Volume of Exercise and Fitness Nonresponse in Sedentary, Postmenopausal Women

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ABSTRACT

SISSON, S. B., P. T. KATZMARZYK, C. P. EARNEST, C. BOUCHARD, S. N. BLAIR, and T. S. CHURCH. Volume of Exercise and Fitness Nonresponse in Sedentary, Postmenopausal Women. *Med. Sci. Sports Exerc.*, Vol. 41, No. 3, pp. 539–545, 2009. There is a wide individual heterogeneity in the maximal aerobic fitness ($\dot{V}O_{2max}$) response to exercise training. **Purpose**: To examine predictors of $\dot{V}O_{2max}$ nonresponse after aerobic exercise training in postmenopausal women. **Methods**: The Dose Response to Exercise in Women (DREW) study was a randomized, controlled trial examining the effects of incremental training doses on sedentary postmenopausal women (45–75 yr). Participants were randomized to one of three exercise treatment groups (4, 8, or 12 $\text{kcal·kg}^{-1}\text{·wk}^{-1}$) for 6 months. Participants exercised 3–4 d·wk^{-1} at 50% $\dot{V}O_{2max}$. Predictors of baseline $\dot{V}O_{2max}$ were determined by ANOVA. We used a logistic regression analyses with categorical (ethnicity and treatment group) and standardized continuous variables (age, body mass index [BMI], and baseline $\dot{V}O_{2max}$) to determine predictors of nonresponse ($\Delta \leq 0\ \text{L·min}^{-1}$). Our analysis included 310 women because the control group was excluded. **Results**: A total of 44.9%, 23.8%, and 19.3% of the 4-, the 8-, and the 12-$\text{kcal·kg}^{-1}\text{·wk}^{-1}$ treatment groups ($P < 0.0001$), respectively, were nonresponders. Maximal effort, BMI, age, and race significantly predicted baseline $\dot{V}O_{2max}$. Treatment group (8 and 12 $\text{kcal·kg}^{-1}\text{·wk}^{-1}$ vs 4 $\text{kcal·kg}^{-1}\text{·wk}^{-1}$; $P = 0.0003$), baseline $\dot{V}O_{2max}$ ($P < 0.0001$), and age ($P < 0.05$) were significant predictors of nonresponse. Odds ratios and 95% confidence intervals were 2.13 (1.53–2.95) for baseline $\dot{V}O_{2max}$; 1.35 (1.00–1.83) for age; 0.45 (0.24–0.85) for the 8- versus the 4-$\text{kcal·kg}^{-1}\text{·wk}^{-1}$ group; and 0.27 (0.13–0.53) for the 12- versus the 4-$\text{kcal·kg}^{-1}\text{·wk}^{-1}$ group. **Conclusion**: Women that were younger, less fit, or exercised more during the DREW trial had greater odds of improving their fitness with training. The most important finding of this study was that greater volumes of exercise were associated with a lower probability of being a nonresponder. **Key Words:** INDIVIDUAL VARIABILITY, TRAINABILITY, AEROBIC TRAINING, DOSE RESPONSE

Low levels of maximal aerobic fitness ($\dot{V}O_{2max}$) are associated with a higher risk of mortality, and improvements in $\dot{V}O_{2max}$ are associated with lower mortality (2,3). Theoretically, if untrained or sedentary individuals with initially low levels of $\dot{V}O_{2max}$ are exposed to cardiorespiratory endurance training, $\dot{V}O_{2max}$ should improve. However, previous studies show that this is not always the case (4,7,10–12,17). Wide individual variability or heterogeneity in response to exercise has been reported (−4.7% to +58.0%), even when the exercise training volume was the same for all participants (11,18).

Earlier reports have examined factors that may influence an individual's response to cardiorespiratory endurance training (10,11,17). Age, sex, race, and initial $\dot{V}O_{2max}$ have all been reported not to influence the heterogeneity of responses to exercise training (7,11,17). Other reports determined age to be a predictor for nonresponse to training such that the older participants were less trainable than the younger (10), but there are contradictory reports (17). Because so few studies have examined this phenomenon, further investigation is warranted into possible phenotypes associated with lack of $\dot{V}O_{2max}$ response to supervised exercise training.

The Dose Response to Exercise in Women (DREW) study provides data on a large sample ($N = 464$) of healthy, postmenopausal women who participated in a nonexercise control or one of three exercise treatments (4, 8, or 12 $\text{kcal·kg}^{-1}\text{·wk}^{-1}$) for 6 months (14). Adherence to the training protocol, which is vital to studying the affect of exercise dose on changes in fitness, was excellent (~92%) (8). The dose–response design of DREW allows for the investigation of $\dot{V}O_{2max}$ nonresponse across varied exercise doses, an aspect that has not been previously examined in a sample of women. The purpose of our current analysis is to examine the predictors of $\dot{V}O_{2max}$ nonresponse to 6 months

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of cardiorespiratory endurance training in a sample of sedentary, postmenopausal women.

METHODS

Study Design and Participants

A complete and detailed description of the design and rationale of the DREW study has been previously published (14). Briefly, DREW was a randomized, controlled trial examining the effects of incremental doses of cardiorespiratory endurance training on 464 sedentary postmenpausal women aged 45 to 75 yr on aerobic fitness and blood pressure. Women recruited for participation were overweight or obese (body mass index [BMI] of 25.0 to 43.0 $kg \cdot m^{-2}$), postmenopausal, healthy, and capable of engaging in the prescribed exercise training. Additionally, volunteers were sedentary (<35 $kcal \cdot kg^{-1} \cdot d^{-1}$ in energy expenditure (1)) and had elevated blood pressure (systolic blood pressure = 125.0–159.0 mm Hg). Women were excluded if they had significant cardiovascular disease or other significant medical disorders, had elevated low-density lipoproteins, or had lost 20 lb or more in the previous year (14).

The study was originally reviewed annually by The Cooper Institute and was subsequently approved by the Pennington Biomedical Research Center IRB for continued analysis. Before participation, all volunteers signed a written informed consent document outlining the procedures involved in the DREW study.

Exercise Training

After a prerandomization run-in period of several visits to the site to become acquainted with staff, location, and logistics of participation, screening, and baseline measurements, participants were randomized into one of three exercise treatments or a nonexercise control group. Women in the control group were asked to maintain regular habits of daily physical activity. Daily physical activity behavior was monitored for all women in the treatment and the control groups by the use of a pedometer (Accusplit Eagle, Japan) and the recording of daily steps. At the end of each month, the activity calendar with daily steps was returned to the study center. Women in the treatment groups removed the pedometer during their scheduled training so that only extracurricular physical activity was assessed.

The three exercise treatment groups were based on the National Institutes of Health (NIH) Consensus Development Panel recommendation that adults should accumulate a minimum of 30 min of moderate- to vigorous-intensity physical activity most days of the week (15). We calculated that 8 $kcal \cdot kg^{-1} \cdot wk^{-1}$ is what a typical, overweight, sedentary, postmenopausal woman would expend when starting an exercise program based on the NIH recommendation and randomized women to this group (14). The remaining two exercise treatment groups were scaled to 50% above and 50% below the 8-$kcal \cdot kg^{-1} \cdot wk^{-1}$ group (i.e., 12 and 4 $kcal \cdot kg^{-1} \cdot wk^{-1}$, respectively). The 4-$kcal \cdot kg^{-1} \cdot wk^{-1}$ was used to examine if exercise in an amount less than the NIH Consensus Development Panel would still provide health and fitness benefits to this sedentary, overweight female population. The 12-$kcal \cdot kg^{-1} \cdot wk^{-1}$ group was designed to examine if more exercise would translate into a proportionally greater increase in the health benefits of the population of interest. These findings have been previously published and are available elsewhere (8).

All treatment participants exercised for 6 months, 3 to 4 $d \cdot wk^{-1}$ at an HR associated with 50% baseline $\dot{V}O_{2max}$ under the supervision of trained technicians in an exercise laboratory. Participants exercised alternatively on a recumbent cycle ergometer and treadmill for a duration long enough to reach their energy expenditure goal based on the treatment group (4, 8, or 12 $kcal \cdot kg^{-1} \cdot wk^{-1}$). After each session, the energy expended was recorded in a log and summed over the course of the training. A ramping protocol was used to get each participant to their recommended exercise level. During the first week, each group expended 4 $kcal \cdot kg^{-1} \cdot wk^{-1}$. Those assigned to the 4-$kcal \cdot kg^{-1} \cdot wk^{-1}$ group remained at this dose for the duration of the study, whereas those assigned to the 8- and the 12-$kcal \cdot kg^{-1} \cdot wk^{-1}$ groups increased their energy expenditure 1 $kcal \cdot kg^{-1} \cdot wk^{-1}$ until their assigned exercise level was reached. In a previous report, we examined if whether the potential for HR drift influenced participant workloads during their exercise sessions. In this article, we reported no presence of HR drift or variance in prescribed versus actual work intensity for any treatment group throughout the course of the study (13).

Clinical Measures

Demographics. Ethnicity, age, physical-activity history, smoking, alcohol use, and dietary habits were all self-reported by participants at baseline and posttraining (14).

Anthropometrics. Height was measured using a standard wall stadiometer, and weight was measured on an electronic scale (Siemens Medical Solutions, Malvern, PA). Body fat percent was estimated from skinfold measurements (bicep, triceps, midaxillary, subscapular, abdominal, suprailiac, thigh, and calf) (14).

Fitness testing. The baseline and the posttraining $\dot{V}O_{2max}$ values were an average of two maximal exercise tests completed on separate days (14). The intraclass correlation for both baseline and follow-up for the two tests was 0.88 (8). $\dot{V}O_{2max}$ testing was conducted on a Lode Excalibur Sport cycle ergometer (Groningen, The Netherlands), an electronic, rate-independent ergometer. Participants exercised at 30 W for 2 min, 50 W for 4 min, followed by increases of 20 W every 2 min until volitional fatigue (14). Gas exchange variables ($\dot{V}O_2$, CO_2 production, ventilation, and respiratory exchange ratio [RER]) were measured using a Parvomedics True Max 2400 Metabolic Measurement Cart.

Statistical Analyses

The purpose of this analysis was to examine determinants of change in maximal aerobic fitness ($\dot{V}O_{2\max}$) in response to exercise training; therefore, participants were excluded from the final data set if they were in the nonexercise control group (n = 93), did not have follow-up data (n = 40), had an exercise compliance (i.e., percentage of expended calories with respect to the prescribed calories) less than 90% (n = 17), or reported ethnicity as Asian or other due to the small sample size (n = 4). This resulted in a study population of 310 participants. Delta values (Δ) were calculated (posttraining minus baseline values) for absolute $\dot{V}O_{2\max}$ ($L \cdot min^{-1}$), and participants were categorized as responders ($\Delta > 0$) or nonresponders ($\Delta \leq 0$) to aerobic endurance training.

Means and SD were calculated. One-way ANOVA and chi-square analyses were conducted to determine whether there was a significant difference between treatment groups for baseline continuous and categorical variables, respectively. Determinants of $\dot{V}O_{2\max}$ before training (i.e., baseline) were determined using an ANOVA containing the following variables: age, ethnicity, BMI, and baseline steps. Continuous variables were standardized by subtracting their respective group mean and then dividing by the corresponding SD (i.e., z-score). The standardized predictor variables were then included in a logistic regression model. Interpretation of the results from the model is such that a significant odds ratio as a measure of effect size of 2.0 represents a twofold increase in the odds of fitness nonresponse for every one unit increase (on the standardized scale). Note that a one unit increase on the standardized scale corresponds to an increase equal to one SD of the predictor variable. Forced-entry logistic regression was then used to determine which variables were significant predictors of fitness nonresponse for the total exercising sample as well as for each individual treatment group. Variables of interest included age, baseline fitness, ethnicity (White, Black, and Hispanic), treatment group, BMI, and smoking status.

RESULTS

Baseline characteristics for our current analysis can be found in Table 1. Percent body fat ($P < 0.04$) and relative $\dot{V}O_{2\max}$ ($mL \cdot kg^{-1} \cdot min^{-1}$) were significantly different across groups at baseline ($P < 0.03$). The 4-$kcal \cdot kg^{-1} \cdot wk^{-1}$ group had significantly lower body fat percentage than the 8-$kcal \cdot kg^{-1} \cdot wk^{-1}$ group, and the 12-$kcal \cdot kg^{-1} \cdot wk^{-1}$ group had significantly higher relative $\dot{V}O_{2\max}$ than the 8-$kcal \cdot kg^{-1} \cdot wk^{-1}$ group. Average absolute baseline $\dot{V}O_{2\max}$ ($L \cdot min^{-1}$) was significantly different between ethnicities ($P < 0.02$) such that blacks had lower baseline $\dot{V}O_{2\max}$ compared with whites. Smoking status and baseline daily step average were not significant predictors of baseline $\dot{V}O_{2\max}$ for the group. Significant positive determinants of absolute baseline $\dot{V}O_{2\max}$ in the ANOVA model were max RER during baseline testing ($P < 0.002$) and BMI ($P < 0.0001$) (i.e., as BMI increased so did absolute $\dot{V}O_{2\max}$). Age was a significantly negative determinant of baseline absolute $\dot{V}O_{2\max}$ (i.e., as age increased baseline $\dot{V}O_{2\max}$ decreased) in the ANOVA model ($P < 0.0001$). Race was also a significant predictor of baseline $\dot{V}O_{2\max}$ in the model ($P < 0.005$).

As was reported in a previous manuscript (8), we observed a significant difference in the mean absolute and

TABLE 1. Baseline characteristics of DREW study participants (N = 310) by treatment group.

Variables	**4 $kcal \cdot kg^{-1} \cdot wk^{-1}$ (n = 138)**	**8 $kcal \cdot kg^{-1} \cdot wk^{-1}$ (n = 84)**	**12 $kcal \cdot kg^{-1} \cdot wk^{-1}$ (n = 88)**
Age (yr)	58.0 ± 6.5	56.7 ± 6.4	56.3 ± 6.0
Exercise compliance (%)	99.5 ± 2.1	99.4 ± 1.6	99.6 ± 1.6
Fitness nonresponse ($\Delta \leq 0$ $L \cdot min^{-1}$)	44.9%*	23.8%*	19.3%*
Married (yes)	94.2%	91.3%	87.5%
Ethnicity			
White	59.4%	58.3%	73.9%
Black	34.1%	33.3%	23.9%
Hispanic	6.5%	8.3%	2.3%
BMI ($kg \cdot m^{-2}$)	31.4 ± 3.7	32.3 ± 4.1	31.0 ± 3.5
Waist circumference (cm)	100.0 ± 11.3	101.6 ± 11.8	99.2 ± 12.3
Hip circumference (cm)	114.2 ± 8.6	114.9 ± 9.2	114.0 ± 9.1
Body fat (%)	27.6 ± 4.1*	29.1 ± 4.5*	28.6 ± 4.7
$\dot{V}O_{2\max}$ ($L \cdot min^{-1}$)	1.3 ± 0.3	1.3 ± 0.2	1.3 ± 0.2
$\dot{V}O_{2\max}$ ($mL \cdot kg^{-1} \cdot min^{-1}$)	15.4 ± 3.0	14.9 ± 2.3*	16.1 ± 3.0*
Resting HR (BMP)	65.0 ± 7.7	67.1 ± 8.9	65.0 ± 7.3
Steps per day	4792 ± 1870	4787 ± 1881	5095 ± 1830
Energy intake ($kcal \cdot d^{-1}$)	2186 ± 978	2304 ± 959	2287 ± 1073
Beers per week (12 oz)	0.8 ± 1.1	0.7 ± 0.8	1.0 ± 1.4
Wine per week (5 oz)	2.2 ± 2.1	1.6 ± 2.1	2.7 ± 2.8
Shots per week (1.5 oz)	1.0 ± 1.4	1.8 ± 2.6	1.7 ± 2.6
Current smoker (yes)	5.8%	3.6%	9.1%

Data are presented as mean ± SD or frequency (%)

* Significant differences between groups ($P < 0.05$)

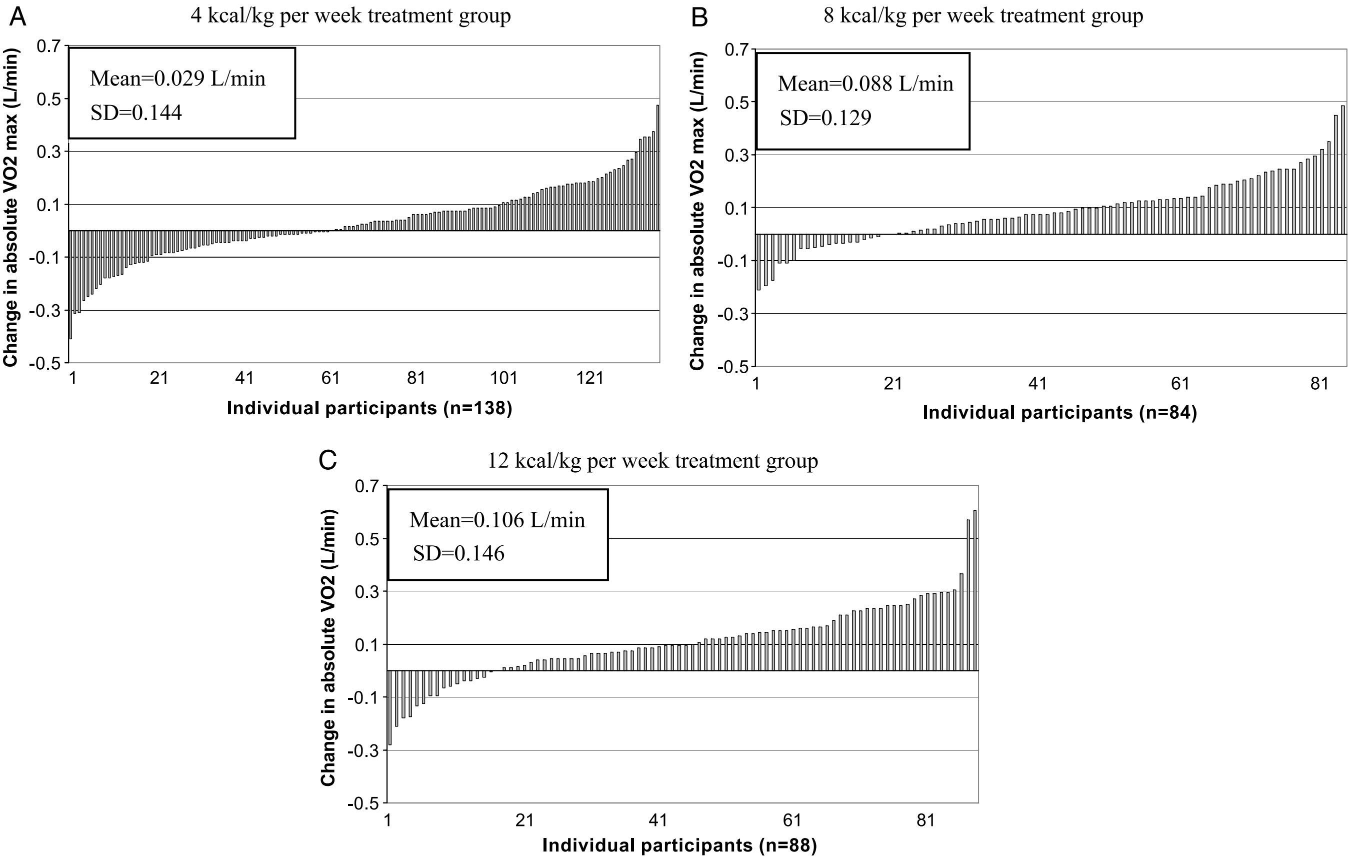

FIGURE 1—Individual variability in absolute $\dot{V}O_2$ response to exercise training by treatment group.

relative $\dot{V}O_{2\max}$ response to training for all pairwise treatment groups except 4 versus 8 $kcal{\cdot}kg^{-1}{\cdot}wk^{-1}$. For the 4-$kcal{\cdot}kg^{-1}{\cdot}wk^{-1}$ group (n = 138), Δ $\dot{V}O_{2\max}$ was 0.029 ± 0.144 $L{\cdot}min^{-1}$ (range = −0.41 to 0.475 $L{\cdot}min^{-1}$); for the 8-$kcal{\cdot}kg^{-1}{\cdot}wk^{-1}$ group (n = 84), Δ $\dot{V}O_{2\max}$ was 0.088 ± 0.129 $L{\cdot}min^{-1}$ (range = −0.21 to 0.485 $L{\cdot}min^{-1}$); and for the 12-$kcal{\cdot}kg^{-1}{\cdot}wk^{-1}$ group (n = 88), Δ $\dot{V}O_{2\max}$ was 0.106 ± 0.146 $L{\cdot}min^{-1}$ (range = −0.28 to 0.605 $L{\cdot}min^{-1}$). The ranges in percent change in absolute $\dot{V}O_{2\max}$ for the 4-, the 8-, and the 12-$kcal{\cdot}kg^{-1}{\cdot}wk^{-1}$ groups were −33.2% to 76.0%, −25.2% to 41.7%, and −14.3% to 58.7%, respectively. Relative Δ $\dot{V}O_{2\max}$ was 0.638 ± 1.867 for the 4-$kcal{\cdot}kg^{-1}{\cdot}wk^{-1}$ group, 1.460 ± 1.581 for the 8-$kcal{\cdot}kg^{-1}{\cdot}wk^{-1}$ group, and 1.554 ± 1.722 for the 12-$kcal{\cdot}kg^{-1}{\cdot}wk^{-1}$ group. Figure 1 depicts the heterogeneity of $\dot{V}O_{2\max}$ response to training for the each treatment group (Fig. 1A–C). For the groups, 44.9%, 23.8%, and 19.3% of the 4-, the 8-, and the 12-$kcal{\cdot}kg^{-1}{\cdot}wk^{-1}$ groups (P < 0.0001), respectively, were $\dot{V}O_{2\max}$ nonresponders, meaning that 55.1%, 76.2%, and 80.7%, respectively, improved $\dot{V}O_{2\max}$ with training.

For the logistic regression analyses, all continuous variables were standardized, and the standardized values were used in the analyses (Table 2). Between 61% and 69% of the participants met the max criterion (14) during the baseline and the posttests. RER was not significant in the

TABLE 2. OR for predictors of nonresponse with all continuous variables standardized to mean of zero and unit SD.

		Model 1		Model 2	
Variable	**SD unit**	**OR**	**95% CI**	**OR**	**95% CI**
Baseline $\dot{V}O_{2\max}$	0.24 $L{\cdot}min^{-1}$	2.01	(1.47–2.74)*	2.10	(1.52–2.91)*
Age	6.4 yr	1.45	(1.08–1.94)*	1.35	(1.00–1.83)*
Black (vs white)		2.04	(1.14–3.66)*	1.81	(0.99–3.30)
Hispanic (vs white)		1.67	(0.57–4.90)	1.41	(0.46–4.38)
BMI	3.8 $kg{\cdot}m^{-2}$	0.82	(0.63–1.06)	0.80	(0.60–1.05)
Smoking status (yes vs no)		1.01	(0.36–2.85)	0.90	(0.30–2.63)
Treatment (8 vs 4 KKW)				0.43	(0.23–0.80)*
Treatment (12 vs 4 KKW)				0.26	(0.13–0.51)*

Predictors included in model 1: age, baseline $\dot{V}O_{2\max}$, age of menopause, ethnicity, BMI, and smoking status. Predictors included in model 2: age, baseline $\dot{V}O_{2\max}$, age of menopause, ethnicity, BMI, smoking status, and treatment group assignment. 4 KKW group was the referent group in model 2.
* Significant predictors (P < 0.05).
KKW, $kcal{\cdot}kg^{-1}{\cdot}wk^{-1}$.

preliminary analyses and was subsequently removed from later analyses. Possible predictors included in logistic regression model 1 were age, baseline $\dot{V}O_{2max}$, BMI, ethnicity, and smoking status. Baseline absolute $\dot{V}O_{2max}$ ($P < 0.0001$), age ($P < 0.02$), and black ethnicity were significant predictors of response in model 1. Interpretation of the significant predictors from model 1 is such that as baseline $\dot{V}O_{2max}$ was higher by 0.24 $L \cdot min^{-1}$, the odds of not responding to endurance training were approximately two times higher. Additionally, as age was 6.4 yr higher, the odds of nonresponse were by 45% higher. Finally, black participants are two times more likely to be nonresponders when compared with white participants; however, this relationship ceased to be significant when treatment group was included in model 2.

All the predictors from model 1 were included in model 2, with the addition of treatment group assignment (i.e., volume of exercise). Treatment group (8 and 12 $kcal \cdot kg^{-1} \cdot wk^{-1}$ vs 4 $kcal \cdot kg^{-1} \cdot wk^{-1}$; $P = 0.0003$), baseline absolute $\dot{V}O_{2max}$ ($P < 0.0001$), and age ($P < 0.05$) were significant predictors of response in model 2. Interpretation of the significant predictors from model 2 is such that as baseline $\dot{V}O_{2max}$ was higher by 0.24 $L \cdot min^{-1}$, the odds of not responding to endurance training were over twofold higher. Additionally, as age was 6.4 yr higher, the odds of nonresponse were 35% higher. When the NIH-recommended treatment group (i.e., 8 $kcal \cdot kg^{-1} \cdot wk^{-1}$) was compared with the group with the lowest volume of training (i.e., 4 $kcal \cdot kg^{-1} \cdot wk^{-1}$), the likelihood of not responding to the training was 57% lower. Furthermore, in the highest volume group (12 $kcal \cdot kg^{-1} \cdot wk^{-1}$), the likelihood of not responding to the exercise training was 74% lower when compared with the lowest volume group.

Logistic regression analyses were also conducted for each of the three treatment groups separately. Predictors included in the analyses were age, baseline absolute $\dot{V}O_{2max}$, BMI, ethnicity, and smoking status. The only significant predictor in the 4- and the 12-$kcal \cdot kg^{-1} \cdot wk^{-1}$ groups was standardized baseline $\dot{V}O_{2max}$ ($P < 0.002$, odds ratio [OR] = 2.40, 95% confidence interval [CI] = 1.41–4.10; and $P < 0.005$, OR = 4.00, 95% CI = 1.53–10.44, respectively). There were no significant predictors in the 8-$kcal \cdot kg^{-1} \cdot wk^{-1}$ group.

DISCUSSION

The primary aim of our current analysis was to examine predictors of no change in maximal aerobic fitness ($\dot{V}O_{2max}$) across different doses of cardiorespiratory endurance training in a sample of sedentary, overweight/obese, moderately hypertensive, postmenopausal women. Despite a high retention rate and a uniform high compliance within each treatment group, there was a large amount of individual variability in response to exercise. The overall predictors of $\dot{V}O_{2max}$ nonresponse to cardiorespiratory training were baseline $\dot{V}O_{2max}$, age, and volume of training, with those groups exercising for longer durations (all participants exercised at the same intensity) having a lower prevalence of nonresponse to training. Variables that were not significant included the participant's level of exertion (i.e., RER), ethnicity, BMI, body composition, and smoking status. Within the treatment groups, findings were similar. The most important finding of this study, especially pertaining to future exercise program development, is that as women increase the volume of exercise, the percent who do not improve $\dot{V}O_{2max}$ significantly decreases. Additionally, on the individual level, there was a decrease in prevalence of nonresponse with increasing training volume.

The large range of individual variability in response to training (−33.2% to 76.0% change) is similar to other trials (9,11,18). Approximately 32% of the participants in the entire sample were nonresponders to the exercise training but varying between treatment groups. Although few studies have examined the response to exercise in this manner, those studies that have do not show such a large proportion of nonresponsive individuals (5,9). This phenomenon may be due to the uniqueness of the study design and training protocol. All DREW participants exercised at an HR-established intensity corresponding to 50% of baseline $\dot{V}O_{2max}$. Participants in other trials exercised between 70% and 85% $\dot{V}O_{2max}$ (6,9,11). The higher intensity of these other trials may partially explain the discrepancy in the proportion of nonresponders between our trial and previous studies. Nonetheless, although the exercise prescription in our current study was lower than in other studies, it was of a significant intensity to increase $\dot{V}O_{2max}$ in most participants. The increase in $\dot{V}O_{2max}$ was especially strong in the group that exercised 50% above the current recommendation (i.e., 192 $min \cdot wk^{-1}$ (8)).

In contrast to our findings, the HERITAGE Family Study (7) did not find initial $\dot{V}O_{2max}$ to be a significant predictor of heterogeneity of response. A trend toward the significance of initial $\dot{V}O_{2max}$ was reported in another trial of older adults (11) and 30- to 40-yr-old men (16); however, the HERITAGE Family Study had the largest sample size of the trials examining nonresponse to training. Volume of exercise was a significant predictor in the DREW trial, meaning that those exercising at a level of 8 $kcal \cdot kg^{-1} \cdot wk^{-1}$ were 55% more likely to increase their $\dot{V}O_{2max}$ than participants exercising at 4 $kcal \cdot kg^{-1} \cdot wk^{-1}$. Furthermore, those in the 12-$kcal \cdot kg^{-1} \cdot wk^{-1}$ were 87% more likely to increase their $\dot{V}O_{2max}$ than the 4-$kcal \cdot kg^{-1} \cdot wk^{-1}$ group. These findings are in contrast to an 8-wk aerobic exercise trial in men where no difference was found between moderate and high-volume treatment groups (10). Specifically, Hautala et al. (10) ($n = 39$), the men in the moderate group engaged in 180 min of exercise at 70–80% HR max per week. This level of exercise corresponds well with the highest dose group in our current cohort who exercised approximately 192 $min \cdot wk^{-1}$ or exercise at 50% $\dot{V}O_{2max}$ (8). Kohrt et al. (11) also examined this issue by separating participants into quartiles based on percent improvement in

$\dot{V}O_{2max}$. When their exercise volume and intensity were examined, no differences were found; however, these participants all received the same exercise treatment (11). Additionally, existing studies show mixed findings for the influence of age on fitness nonresponse with one trial showing significance of age (10), one showing a trend (11), and another showing no influence (7,17). Further, the age range of our current cohort was relatively narrow. Thus, studies examining a greater range of ages may offer better insights regarding the influence of age and exercise training response.

The primary limitation of this trial is the homogenous nature of the participants. Therefore, the generalizability of our findings to other populations of women or to men is not possible. However, this was an efficacy trial, and the limited variability of the sample allowed for the examination of the effectiveness of the dose–response exercise intervention. Another possible limitation could be the sensitivity of the $\dot{V}O_{2max}$ testing to detect a change between groups and over time; however, there were no significant differences between test 1 and test 2 at baseline or posttest, and the differences between test 1 and test 2 were significantly smaller than the difference between baseline and posttest (data not shown). Furthermore, the intraclass correlation was high at both time points (8). It is also important to note that due to the ramping protocol, participants in the 8- and the 12-kcal·kg^{-1}·wk^{-1} groups spent less time, 5 and 4 months rather than 6 months, at their maximum training volume. It is not expected that this difference would yield any meaningful differences in these findings. A strength of the DREW study is that it includes a large sample of sedentary, overweight, postmenopausal women. Additionally, the adherence to the tightly controlled and supervised exercise training was extremely high, and the attrition rate in all groups was low, maintaining adequate sample sizes within each group for these analyses. Another strength of this study was the dose–response exercise recommendation that allowed for the examination of nonresponse to exercise training in three different treatment groups.

In conclusion, initial levels of $\dot{V}O_{2max}$, volume of training, and age were significant predictors of $\dot{V}O_{2max}$ nonresponse following a training program in this sample of sedentary, overweight, postmenopausal women. Those women that were younger, less fit initially, or exercised more during the trial had greater odds of improving their $\dot{V}O_{2max}$ with training. The most important finding of this study, especially pertaining to future exercise program development, is that as women increase the volume of exercise, the more likely they were to improve their $\dot{V}O_{2max}$. Practically speaking, older, postmenopausal women continuing or beginning an exercise regimen interested in increasing aerobic fitness should consider increasing the total volume of exercise to increase the likelihood of reaching their goals. In this relatively homogeneous sample of women, race does not appear to have an influence on which participants improve with training and which do not. Future research should explore training programs of longer durations, diverse populations, and different intensities to better examine why some profiles of women appear to not respond to cardiorespiratory endurance training.

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