HRR and $\dot{V}O_2R$ Fractions Are Not Equivalent: Is It Time to Rethink Aerobic Exercise Prescription Methods?

CARLO FERRI MARINI[1], DAVIDE SISTI[2], ARTHUR S. LEON[3], JAMES S. SKINNER[4], MARK A. SARZYNSKI[5], CLAUDE BOUCHARD[6], MARCO B. L. ROCCHI[2], GIOVANNI PICCOLI[1], VILBERTO STOCCHI[1], ARIO FEDERICI[1], and FRANCESCO LUCERTINI[1]

[1]Department of Biomolecular Sciences, Division of Exercise and Health Sciences, University of Urbino Carlo Bo, Urbino, ITALY; [2]Department of Biomolecular Sciences, Unit of Biostatistics, University of Urbino Carlo Bo, Urbino, ITALY; [3]Department of Kinesiology, University of Minnesota, Minneapolis, MN; [4]Department of Kinesiology, Indiana University, Bloomington, IN; [5]Department of Exercise Science, Arnold School of Public Health, University of South Carolina, Columbia, SC; and [6]Human Genomics Laboratory, Pennington Biomedical Research Center, Louisiana State University System, Baton Rouge, LA

ABSTRACT

FERRI MARINI, C., D. SISTI, A. S. LEON, J. S. SKINNER, M. A. SARZYNSKI, C. BOUCHARD, M. B. L. ROCCHI, G. PICCOLI, V. STOCCHI, A. FEDERICI, and F. LUCERTINI. HRR and $\dot{V}O_2R$ Fractions Are Not Equivalent: Is It Time to Rethink Aerobic Exercise Prescription Methods? *Med. Sci. Sports Exerc.*, Vol. 53, No. 1, pp. 174–182, 2021. **Introduction:** According to current guidelines, the intensity of health-enhancing aerobic exercise should be prescribed using a percentage of heart rate reserve (%HRR), which is considered to be more closely associated (showing a 1:1 relation) with the percentage of oxygen uptake reserve (%$\dot{V}O_2R$) rather than with the percentage of maximal oxygen uptake (%$\dot{V}O_{2max}$) during incremental exercise. However, the associations between %HRR and %$\dot{V}O_2R$ and between %HRR and %$\dot{V}O_{2max}$ are under debate; hence, their actual relationships were investigated in this study. **Methods:** Data from each stage of a maximal incremental exercise test performed by 737 healthy and physically inactive participants of the HERITAGE Family Study were screened and filtered then used to calculate the individual linear regressions between %HRR and either %$\dot{V}O_2R$ or %$\dot{V}O_{2max}$. For each relationship, the mean slope and intercept of the individual linear regression were compared with 1 and 0 (i.e., the identity line), respectively, using one-sample *t*-tests. The individual root mean square errors of the actual versus the 1:1 predicted %HRR were calculated for both relationships and compared using a paired-sample *t*-test. **Results:** The mean slopes (%HRR–%$\dot{V}O_2R$, 0.972 ± 0.189; %HRR–%$\dot{V}O_{2max}$, 1.096 ± 0.216) and intercepts (%HRR–%$\dot{V}O_2R$, 8.855 ± 16.022; %HRR–%$\dot{V}O_{2max}$, −3.616 ± 18.993) of both relationships were significantly different from 1 and 0, respectively, with high interindividual variability. The average root mean square errors were high and revealed that the %HRR–%$\dot{V}O_{2max}$ relationship was more similar to the identity line ($P < 0.001$) than the %HRR–%$\dot{V}O_2R$ relationship (7.78% ± 4.49% vs 9.25% ± 5.54%). **Conclusions:** Because both relationships are different from the identity line and using a single equation may not be appropriate to predict exercise intensity at the individual level, a rethinking of the relationships between the intensity variables may be necessary to ensure that the most suitable health-enhancing aerobic exercise intensity is prescribed. **Key Words:** HEART RATE, OXYGEN UPTAKE, RESERVE, RELATIONSHIP, EXERCISE INTENSITY

Cardiorespiratory fitness is positively associated with health status, and structured and individually tailored aerobic exercise training programs are recommended to improve cardiorespiratory fitness (1–5). Structuring an aerobic exercise program involves the manipulation of several parameters (6) related to both the overall training regimen (e.g., weekly exercise frequency, volume, progression, etc.) and the single exercise session (e.g., duration, intensity, etc.). The aerobic exercise intensity continuum has long been divided into moderate, heavy, and severe domains, based on clearly identifiable physiological demarcation points (7). However, most of the world's preeminent organizations have adopted a different approach, also used in the present investigation, which uses five intensity zones (e.g., see [1]). Although the domains and zones do not match perfectly, mainly because of the highly individualized nature of responses to exercise (8), heavy and severe domains correspond approximately to the intensity zones vigorous and near-maximal to maximal, respectively, whereas the moderate domain comprises the intensity zones very light to light, light, and moderate.

Intensity is a fundamental consideration when tailoring an aerobic exercise prescription: light intensities are considered safe but may be insufficient to elicit the biological responses necessary to improve cardiorespiratory fitness

---

Address for correspondence: Francesco Lucertini, Ph.D., University of Urbino Carlo Bo, Via I Maggetti 26/2, 61029 Urbino (PU), Italy, E-mail: francesco.lucertini@uniurb.it.

C. F. M. and D. S. contributed equally to this work.
Submitted for publication November 2019.
Accepted for publication June 2020.
Supplemental digital content is available for this article. Direct URL citations appear in the printed text and are provided in the HTML and PDF versions of this article on the journal's Web site (www.acsm-msse.org).

0195-9131/20/5301-0174/0
MEDICINE & SCIENCE IN SPORTS & EXERCISE®

DOI: 10.1249/MSS.0000000000002434

(9), whereas vigorous intensity, although effective in improving cardiorespiratory fitness, may increase the health risks associated with exercise when individuals are not accustomed to it (6,9).

Aerobic exercise intensity is usually prescribed and monitored with parameters calculated using either oxygen uptake ($\dot{V}O_2$) or heart rate (HR), both of which increase with increasing aerobic exercise intensity. Indeed, studies investigating the association between $\dot{V}O_2$ and HR during incremental exercise have generally found a linear relationship when values were expressed as percentages of maximal $\dot{V}O_2$ ($\dot{V}O_{2max}$) and maximal HR (HR_{max}), respectively (10–12). However, the relationship between $\%\dot{V}O_{2max}$ and $\%HR_{max}$ may be affected by interindividual differences in the maximal (as suggested by Swain and Leutholtz [13]) and/or resting values. On the contrary, using the "reserve" values, i.e., the difference between maximal and resting values, allows the correction for nonzero resting values. The concept of reserve, which was introduced by Karvonen et al. for HR (14), was applied to $\dot{V}O_2$ by Swain and Leutholtz (13) in light of previous findings of Davis and Convertino (15). These investigations, focusing on young adults, showed that: (a) the percentages of the reserve values of $\dot{V}O_2$ ($\%\dot{V}O_2R$) and HR (%HRR) did not differ significantly at four different exercise intensities (15) and (b) $\%\dot{V}O_2R$ and %HRR were strongly correlated and their regression was not distinguishable from the line of identity (13), i.e., slope = 1 and intercept = 0. Subsequent studies confirmed that $\%\dot{V}O_2R$ and %HRR regressions did not significantly differ from the line of identity in healthy subjects (16,17), in myocardial infarction (18), obese (19), and diabetic (20) patients, or in elite amateur and professional cyclists (21).

However, it has been known for years (22) that the association between $\dot{V}O_2$ and HR, even under controlled conditions, may be affected by several factors such as body temperature, hydration, emotional state, physical activity level, sex, and day-to-day variability in HR response to exercise. Indeed, the actual association between $\%\dot{V}O_2R$ and %HRR has been questioned in several reports. Swain et al. (23) found that regression parameters differed significantly from those of the identity line in healthy adults, and subsequently, the same discrepancies have been found in children and adolescents (24), in overweight and obese pregnant women (25), and in obese (26), CHF (17,18), CAD (18), and heart transplant recipient (27) patients. Furthermore, Cunha et al. (28) found that the $\%\dot{V}O_2R$–%HRR relationship was significantly affected by the exercise testing protocol used. Importantly, they also found that %HRR was more closely associated with $\%\dot{V}O_{2max}$ than it was with $\%\dot{V}O_2R$ (28), confirming the results of a previous study (24). According to data from a review on this topic (29), the HRR percentage point errors yielded by using the identity line to describe the relationship between %HRR and $\dot{V}O_2R$ of the above-mentioned studies ranged from −8% to +10% at 50% HRR and from −6% to +14% at 70% HRR. This means that, even close to the midpoints of moderate (40%–59% HRR) and vigorous (60%–89% HRR) ranges of the two recommended health-enhancing aerobic exercise intensity categories, the actual exercise intensity may be very close to, or even fall within, other intensity categories. This could lead to major errors in exercise intensity prescription and monitoring because HR is mostly used for this purpose.

Nonetheless, since 1998 (30), the regression between $\%\dot{V}O_2R$ and %HRR has been widely accepted as nonsignificantly different from the line of identity, as reported in the latest position stands of the major internationally recognized leading bodies in the field of physical activity and exercise (e.g., see [9]). Therefore, the main aim of the present study was to assess the actual relationships between %HRR and $\%\dot{V}O_2R$ and between %HRR and $\%\dot{V}O_{2max}$ using the large data set of the HERITAGE Family Study (31).

METHODS

Sample

The sample of the present investigation was composed of 737 members of Caucasian and African American families participating in the pretraining assessments of the HERITAGE Family Study (HERITAGE) (for details regarding ethics committee approval, inclusion and exclusion criteria, and study design, see Bouchard et al. [31]).

All subjects enrolled in the HERITAGE study (ranging in age from 17 to 65, in $\dot{V}O_{2max}$ from 15.2 to 54.9 $mL \cdot min^{-1} \cdot kg^{-1}$, and in HR_{max} from 136 to 214 bpm) were healthy (i.e., with no significant medical conditions or diseases), not physically active (i.e., they had not engaged in regular physical activity in the previous 6 months), and were not taking any medication that could affect resting and/or exercise HR.

HERITAGE Assessments

The design of the HERITAGE study included several exercise and nonexercise tests performed before and after an aerobic exercise training intervention. In the present study, only baseline (body weight and preexercise HR) and exercise testing ($\dot{V}O_{2max}$ tests) data of selected pretraining assessments were used (see below).

Body weight and preexercise heart rate. Body mass was measured to the nearest 0.1 kg using a balance beam scale. Resting HR (HR_{rest}) was measured immediately before the exercise test at the end of a 5-min rest period, with the subject sitting quietly in a chair.

Maximal oxygen uptake. Participants' $\dot{V}O_{2max}$ was defined based on the results of two cardiorespiratory fitness tests. First, a continuous, step-incremental exercise test to exhaustion (T1) was performed on a cycle ergometer (model 800S; Sensor Medics, Yorba Linda, CA) connected to a mixing-chamber metabolic cart (model 2900, Sensor Medics). In the first 3-min stage, participants pedaled at 50 W, then the resistance of the ergometer was increased by 25 W every 2 min until volitional exhaustion (in older, smaller, or less fit subjects, starting the test with a lower power output (PO) and/or making smaller increases every 2 min was permitted). At least 48 h later, a submaximal, steady-state exercise test, followed by a progressive test to maximum (T2), was performed. After the first phase of

APPLIED SCIENCES

the test (which is not relevant to the present investigation and involved having the subjects exercise at a steady-state intensity of about 60% of the $\dot{V}O_{2max}$ measured in T1), participants pedaled for 3 min at the PO that was intended to correspond approximately to 80% of the $\dot{V}O_{2max}$ measured in T1. This PO was calculated using a linear interpolation of the $\dot{V}O_2$ versus PO data recorded in T1. Thereafter, a 2-min stage at the highest PO attained in T1 was performed, and the resistance was then increased, if necessary, by the same increment used in T1, every 2 min until volitional exhaustion. Because the cycle ergometer was able to keep the PO constant regardless of the pedaling frequency, each participant was allowed to choose his/her own "comfortable" cadence (usually around 60 rpm).

In both tests, $\dot{V}O_2$ (along with other gas exchange variables that were not used in the present investigation) was determined every 20 s and retained for subsequent analysis as the average of the last three 20-s values of each stage, whereas HR was measured continuously by means of ECG (to confirm HR, ECG rhythm strips were taken within the last 15 s of each stage and at maximum).

The criteria used for the attainment of $\dot{V}O_{2max}$ were as follows: (a) a plateau in $\dot{V}O_2$ (i.e., a change <100 $mL \cdot min^{-1}$ in the last three consecutive 20-s intervals), (b) an HR within 10 bpm of the age-predicted HR_{max}, and (c) a respiratory exchange ratio >1.1. All participants met at least one of these criteria in one of the two tests (32), but most subjects met two or more (33). Hence, when the $\dot{V}O_2$ peak of only one test met at least one criterion, it was assumed to be the $\dot{V}O_{2max}$. When both T1 and T2 $\dot{V}O_2$ peaks met the criteria and the values were within 5% of each other, their average was calculated and assumed to be the $\dot{V}O_{2max}$; otherwise, the highest value was assumed to be the $\dot{V}O_{2max}$ (32). HR_{max} was assumed to be the highest value attained during either of the two maximal exercise tests.

Study Data Set Implementation

Before performing the calculations necessary to implement the data set used in the present study, the HERITAGE data were screened and filtered.

HERITAGE data set screening and filtering. Participants whose records had missing data in the $\dot{V}O_{2max}$ (and/or body weight), HR_{rest}, or HR_{max} fields were excluded. Subsequently, each stage of the T1 was inspected and deleted if either the $\dot{V}O_2$ or the HR fields were missing. Finally, the data integrity of all the above-mentioned variables was assessed by means of range checks: when implausible physiological data were found, the whole participant record and/or the relevant stage(s) of the T1 were excluded (see Fig. 1 for details).

Data preparation and processing. Each $\dot{V}O_2$ and HR recorded for each stage of the T1 was computed as a percentage of both the reserve and the maximum values using, respectively, the following two formulae: (a) 100 × (recorded value − resting value) / (maximal value − resting value) and (b) 100 × recorded value / maximal value. In the calculation of $\%\dot{V}O_2R$, the resting $\dot{V}O_2$ was assumed to be 3.5 $mL \cdot min^{-1} \cdot kg^{-1}$, as suggested by the current American College of Sports Medicine guidelines (6).

Once calculated, $\%\dot{V}O_2R$, $\%\dot{V}O_{2max}$, and %HRR paired data points were used to perform the individual linear

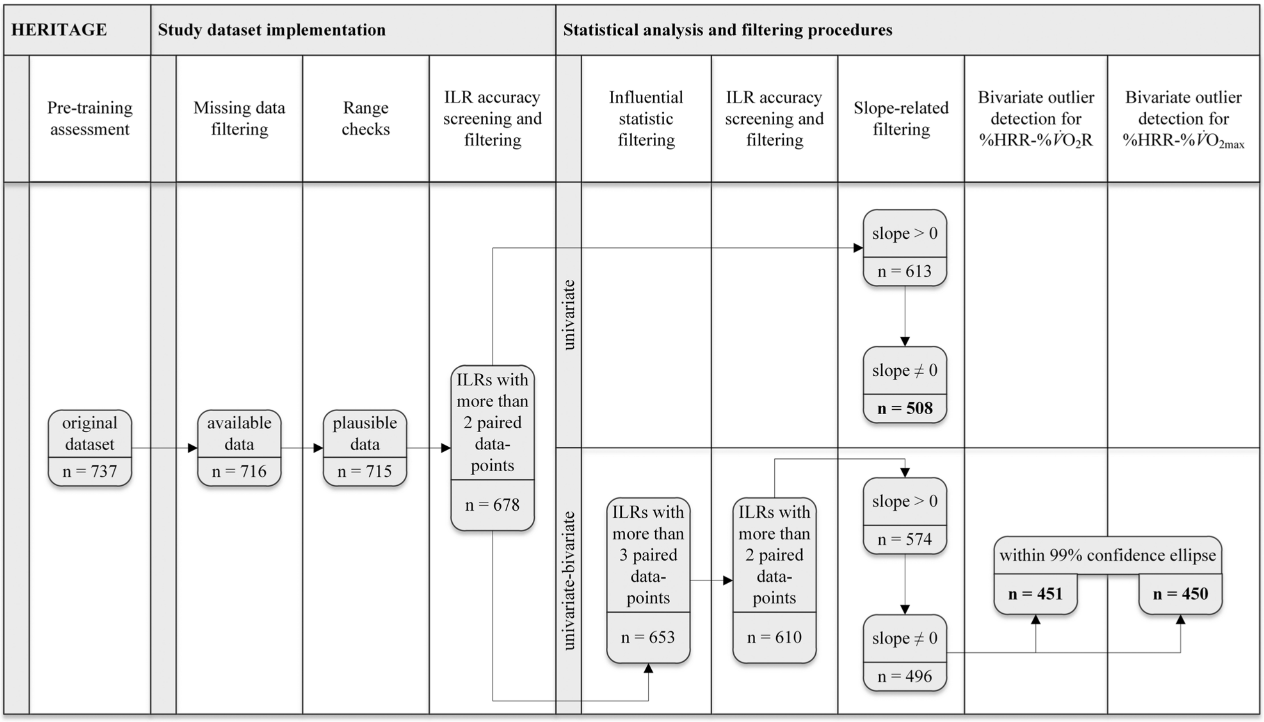

FIGURE 1—Flowchart illustrating the number of subjects (*n*) retained after each step of the screening and filtering procedures applied to the original HERITAGE Family Study data set. ILR, individual linear regression.

TABLE 1. Baseline characteristics of the subjects retained after applying the screening and filtering procedures to the original data set of the HERITAGE family study.

	Univariate Approach for %HRR–%$\dot{V}O_2R$ and %HRR–%$\dot{V}O_{2max}$ Relationships (n = 508)	Univariate–Bivariate Blended Approach for %HRR–%$\dot{V}O_2R$ Relationship (n = 451)	Univariate–Bivariate Blended Approach for %HRR–%$\dot{V}O_{2max}$ Relationship (n = 450)
Sex and race			
Female			
n	281	226	226
AA (%)	36.9	32.9	33.3
C (%)	64.1	68.1	67.7
Male			
n	227	225	224
AA (%)	24.7	22.7	22.8
C (%)	75.3	77.3	77.2
Age (yr)	35.0 ± 13.4	34.9 ± 13.2	34.7 ± 13.1
Height (m)	1.70 ± 0.09	1.71 ± 0.09	1.71 ± 0.09
Weight (kg)	76.6 ± 17.8	77.7 ± 17.2	77.7 ± 17.2
Fat mass (%)	27.4 ± 10.5	27.0 ± 10.3	27.0 ± 10.4
HR_{rest} (bpm)	65.4 ± 8.9	65.0 ± 8.7	65.0 ± 8.7
HR_{max} (bpm)	184.4 ± 13.9	185.0 ± 13.4	185.0 ± 13.4
$\dot{V}O_{2max}$ (mL·min^{-1}·kg^{-1})	31.6 ± 8.6	32.6 ± 8.7	32.6 ± 8.6

Values are expressed as mean ± SD, except for sex and race parameters.

%$\dot{V}O_2R$, percentage of oxygen uptake reserve; $\dot{V}O_{2max}$, maximal oxygen uptake; n, number of subjects; AA, African American; C, Caucasian; HR_{rest}, resting heart rate; %HRR, percentage of heart rate reserve; HR_{max}, maximal heart rate.

regressions (ILR) for the %HRR–%$\dot{V}O_2R$ and the %HRR–%$\dot{V}O_{2max}$ relationships. As suggested by Swain et al. (12,13), a regression was performed for each participant, and the %HRR was set as the dependent variable. Data from ILR resulting from fewer than three paired data points were excluded because they were assumed to be potentially not accurate in representing the true underlying physiological relationship.

Statistical Analysis

The analyses were performed using Excel (Microsoft Office, version 2016), SPSS Statistics (IBM, version 20), and R (R Core Team, version 3.2.3; "Robust" package, version 0.4/16) software, with an α level of 0.05.

The study data set was filtered and analyzed twice using a univariate approach and a univariate–bivariate blended approach.

The procedures of the univariate approach were performed according to the methods of analysis routinely used in the literature to facilitate comparability among studies. Such procedures, which have been widely used in previous investigations (13,16–19,21,23–26), were adopted in this study to verify the currently accepted HR–$\dot{V}O_2$ relationships using the large and heterogeneous HERITAGE study data set, whose quality assurance and control have been supported by several reports (34–37). Because the results of the univariate approach did not confirm those on which currently available guidelines are based, the data were also reanalyzed using a univariate–bivariate blended approach with more stringent data filtering procedures (to avoid any potential outlier-related bias) and multivariate analyses, providing additional statistically robust interpretations of the data.

In both approaches, data were adjusted for the familial clusters of the original HERITAGE data set (see the specific paragraph below for details). A flowchart illustrating the number of cases resulting from the analyses is presented in Figure 1. See Table 1 for details of the characteristics of the participants and Table 2 for the results of the analyses.

Univariate Approach

Data filtering. After excluding the linear regressions whose slopes were lower than zero, the slope of each linear regression was compared with zero using a two-tailed regression slope t-test. The regressions whose slopes were not significantly different from zero were excluded.

Statistics. For each relationship, the mean slope and intercept were compared with the line of identity (i.e., to 1 and 0,

TABLE 2. Average values, familial-cluster adjustments, and statistics for the univariate and the univariate–bivariate blended approaches.

	Univariate Approach				Univariate–Bivariate Blended Approach			
	%HRR–%$\dot{V}O_2R$		%HRR–%$\dot{V}O_{2max}$		%HRR–$\dot{V}O_2R$		%HRR–$\dot{V}O_{2max}$	
	Slope	**Intercept**	**Slope**	**Intercept**	**Slope**	**Intercept**	**Slope**	**Intercept**
Mean	0.979	7.578	1.112	−5.706	0.972	8.855	1.096	−3.616
SD	0.214	16.509	0.243	19.547	0.189	16.022	0.216	18.993
CV	0.219	2.179	0.219	3.426	0.195	1.809	0.197	5.252
ES	0.098	0.459	0.461	0.292	0.148	0.553	0.444	0.190
ICC	0.431	0.411	0.476	0.445	0.418	0.501	0.414	0.440
VIF	1.821	1.782	1.906	1.847	1.762	1.914	1.756	1.803
n^{corr}	279.1	285.1	266.6	275.1	255.3	235.1	256.3	249.6
t	1.662	7.750	7.483	4.841	2.377	8.475	7.085	3.008
$P(t)$	0.098[a]	<0.001[b]	<0.001[c]	<0.001[b]	0.018[c]	<0.001[b]	<0.001[c]	0.003[b]

[a] Nonsignificantly different from 1.

[b] Significantly different from 0.

[c] Significantly different from 1.

%$\dot{V}O_2R$, percentage of oxygen uptake reserve; %$\dot{V}O_{2max}$, percentage of maximal oxygen uptake; CV, coefficient of variation; ES, Cohen's d effect size; ICC, intraclass correlation coefficient; VIF, variance inflation factor; %HRR, percentage of heart rate reserve; n^{corr}, corrected number of subjects; $P(t)$, level of statistical significance.

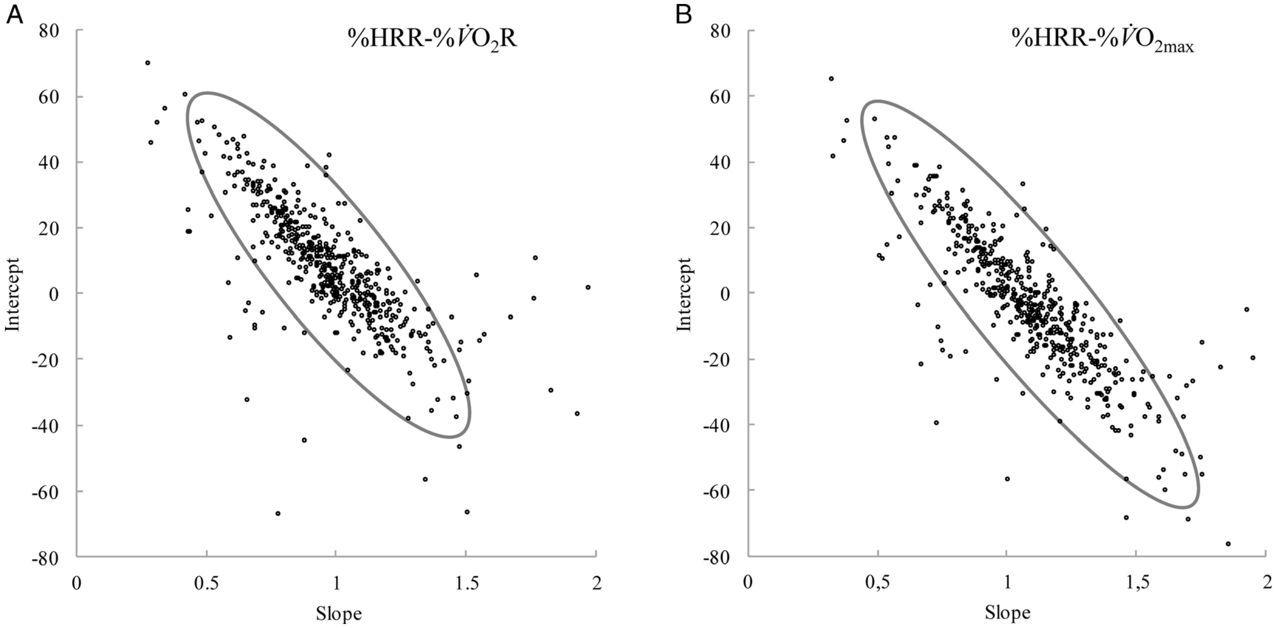

FIGURE 2—Bivariate 99% confidence ellipses calculated for the %HRR–%$\dot{V}O_2$R (A) and the %HRR–%$\dot{V}O_{2max}$ (B) relationships. %$\dot{V}O_2$R, percentage of oxygen uptake reserve; %HRR, percentage of heart rate reserve; %$\dot{V}O_{2max}$, percentage of maximal oxygen uptake.

respectively) using two two-tailed one-sample *t*-tests with degrees of freedom corrected for familial clusters.

Univariate–Bivariate Blended Approach

Data filtering. For each relationship, paired data points were filtered using the DFFITS influential statistics and those having an absolute value of DFFITS larger than the size adjusted cutoff (i.e., double the square root of the ratio between the number of the regression's parameters and the number of paired data points) were excluded, as proposed by Belsley et al. (38). Because the DFFITS procedure requires at least four values to be performed, all the regressions resulting from fewer than four paired data points were also excluded. Subsequently, the ILR was run using the remaining paired data points, and those resulting from fewer than three paired data points and those with a slope lower than zero or not significantly different from zero (two-tailed regression slope *t*-test) were excluded as well (see Fig. 1).

Thereafter, because the dependent variables for both relationships showed significant correlations, slopes and intercepts were filtered using a bivariate procedure by adapting the ISO 13528:2015 rule (39). Briefly, the 99% confidence ellipse was created using the robust mean and the variance–covariance matrix (calculated using the Huber M-estimator), and all paired data lying outside the ellipse were assumed to be bivariate outliers and excluded (Fig. 2).

Statistics. A test for Pearson's *r* significance was performed to evaluate the correlation between intercepts and slopes of both the %HRR–%$\dot{V}O_2$R and the %HRR–%$\dot{V}O_{2max}$ relationships.

The slopes and intercepts were used to build a mean vector $\binom{a}{b}$ that was compared with the expected vector $\binom{0}{1}$ using the bivariate Mahalanobis distance and the Wishart distribution. *Post hoc* univariate analyses were then performed using two two-tailed one-sample *t*-tests to compare the average slopes and intercepts to 1 and 0, respectively. The degrees of freedom used for Mahalanobis distance and *post hoc* tests were those obtained from familial-cluster adjusted calculations.

The equations of the ILR retained were also used to calculate the predicted %HRR over the $\dot{V}O_2$R and $\dot{V}O_{2max}$ continua (0% to 100%) for each subject. The mean %HRR predicted at 30%, 40%, 50%, 60%, 70%, 80%, and 90% of $\dot{V}O_2$R and $\dot{V}O_{2max}$ were then reported in Table 3 along with the relevant descriptive statistics and the 95% confidence intervals (CI) of the Cohen's *d* effect size (ES). To be as conservative as possible, the CI values of the ES were calculated according to Lakens (40), using the lower sample size resulting from the correction for familial clusters (i.e., 235; see the n^{corr} row of Table 2).

TABLE 3. %HRR calculated averaging the predicted %HRR resulting from each ILR, and relevant descriptive statistics, at different %$\dot{V}O_2$R and %$\dot{V}O_{2max}$.

	%HRR	SD	Diff	PE	ES	CI_{INF}		CI_{SUP}
%$\dot{V}O_2$R								
30	38.0	11.3	8.0	−26.7	0.709	0.565	[a]	0.852
40	47.7	9.9	7.7	−19.3	0.777	0.630	[a]	0.922
50	57.4	8.8	7.4	−14.9	0.846	0.697	[a]	0.995
60	67.2	7.9	7.2	−11.9	0.902	0.749	[a]	1.053
70	76.9	7.5	6.9	−9.8	0.919	0.766	[a]	1.072
80	86.6	7.5	6.6	−8.2	0.881	0.730	[a]	1.031
90	96.3	8.0	6.3	−7.0	0.792	0.644	[a]	0.938
Mean	–	–	7.2	−14.0	0.832	–		–
%$\dot{V}O_{2max}$								
30	29.3	13.3	−0.7	2.5	−0.056	−0.183		0.072
40	40.2	11.6	0.2	−0.5	0.018	−0.110		0.146
50	51.2	10.1	1.2	−2.3	0.116	−0.012		0.244
60	62.1	8.8	2.1	−3.5	0.241	0.111	[a]	0.370
70	73.1	8.0	3.1	−4.4	0.387	0.254	[a]	0.519
80	84.0	7.7	4.0	−5.1	0.527	0.390	[a]	0.663
90	95.0	8.0	5.0	−5.6	0.629	0.488	[a]	0.768
Mean	–	–	2.1	−2.7	0.266	–		–

[a] When the zero expected ES does not lie within the CI.

%HRR, percentage of heart rate reserve (average of the predicted); ILR, individual linear regression; %$\dot{V}O_2$R, percentage of oxygen uptake reserve; %$\dot{V}O_{2max}$, percentage of maximal oxygen uptake; Diff, difference between the predicted and the expected percentage; PE, percentage error (of the diff); ES, Cohen's *d* effect size; CI, inferior (INF) and superior (SUP) 95% CI of the ES.

Finally, for each relationship, the average root mean square error (RMSE) was calculated as follows. For each participant, the difference between the actual %HRR and the %$\dot{V}O_2R$ or %$\dot{V}O_{2max}$ of each stage of the T1 was calculated. The sum of the squared differences was then divided by the number of stages completed before calculating the square root of each relationship and their averages. The RMSE values of the two relationships were compared using a two-tailed, paired-sample *t*-test (for the same reason described above, the sample size was set to 235).

Familial-cluster adjustments

To take into account the familial relatedness effect on each regression variable (see Table 2), the following procedure was performed: (a) the eta squared (η^2) for univariate ANOVA with random effect (family membership) was calculated (the dependent variables were either slope or intercept); (b) the η^2 was computed in the equation of Shieh (41) and an intraclass correlation coefficient was obtained; (c) the variance inflation factor was calculated using the intraclass correlation coefficient and the mean size of the grouped data; and (d) the variance inflation factor was used to calculate the corrected sample size (n^{corr}) for clustered data (42).

RESULTS

The results are presented separately for each approach used.

Univariate approach. The intercepts of both %HRR–%$\dot{V}O_2R$ and %HRR–$\dot{V}O_{2max}$ regressions were significantly different from 0, whereas only the slope of the %HRR–%$\dot{V}O_{2max}$ regression was significantly different from 1 (see Table 2). Additional information regarding the goodness of fit of the ILR can be found in the supplemental content (see Table, Supplemental Digital Content 1, Descriptive statistics of the goodness of fit of the ILR retained after applying the screening and filtering procedures to the original dataset of the HERITAGE Family Study, http://links.lww.com/MSS/C42).

Univariate–bivariate blended approach. The *t*-test for the correlation index between the slopes and the intercepts revealed a significant correlation for both the %HRR–%$\dot{V}O_2R$ ($r = -0.72$, $P < 0.0001$) and the %HRR–%$\dot{V}O_{2max}$ ($r = -0.79$, $P < 0.0001$) relationships.

The Mahalanobis distance showed a highly significant difference between the mean vector $\binom{a}{b}$ and the expected vector $\binom{0}{1}$ for both the %HRR–%$\dot{V}O_2R$ ($\chi^2_{(2)} = 186$, $P < 0.0001$) and the %HRR–%$\dot{V}O_{2max}$ ($\chi^2_{(2)} = 98$, $P < 0.0001$) relationships. *Post hoc* univariate *t*-tests (see Table 2) revealed that the slopes and the intercepts were significantly different from 1 and 0, respectively in both relationships (see Fig. 3 for a graphical representation of the regressions over the expected identity line). Additional information regarding the goodness of fit of the ILR can be found in the Table of the Supplemental Digital Content 1, which reports their R^2, *r*, and SEE, http://links.lww.com/MSS/C42.

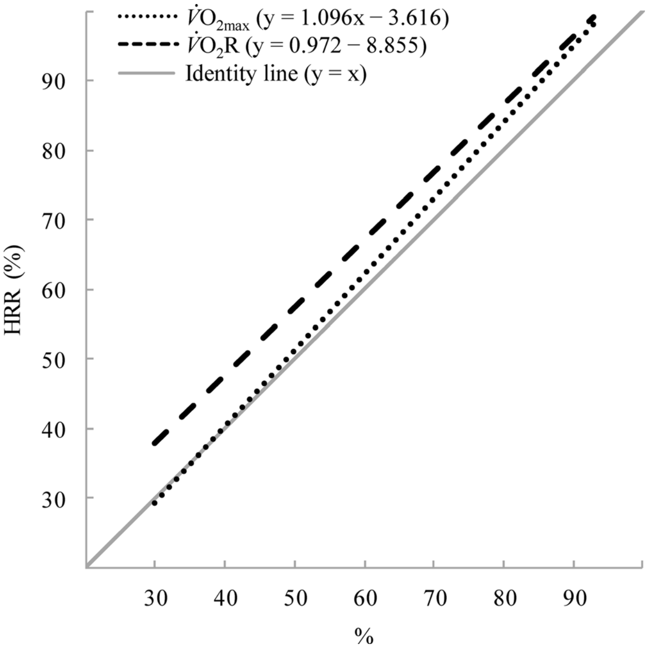

FIGURE 3—The regression lines of the %HRR–%$\dot{V}O_2R$ and %HRR–%$\dot{V}O_{2max}$ relationships are plotted over the expected identity line. The regression lines were created using the average slopes and intercepts deriving from the ILR. %HRR, percentage of heart rate reserve; $\dot{V}O_{2max}$, maximal oxygen uptake; $\dot{V}O_2R$, oxygen uptake reserve; ILR, individual linear regression.

The predicted %HRR values were different from the identity line (i.e., the expected zero ES did not lie within the 95% CI of the ES) for all the percentages calculated for the %HRR–$\dot{V}O_2R$ relationship, whereas for the %HRR–$\dot{V}O_{2max}$ relationship, they differed significantly from the identity line above 50% of $\dot{V}O_{2max}$ (Table 3).

Compared with the %HRR–%$\dot{V}O_2R$ relationship, the average RMSE of the %HRR–%$\dot{V}O_{2max}$ relationship was significantly lower (7.78% ± 4.49% vs 9.25% ± 5.54%; $t = 6.348$, $P < 0.001$), with a mean difference of 1.47% ± 3.55% and an ES of 0.41.

DISCUSSION

The main finding of the present study was that the regression between %HRR and %$\dot{V}O_2R$ differed from the identity line, which conflicts with the currently accepted 1:1 relationship commonly recommended to prescribe and monitor aerobic exercise intensity. Furthermore, the %HRR–%$\dot{V}O_{2max}$ relationship appeared to be more similar to the identity line than the %HRR–%$\dot{V}O_2R$ relationship. However, the %HRR–%$\dot{V}O_{2max}$ relationship was not 1:1 either, and the similarity between the two percentages was disrupted at intensities above 50% of the $\dot{V}O_{2max}$. In the present study, both the univariate and the univariate–bivariate blended approach provided results oriented in the same direction.

Univariate approach. When straight *t*-tests were performed on the data retained for the univariate approach, only the slope of the %HRR–%$\dot{V}O_2R$ relationship was nonsignificantly different from the expected result, whereas all the other comparisons showed significant differences.

The results of the univariate approach support those of several studies which found the %HRR–%$\dot{V}O_2R$ relationship to be different from the identity line during incremental exercises (17,18,23–27), yet they conflict with the observations of other investigations that reported no difference between the relationship and the identity line (13,16–21). Such conflicting results, however, may stem from methodological limitations and differences among the studies. First, several investigators (17,27) set the %HRR as the independent rather than the dependent variable of the ILR, as suggested by Swain and Leutholtz (13). Second, in some of the investigations, the linear regressions were performed also including the resting values of the percentages of the reserve (13,16,17,21,23–25); along with the maximal values, this could induce the slope and intercept to tend to 1 and 0, respectively. Third, in several studies (16–19,23,24,26), the resting HR was not adequately measured, which could affect the extent of the reserve. As suggested by Swain et al. (12), a regression was performed for each participant in this study (resting values were excluded), and the %HRR was set as the dependent variable to accurately reflect the variability within the data and not to obscure the individual relationships. This method is theoretically correct from a physiological standpoint because HR does not elicit whole body $\dot{V}O_2$, although $\dot{V}O_2$ is the main factor determining the demand for HR. This method is also statistically correct because the transposition of a linear regression equation does not yield the same values as those that would be obtained if the regression had initially been performed with the dependent and independent variables reversed. In addition, another strength of the data retrieved from the HERITAGE study is that the procedure used to measure resting HR was in line with current guidelines, which recommend that it should be measured after at least 5 min of quiet rest, preferably with the subject in a position similar to the one assumed during the prescribed exercise mode (e.g., see [43]). On the contrary, the resting $\dot{V}O_2$ was not measured in all subjects of the HERITAGE study; thus, it was assumed to be 3.5 mL·min^{-1}·kg^{-1} in the present investigation. Although this value is routinely used in the calculations performed for aerobic exercise intensity prescription (6), its use may represent a limitation of the present study. Indeed, using the recommended resting value of $\dot{V}O_2$ yields results that reflect more directly the daily practice of exercise specialists who prescribe the intensity of aerobic exercise for health-related purposes.

Univariate–bivariate blended approach. The multivariate inferential statistics showed that both the %HRR–%$\dot{V}O_2$R and the %HRR–%$\dot{V}O_{2max}$ relationships were significantly different from the identity line, with all slopes and intercepts significantly different from 1 and 0, including the slope of the %HRR–%$\dot{V}O_2$R relationship, which was not significantly different from 1 in the univariate approach. Compared with the results of the univariate approach, the ES and the mean differences of the slope and the intercept versus the identity line of the %HRR–%$\dot{V}O_2$R relationship increased in the univariate–bivariate blended approach, whereas those of the %HRR–%$\dot{V}O_{2max}$ relationship decreased.

When the %HRR values predicted using the identity line were compared at different intensities to the %HRR values predicted using the ILR, the identity line showed an overall low accuracy for prescribing and monitoring different exercise intensities. Indeed, the HRR values predicted using the ILR were different from those predicted using the identity line for any $\dot{V}O_2$ ranging from 30% to 90% of the reserve, whereas they differed from the prediction of the identity line for any $\dot{V}O_2$ higher than 50% of the maximal. From a practical standpoint, when HR is used to prescribe exercise intensity according to the 1:1 relationship between %HRR and either %$\dot{V}O_2$R or %$\dot{V}O_{2max}$, the exercise $\dot{V}O_2$ tends to be overestimated. This means that the actual exercise intensities are lower than those expected close to the midpoints of both the moderate and the vigorous range of exercise intensity. Exercise intensity also affects the prediction error of the 1:1 relationship, which increases in the %HRR–%$\dot{V}O_{2max}$ relationship and decreases in the %HRR–%$\dot{V}O_2$R relationship as the exercise intensity rises.

When %HRR–%$\dot{V}O_2$R and %HRR–%$\dot{V}O_{2max}$ relationships were compared with the identity line, the difference between predicted and expected HRR, their percentage error, and ES appear to be higher in the %HRR–%$\dot{V}O_2$R relationship than in the %HRR–%$\dot{V}O_{2max}$ relationship, suggesting that the %HRR–%$\dot{V}O_{2max}$ relationship is more similar to the identity line than the %HRR–%$\dot{V}O_2$R relationship. Likewise, when the predictions of the identity line were compared with the actual values of the %HRR for each subject, the errors in using the identity lines were higher for the %HRR–%$\dot{V}O_2$R relationship than for the %HRR–%$\dot{V}O_{2max}$ relationship, which confirms that the %HRR–%$\dot{V}O_{2max}$ relationship is more similar to the identity line than the %HRR–%$\dot{V}O_2$R relationship.

The univariate–bivariate blended approach highlights that the relationships are different from the identity line and that %HRR–%$\dot{V}O_{2max}$ relationship has better agreement with the identity line. The latter result is in line with previous studies (24,28) and in contrast with the postulated 1:1 relationship between the reserve values. This is particularly evident at lower exercise intensities despite the relatively high error, which is observed in both relationships but is higher for %$\dot{V}O_2$R–%HRR.

Therefore, assuming a 1:1 relationship for the %HRR–%$\dot{V}O_2$R and %HRR–%$\dot{V}O_{2max}$ relationships will yield high average errors in both relationships, although the average errors are lower in the %HRR–%$\dot{V}O_{2max}$ relationship, calling into question current guidelines.

Future directions. In the present study, we chose not to create subject subgroups (e.g., age, sex, and race) because the current guidelines adopt a 1:1 relationship between %HRR–%$\dot{V}O_2$R for all subjects. However, the influence of those and other variables (e.g., body composition, $\dot{V}O_{2max}$, resting HR, type of ergometer used, and incremental exercise adopted) on both relationships has not been adequately investigated. Therefore, future studies that consider all of these variables may be able to help account for the high variability of the HR–$\dot{V}O_2$ relationships among different persons found in this study and enhance the accuracy of aerobic exercise intensity prescription.

Finally, the transferability of the relationships between HR and $\dot{V}O_2$ from incremental to constant-load exercise is a much debated and controversial topic (44,45) that has implications on the applicability of current aerobic exercise prescription guidelines. Indeed, studies have shown that the actual constant-load exercise intensity is mostly not predictable with accuracy by calculating fixed and standard percentages of $\dot{V}O_{2\max}$, $HR_{\max}$, or HRR measured using an incremental exercise test to exhaustion (46,47). However, although prediction accuracy may be increased by using incremental exercise protocols with specific characteristics (48,49), the prolonged duration of constant-load exercise yields physiological responses, such as cardiovascular drift, whose implications on the parameters usually adopted to control for exercise intensity (i.e., HR) need to be carefully considered (50). Clearly, this topic is of great interest and still warrants further investigation.

CONCLUSIONS

The %HRR–%$\dot{V}O_2$R and %HRR–%$\dot{V}O_{2\max}$ relationships are slightly but significantly different from the identity line, and the %HRR is more closely associated with %$\dot{V}O_{2\max}$ than %$\dot{V}O_2$R. Importantly, the interindividual variability of the ILR (i.e., slopes and intercepts) and of the predicted %HRR at different exercise intensities is high, which suggests that using a standard and unique equation to predict aerobic exercise intensity can yield relatively high error in a single subject. In both relationships, the potential prediction errors of using the 1:1 relationship are relatively high. This shows the inadequacy of the 1:1 relationship in predicting exercise intensity and should raise the question of whether relying on the currently recommended equivalence between HRR and $\dot{V}O_2$R to prescribe and monitor aerobic exercise intensity is still acceptable.

The authors thank Professor Steven E. Gaskill, who provided them with important information that gave them the initial impetus for this research, and Mr. Timothy C. Bloom for his linguistic revision of the manuscript. The HERITAGE Family Study was supported by multiple grants from the NIH (HL45670, HL47323, HL47317, HL47327, and HL47321). The authors state that the results of the study are presented clearly, honestly, and without fabrication, falsification, or inappropriate data manipulation. The authors report no conflict of interest. The results of the present study do not constitute endorsement by the American College of Sports Medicine.

REFERENCES

1. 2018 Physical Activity Guidelines Advisory Committee. *2018 Physical Activity Guidelines Advisory Committee Scientific Report*. Washington (DC): U.S. Department of Health and Human Services; 2018. Available from: U.S. Department of Health and Human Services.
2. Brown WJ, Bauman AE, Bull FC, Burton NW. *Development of Evidence-Based Physical Activity Recommendations for Adults (18–64 years). Report Prepared for the Australian Government Department of Health, August 2012*. Australia: Commonwealth of Australia; 2013.
3. Haskell WL, Lee IM, Pate RR, et al. Physical activity and public health: updated recommendation for adults from the American College of Sports Medicine and the American Heart Association. *Med Sci Sports Exerc*. 2007;39(8):1423–34.
4. O'Donovan G, Blazevich AJ, Boreham C, et al. The ABC of physical activity for health: a consensus statement from the British Association of Sport and Exercise Sciences. *J Sports Sci*. 2010;28(6):573–91.
5. Weggemans RM, Backx FJG, Borghouts L, et al, Committee Dutch Physical Activity Guidelines 2017. The 2017 Dutch physical activity guidelines. *Int J Behav Nutr Phys Act*. 2018;15(1):58.
6. American College of Sports Medicine, Riebe D, Ehrman JK, Liguori G, Magal M. *ACSM's Guidelines for Exercise Testing and Prescription*. 10th ed. Philadelphia: Wolters Kluwer; 2018.
7. Whipp BJ. Domains of aerobic function and their limiting parameters. In: Steinacker JM, Ward SA, editors. *The Physiology and Pathophysiology of Exercise Tolerance*. Boston (MA): Springer; 1996.
8. Poole DC, Burnley M, Vanhatalo A, Rossiter HB, Jones AM. Critical power: an important fatigue threshold in exercise physiology. *Med Sci Sports Exerc*. 2016;48(11):2320–34.
9. Garber CE, Blissmer B, Deschenes MR, et al. American College of Sports Medicine position stand. Quantity and quality of exercise for developing and maintaining cardiorespiratory, musculoskeletal, and neuromotor fitness in apparently healthy adults: guidance for prescribing exercise. *Med Sci Sports Exerc*. 2011;43(7):1334–59.
10. Franklin BA, Hodgson J, Buskirk ER. Relationship between percent maximal O_2 uptake and percent maximal heart rate in women. *Res Q Exerc Sport*. 1980;51(4):616–24.
11. Katch V, Weltman A, Sady S, Freedson P. Validity of the relative percent concept for equating training intensity. *Eur J Appl Physiol Occup Physiol*. 1978;39(4):219–27.
12. Swain DP, Abernathy KS, Smith CS, Lee SJ, Bunn SA. Target heart rates for the development of cardiorespiratory fitness. *Med Sci Sports Exerc*. 1994;26(1):112–6.
13. Swain DP, Leutholtz BC. Heart rate reserve is equivalent to %$\dot{V}O_2$ reserve, not to %$\dot{V}O_{2\max}$. *Med Sci Sports Exerc*. 1997;29(3):410–4.
14. Karvonen MJ, Kentala E, Mustala O. The effects of training on heart rate; a longitudinal study. *Ann Med Exp Biol Fenn*. 1957;35(3):307–15.
15. Davis JA, Convertino VA. A comparison of heart rate methods for predicting endurance training intensity. *Med Sci Sports*. 1975;7(4):295–8.
16. Dalleck LC, Kravitz L. Relationship between %heart rate reserve and %$\dot{V}O_2$ reserve during elliptical crosstrainer exercise. *J Sports Sci Med*. 2006;5(4):662–71.
17. Mezzani A, Corrà U, Giordano A, Cafagna M, Adriano EP, Giannuzzi P. Unreliability of the %$\dot{V}O_2$ reserve versus %heart rate reserve relationship for aerobic effort relative intensity assessment in chronic heart failure patients on or off beta-blocking therapy. *Eur J Cardiovasc Prev Rehabil*. 2007;14(1):92–8.
18. Brawner CA, Keteyian SJ, Ehrman JK. The relationship of heart rate reserve to $\dot{V}O_2$ reserve in patients with heart disease. *Med Sci Sports Exerc*. 2002;34(3):418–22.
19. Byrne NM, Hills A. Relationships between HR and $\dot{V}O_2$ in the obese. *Med Sci Sports Exerc*. 2002;34(9):1419–27.
20. Colberg SR, Swain DP, Vinik AI. Use of heart rate reserve and rating of perceived exertion to prescribe exercise intensity in diabetic autonomic neuropathy. *Diabetes Care*. 2003;26(4):986–90.
21. Lounana J, Campion F, Noakes TD, Medelli J. Relationship between %$HR_{\max}$, %HR reserve, %$\dot{V}O_{2\max}$, and %$\dot{V}O_2$ reserve in elite cyclists. *Med Sci Sports Exerc*. 2007;39(2):350–7.
22. Montoye HJ, Taylor HL. Measurement of physical activity in population studies: a review. *Hum Biol*. 1984;56(2):195–216.
23. Swain DP, Leutholtz BC, King ME, Haas LA, Branch JD. Relationship between % heart rate reserve and %$\dot{V}O_2$ reserve in treadmill exercise. *Med Sci Sports Exerc*. 1998;30(2):318–21.
24. Hui SS, Chan JW. The relationship between heart rate reserve and oxygen uptake reserve in children and adolescents. *Res Q Exerc Sport*. 2006;77(1):41–9.
25. Davenport MH, Charlesworth S, Vanderspank D, Sopper MM, Mottola MF. Development and validation of exercise target heart rate

zones for overweight and obese pregnant women. *Appl Physiol Nutr Metab*. 2008;33(5):984–9.

26. Pinet BM, Prud'homme D, Gallant CA, Boulay P. Exercise intensity prescription in obese individuals. *Obesity*. 2008;16(9):2088–95.
27. Carvalho VO, Bocchi EA, Pascoalino LN, Guimaraes GV. The relationship between heart rate and oxygen consumption in heart transplant recipients during a cardiopulmonary exercise test: heart rate dynamic during exercise test. *Int J Cardiol*. 2010;145(1):158–60.
28. Cunha FA, Midgley AW, Monteiro WD, Farinatti PT. Influence of cardiopulmonary exercise testing protocol and resting $\dot{V}O_2$ assessment on $\%HR_{max}$, %HRR, $\%\dot{V}O_{2max}$ and $\%\dot{V}O_2R$ relationships. *Int J Sports Med*. 2010;31(5):319–26.
29. da Cunha FA, Farinatti Pde T, Midgley AW. Methodological and practical application issues in exercise prescription using the heart rate reserve and oxygen uptake reserve methods. *J Sci Med Sport*. 2011;14(1):46–57.
30. Pollock ML, Gaesser GA, Butcher JD, et al. American College of Sports Medicine position stand. The recommended quantity and quality of exercise for developing and maintaining cardiorespiratory and muscular fitness, and flexibility in healthy adults. *Med Sci Sports Exerc*. 1998;30(6):975–91.
31. Bouchard C, Leon AS, Rao DC, Skinner JS, Wilmore JH, Gagnon J. The HERITAGE Family Study. Aims, design, and measurement protocol. *Med Sci Sports Exerc*. 1995;27(5):721–9.
32. Bouchard C, Daw EW, Rice T, et al. Familial resemblance for $\dot{V}O_{2max}$ in the sedentary state: the HERITAGE Family Study. *Med Sci Sports Exerc*. 1998;30(2):252–8.
33. Skinner JS, Gaskill SE, Rankinen T, et al. Heart rate versus % $\dot{V}O_{2max}$: age, sex, race, initial fitness, and training response–HERITAGE. *Med Sci Sports Exerc*. 2003;35(11):1908–13.
34. Gagnon J, Province MA, Bouchard C, et al. The HERITAGE Family Study: quality assurance and quality control. *Ann Epidemiol*. 1996; 6(6):520–9.
35. Skinner JS, Wilmore KM, Jaskolska A, et al. Reproducibility of maximal exercise test data in the HERITAGE Family Study. *Med Sci Sports Exerc*. 1999;31(11):1623–8.
36. Stanforth PR, Gagnon J, Rice T, et al. Reproducibility of resting blood pressure and heart rate measurements. The HERITAGE Family Study. *Ann Epidemiol*. 2000;10(5):271–7.
37. Wilmore JH, Stanforth PR, Domenick MA, et al. Reproducibility of anthropometric and body composition measurements: the HERITAGE Family Study. *Int J Obes Relat Metab Disord*. 1997; 21(4):297–303.
38. Belsley DA. *Regression Diagnostics: Identifying Influential Data and Sources of Collinearity*. Hoboken (NJ): Wiley-Interscience; 2004. p. 28.
39. ISO. ISO-Standards: statistical methods for use in proficiency testing by interlaboratory comparison. In: ISO 13528:2015 [available at https://www.iso.org/standard/56125.html].
40. Lakens D. Calculating and reporting effect sizes to facilitate cumulative science: a practical primer for *t*-tests and ANOVAs. *Front Psychol*. 2013;4:863.
41. Shieh G. A comparison of two indices for the intraclass correlation coefficient. *Behav Res Methods*. 2012;44(4):1212–23.
42. Rutterford C, Copas A, Eldridge S. Methods for sample size determination in cluster randomized trials. *Int J Epidemiol*. 2015;44(3):1051–67.
43. Swain DP, American College of Sports Medicine. *ACSM's Resource Manual for Guidelines for Exercise Testing and Prescription*. 7th ed. Philadelphia: Wolters Kluwer Health/Lippincott Williams & Wilkins; 2014. p. 473.
44. Cunha FA, Midgley AW, Monteiro WD, Campos FK, Farinatti PT. The relationship between oxygen uptake reserve and heart rate reserve is affected by intensity and duration during aerobic exercise at constant work rate. *Appl Physiol Nutr Metab*. 2011;36(6):839–47.
45. Wingo JE, Ganio MS, Cureton KJ. Cardiovascular drift during heat stress: implications for exercise prescription. *Exerc Sport Sci Rev*. 2012;40(2):88–94.
46. Iannetta D, Inglis EC, Mattu AT, et al. A critical evaluation of current methods for exercise prescription in women and men. *Med Sci Sports Exerc*. 2020;52(2):466–73.
47. Weatherwax RM, Harris NK, Kilding AE, Dalleck LC. Incidence of $\dot{V}O_{2max}$ responders to personalized versus standardized exercise prescription. *Med Sci Sports Exerc*. 2019;51(4):681–91.
48. Keir DA, Paterson DH, Kowalchuk JM, Murias JM. Using ramp-incremental $\dot{V}O_2$ responses for constant-intensity exercise selection. *Appl Physiol Nutr Metab*. 2018;43(9):882–92.
49. Iannetta D, de Almeida Azevedo R, Keir DA, Murias JM. Establishing the $\dot{V}O_2$ versus constant–work–rate relationship from ramp-incremental exercise: simple strategies for an unsolved problem. *J Appl Physiol (1985)*. 2019;127(6):1519–27.
50. Zuccarelli L, Porcelli S, Rasica L, Marzorati M, Grassi B. Comparison between slow components of HR and $\dot{V}O_2$ kinetics: functional significance. *Med Sci Sports Exerc*. 2018;50(8):1649–57.