonly used formulas of multiplying by either 35 or 40 (16,17). The ratios of $\dot{V}_{\text{Epeak}}/\text{MVV}$ were calculated using both MVV equations to assess the range of these values in the FRIEND cohort. Values >0.8 for $\dot{V}_{\text{Epeak}}/\text{MVV}$ ratio were observed in approximately 37% of women and 60% of men when using $\text{FEV}_1 \times 35$ to predict MVV and $\sim 18\%$ of women and 32% of men if using $\text{FEV}_1 \times 40$ (Table 4). Additionally, values >1.0 for $\dot{V}_{\text{Epeak}}/\text{MVV}$ ratio were observed in $\sim 7\%$ of women

TABLE 1. Descriptive characteristics of the FRIEND cohort.

	Men (<i>n</i> = 3043)	Women (<i>n</i> = 2189)
Age (yr)	46.4 ± 13.5	46.4 ± 14.1
\dot{V}_{Epeak} ($\text{L}\cdot\text{min}^{-1}$)	110.9 ± 29.2*	71.6 ± 19.7
$\text{VO}_{2\text{peak}}$ ($\text{mL}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$)	34.0 ± 9.6*	26.5 ± 7.9
Height (inches)	70.1 ± 2.8*	64.5 ± 2.6
Weight (kg)	91.0 ± 17.7*	74.3 ± 18.1
Body mass index ($\text{kg}\cdot\text{m}^{-2}$)	28.7 ± 5.2	27.7 ± 6.4
Waist (cm)	98.1 ± 14.9*	84.1 ± 14.8
Resting HR (bpm)	67 ± 12	69 ± 10
Maximal HR (bpm)	172 ± 18	172 ± 17
Resting SBP/DBP (mm Hg)	126/81 ± 15/10*	118/74 ± 15/10
FEV_1 (L)	3.690 ± 0.760*	2.696 ± 0.573

Data are mean ± SD.

*Significantly different between men and women, $P < 0.05$.

DBP, diastolic blood pressure; SBP, systolic blood pressure.

TABLE 2. Peak ventilation ($L \cdot \text{min}^{-1}$) during CPX data from the FRIEND registry ($n = 5232$).

Age (yr)*	20–29	30–39	40–49	50–59	60–69	70–79
Men ($n = 3043$)**	130 ± 30 (434)	121 ± 25 (524)	113 ± 25 (756)	103 ± 25 (748)	93 ± 24 (458)	80 ± 24 (123)
Women ($n = 2189$)	89 ± 21 (324)	78 ± 19 (360)	74 ± 16 (536)	67 ± 15 (557)	59 ± 14 (325)	53 ± 12 (87)

Data are mean ± SD.

* $P < 0.05$ Each age-group different from all other age-groups.

** $P < 0.05$ Men different from women in each age group.

and 15% of men if using $FEV_1 \times 35$ to predict MVV and ~6% of men if using $FEV_1 \times 40$.

Stepwise multiple regression analyses revealed that sex, followed by age and then height all made significant contributions to estimating \dot{V}_{Epeak} from the data of the validation sample group. The equation was found to be accurate because there was no significant difference between the predicted and measured \dot{V}_{Epeak} in the cross-validation group (93.9 ± 23.1 vs $93.6 \pm 31.9 L \cdot \text{min}^{-1}$; $P > 0.05$). The Pearson correlation coefficient between the predicted and measured \dot{V}_{Epeak} was 0.74. Given the demonstrated accuracy of the prediction equation from the cross-validation procedure, the stepwise multiple regression analyses were repeated with the entire sample to produce the final prediction equation: \dot{V}_{Epeak} ($L \cdot \text{min}^{-1}$) = $17.32 - 28.33$ (sex; men = 0, women = 1) - 0.79 (age [yr]) - 1.85 (height [inches]); SEE = 21.7. The correlation for the model using the whole sample was $r = 0.73$. FEV_1 is often available as it may be measured in some laboratories, thus a linear regression equation ($r = 0.73$) was developed: \dot{V}_{Epeak} ($L \cdot \text{min}^{-1}$) = $5.51 + 26.79$ (FEV_1 [L]), SEE = 21.6.

DISCUSSION

Although it is generally understood that \dot{V}_{Epeak} is greater in men than in women and declines with age, there are no reference values available to interpret \dot{V}_{Epeak} . The data from the FRIEND registry show that, on average, \dot{V}_{Epeak} is 34% higher in men than women, and \dot{V}_{Epeak} declines approximately 8% per decade in both men and women from the 3rd to 8th decades.

Commonly, if \dot{V}_{Epeak} from CPX is interpreted at all, it is done so in relationship to MVV, which is then used to determine breathing reserve (3,12,13). This interpretation typically considers normal \dot{V}_{Epeak} to be 50% to 80% of MVV. Interestingly, these data from an apparently healthy population

from FRIEND, found more than a third of women and half of men exceeded the upper end of the range of normal (80%) using the common estimation of MVV calculated as $35 \times FEV_1$. Compared with another common estimation of MVV ($=40 \times FEV_1$) approximately a fifth of the women and a third of the men from FRIEND exceeded the upper end of the range of normal. Additionally, 15% of men and 7% of women had \dot{V}_{Epeak} values greater than MVV ($=35 \times FEV_1$) and 6% of men had \dot{V}_{Epeak} values greater than MVV ($=40 \times FEV_1$). These findings demonstrate the limitations to using this approach for interpreting \dot{V}_{Epeak} values.

A more direct approach to interpret \dot{V}_{Epeak} would be to apply the FRIEND reference standards for \dot{V}_{Epeak} from CPX. This would be done by comparing the measured \dot{V}_{Epeak} to that from FRIEND age- and sex-specific reference values for the means ± SD from Table 1 or as a percentile (Table 5). The interpretation of \dot{V}_{Epeak} as either a percent of predicted or as a percentile will allow future studies to consider the importance of this variable as a contributor to existing CPX-derived diagnostic or prognostic algorithms (3). For example, it would be of interest to explore factors related to the gender differences in \dot{V}_{Epeak} compared to differences in $\dot{V}O_{2peak}$. The rate of decline in \dot{V}_{Epeak} is slightly lower (8% per decade) than that previously shown for $\dot{V}O_{2peak}$ (9.2 and 10.3% per decade for men and women, respectively) from the FRIEND registry (5). However, the average difference in \dot{V}_{Epeak} between men and women was slightly higher for \dot{V}_{Epeak} (34%) than that for $\dot{V}O_{2peak}$ (27%).

Two larger studies from Norway did report mean \dot{V}_{Epeak} data in their studies focused on CRF (Fig. 1) (21,22). These studies from the Norwegian cohort's men and women had higher $\dot{V}O_{2peak}$ compared with those in the FRIEND registry and a similar population difference for \dot{V}_{Epeak} was observed. Mean \dot{V}_{Epeak} values by decade were higher by 11 to 19 $L \cdot \text{min}^{-1}$ and 3 to 14 $L \cdot \text{min}^{-1}$ for men and women,

TABLE 3. FEV_1 (L) from the FRIEND registry.

Method	Age* (yr)	20–29	30–39	40–49	50–59	60–69	70–79
Measured	Men** ($n = 1973$)	4.17 ± 0.81	3.99 ± 0.74	3.78 ± 0.67	3.51 ± 0.65	3.19 ± 0.65	2.90 ± 0.65
Predicted	Men*** ($n = 1973$)	4.62 ± 0.34	4.36 ± 0.32	4.11 ± 0.30	3.87 ± 0.30	3.57 ± 0.30	3.31 ± 0.32
Predicted	Men** ($n = 3043$)	4.65 ± 0.34	4.37 ± 0.30	4.11 ± 0.29	3.86 ± 0.41	3.58 ± 0.30	3.32 ± 0.30
Measured	Women ($n = 1461$)	3.19 ± 0.57	3.00 ± 0.52	2.75 ± 0.45	2.50 ± 0.43	2.24 ± 0.42	1.95 ± 0.41
Predicted	Women*** ($n = 1461$)	3.47 ± 0.25	3.19 ± 0.23	2.91 ± 0.24	2.62 ± 0.25	2.35 ± 0.22	2.04 ± 0.27
Predicted	Women ($n = 2189$)	3.50 ± 0.25	3.19 ± 0.23	2.92 ± 0.24	2.63 ± 0.24	2.36 ± 0.23	2.07 ± 0.25

Data are mean ± SD.

* $P < 0.05$ Each age group different from all other age groups.

** $P < 0.05$ Men different from women in each age group.

*** $P < 0.05$ Predicted different from measured FEV_1 in each age group.

Measured with pulmonary function testing; predicted using Crapo et al equations.

TABLE 4. Sex-specific percentiles for \dot{V}_{Epeak}/MVV ratio. \dot{V}_E from CPX obtained from the FRIEND registry and MVV estimated from $FEV_1 \times 35$ [A] and from $FEV_1 \times 40$ [B].

Age Groups (yr)/Percentiles	5	10	25	50	75	90	95
A							
Men							
20–29	0.40	0.51	0.61	0.71	0.81	0.88	0.93
30–39	0.45	0.53	0.61	0.70	0.78	0.87	0.91
40–49	0.44	0.48	0.59	0.69	0.79	0.89	0.93
50–59	0.42	0.48	0.56	0.67	0.77	0.88	0.94
60–69	0.40	0.46	0.55	0.64	0.75	0.84	0.91
70–79	0.36	0.40	0.50	0.59	0.71	0.85	0.94
Women							
20–29	0.40	0.45	0.53	0.64	0.73	0.82	0.86
30–39	0.37	0.42	0.50	0.61	0.71	0.81	0.88
40–49	0.42	0.46	0.53	0.63	0.73	0.81	0.86
50–59	0.41	0.45	0.54	0.63	0.73	0.81	0.87
60–69	0.41	0.45	0.53	0.62	0.72	0.80	0.86
70–79	0.43	0.47	0.55	0.65	0.76	0.84	0.90
B							
Men							
20–29	0.46	0.58	0.70	0.81	0.92	1.00	1.06
30–39	0.52	0.61	0.69	0.80	0.90	0.99	1.04
40–49	0.50	0.55	0.68	0.79	0.90	1.02	1.06
50–59	0.48	0.55	0.64	0.76	0.88	1.00	1.07
60–69	0.45	0.52	0.62	0.73	0.86	0.96	1.03
70–79	0.41	0.46	0.57	0.67	0.81	0.98	1.07
Women							
20–29	0.45	0.51	0.61	0.73	0.84	0.94	0.99
30–39	0.42	0.48	0.57	0.69	0.81	0.93	1.01
40–49	0.48	0.52	0.61	0.72	0.83	0.93	0.99
50–59	0.47	0.52	0.62	0.72	0.84	0.92	1.00
60–69	0.47	0.52	0.61	0.71	0.83	0.92	0.98
70–79	0.49	0.53	0.63	0.74	0.86	0.96	1.02

respectively, in the Loe et al. (21) study and higher by 9 to 20 $L \cdot \text{min}^{-1}$ and 2 to 14 $L \cdot \text{min}^{-1}$ for men and women, respectively in the Evadsen et al. (22) study across the six decades compared with those in the FRIEND cohort. The Norwegian cohorts also showed a similar rate of decline in \dot{V}_{Epeak} data with age of 7% to 9% per decade. The difference in mean values per decade between men and women ranged between 30 and 39 $L \cdot \text{min}^{-1}$ (~34% higher in men) for FRIEND and both Norwegian cohorts. Another study of a small ($n = 231$) cohort from Canada, with cycle ergometry as the test mode, showed similar rates of decline with age (8%–9% per decade) and similar, albeit slightly smaller differences between men and women (28%) in \dot{V}_{Epeak} (23). Although there are no other large data sets that have reported \dot{V}_{Epeak} data, some studies related to exercise training, with small sample sizes, have included this measure along with $\dot{V}O_{2peak}$

in their reports. For example, a study of athletes by Saltin and Astrand reported $\dot{V}_{E_{max}}$ of 156 ± 19 and $112 \pm 11 L \cdot \text{min}^{-1}$ for 15- to 33-yr-old men and women, respectively (24). Heath et al. (25) compared young and old endurance trained men with untrained older men. They reported both the trained younger ($n = 16$, ages 19–27 yr) and older subjects ($n = 16$, 50–72 yr) had similar $\dot{V}_{E_{max}}$ values of 125 ± 17 and $129 \pm 19 L \cdot \text{min}^{-1}$, respectively, whereas untrained older men ($n = 16$, 51 yr) had an average $\dot{V}_{E_{max}}$ of $97 L \cdot \text{min}^{-1}$. Another report by Trappe et al. (26) compared octogenarian athletic men ($n = 8$) to untrained men ($n = 8$). The mean $\dot{V}_{E_{max}}$ values were $79 \pm 3 L \cdot \text{min}^{-1}$ and $63 \pm 6 L \cdot \text{min}^{-1}$ for these older athletes and untrained men, respectively. This could suggest that exercise training may provide some protection against the rate of decline in $\dot{V}_{E_{max}}$ with age, although this will need to be explored in future studies.

TABLE 5. Sex-specific percentiles for peak treadmill exercise ventilation ($L \cdot \text{min}^{-1}$) from CPX obtained from the FRIEND registry.

Age Groups (yr)/Percentiles	5	10	25	50	75	90	95
A. Men							
20–29	72	89	113	132	151	168	176
30–39	79	93	106	121	137	152	162
40–49	72	81	96	114	130	146	156
50–59	63	73	86	102	120	136	145
60–69	55	64	77	91	108	122	130
70–79	45	50	63	76	90	115	129
B. Women							
20–29	53	60	74	89	103	116	122
30–39	48	53	63	76	91	105	111
40–49	46	52	62	74	85	94	101
50–59	44	47	56	65	76	86	93
60–69	39	42	49	58	69	78	79
70–79	33	36	45	52	63	68	75

All subjects were considered free from known CVD and COPD.

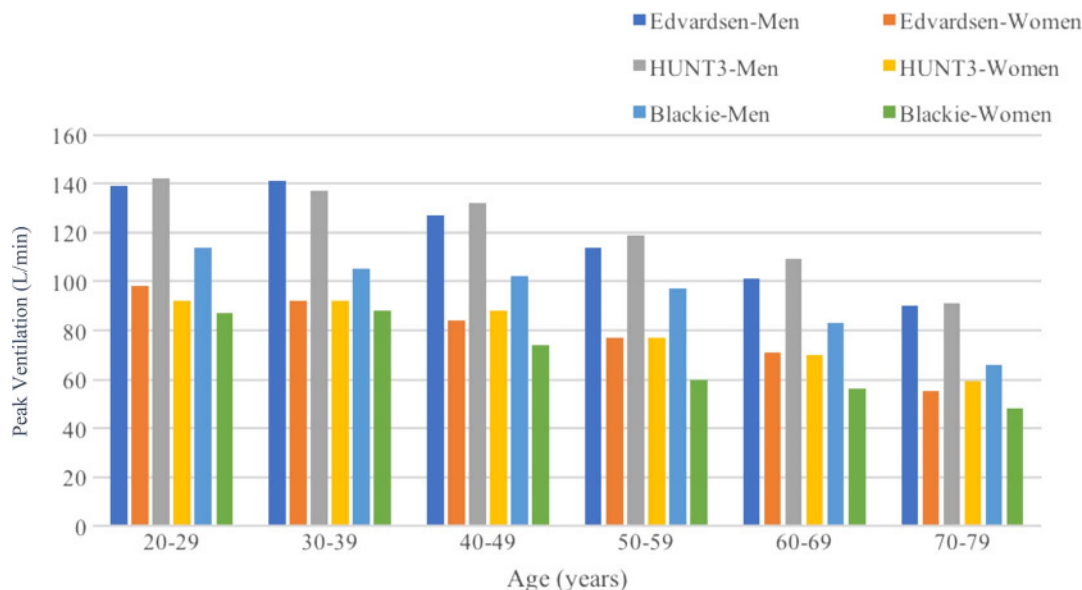


FIGURE 1—Peak ventilation ($L \cdot \text{min}^{-1}$) during cardiopulmonary testing data for men and women from three previous studies (11–13).

Common to studies using retrospective data, there are some limitations that should be considered. Subjects with previously diagnosed CVD and COPD were excluded from this data set. However, the population did have some chronic diseases (e.g., diabetes, obesity) and musculoskeletal concerns (e.g., back pain, osteoarthritis). Although all tests were performed for functional capacity measurement, the individual referral for the tests varied (clinical assessment, fitness screening, and research evaluation). Additionally, the choice of test protocols (~56% with ramp type and 45% with incremental type), measurement equipment, and data collection procedures although consistent with recommendations provided in recently published guidelines, was specific to each contributing laboratory (1,27,28).

These reference standards from FRIEND provide an alternative for investigators to derive an estimation of expected values for $\dot{V}_{E\text{peak}}$ for men and women from CPX (Table 4). Alternatively, estimates of $\dot{V}_{E\text{peak}}$ could be obtained using the regression equation incorporating sex, age, and height or with the simple equation with FEV_1 as the sole predictor. This simple equation, which could be an easy to remember rule of thumb ($\dot{V}_{E\text{peak}} = [FEV_1 \times 27] + 5$), may be helpful in clinical practice. This approach would allow interpretation of the measured value as a percentage of predicted.

REFERENCES

- Balady GJ, Arena R, Sietsema K, et al. Clinician's guide to cardiopulmonary exercise testing in adults: a scientific statement from the American Heart Association. *Circulation*. 2010;122:191–225.
- Guazzi M, Adams V, Conraads V, et al. Clinical recommendations for cardiopulmonary exercise testing data assessment in specific patient populations. *Circulation*. 2012;126:2261–74.
- Guazzi M, Arena R, Halle M, Piepoli MF, Myers J, Lavie CJ. 2016 Focused update: clinical recommendations for cardiopulmonary exercise testing data assessment in specific patient populations. *Circulation*. 2016;133:e694–711.
- Kaminsky LA, Arena R, Beckie TM, et al. American Heart Association Advocacy Coordinating Committee, Council on Clinical Cardiology, and Council on Nutrition, Physical Activity and Metabolism. The importance of cardiorespiratory fitness in the United States: the need for a national registry: a policy statement from the American Heart Association. *Circulation*. 2013;127:652–62.
- Kaminsky LA, Arena R, Myers J. Reference standards for cardiorespiratory fitness measured with cardiopulmonary exercise testing: data from the fitness registry and the importance of exercise national database. *Mayo Clin Proc*. 2015;90:1515–23.

CONCLUSIONS

Reference standards for $\dot{V}_{E\text{peak}}$ were established from the FRIEND Registry from CPX data in the United States. These standards can be applied for the interpretation of $\dot{V}_{E\text{peak}}$ along with other measures obtained in CPX. Future studies should explore the potential contribution of individuals $\dot{V}_{E\text{peak}}$ response related to health and disease outcomes. Additionally, factors that may influence $\dot{V}_{E\text{peak}}$ and its change with age, such as exercise training should be explored.

FRIEND Consortium Contributors: Ball State University (Leonard Kaminsky), Brooke Army Medical Center (Kenneth Leclerc), Cone Health (Paul Chase), Johns Hopkins University (Kerry Stewart), University of Kansas Medical Center (Sandra Billinger), Southern Connecticut State University (Robert Axtell), Taylor University (Erik Hayes), VA Palo Alto Healthcare System (Jon Myers).

The results of the study are presented clearly, honestly, and without fabrication, falsification, or inappropriate data manipulation, and statement that results of the present study do not constitute endorsement by ACSM.

L. K.: The project described was partially supported by TKC Global through Grant No. GS04T11BFP0001 to Ball State University and L. K. serves as a Scientific Advisor for ENDO Medical, Inc. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health. M. Harber, M. Imboden, R. Arena, and J. Myers: nothing to disclose.

6. Kaminsky LA, Imboden MT, Arena R, Myers J. Reference standards for Cardiorespiratory fitness measured with cardiopulmonary exercise testing using cycle ergometry: data from the fitness registry and the importance of exercise National Database (FRIEND) registry. *Mayo Clin Proc.* 2017;92:228–33.
7. Myers J, Kaminsky LA, Lima R, Christle JW, Ashley E, Arena R. A reference equation for normal standards for VO₂ max: analysis from the Fitness Registry and the Importance of Exercise National Database (FRIEND registry). *Prog Cardiovasc Dis.* 2017;60:21–9.
8. Ross R, Blair SN, Arena R, et al. Importance of assessing cardiorespiratory fitness in clinical practice: a case for fitness as a clinical vital sign: a scientific statement from the American Heart Association. *Circulation.* 2016;134:e653–99.
9. Harber MP, Kaminsky LA, Arena R, et al. Impact of cardiorespiratory fitness on all-cause and disease-specific mortality: advances since 2009. *Prog Cardiovasc Dis.* 2017;60:11–20.
10. Nauman J, Tauschek LC, Kaminsky LA, Nes BM, Wisløff U. Global fitness levels: findings from a web-based surveillance report. *Prog Cardiovasc Dis.* 2017;60(1):78–88.
11. Killian KJ, Leblanc P, Martin DH, Summers E, Jones NL, Campbell EJ. Exercise capacity and ventilatory, circulatory, and symptom limitation in patients with chronic airflow limitation. *Am Rev Respir Dis.* 1992;146:935–40.
12. Hansen JE, Sue DY, Wasserman K. Predicted values for clinical exercise testing. *Am Rev Respir Dis.* 1984;129(2 Pt 2):S49–54.
13. Wasserman K, Hansen JE, Sue DY, Whipp BJ, Casaburi R. *Principles of Exercise Testing and Interpretation.* 2nd ed. Philadelphia: Lea & Febiger; 1994. p. 124.
14. Miller MR, Hankinson V, Brusasco F, et al. Standardization of lung function testing. *Eur Respir J.* 2005;26:319–38.
15. Crapo RO, Morris AH, Gardner RM. Reference spirometric values using techniques and equipment that meet ATS recommendations. *Am Rev Respir Dis.* 1981;123:659–64.
16. Cotes JE. *Lung Function: Assessment and Application in Medicine.* 3rd ed. Oxford: Blackwell Scientific Publications; 1975. p. 104.
17. Gandevia B, Hugh-Jones P. Terminology for measurements of ventilatory capacity; a report to the thoracic society. *Thorax.* 1957;12:290–3.
18. Pedhazur EJ, Schmelkin LP. *Measurement, Design, and Analysis: An Integrated Approach.* Hillsdale: Lawrence Erlbaum Associates, Publishers; 1991. p. 433.
19. U.S. Department of Labor. Spirometry prediction tables for normal males and females. Occupational safety and health standards. 1910. 1043 App C. Assessed on July 15, 2018: https://www.osha.gov/pls/oshaweb/owadisp.show_document?p_table=STANDARDS&p_id=10058.
20. Palmer PB, O’Connell DG. Regression analysis for prediction: understanding the process. *Cardiopulm Phys Ther J.* 2009;20:23–6.
21. Loe H, Rognmo Ø, Saltin B, Wisløff U. Aerobic capacity reference data in 3816 healthy men and women 20-90 years. *PLoS One.* 2013;8:e64319.
22. Edvardsen E, Scient C, Hansen BH, Holme IM, Dyrstad SM, Anderssen SA. Reference values for cardiorespiratory response and fitness on the treadmill in a 20- to 85-year-old population. *Chest.* 2013;144:241–8.
23. Blackie SP, Fairbairn MS, McElvaney NG, et al. *Chest.* 100:136–42.
24. Saltin B, Astrand PO. Maximal oxygen uptake in athletes. *J Appl Physiol.* 1967;23:353–8.
25. Heath GW, Hagberg JM, Ehsani AA, Holloszy JO. A physiological comparison of young and older endurance athletes. *J Appl Physiol Respir Environ Exerc Physiol.* 1981;51:634–40.
26. Trappe S, Hayes E, Galpin A, et al. New records in aerobic power among octogenarian lifelong endurance athletes. *J Appl Physiol (1985).* 2013;114:3–10.
27. Myers J, Arena R, Franklin B, et al. Recommendations for clinical exercise laboratories: a scientific statement from the American Heart Association. *Circulation.* 2009;119(24):3144–61.
28. Myers J, Forman DE, Balady GJ, et al. Supervision of exercise testing by nonphysicians: a scientific statement from the American Heart Association. *Circulation.* 2014;130(12):1014–27.