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Association Between Change in Nonexercise Estimated Cardiorespiratory Fitness and Mortality in Men

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Abstract

Objective: To examine the association between change in nonexercise estimated cardiorespiratory fitness (eCRF) and mortality risk in adult men.

Patients and Methods: A total of 10,445 men (mean age, 44.6±9.3 years) from the Aerobics Center Longitudinal Study underwent 2 comprehensive medical examinations and peak work rate tests between January 1, 1979, and December 31, 2002, with an average time between measures of 5.7±4.9 years. Participants were observed for 11.6±6.4 years after their second examination until death or December 31, 2003. The eCRF was calculated with the Jackson et al (2012) and Nes et al (2011) published nonexercise estimation equations. Cox proportional hazards models were performed to examine the association between change in eCRF and all-cause and cardiovascular disease (CVD) mortality.

Results: There were 601 deaths (192 CVD deaths) during the follow-up period. For both eCRF equations, a higher eCRF at baseline was associated with significant reductions in mortality risk from all causes and CVD ($P<.001$). Change in eCRF by the Jackson equation remained significantly associated with all-cause mortality ($P<.001$) and CVD mortality ($P=.02$) after multivariable adjustment. Every 1 metabolic equivalent (3.5 mL·kg^{-1}·min^{-1}) increase in eCRF was associated with a 21% and 22% reduction in mortality risk from all causes or CVD, respectively. No significant associations were observed between change in eCRF by the Nes equation and all-cause ($P=.69$) or CVD ($P=.85$) mortality risk after multivariable adjustment.

Conclusion: The association between change in nonexercise eCRF and mortality risk may be equation dependent.

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It is well established that cardiorespiratory fitness (CRF) is a strong, independent predictor of cardiovascular disease (CVD) and all-cause mortality risk.[1-3] The addition of CRF to traditional models used to estimate CVD risk significantly improves the risk reclassification.[4-6] Consequently, the American Heart Association has recommended that CRF be classified as a vital sign to be measured in clinical settings.[1] Despite this evidence, CRF has not been adopted as a routine measure in clinical settings as it is neither feasible nor appropriate to perform exercise testing during most patient encounters.[7-9]

Nonexercise estimated CRF (eCRF) has been suggested as a pragmatic alternative to objectively measured CRF (mCRF) during submaximal or maximal exercise testing.

These equations incorporate known determinants of CRF including age, sex, body composition phenotype, resting heart rate (RHR), and physical activity (PA) level into a regression model to predict CRF.[10-13] Many of these variables are commonly measured in clinical settings, underscoring the feasibility of eCRF assessment.

Initial evidence suggests that eCRF is a strong predictor of CVD and all-cause mortality.[9,14,15] These findings are based on observational evidence using a single assessment of eCRF, which may fail to account for the nonlinear decline in CRF associated with aging, genetic factors, and changes in other confounding factors, such as lifestyle behaviors, that may influence the relationship between CRF and mortality. Examining the change in

eCRF with 2 distinct measures would provide more information on long-term mortality risk than could be obtained from a single measure alone.

Although the association between change in mCRF and mortality is clear, yet to be considered is whether change in eCRF is associated with mortality risk. In this study, we examined the association between change in eCRF and the risk of all-cause and CVD mortality in healthy men using 2 published eCRF equations.

PATIENTS AND METHODS

A sample of 10,445 healthy men, ranging in age from 18 to 81 years at baseline, was obtained from the Aerobics Center Longitudinal Study cohort between 1979 and 2002. Study participants were referred by their employer or physician or were self-referred. All men were considered healthy, defined as free of known CVD and cancer at both examinations. Participants were included if they were 18 years of age or older at the baseline examination and had completed at least 2 comprehensive medical examinations with all data required to derive both eCRF equations. The minimum time between examinations was 2 months. Participants were excluded if there was less than 1 year of mortality follow-up from the final examination in attempts to control for underlying disease. All participants provided written informed consent before participation. Ethics approval was obtained from the Cooper Institutional Review Board.

Clinical Examination

A full description of the procedures involved in the 2 clinical examinations has been reported previously.[16] In summary, participants underwent extensive medical examinations including resting electrocardiography, anthropometric measurements, blood pressure measurement, and a blood test following an overnight fast of at least 12 hours. Participants performed a maximal exercise tolerance test on a treadmill at both examinations. Complete details of the testing protocol have been reported elsewhere.[2] A self-administered personal and family medical history was completed at both examinations.

Physical Activity

All participants completed a self-administered PA questionnaire at both examinations. The Jackson PA index was derived using a 5-level scale (0-4), where 0 indicates no regular PA and 4 indicates that the participant jogged or walked more than 20 miles (32 km) per week. Full descriptions of the PA criteria that describe the 5-level scale are published elsewhere.[16] The PA score used for the Nes eCRF equation was derived by converting the Jackson PA score to the equivalent Nes PA score as described by Peterman et al.[17]

Resting Heart Rate

Resting heart rate was measured by a clinician before each mCRF test. The average RHR recorded was 58.9 ($\pm$10.4) beats/min at the first test and 58.0 ($\pm$9.9) beats/min at the second test. However, the protocol for measuring RHR was not consistent across examinations, which led to substantial individual variability in RHR (range of observed change in RHR, -50 beats/min to $+95$ beats/min). Therefore, the average RHR values for age and sex taken from the Canadian Health Measures Survey were used to estimate RHR.[18]

Estimated Cardiorespiratory Fitness

The eCRF was computed by 2 sex-specific nonexercise equations (Table 1). The eCRF values of the Nes equation ($mL \cdot kg^{-1} \cdot min^{-1}$) were converted to units of METs by dividing the values by 3.5 $mL \cdot kg^{-1} \cdot min^{-1}$. These 2 equations were selected on the basis of prior validation studies and the equations' ability to predict mortality by a single measure of eCRF.[9,19] In addition, both eCRF equations were derived using objective measures of CRF; the Nes eCRF equation was derived using mCRF measures obtained by indirect calorimetry. Change in eCRF, expressed as a continuous variable, was calculated as the difference in eCRF (METs) between the 2 examinations.

Mortality Surveillance

Participants were observed from the date of the second examination until death or December 31, 2003. Mortality data were obtained from the National Death Index. The underlying cause of death was obtained from

TABLE 1. Male-Specific eCRF Equations	
Nes et al[13] Converted to METs	$eCRF_{men} = [92.05 - (0.327*age) - (0.933*BMI) - (0.167*RHR) + (0.257*PAI)]/3.5$
Jackson et al[19] METs	$eCRF_{men} = 20.8013 + (0.1610*age) - (0.0022*age^2) - (0.2240*BMI) - (0.0334*WC) - (0.0375*RHR) + (0.2163*1$ if PAI=1$) + (0.3447*1$ if PAI=2$) + (0.7877*1$ if PAI=3$) + (1.1961*1$ if PAI=4$) - (0.4306*current smoker)$

BMI, body mass index; eCRF, estimated cardiorespiratory fitness; METs, metabolic equivalents; PAI, physical activity index; RHR, resting heart rate; WC, waist circumference.

official death certificates and CVD mortality was noted when applicable.

Statistical Analyses

SPSS version 27 (IBM) was used for all statistical analyses. Descriptive statistics were performed to summarize participants' characteristics at baseline and follow-up examinations. Paired *t*-tests were performed to assess differences in participants' characteristics between examinations. Statistical assumptions were addressed to ensure that the data set met the criteria required to perform a Cox proportional hazards analysis. These included ensuring that survival times between participants were independent and that the hazard ratio was constant over time on examination of the log minus log survival time graph. Cox proportional hazards models were performed to determine hazard ratios and 95% CIs associated with the change in eCRF and mCRF as they relate to all-cause and CVD mortality. Changes in eCRF and mCRF were computed as the difference in eCRF or mCRF (in METs) between the baseline and follow-up examination values, expressed as a continuous variable. The follow-up period was calculated as the time from the second examination until death or censor date. The Cox proportional hazards models were fit to the data unadjusted (model 1), adjusted for baseline eCRF or mCRF and age (model 2), then with further adjustment for baseline examination year and time between measures (model 3), and finally adjusted for baseline and change in traditional CVD risk factors (resting systolic blood pressure, total cholesterol concentration, fasting blood glucose level, triglycerides; model 4). Additional analyses were performed with change in eCRF as a categorical variable with data split into tertiles (Supplemental Table, available online at http://www.mcpiqojournal.org). The reference group categorized as tertile 1 contained the lowest change in eCRF scores (ie, showing a decrease in eCRF). Cox regression analyses were also performed to examine the association between baseline eCRF or mCRF and mortality. Linear regression was performed to examine the associations between eCRF and mCRF. Significance was set at $P<.05$ for all statistics.

RESULTS

Baseline Characteristics

A total of 10,445 men were included in the analyses (Table 2). Participants were observed for 11.6 ± 6.4 years from the second examination until the censor date or death. During this time, 601 men died from all causes, with 192 of those deaths attributable to CVD.

Associations Between eCRF and mCRF

A moderate relationship was observed between eCRF and mCRF at baseline ($r=0.66$ [$P<.001$] for Jackson eCRF; $r=0.68$ [$P<.001$] for Nes eCRF); a stronger relationship was observed between the 2 eCRF equations ($r=0.90$; $P<.001$). Although both eCRF and mCRF decreased between measures (Table 2), only moderate associations were observed between corresponding changes in eCRF and mCRF ($r=0.63$ [$P<.001$] for change in Jackson eCRF; $r=0.55$ [$P<.001$] for change in Nes eCRF). A significant association was observed for change in eCRF between the 2 equations ($r=0.87$; $P<.001$).

TABLE 2. Characteristics of the Participants[a,b]		
	Baseline	Follow-up
Age, years	44.6 (9.3)	50.3 (10.2)[c]
BMI, kg/m^2	26.0 (3.3)	26.3 (3.4)[c]
WC, cm	92.6 (9.7)	93.5 (9.8)[c]
RHR, beats/min	66.8 (0.8)	66.4 (1.2)[c]
Glucose, mmol/L	5.5 (0.8)	5.6 (0.9)[c]
Cholesterol, mmol/L	5.5 (1.1)	5.3 (1.3)[c]
Triglycerides, mmol/L	1.5 (1.1)	1.5 (1.2)
Systolic blood pressure, mm Hg	119.8 (12.9)	121.9 (14.0)[c]
Diastolic blood pressure, mm Hg	80.3 (9.3)	81.1 (9.3)[c]
Physical activity		
Jackson PA (code, 0-4)	1.7 (1.2)	1.7 (1.2)[c]
Nes PA (code, 0-45)	7.9 (10.1)	7.9 (10.3)
Cardiorespiratory fitness, METs		
eCRF, Jackson	12.3 (1.2)	11.9 (1.4)[c]
eCRF, Nes	12.6 (1.5)	12.0 (1.6)[c]
mCRF	12.2 (2.3)	12.1 (2.4)[c]
Events		
All-cause mortality (No.)		601
CVD mortality (No.)		192
Follow-up		
Time between examinations, years		5.7 (4.9)
Follow-up, years		11.6 (6.4)
Follow-up, person-years		120,768.7

[a]BMI, body mass index; CVD, cardiovascular disease; eCRF, estimated cardiorespiratory fitness; mCRF, measured cardiorespiratory fitness; METs, metabolic equivalents; PA, physical activity; RHR, resting heart rate; WC, waist circumference.
[b]Values are means (standard deviation); N=10,445.
[c]Significantly different from the baseline measure ($P<.05$).

Baseline eCRF and Mortality Risk

For both eCRF equations, a higher eCRF at baseline was associated with significant reductions in mortality risk from all causes and CVD. Specifically, every 1 MET higher baseline eCRF was associated with a 25% or 29% reduction in all-cause mortality risk after multivariable adjustment using the Jackson or Nes equation, respectively ($P<.001$; Table 3). Statistically significant associations were also observed between baseline eCRF and CVD mortality as every 1 MET higher eCRF was associated with a 30% or 33% reduction in CVD mortality risk using the Jackson or Nes equation, respectively ($P<.001$; Table 3).

Change in eCRF and Mortality Risk

When considered continuously, change in eCRF using the Jackson equation remained significantly associated with both all-cause mortality ($P<.001$) and CVD mortality ($P=.02$) after multivariable adjustment (Table 4). Every 1 MET increase in eCRF was associated with a 21% or 22% reduction in mortality risk from all causes or CVD, respectively. When considered categorically, those with the largest improvements in eCRF (tertile 3) had the lowest risk of mortality (Table 5). These associations remained significant after multivariable adjustment ($P=.001$ for all-cause mortality; $P=.005$ for CVD mortality).

Change in eCRF using the Nes equation was associated with all-cause mortality ($P<.001$) and CVD mortality ($P=.01$) after control for baseline eCRF but did not remain significant after multivariable adjustment when it was examined as a continuous variable ($P=.69$ for all-cause mortality; $P=.85$ for CVD mortality; Table 4) or as a categorical variable ($P=.81$ for all-cause mortality; $P=.90$ for CVD mortality; Table 5).

Change in Variables Within the eCRF Equations

Examination of the change in eCRF equation variables revealed age to be the only variable that changed substantially (increase of 5.7 ± 4.9 years; $P<.001$). Extremely small changes were observed for BMI ($+0.4\pm1.8$ kg/m^2), waist circumference ($+0.9\pm6.6$ cm), RHR (-0.4 ± 1.0 beats/min), and smoking status (-0.04 ± 0.3). Over time, 6192 participants changed PA levels (increased or decreased) with use of the Jackson PA index compared with 5127 participants when the Nes PA index was used.

DISCUSSION

We sought to determine whether changes in eCRF were associated with all-cause and CVD mortality in previously healthy adults. To our knowledge, this is the first study that linked change in nonexercise eCRF to mortality. Our primary finding suggests that the association between change in eCRF and mortality is equation dependent. Whereas the change in eCRF by the Jackson equation

TABLE 3. Hazard Ratios for All-Cause and CVD Mortality per 1 MET Higher Baseline CRF

	Jackson eCRF, HR (95% CI)		Nes eCRF, HR (95% CI)		mCRF, HR (95% CI)	
	All-cause mortality	CVD mortality	All-cause mortality	CVD mortality	All-cause mortality	CVD mortality
Model 1	0.75 (0.71-0.80)[b]	0.68 (0.62-0.75)[b]	0.71 (0.68-0.75)[b]	0.65 (0.59-0.71)[b]	0.83 (0.80-0.86)[b]	0.78 (0.73-0.84)[b]
Model 2	0.72 (0.68-0.77)[b]	0.65 (0.59-0.72)[b]	0.69 (0.66-0.73)[b]	0.63 (0.57-0.69)[b]	0.95 (0.92-0.99)[b]	0.92 (0.86-0.99)[b]
Model 3	0.75 (0.70-0.80)[b]	0.70 (0.63-0.78)[b]	0.71 (0.67-0.76)[b]	0.67 (0.61-0.75)[b]	0.96 (0.92-1.00)[b]	0.94 (0.87-1.01)

[a]CRF, cardiorespiratory fitness; CVD, cardiovascular disease; eCRF, estimated cardiorespiratory fitness; HR, hazard ratio; mCRF, measured cardiorespiratory fitness; MET, metabolic equivalent.
[b]Statistically significant (*P*<.05).
Model 1 unadjusted.
Model 2 adjusted for examination year (and age for mCRF).
Model 3 adjusted for model 2 plus baseline CVD risk factors (resting systolic blood pressure, cholesterol concentration, glucose level, triglycerides).

was independently related to mortality, change in eCRF determined by the Nes equation was not associated with either CVD or all-cause mortality.

The observation that both eCRF equations in this study identified adults at risk of all-cause and CVD mortality confirms a growing body of evidence and reinforces the usefulness of eCRF to stratify health risk beyond that identified by commonly obtained risk factors.[9,14,15] However, the established associations between eCRF and mortality rely on observational studies that use a single baseline assessment with subsequent follow-up and thus are vulnerable to confounders including genetics, undetected preexisting disease, and unknown changes in PA or CRF. Some of these limitations are mitigated by evaluating the associations between mortality and change in eCRF over time.

The observation that every 1 MET increase in eCRF using the Jackson equation was associated with an approximately 21% reduction in mortality risk is promising and provides additional evidence underscoring the value of eCRF across health care settings. Our optimism is tempered, however, as the Jackson equation was originally derived using the Aerobics Center Longitudinal Study cohort. Whether change in eCRF by the Jackson equation is associated with CVD or all-cause mortality in an independent cohort remains to be determined.

Our findings using the Jackson equation counter those observed using the Nes equation. A comparison of the 2 equations reveals differences that may help explain the discrepant findings. Whereas the PA variable within the Jackson equation is sensitive to

TABLE 4. Hazard Ratios for All-Cause and CVD Mortality per 1 MET Improvement in CRF[a]

	Jackson eCRF, HR (95% CI)		Nes eCRF, HR (95% CI)		mCRF, HR (95% CI)	
	All-cause mortality	CVD mortality	All-cause mortality	CVD mortality	All-cause mortality	CVD mortality
Model 1	0.72 (0.66-0.78)[b]	0.71 (0.61-0.83)[b]	0.96 (0.89-1.04)	1.01 (0.88-1.17)	0.80 (0.76-0.84)[b]	0.82 (0.74-0.90)[b]
Model 2	0.65 (0.60-0.71)[b]	0.63 (0.54-0.72)[b]	0.81 (0.74-0.88)[b]	0.81 (0.70-0.95)[b]	0.80 (0.75-0.85)[b]	0.82 (0.74-0.92)[b]
Model 3	0.74 (0.66-0.82)[b]	0.71 (0.59-0.86)[b]	0.95 (0.86-1.04)	0.97 (0.82-1.15)	0.86 (0.81-0.92)[b]	0.90 (0.80-1.01)
Model 4	0.79 (0.70-0.88)[b]	0.78 (0.64-0.96)[b]	0.98 (0.89-1.08)	1.02 (0.86-1.21)	0.87 (0.82-0.93)[b]	0.91 (0.81-1.02)

[a]CRF, cardiorespiratory fitness; CVD, cardiovascular disease; eCRF, estimated cardiorespiratory fitness; HR, hazard ratio; mCRF, measured cardiorespiratory fitness; MET, metabolic equivalent.
[b]Statistically significant (*P*<.05).
Model 1 unadjusted.
Model 2 adjusted for baseline eCRF (and baseline age for mCRF).
Model 3 adjusted for model 2 plus examination year and time between measures.
Model 4 adjusted for model 3 plus baseline CVD risk factors (resting systolic blood pressure, cholesterol concentration, glucose level, triglycerides) and change in CVD risk factors.

TABLE 5. Hazard Ratios for All-Cause and CVD Mortality by Change in eCRF by Tertile

	All-cause mortality, HR (95% CI)				CVD mortality, HR (95% CI)			
	Model 1	Model 2	Model 3	Model 4	Model 1	Model 2	Model 3	Model 4
Jackson eCRF change								
Tertile 1	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
2	0.59 (0.49-0.72)[b]	0.57 (0.46-0.69)[b]	0.74 (0.59-0.92)[b]	0.79 (0.63-0.99)[b]	0.56 (0.40-0.79)[b]	0.53 (0.37-0.75)[b]	0.68 (0.46-0.99)[b]	0.77 (0.52-1.14)
3	0.54 (0.44-0.66)[b]	0.44 (0.36-0.54)[b]	0.61 (0.48-0.77)[b]	0.68 (0.53-0.86)[b]	0.45 (0.31-0.64)[b]	0.34 (0.24-0.49)[b]	0.46 (0.30-0.70)[b]	0.53 (0.35-0.82)[b]
Nes eCRF change								
Tertile 1	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
2	0.91 (0.73-1.12)	0.70 (0.57-0.88)[b]	1.04 (0.81-1.33)	1.10 (0.86-1.40)	0.96 (0.65-1.42)	0.71 (0.48-1.05)	1.08 (0.69-1.67)	1.15 (0.74-1.79)
3	0.89 (0.72-1.10)	0.60 (0.48-0.75)[b]	0.98 (0.76-1.27)	1.03 (0.80-1.34)	0.95 (0.65-1.39)	0.58 (0.39-0.86)[b]	0.99 (0.62-1.57)	1.03 (0.64-1.66)

[a]CVD, cardiovascular disease; eCRF, estimated cardiorespiratory fitness; HR, hazard ratio.

[b]Statistically significant ($P<.05$).

Tertile 1 (n=3482), tertile 2 (n=3481), tertile 3 (n=3482).

Model 1 unadjusted.

Model 2 adjusted for baseline eCRF.

Model 3 adjusted for model 2 plus examination year and time between measures.

Model 4 adjusted for model 3 plus baseline CVD risk factors (resting systolic blood pressure, cholesterol concentration, glucose level, triglycerides) and change in CVD risk factors.

changes in frequency and amount of PA, change in PA within the Nes equation is largely dependent on PA intensity. Within the Jackson equation, inclusion of age reflects the nonlinear relationship between age and CRF, and smoking status is included. Whether change in smoking behavior captured variance in mortality not explained by change in eCRF is unclear. However, given that smoking is a strong determinant of mortality,[20,21] speculation that smoking behavior may partially explain the ability of the Jackson eCRF equation to predict mortality seems reasonable.

Development of nonexercise equations to estimate CRF represents a feasible option with the potential to increase the adoption of CRF as a routine measure in health care settings. In most health care settings, it is likely that eCRF will first be used to interpret the benefits of increasing PA. Accordingly, regardless of the eCRF equation chosen, its use for the purpose of evaluating the utility of PA to improve CRF has limitations. Common to eCRF equations are the well-recognized determinants of CRF: biological sex, age, body weight (BMI), RHR, and PA. In the short term, some of these variables will not change (sex and age) and others (weight and RHR) will likely change very little. The immediate increases in eCRF that result on the first adoption of PA will clearly precede true improvements in CRF. Health care practitioners should be aware of these limitations but embrace the opportunity to counsel their patients on the benefits of PA as the primary modifiable determinant of CRF and the associated benefits of increasing PA across a wide range of health outcomes.

Strengths of this report include the study of a large sample with a wide range in age and a comprehensive CVD risk factor profile and extensive follow-up for mortality. Limitations include a small number of CVD deaths, that PA was self-reported, and that the cohort consists primarily of well-educated white men from the middle to upper socioeconomic strata. Only 2 eCRF equations were considered, and thus the utility of other eCRF equations to predict change in CVD and all-cause mortality remains to be determined.

CONCLUSION
The primary finding of this study provides partial support for the notion that changes in eCRF predict CVD and all-cause mortality. That estimates of CRF are associated with mortality with use of the Jackson equation requires validation in an independent sample.

SUPPLEMENTAL ONLINE MATERIAL
Supplemental material can be found online at http://www.mcpiqojournal.org. Supplemental material attached to journal articles has not been edited, and the authors take responsibility for the accuracy of all data.

Abbreviations and Acronyms: **BMI,** body mass index; **CRF,** cardiorespiratory fitness; **CVD,** cardiovascular disease; **eCRF,** estimated cardiorespiratory fitness; **mCRF,** measured cardiorespiratory fitness; **MET,** metabolic equivalent; **PA,** physical activity; **RHR,** resting heart rate

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REFERENCES
1. Ross NR, Blair SS, Arena AR, 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(24):e653-e699.
2. Blair SN, Kohl HW, Paffenbarger RS, Clark DG, Cooper KH, Gibbons LW. Physical fitness and all-cause mortality: a prospective study of healthy men and women. *JAMA.* 1989;262(17): 2395-2401.
3. Kodama S. Cardiorespiratory fitness as a quantitative predictor of all-cause mortality and cardiovascular events in healthy men and women. *JAMA.* 2009;301(19):2024.
4. Gupta S, Rohatgi A, Ayers CR, et al. Cardiorespiratory fitness and classification of risk of cardiovascular disease mortality. *Circulation.* 2011;123(13):1377-1383.
5. Myers J, Nead KT, Chang P, Abella J, Kokkinos P, Leeper NJ. Improved reclassification of mortality risk by assessment of physical activity in patients referred for exercise testing. *Am J Med.* 2015;128(4):396-402.
6. Blair SN, Kampert JB, Kohl HW 3rd, et al. Influences of cardiorespiratory fitness and other precursors on cardiovascular disease and all-cause mortality in men and women. *JAMA.* 1996; 276(3):205-210.

7. Cooney JK, Moore JP, Ahmad YA, et al. A simple step test to estimate cardiorespiratory fitness levels of rheumatoid arthritis patients in a clinical setting. *Int J Rheumatol*. 2013;2013:174541.

8. Poole DC, Jones AM. Measurement of the maximum oxygen uptake $\dot{V}o_{2max}$:$\dot{V}o_{2peak}$ is no longer acceptable. *J Appl Physiol*. 2017;122(4):997-1002.

9. Stamatakis E, Hamer M, O'Donovan G, Batty GD, Kivimaki M. A non-exercise testing method for estimating cardiorespiratory fitness: associations with all-cause and cardiovascular mortality in a pooled analysis of eight population-based cohorts. *Eur Heart J*. 2013;34(10):750-758.

10. Heil DP, Freedson PS, Ahlquist LE, Price J, Rippe JM. Nonexercise regression models to estimate peak oxygen consumption. *Med Sci Sports Exerc*. 1995;27(4):599-606.

11. 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(6):863-870.

12. Jurca R, Jackson AS, LaMonte MJ, et al. Assessing cardiorespiratory fitness without performing exercise testing. *Am J Prev Med*. 2005;29(3):185-193.

13. Nes BM, Janszky I, Vatten LJ, Nilsen T, Aspenes ST, Wisløff U. Estimating $\dot{V}o_{2peak}$ from a nonexercise prediction model: the HUNT Study, Norway. *Med Sci Sports Exerc*. 2011;43(11):2024-2030.

14. Artero EG, Jackson AS, Sui X, et al. Longitudinal algorithms to estimate cardiorespiratory fitness: associations with nonfatal cardiovascular disease and disease-specific mortality. *J Am Coll Cardiol*. 2014;63(21):2289-2296.

15. Nes BM, Vatten LJ, Nauman J, Janszky I, Wisløff U. A simple nonexercise model of cardiorespiratory fitness predicts long-term mortality [erratum appears in *Med Sci Sports Exerc*. 2020;52(6):1440]. *Med Sci Sports Exerc*. 2014;46(6):1159-1165.

16. Blair SN, Goodyear NN, Gibbons LW, Cooper KH. Physical fitness and incidence of hypertension in healthy normotensive men and women. *JAMA*. 1984;252(4):487-490.

17. Peterman JE, Whaley MH, Harber MP, et al. Comparison of non-exercise cardiorespiratory fitness prediction equations in apparently healthy adults. *Eur J Prev Cardiol*. 2021;28(2):142-148.

18. Statistics Canada. Average resting heart rate, by age and sex, household population, Canada, 2009 to 2011. 2015. https://www150.statcan.gc.ca/n1/pub/82-626-x/2013001/t004-eng.htm. Accessed May 21, 2021.

19. Jackson AS, Sui X, O'Connor DP, et al. Longitudinal cardiorespiratory fitness algorithms for clinical settings. *Am J Prev Med*. 2012;43(5):512-519.

20. Thun MJ, Day-Lally CA, Calle EE, Flanders WD, Heath CW Jr. Excess mortality among cigarette smokers: changes in a 20-year interval. *Am J Public Health*. 1995;85(9):1223-1230.

21. National Center for Chronic Disease Prevention and Health Promotion (US) Office on Smoking and Health. *The Health Consequences of Smoking—50 Years of Progress: A Report of the Surgeon General*. Atlanta, GA: Centers for Disease Control and Prevention; 2014.