Published in final edited form as:

Int J Sports Med. 2016 October ; 37(11): 863–869. doi:10.1055/s-0042-110572.

The Role of Body Habitus in Predicting Cardiorespiratory Fitness: The FRIEND Registry

T. Baynard¹, R. A. Arena², J. Myers³, and L. A. Kaminsky⁴

¹Kinesiology & Nutrition, University of Illinois at Chicago, Chicago, United States

²Department of Physical Therapy, University of Illinois at Chicago, Chicago, United States

³Cardiology Division, VA Palo Alto Health Care System, Palo Alto, California, United States

⁴School of Kinesiology, Ball State University, Muncie, Indiana, United States

Abstract

This study aimed to validate and cross-validate a non-exercise prediction model from a large and apparently healthy US cohort of individuals who underwent an analysis of body habitus (waist circumference (WC) and body mass index (BMI)) with measured CRF. The large cohort (5 030 individuals) was split into validation (4 030) and cross-validation (1 000) groups, whereby waist circumference and maximal aerobic capacity ($\text{VO}_{2\text{max}}$) were assessed by rigorously approved laboratories. $\text{VO}_{2\text{max}}$ was estimated in 2 multiple regression equations using age, sex and either WC ($r = 0.77$; standard error of the estimate (SEE) $6.70 \text{ mL O}_2 \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$) or BMI ($r = 0.76$; SEE $6.89 \text{ mL O}_2 \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$). Cross-validation yielded similar results. However, as $\text{VO}_{2\text{max}}$ increased, there was increased bias, suggesting $\text{VO}_{2\text{max}}$ may be underestimated at higher values. Both WC and BMI prediction models yielded similar findings, with WC having a slightly smaller SEE. These measures of body habitus appear to be adequate in predicting CRF using non-exercise parameters, even without a measure of physical activity. Caution should be taken when using these equations in more fit individuals.

Keywords

waist circumference; body mass index; prediction equation; maximal aerobic capacity

Introduction

The quantification of cardiorespiratory fitness (CRF) portends a wealth of clinically valuable information. In fact, CRF may be one of the most important vital signs that a clinician can ascertain [2]. CRF is a major predictor of all-cause and cardiovascular disease (CVD) mortality in apparently healthy populations [9, 19, 21, 27, 41], as well as in populations with conditions that significantly increase CVD risk, such as hypertension [6], obesity [4, 41] and type 2 diabetes [40]. Quantification of CRF is also an important prognostic tool in patients

Correspondence: Dr. Tracy Baynard, Kinesiology & Nutrition, University of Illinois at Chicago, 1919W. Taylor St. MC-517, 60612 Chicago, United States, Tel.: + 1/312/4131 962, Fax: + 1/312/4130 319, tbaynard@uic.edu.

Conflict of interest: The authors have no conflict of interest to declare.

already diagnosed with CVD [33]. Outside of the cardiovascular realm, CRF is also highly related to other important health-related outcomes, such as depression/anxiety, Alzheimer's disease, lung diseases and cancer mortalities [20, 23, 24, 29, 36–38].

Despite the clear value of the quantification of CRF, submaximal or maximal exercise testing is not common nor feasible in all settings [16]. The recent AHA scientific statement supporting the appropriateness of non-physician supervision of maximal exercise testing and the increasing evidence base for the value of cardiopulmonary exercise testing are encouraging more widespread consideration, particularly for clinical populations [10, 26]. Therefore, the ability to obtain reasonable estimations of CRF from non-exercise based parameters (e. g., age, sex, etc.) that are easily obtained during a regular physical exam would provide high clinical value, allowing for the identification of individuals who are more likely to have a low CRF and thus likely to be prescribed exercise. Moreover, there is utility in using an accurate prediction equation to compare to measured CRF values obtained in those undergoing an exercise test, generating a percent-predicted value. In fact, previous studies have demonstrated percent-predicted CRF values portend important prognostic information [1, 34].

3 large studies have provided estimates of CRF using non-exercise parameters [13, 28, 42, 43], all of which included careful evaluation and scoring of physical activity, a practice not normally performed clinically [32]. These previous studies fared well in predicting CRF with physical activity included (SEE between 4.8 and 5.8 mL/kg/min). While physical inactivity is an important CVD risk factor and may be a common goal to record in a patient's medical records, unfortunately, it is not commonly done in clinical practice [35]. While physical activity should be recorded clinically, there is no current consensus on an optimal physical activity assessment tool, which can introduce possible discrepancies between prediction models. Therefore, developing an equation to easily estimate CRF based on data usually obtained during a standard clinic visit is of particular value. Importantly, these currently available equations [13, 28, 43] demonstrated the value of including a measure of body habitus [i. e. percent body fat, waist circumference (WC) or body mass index (BMI)] in their models. Considering the current prevalence of obesity in the US [25], a continued analysis of the impact of body habitus on CRF prediction is warranted. Specifically, none of the previous investigations developed their prediction equations using a large US database, allowing for simultaneous validation and cross-validation. As such, it is important to develop a non-exercise model that is easily accessible from a clinical perspective, with variables commonly recorded, such as age, sex and BMI. Therefore, the purpose of this study was to determine whether an accurate prediction model could be developed and validated from a large US cohort of individuals, without overt CVD or COPD, who underwent an analysis of body habitus and subsequently completed a maximal cardiopulmonary exercise test (CPX).

Methods

In 2014 a multi-institutional initiative, the “Fitness Registry and the Importance of Exercise: A National Database” (FRIEND) Registry was established by the cardiorespiratory fitness (CRF) advisory board (listed in the acknowledgments) with the primary charge of

establishing normative CRF values in the United States across the adult lifespan [17]. Briefly, CPX laboratories from within the US that contributed data to the FRIEND Registry were all determined to be, by the CRF advisory board, well-established, demonstrating valid and reliable calibration and testing procedures as well as employing experienced personnel qualified to conduct exercise tests. Participating CPX laboratories were responsible for obtaining local IRB approval for inclusion in the FRIEND Registry, providing documentation that they were authorized to submit de-identified, coded data to the core CPX laboratory housed at the University of Illinois at Chicago (UIC). Institutional review board approval for the core CPX laboratory was also obtained at UIC. In addition, this study meets the ethical standards of the International Journal of Sports Medicine [11]. The FRIEND advisory board reviewed data from each CPX laboratory for uniformity of the data prior to inclusion in the registry, which has been described recently [3, 17]. For example, the data was examined for outliers and skewness. Databases from each participating site included key baseline characteristics and CPX measures. The UIC core CPX laboratory performed an analysis of all submitted data to ensure data points were within expected normal ranges and subsequently created a single merged database. In the event errors were identified or data points were outside of the normal expected range, the CPX laboratory submitting the data in question were contacted for clarification, data validation and, if needed, correction. Additional details regarding the registry can be obtained in these recent papers [3, 17].

Cohort and study data points

The current analysis included 5 030 tests from the FRIEND consortium data contributors (see acknowledgements). Tests were conducted between September 1998 and January 2015. Inclusion criteria for the current analysis included CPX data on men and women: 1) aged 20 years; 2) a maximal exercise test performed on a treadmill; and 3) measurement of both body mass index (BMI; in kg/m²) and WC (measured in cm). Because the FRIEND registry collected data from various laboratories that were conducting different study protocols, WC was measured with various methods, including at the umbilicus, at the midpoint between the iliac crest and lowest rib, or directly above the iliac crest. Importantly, WC measured at different sites is reportedly equally reliable at identifying increased risk [30, 39], which we believe justifies the different techniques utilized. Any subject was excluded who was identified as having a pre-existing medical condition at the time of testing (i. e. coronary artery disease, peripheral artery disease, heart failure or chronic obstructive pulmonary disease) and/or was taking a beta-blocking agent. Some chronic conditions were prevalent in the FRIEND Registry due to the nature of the data included, such as hypertension, hyperlipidemia and obesity. Maximal oxygen consumption (VO_{2max}), and the peak respiratory exchange ratio (RER) were the CPX variables reported in the current study and utilized for analysis. Additional details can be found elsewhere [17].

Statistical analysis

Subjects were randomly assigned to a validation (n = 4 030) or cross-validation (n = 1 000) cohort. The independent sample *t*-test and χ^2 tests were used to compare differences in key continuous and categorical variables, respectively, in the validation and cross-validation cohorts. Normality was tested and it was observed that neither WC nor BMI were normally distributed. Considering that the primary aim was to execute regression analyses, it is more

relevant for residuals to demonstrate linearity, which they did when P-P plots were examined (plots not included). 2 stepwise linear regression analyses were used to derive $\text{VO}_{2\text{max}}$ prediction equations in the validation cohort. Both regressions included age and sex; one equation also included BMI, while the other included WC. The same linear regression analyses were then run in the cross-validation cohort for comparison. The difference between measured and predicted $\text{VO}_{2\text{max}}$ values, the latter using the regressions developed in the validation cohort, was compared in the cross-validation cohort using a one-sample *t*-test. The Bland-Altman [5] plot was used to further assess the agreement between measured and predicted $\text{VO}_{2\text{max}}$ values in the cross-validation cohort. Linear regression analyses, using the difference between (y-axis) and mean of (x-axis) measured and predicted $\text{VO}_{2\text{max}}$ values in the cross-validation cohort, were used to assess the presence of proportional bias for each regression. In addition, curve estimation was used to determine the best fit for the difference between (y-axis) and the mean of (x-axis) the measured and predicted $\text{VO}_{2\text{max}}$ values in the cross-validation cohort. Continuous data are reported as mean and standard deviation, while categorical data are reported as frequencies and percentages. The SPSS 22.0 (IBM, Armonk, New York) statistical software package was used for all analyses. All tests with an $\alpha < 0.05$ were considered statistically significant.

Results

Key comparisons between the validation and cross-validation cohorts are listed in Table 1; no significant differences were detected. Mean $\text{VO}_{2\text{max}}$ values approximated the 50th percentile for recently published normative values for both men and women [17], and mean peak RER values indicated excellent exercise effort for the cohort. Both cohorts were predominantly male, but given the large sample size there was a significant number of females included in the analysis.

The linear regression analyses are listed in Table 2, 3. Table 2, 3, both WC and BMI-based regression equations were significant ($p < 0.001$). Moreover, in the cross-validation cohorts, the *r*-values, standard errors of the estimate and the beta-coefficients closely approximated results in the validation cohort. Table 2, 3 also list the model summary results for validation analyses in the WC and BMI-based linear regression models. In each model summary, addition of the independent variable representing body habitus resulted in the largest improvement in prediction accuracy.

The one-sample *t*-test indicated that the mean difference between the measured $\text{VO}_{2\text{max}}$ and predicted $\text{VO}_{2\text{max}}$ in the cross-validation cohort was not different from 0 for both the WC (mean = -0.0438 , $p = 0.84$) and BMI-based (mean = -0.083 , $p = 0.97$) regression equations. The Bland-Altman analysis is illustrated in Fig. 1a, b, and reveals comparable limits of agreement for the WC (upper = 13.01 and lower = -13.10 , range 26.11 $\text{mLO}_2\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$) and BMI-based (upper = 13.48 and lower = -13.49 , range 26.97 $\text{mLO}_2\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$) regression equations. The slopes of the Bland-Altman plots are zero. Both Bland-Altman analyses revealed a positive trend, as the measured $\text{VO}_{2\text{max}}$ and predicted $\text{VO}_{2\text{max}}$ mean (x-axis) increased.

Linear regression analysis using the difference between (y-axis) and mean of (x-axis) $\text{VO}_{2\text{max}}$ and predicted $\text{VO}_{2\text{max}}$ revealed a significant relationship for both the WC [$r = 0.39$, $p < 0.001$; equation = $-10.07 - 0.29 (\text{VO}_{2\text{max}} - \text{predicted } \text{VO}_{2\text{max}} \text{ mean})$, standard error of the estimate = 6.14] and BMI-based [$r = 0.41$, $p < 0.001$; equation = $-11.02 - 0.32 (\text{VO}_{2\text{max}} - \text{predicted } \text{VO}_{2\text{max}} \text{ mean})$, standard error of the estimate = 6.28] regression equations, indicating a proportional bias for both. However, curve estimation analysis revealed that, compared to the linear model, a cubic curve fit afforded a substantially improved reflection of the difference between (y-axis) and the mean of (x-axis) the $\text{VO}_{2\text{max}}$ and predicted $\text{VO}_{2\text{max}}$ values for both WC ($r = 0.56$ cubic vs. 0.39 linear) and BMI-based ($r = 0.61$ vs. 0.41) regression models (Fig. 1c, d).

Discussion

Our main findings suggest that 2 markers of body habitus, BMI and waist circumference, add significant predictive value (i. e. largest r-square change) to age and sex in developing a prediction model to estimate CRF in a large cohort of men and women from the US, which does not include a physical activity parameter. These prediction variables are readily and rapidly obtainable in the clinical setting, enhancing the clinical applicability of the proposed CRF prediction equations. Furthermore, cross-validation demonstrated quite stable models for both WC and BMI, with $R^2 = 0.58$ and 0.61 , and SEEs 6.7 and $6.9 \text{ mL O}_2 \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$, respectively. Previous research has also reported body habitus (e. g., BMI, waist circumference or percent body fat) to be robust in CRF predictive equations; These previous models have all included measures of physical activity [12, 13, 28, 43]. Collectively, these previous models appear to result in slightly more accurate non-exercise prediction models, with SEEs ranging between 4.72 [43] to $5.85 \text{ mL O}_2 \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ [28] and relative standard errors between 12.6% [13] and 14.6% [28]. Despite having slightly higher SEE and relative standard error values (6.7 – $6.9 \text{ SEE mL O}_2 \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$; 19.4 – 20% SEE %) compared to the current prediction equations, our data demonstrate that using either BMI or WC is indeed informative in predicting CRF, and that these equations may have utility in the clinical setting where a detailed assessment of physical activity is commonly not performed.

The degree and type of physical activity that an individual participates in on a daily basis certainly influences CRF and can therefore be an important dependent variable for CRF prediction equations. While accuracy for the equations proposed in the current study may be slightly compromised without any physical activity indices included in the prediction models, as other equations may suggest, it is important to note that the relative standard error is within the normal relative error for submaximal exercise tests used to predict aerobic capacity (i. e., 10 – 20%) [7, 18, 22, 31], with SEEs ranging from 3.8 – $5.7 \text{ mL O}_2 \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$. It is important to note that a detailed assessment of physical activity patterns is currently not common practice in the clinical setting. As a result, CRF prediction equations are needed in these settings using data that is regularly assessed in clinical practice. The enhanced broad applicability of the proposed regression equations more than compensates for the slight increase in prediction error.

Cross-validation typically establishes the stability of the developed models onhand. The moderately high r for both the validated and cross-validated models (Table 2, 3) indicate

good overall stability for both the WC and BMI models. Waist circumference may more readily identify an excess body mass phenotype that is more closely aligned with adipose tissue in a particularly unfavorable location associated with low CRF – the abdomen [8, 14]. Conversely, higher BMI values, which on the surface are assumed to be aligned with unhealthy amounts of excess adipose tissue, may actually be associated with higher lean mass values in certain individuals, a phenotype not necessarily associated with lower CRF. This may be particularly true in individuals who are classified within the lower end of the overweight BMI range (i. e., $\approx 25\text{--}27\text{ kg/m}^2$). For this reason, measuring waist circumference, which is not a difficult task and is rapidly obtainable, should be considered as a clinical standard for assessment of body habitus, along with measurement of BMI. Even so, the prediction equations using both measures of body habitus were comparable and both therefore appear to be of value.

Other studies have demonstrated very good stability of their non-exercise prediction equations [12, 13, 28, 43]. However, some of this previous work has found their non-exercise prediction equations to underestimate $\text{VO}_{2\text{max}}$ among subgroups with higher fitness values (e. g. $> 55\text{ mL O}_2\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$) [12, 13, 43]. While the mean difference between measured $\text{VO}_{2\text{max}}$ and predicted $\text{VO}_{2\text{max}}$ in the cross-validation cohort was not significantly different from 0, further analyses did reveal concerns over prediction accuracy in certain circumstances. When examining the Bland-Altman plots, it is clear that there is a proportional bias, where our results also appear to indicate a higher underestimation of CRF in those who exhibit a high level of fitness, particularly when measured $\text{VO}_{2\text{max}}$ values exceed $50\text{ mL O}_2\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$. We took the proportional bias analysis a step further in the current study, performing a curve fit analysis on the difference between $\text{VO}_{2\text{max}}$ (y-axis) and the means of measured and predicted $\text{VO}_{2\text{max}}$ (x-axis); This appears to be a novel analysis not previously performed in this area. This additional analysis found that a cubic curve fit was superior to the linear model, further indicating a proportional bias. Specifically, it appears that the prediction equations developed and cross-validated in the current study also underestimated CRF when measured $\text{VO}_{2\text{max}}$ was particularly low; Admittedly the underestimation was greater in those individuals with a particularly high measured $\text{VO}_{2\text{max}}$. It is unclear whether proportional bias is a common phenomenon and this requires further investigation. Clearly, our findings indicate the ability to predict CRF has limitations and variable error. Specifically, when the regression equation produces a particularly high (i. e., $> 50\text{ mL O}_2\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$) or particularly low (i. e., $< 20\text{ mL O}_2\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$) prediction, there is a greater concern for underestimation, especially in those who are predicted to have a high CRF. Additional research is needed to further explore improved prediction equation models, such as age-specific models, in order to reduce the associated degree of error. Importantly, this equation could be useful for all adults seen in the primary care setting (with the exception of the exclusion criteria outlined here in this study, as well as those with known CVD or COPD). CRF is an important vital measure to be assessed that is currently not being assessed in clinical practice. This equation can be built into to existing electronic record reports to calculate the estimated CRF from the other measures that are obtained on patients in the primary care setting. This information can help clinicians and additional healthcare professionals to inform and counsel patients about CRF.

The primary strength of this study is the size of the cohort and the representation of SEE values along with the cross-validation analyses. In fact, the current analysis appears to consist of the largest combined validation and cross-validation cohort to date. The statistical analyses employed in the current analyses should be considered an additional strength. Furthermore, the use of indirect calorimetry to assess measured $\text{VO}_{2\text{max}}$ is an important strength, as previous work has demonstrated that measured $\text{VO}_{2\text{max}}$ is better correlated to prediction equations vs. cohorts using indirect assessments of fitness [15]. Along these lines, not only was fitness measured, but it was done in a well-controlled manner across numerous laboratories around the United States, with well-defined criteria for inclusion in the database. Furthermore, easily accessible markers of body habitus were included. Other studies have included percent body fat in their non-exercise prediction equations [12, 13, 43], which have yielded good models. However, percent body fat is rarely ever measured clinically and requires either expensive technical equipment (e. g., dual energy x-ray absorptiometry) or less-expensive equipment that necessitates a high degree of experience and competence (e. g., skinfold measures).

Several limitations exist with respect to this study. The cohort is relatively healthy and therefore generalizability cannot be made to other populations, such as those with CVD. As registries containing CRF data grow, it is inevitable that similar prediction equations will be analyzed if chronic disease significantly adds to the predictive power of such equations over and above the relationships between age, body habitus and sex. Certain parameters were not collected in the current dataset, particularly a valid measure of physical activity. This limits the ability to perform an analysis similar to previous studies [13, 28, 43] and provide a more closely aligned comparison. However, we feel this is not a limitation per se, because physical activity is not regularly assessed in clinical practice, which supports the need for such non-exercise models. It is important to remember that differences in testing protocols, cohorts and even equipment can introduce some degree of artifact between the available studies examining non-exercise prediction equations. However, the FRIEND registry did employ a stringent vetting procedure for participating CPX laboratories, which substantially increases confidence in the consistency of the data analyzed across laboratories.

In conclusion, both WC and BMI appear to be valuable and meaningful contributors to the estimation of CRF among individuals without overt CVD or COPD, using additional non-exercise parameters of age and sex. The cross-validation demonstrated good stability for both the WC and BMI models. While physical activity indices may improve accuracy slightly according to previous non-exercise models, these measures are largely lacking from clinical practice. Applying the current models in a clinical setting may be useful in tracking an important component and marker of overall health – cardiorespiratory fitness.

Acknowledgments

Cardiorespiratory Fitness Registry Board Members: Co-Chairs: Lenny Kaminsky and Ross Arena, Paige Briggs, Peter Brubaker, Daniel Forman, Carol Garber, Chip Lavie, Jonathan Myers, Mahesh Patel FRIEND Consortium Contributors: Ball State University (Leonard Kaminsky), Cleveland Clinic (John Kirwan and Jacob Haus), Johns Hopkins University (Kerry Stewart). This project was supported, in part, by a grant from TKC Global Solutions, LLC. The National Center for Advancing Translational Sciences, National Institutes of Health, (UL1TR000050) provided additional support. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

References

1. Arena R, Myers J, Abella J, Pinkstaff S, Brubaker P, Moore B, Kitzman D, Peberdy MA, Bensimhon D, Chase P, Forman D, West E, Guazzi M. Determining the preferred percent-predicted equation for peak oxygen consumption in patients with heart failure. *Circ Heart Fail*. 2009; 2:113–120. [PubMed: 19808326]
2. Arena R, Myers J, Guazzi M. The future of aerobic exercise testing in clinical practice: Is it the ultimate vital sign? *Future Cardiol*. 2010; 6:325–342. [PubMed: 20462339]
3. Arena R, Myers J, Kaminsky LA. Revisiting age-predicted maximal heart rate: Can it be used as a valid measure of effort? *Am Heart J*. 2016; 173:49–56. [PubMed: 26920596]
4. Barry VW, Baruth M, Beets MW, Durstine JL, Liu J, Blair SN. Fitness vs. Fatness on all-cause mortality: A meta-analysis. *Prog Cardiovasc Dis*. 2014; 56:382–390. [PubMed: 24438729]
5. Bland JM, Altman DG. Statistical methods for assessing agreement between two methods of clinical measurement. *Lancet*. 1986; 1:307–310. [PubMed: 2868172]
6. Church TS, Kampert JB, Gibbons LW, Barlow CE, Blair SN. Usefulness of cardiorespiratory fitness as a predictor of all-cause and cardiovascular disease mortality in men with systemic hypertension. *Am J Cardiol*. 2001; 88:651–656. [PubMed: 11564389]
7. Cink RE, Thomas TR. Validity of the Åstrand-Ryhming nomogram for predicting maximal oxygen intake. *Br J Sports Med*. 1981; 15:182–185. [PubMed: 7272663]
8. Despres JP, Lemieux I. Abdominal obesity and metabolic syndrome. *Nature*. 2006; 444:881–887. [PubMed: 17167477]
9. Farrell SW, Braun L, Barlow CE, Cheng YJ, Blair SN. The relation of body mass index, cardiorespiratory fitness, and all-cause mortality in women. *Obes Res*. 2002; 10:417–423. [PubMed: 12055316]
10. Guazzi M, Arena R. Cardiopulse. New clinical cardiopulmonary exercise testing joint statement from the European Society of Cardiology and American Heart Association. *Eur Heart J*. 2012; 33:2627–2628. [PubMed: 23281541]
11. Harriss DJ, Atkinson G. Ethical standards in sport and exercise science research: 2016 update. *Int J Sports Med*. 2015; 36:1121–1124. [PubMed: 26671845]
12. Heil DP, Freedson PS, Ahlquist LE, Price J, Rippe JM. Nonexercise regression models to estimate peak oxygen consumption. *Med Sci Sports Exerc*. 1995; 27:599–606. [PubMed: 7791593]
13. Jackson AS, Blair SN, Mahar MT, Wier LT, Ross RM, Stuteville JE. Prediction of functional aerobic capacity without exercise testing. *Med Sci Sports Exerc*. 1990; 22:863–870. [PubMed: 2287267]
14. Janssen I, Katzmarzyk PT, Ross R. Waist circumference and not body mass index explains obesity-related health risk. *Am J Clin Nutr*. 2004; 79:379–384. [PubMed: 14985210]
15. Jurca R, Jackson AS, LaMonte MJ, Morrow JR Jr, Blair SN, Wareham NJ, Haskell WL, van Mechelen W, Church TS, Jakicic JM, Laukkanen R. Assessing cardiorespiratory fitness without performing exercise testing. *Am J Prev Med*. 2005; 29:185–193.
16. Kaminsky LA, Arena R, Beckie TM, Brubaker PH, Church TS, Forman DE, Franklin BA, Gulati M, Lavie CJ, Myers J, Patel MJ, Pina IL, Weintraub WS, Williams MA, American Heart Association Advocacy Coordinating Committee. CoCC, Council on Nutrition PA, 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; 127:652–662. [PubMed: 23295916]
17. 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 (FRIEND Registry). *Mayo Clin Proc*. 2015
18. Kline GM, Porcari JP, Hintermeister R, Freedson PS, Ward A, McCarron RF, Ross J, Rippe JM. Estimation of VO₂max from a one-mile track walk, gender, age, and body weight. *Med Sci Sports Exerc*. 1987; 19:253–259. [PubMed: 3600239]
19. Kodama S, Saito K, Tanaka S, Maki M, Yachi Y, Asumi M, Sugawara A, Totsuka K, Shimano H, Ohashi Y, Yamada N, Sone H. Cardiorespiratory fitness as a quantitative predictor of all-cause

- mortality and cardiovascular events in healthy men and women: A meta-analysis. *JAMA*. 2009; 301:2024–2035. [PubMed: 19454641]
20. Lakoski SG, Willis BL, Barlow CE, Leonard D, Gao A, Radford NB, Farrell SW, Douglas PS, Berry JD, DeFina LF, Jones LW. Midlife cardiorespiratory fitness, incident cancer, and survival after cancer in men: The cooper center longitudinal study. *JAMA Oncol*. 2015; 1:231–237. [PubMed: 26181028]
 21. Lee DC, Artero EG, Sui X, Blair SN. Mortality trends in the general population: The importance of cardiorespiratory fitness. *J Psychopharmacol*. 2010; 24:27–35.
 22. Leger LA, Lambert J. A maximal multistage 20-m shuttle run test to predict VO2 max. *Eur J Appl Physiol Occup Physiol*. 1982; 49:1–12. [PubMed: 7201922]
 23. Liu R, Sui X, Laditka JN, Church TS, Colabianchi N, Hussey J, Blair SN. Cardiorespiratory fitness as a predictor of dementia mortality in men and women. *Med Sci Sports Exerc*. 2012; 44:253–259. [PubMed: 21796048]
 24. Milani RV, Lavie CJ. Impact of cardiac rehabilitation on depression and its associated mortality. *Am J Med*. 2007; 120:799–806. [PubMed: 17765050]
 25. Mozaffarian D, Benjamin EJ, Go AS, Arnett DK, Blaha MJ, Cushman M, de Ferranti S, Despres JP, Fullerton HJ, Howard VJ, Huffman MD, Judd SE, Kissela BM, Lackland DT, Lichtman JH, Lisabeth LD, Liu S, Mackey RH, Matchar DB, McGuire DK, Mohler ER 3rd, Moy CS, Muntner P, Mussolino ME, Nasir K, Neumar RW, Nichol G, Palaniappan L, Pandey DK, Reeves MJ, Rodriguez CJ, Sorlie PD, Stein J, Towfighi A, Turan TN, Virani SS, Willey JZ, Woo D, Yeh RW, Turner MB, American Heart Association Statistics C, Stroke Statistics S. Heart disease and stroke statistics – 2015 update: A report from the American Heart Association. *Circulation*. 2015; 131:e29–e322. [PubMed: 25520374]
 26. Myers J, Forman DE, Balady GJ, Franklin BA, Nelson-Worel J, Martin BJ, Herbert WG, Guazzi M, Arena R, American Heart Association Subcommittee on Exercise CR, Prevention of the Council on Clinical Cardiology CoL, Cardiometabolic Health CoE, Prevention, Council on C, Stroke N. Supervision of exercise testing by nonphysicians: A scientific statement from the American Heart Association. *Circulation*. 2014; 130:1014–1027. [PubMed: 25223774]
 27. Myers J, McAuley P, Lavie CJ, Despres JP, Arena R, Kokkinos P. Physical activity and cardiorespiratory fitness as major markers of cardiovascular risk: Their independent and interwoven importance to health status. *Prog Cardiovasc Dis*. 2015; 57:306–314. [PubMed: 25269064]
 28. Nes BM, Janszky I, Vatten LJ, Nilsen TI, Aspenes ST, Wisloff U. Estimating VO2peak from a nonexercise prediction model: The hunt study, Norway. *Med Sci Sports Exerc*. 2011; 43:2024–2030. [PubMed: 21502897]
 29. Peel JB, Sui X, Adams SA, Hebert JR, Hardin JW, Blair SN. A prospective study of cardiorespiratory fitness and breast cancer mortality. *Med Sci Sports Exerc*. 2009; 41:742–748. [PubMed: 19276861]
 30. Ross R, Berentzen T, Bradshaw AJ, Janssen I, Kahn HS, Katzmarzyk PT, Kuk JL, Seidell JC, Snijder MB, Sorensen TI, Despres JP. Does the relationship between waist circumference, morbidity and mortality depend on measurement protocol for waist circumference? *Obes Rev*. 2008; 9:312–325. [PubMed: 17956544]
 31. Ross RM, Murthy JN, Wollak ID, Jackson AS. The six minute walk test accurately estimates mean peak oxygen uptake. *BMC Pulm Med*. 2010; 10:31. [PubMed: 20504351]
 32. Sallis R, Franklin B, Joy L, Ross R, Sabgir D, Stone J. Strategies for promoting physical activity in clinical practice. *Prog Cardiovasc Dis*. 2015; 57:375–386. [PubMed: 25459975]
 33. Smith JL, Verrill TA, Boura JA, Sakwa MP, Shannon FL, Franklin BA. Effect of cardiorespiratory fitness on short-term morbidity and mortality after coronary artery bypass grafting. *Am J Cardiol*. 2013; 112:1104–1109. [PubMed: 23849973]
 34. Stelken AM, Younis LT, Jennison SH, Miller DD, Miller LW, Shaw LJ, Kargl D, Chaitman BR. Prognostic value of cardiopulmonary exercise testing using percent achieved of predicted peak oxygen uptake for patients with ischemic and dilated cardiomyopathy. *J Am Coll Cardiol*. 1996; 27:345–352. [PubMed: 8557904]

35. Strath SJ, Kaminsky LA, Ainsworth BE, Ekelund U, Freedson PS, Gary RA, Richardson CR, Smith DT, Swartz AM, American Heart Association Physical Activity Committee of the Council on L, Cardiometabolic H, Cardiovascular ECR, Prevention Committee of the Council on Clinical C, Council. Guide to the assessment of physical activity: Clinical and research applications: A scientific statement from the American Heart Association. *Circulation*. 2013; 128:2259–2279. [PubMed: 24126387]
36. Sui X, Laditka JN, Church TS, Hardin JW, Chase N, Davis K, Blair SN. Prospective study of cardiorespiratory fitness and depressive symptoms in women and men. *J Psychiatr Res*. 2009; 43:546–552. [PubMed: 18845305]
37. Sui X, Lee DC, Matthews CE, Adams SA, Hebert JR, Church TS, Lee CD, Blair SN. Influence of cardiorespiratory fitness on lung cancer mortality. *Med Sci Sports Exerc*. 2010; 42:872–878. [PubMed: 19996990]
38. Vidoni ED, Honea RA, Billinger SA, Swerdlow RH, Burns JM. Cardiorespiratory fitness is associated with atrophy in Alzheimer's and aging over 2 years. *Neurobiol Aging*. 2012; 33:1624–1632. [PubMed: 21531480]
39. Wang J, Thornton JC, Bari S, Williamson B, Gallagher D, Heymsfield SB, Horlick M, Kotler D, LaFerrere B, Mayer L, Pi-Sunyer FX, Pierson RN Jr. Comparisons of waist circumferences measured at 4 sites. *Am J Clin Nutr*. 2003; 77:379–384. [PubMed: 12540397]
40. Wei M, Gibbons LW, Kampert JB, Nichaman MZ, Blair SN. Low cardiorespiratory fitness and physical inactivity as predictors of mortality in men with type 2 diabetes. *Ann Intern Med*. 2000; 132:605–611. [PubMed: 10766678]
41. Wei M, Kampert JB, Barlow CE, Nichaman MZ, Gibbons LW, Paffenbarger RS Jr, Blair SN. Relationship between low cardiorespiratory fitness and mortality in normal-weight, overweight, and obese men. *JAMA*. 1999; 282:1547–1553. [PubMed: 10546694]
42. Whaley MH, Kaminsky LA, Dwyer GB, Getchell LH. Failure of predicted VO₂peak to discriminate physical fitness in epidemiological studies. *Med Sci Sports Exerc*. 1995; 27:85–91. [PubMed: 7898344]
43. Wier LT, Jackson AS, Ayers GW, Arenare B. Nonexercise models for estimating VO₂max with waist girth, percent fat, or BMI. *Med Sci Sports Exerc*. 2006; 38:555–561. [PubMed: 16540845]

Fig. 1.

a and **b** represent the Bland-Altman plot in the cross-validation cohort for waist circumference and body mass index regression models predicting VO_{2max} , respectively.

$$VO_{2max} = 88.35 - 14.79 (\text{sex}) - 0.40 (\text{WC}) - 0.27 (\text{age})$$

$$VO_{2max} = 77.96 - 10.35 (\text{sex}) - 0.92 (\text{BMI}) - 0.32 (\text{age})$$

VO_{2max} = maximal oxygen consumption. Sex code: 0 = male, 1 = female

Panels **c** and **d** represent the curve estimation analysis in the cross-validation cohort for waist circumference and body mass index, respectively.

Table 1

Comparison of demographic characteristics of the validation and cross-validation cohorts.

	Validation (n=4 030)	Validation 95 % CI	Cross Validation (n = 1000)
Age (years)	46 ± 12	– 1.79, – 0.13	47 ± 12
Sex (% male)	60	–	60
BMI (kg/m²)	26.8 ± 5.2	– 0.43, 0.29	26.9 ± 5.3
WC (cm)	89.2 ± 13.9	– 0.91, 1.03	89.2 ± 14.3
VO_{2max} (mLO₂·kg⁻¹·min⁻¹)	34.5 ± 10.5	– 0.47, 0.99	34.2 ± 10.6
Peak RER	1.17 ± 0.10	– 0.003, 0.109	1.17 ± 0.10

BMI: Body mass index; WC: Waist circumference; VO_{2max}: Maximal oxygen consumption; RER: Respiratory exchange ratio; Mean ± SD; 95 % CI: Confidence interval; No significant differences

Table 2

Linear regression model summaries for Waist Circumference regressions.

Validation Cohort (n = 4 030)									
Model	Parameters	B	Beta	t	Sig	95 % CI	R value	Adj. R ²	R ² Change SEE
1	constant	38.40	–	202.9	<0.001	38.0, 38.8	0.46	0.21	* 9.32
	sex	– 9.92	– 0.462	– 33.1	<0.001	– 10.5, – 9.3			
2	constant	79.84	–	91.4	<0.001	78.1, 81.6	0.71	0.50	* 7.43
	sex	– 14.0	– 0.698	– 57.4	<0.001	– 15.5, – 14.5			
	WC	– 0.44	– 0.586	– 48.1	<0.001	– 0.46, – 0.42			
3	constant	88.35	–	105.8	<0.001	86.7, 90.0	0.77	0.60	* 6.70
	sex	– 14.79	– 0.689	– 62.8	<0.001	– 15.2, – 14.3			
	WC	– 0.40	– 0.529	– 47.5	<0.001	– 0.42, – 0.38			
	age	– 0.27	– 0.311	– 30.5	<0.001	– 0.29, – 0.26			
Equation: $88.35 - 14.79 (sex) - 0.40(WC) - 0.27(age)$									
Cross-Validation Cohort (n = 1000)									
Full Model	Constant				<0.001		0.78	0.61	– 6.67

B: Unstandardized coefficient; Beta: Standardized coefficient; Sex code: 0 = male, 1 = female; WC (cm); Age (yrs); 95 % CI: Confidence interval for B;

* p < 0.001 for R² change;

SEE: Standard error of the estimate in mL O₂·kg^{–1}·min^{–1}

Table 3

Linear regression model summaries for Body Mass Index regressions.

Validation Cohort (n = 4 030)									
Model	Parameters	B	Beta	t	Sig	95 % CI	R value	Adj. R ²	SEE
1	constant	59.96	–	77.3	< 0.001	58.4, 61.5	0.47	0.22	9.30
	BMI	– 0.95	– 0.467	– 33.5	< 0.001	– 1.0, – 0.90			
2	constant	64.19	–	96.3	< 0.001	62.9, 65.5	0.66	0.44	7.90
	BMI	– 0.96	– 0.472	– 39.8	< 0.001	– 1.0, – 0.91			
	sex	– 10.02	– 0.467	– 39.4	< 0.001	– 10.5, – 9.5			
3	constant	77.96	–	111.5	< 0.001	76.6, 79.3	0.76	0.57	6.89
	BMI	– 0.92	– 0.452	– 43.7	< 0.001	– 0.96, – 0.88			
	sex	– 10.35	– 0.482	– 46.6	< 0.001	– 10.8, – 9.9			
	age	– 0.32	– 0.368	– 35.6	< 0.001	– 0.34, – 0.31			
Equation: $77.96 - 10.35 (\text{sex}) - 0.92 (\text{BMI}) - 0.32 (\text{age})$									
Cross-Validation Cohort (n = 1 000)									
Full Model	Constant				< 0.001		0.76	0.58	6.89

B: Unstandardized coefficient; Beta: Standardized coefficient; Sex code: 0 = male, 1 = female; BMI: Body mass index (kg/m²); Age (yrs); 95 % CI: Confidence interval for B;

* p < 0.001 for R² change;

SEE: Standard error of the estimate in mL O₂ · kg^{–1} · min^{–1}