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Volume of Exercise and Fitness Non-Response in Sedentary, Post-Menopausal Women

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Abstract

There is a wide individual heterogeneity in the maximal aerobic fitness (VO_{2max}) response to exercise training.

Purpose—To examine predictors of VO_{2max} non-response following aerobic exercise training in post-menopausal 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 (45–75y). Participants were randomized to one of three exercise treatment groups (4, 8, or 12 kcal/kg per week) for six months. Participants exercised 3–4 days/week at 50% VO_{2max} . Predictors of baseline VO_{2max} were determined by ANOVA. We used a logistic regression analyses with categorical (ethnicity, treatment group) and standardized continuous variables (age, body mass index [BMI], baseline VO_{2max}) to determine predictors of non-response ($\Delta \leq 0$ L/min). Our analysis included 310 women, as the control group was excluded.

Results—A total of 44.9%, 23.8%, and 19.3% of the 4 kcal/kg per week, 8 kcal/kg per week, and 12 kcal/kg per week treatment groups ($p < 0.0001$), respectively, were non-responders. Maximal effort, BMI, age, and race significantly predicted baseline VO_{2max} . Treatment group (8 kcal/kg per week and 12 kcal/kg per week vs. 4 kcal/kg per week) ($p = 0.0003$), baseline VO_{2max} ($p < 0.0001$), and age ($p < 0.05$) were significant predictors of non-response. Odds ratios and 95% CI were 2.13 (1.53, 2.95) for baseline VO_{2max} ; 1.35 (1.00, 1.83) for age; 0.45 (0.24, 0.85) for the 8 kcal/kg per week vs. 4 kcal/kg per week group; and 0.27 (0.13, 0.53) for the 12 kcal/kg per week vs. 4 kcal/kg per week 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 non-responder.

Keywords

individual variability; trainability; aerobic training; dose-response

Introduction

Low levels of maximal aerobic fitness (VO_{2max}) are associated with a higher risk of mortality, and improvements in VO_{2max} are associated with lower mortality (2,3). Theoretically, if

untrained or sedentary individuals with initially low levels of $\text{VO}_{2\text{max}}$ are exposed to cardiorespiratory endurance training, $\text{VO}_{2\text{max}}$ 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 $\text{VO}_{2\text{max}}$ 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 non-response to training such that the older participants were less trainable than the younger (10) but there are contradictory reports (17). Since so few studies have examined this phenomenon, further investigation is warranted into possible phenotypes associated with lack of $\text{VO}_{2\text{max}}$ response to supervised exercise training.

The Dose-Response to Exercise in Women (DREW) study provides data on a large sample ($N=464$) of healthy, post-menopausal women who participated in a non-exercise control or one of three exercise treatments (4, 8, or 12 kcal/kg/wk) for six 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 $\text{VO}_{2\text{max}}$ non-response 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 $\text{VO}_{2\text{max}}$ non-response to six-months of cardiorespiratory endurance training in a sample of sedentary, post-menopausal 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 postmenopausal women aged 45 to 75 years 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/m²), postmenopausal, healthy and capable of engaging in the prescribed exercise training. Additionally, volunteers were sedentary (<35 kcal/kg/day in energy expenditure (1)) and had elevated blood pressure (SBP 125.0 to 159.0 mmHg). Women were excluded if they had significant cardiovascular disease or other significant medical disorders, elevated low-density lipoproteins, or had lost 20 pounds or more in the previous year (14).

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

Exercise Training

Following a pre-randomization 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 non-exercise 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 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 minutes of moderate-to-vigorous intensity physical activity most days of the week (15). We calculated that 8 kcal/kg per week 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/kg per wk group (i.e., 12 kcal/kg per week and 4 kcal/kg per week, respectively). The 4 kcal/kg per week was utilized 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/kg per week 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 six months, three to four days per week at a heart rate associated with 50% baseline $\text{VO}_{2\text{max}}$ 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/kg per week). 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/kg per week. Those assigned to the 4 kcal/kg per week group remained at this dose for the duration of the study while those assigned to the 8 and 12 kcal/kg per week groups increased their energy expenditure 1 kcal/kg per week until their assigned exercise level was reached. In a previous report, we examined if whether the potential for heart rate (HR) drift influenced participant workloads during their exercise sessions. In this paper, we reported no presence of HR drift, nor 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 post-training (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, mid-axillary, subscapular, abdominal, suprailiac, thigh, and calf) (14).

Fitness testing—The baseline and post-training $\text{VO}_{2\text{max}}$ 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). $\text{VO}_{2\text{max}}$ testing was conducted on a Lode Excalibur Sport cycle ergometer (Groningen, The Netherlands), an electronic, rate-independent ergometer. Participants exercised at 30 watts for 2 minutes, 50 watts for 4 minutes, followed by increases of 20 watts every 2 minutes until volitional fatigue (14). Gas exchange variables (VO_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 ($\text{VO}_{2\text{max}}$) in response to exercise training; therefore participants were excluded from the final data set if they were in the non-exercise 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 (post-training minus baseline values) for absolute $\text{VO}_{2\text{max}}$ (L/min) and participants were categorized as responders ($\Delta > 0$) or non-responders ($\Delta \leq 0$) to aerobic endurance training.

Means and standard deviations were calculated. One-way ANOVA and Chi-Square analyses were conducted to determine if there was a significant difference between treatment groups for baseline continuous and categorical variables, respectively. Determinants of $\text{VO}_{2\text{max}}$ prior to 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 standard deviation (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 2 fold increase in the odds of fitness non-response 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 standard deviation of the predictor variable. Forced-entry logistic regression was then used to determine which variables were significant predictors of fitness non-response for the total exercising sample, as well as for each individual treatment group. Variables of interest included: age, baseline fitness, ethnicity (White, Black, 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 $\text{VO}_{2\text{max}}$ (mL/kg/min) were significantly different across groups at baseline ($p<0.03$). The 4 kcal/kg per week group had significantly lower body fat percentage than the 8 kcal/kg per week group, and the 12 kcal/kg per week group had significantly higher relative $\text{VO}_{2\text{max}}$ than the 8 kcal/kg per week group. Average absolute baseline $\text{VO}_{2\text{max}}$ (L/min) was significantly different between ethnicities ($p<0.02$) such that blacks had lower baseline $\text{VO}_{2\text{max}}$ compared to whites. Smoking status and baseline daily step average were not significant predictors of baseline $\text{VO}_{2\text{max}}$ for the group. Significant positive determinants of absolute baseline $\text{VO}_{2\text{max}}$ 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 $\text{VO}_{2\text{max}}$). Age was a significantly negative determinant of baseline absolute $\text{VO}_{2\text{max}}$ (i.e., as age increased baseline $\text{VO}_{2\text{max}}$ decreased) in the ANOVA model ($p<0.0001$). Race was also a significant predictor of baseline $\text{VO}_{2\text{max}}$ in the model ($p<0.005$).

As was reported in a previous manuscript (8), we observed a significant difference in the mean absolute and relative $\text{VO}_{2\text{max}}$ response to training for all pair-wise treatment groups except 4 vs. 8 kcal/kg per week. For the 4 kcal/kg per week group ($n=138$), $\Delta \text{VO}_{2\text{max}}$ was 0.029 ± 0.144 (range -0.41 to 0.475) L/min; for the 8 kcal/kg per week group ($n=84$), $\Delta \text{VO}_{2\text{max}}$ was 0.088 ± 0.129 (range -0.21 to 0.485) L/min; and for the 12 kcal/kg per week group ($n=88$), $\Delta \text{VO}_{2\text{max}}$ was 0.106 ± 0.146 (range -0.28 to 0.605) L/min. The range in percent change in absolute $\text{VO}_{2\text{max}}$ for the 4, 8, and 12 kcal/kg per week groups were -33.2% to 76.0% , -25.2% to 41.7% , and -14.3% to 58.7% , respectively. Relative $\Delta \text{VO}_{2\text{max}}$ was 0.638 ± 1.867 for the 4 kcal/kg per week group, 1.460 ± 1.581 for the 8 kcal/kg per week group, and 1.554 ± 1.722 for the 12 kcal/kg per week group. Figure 1 depicts the heterogeneity of $\text{VO}_{2\text{max}}$ response to

training for the each treatment group (A–C). For the groups, 44.9%, 23.8%, and 19.3% of the 4 kcal/kg per week, 8 kcal/kg per week, and 12 kcal/kg per week groups ($p<0.0001$), respectively, were $\text{VO}_{2\text{max}}$ non-responders, meaning that 55.1%, 76.2%, and 80.7%, respectively, improved $\text{VO}_{2\text{max}}$ 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 post tests. RER was not significant in the preliminary analyses and was subsequently removed from later analyses. Possible predictors included in logistic regression model 1 were age, baseline $\text{VO}_{2\text{max}}$, BMI, ethnicity, and smoking status. Baseline absolute $\text{VO}_{2\text{max}}$ ($p<0.0001$), 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 $\text{VO}_{2\text{max}}$ was higher by 0.24 L/min, the odds of not responding to endurance training were approximately two times higher. Additionally, as age was 6.4 years higher the odds of non-response were by 45% higher. Finally, black participants are two times more likely to be non-responders when compared to 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 kcal/kg per week and 12 kcal/kg per week versus 4 kcal/kg per week) ($p=0.0003$), baseline absolute $\text{VO}_{2\text{max}}$ ($p<0.0001$), 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 $\text{VO}_{2\text{max}}$ was higher by 0.24 L/min, the odds of not responding to endurance training were over two fold higher. Additionally, as age was 6.4 years higher the odds of non-response were 35% higher. When the NIH recommendation treatment group (i.e., 8 kcal/kg per week) was compared to the group with the lowest volume of training (i.e., 4 kcal/kg per week) the likelihood of not responding to the training was 57% lower. Furthermore, in the highest volume group (12 kcal/kg per week) the likelihood of not responding to the exercise training were 74% lower when compared to 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 $\text{VO}_{2\text{max}}$, BMI, ethnicity, and smoking status. The only significant predictor in the 4 kcal/kg per week and 12 kcal/kg per week groups was standardized baseline $\text{VO}_{2\text{max}}$ ($p<0.002$, OR 2.40, 95% CI 1.41, 4.10; $p<0.005$, OR 4.00, 95% CI 1.53, 10.44, respectively). There were no significant predictors in the 8 kcal/kg per week group.

Discussion

The primary aim of our current analysis was to examine predictors of no change in maximal aerobic fitness ($\text{VO}_{2\text{max}}$) across different doses of cardiorespiratory endurance training in a sample of sedentary, overweight/obese, moderately hypertensive, post-menopausal women. Despite a high retention rate and uniform high compliance within each treatment group, there was a large amount of individual variability in response to exercise. The overall predictors of $\text{VO}_{2\text{max}}$ non-response to cardiorespiratory training were baseline $\text{VO}_{2\text{max}}$, age, and volume of training, with those groups exercising for longer durations (all participants exercised at the same intensity) having a lower prevalence of non-response 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 $\text{VO}_{2\text{max}}$

significantly decreases. Additionally, on the individual level there was a decrease in prevalence of non-response 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 non-responders to the exercise training but that varying between treatment groups. While few studies have examined the response to exercise in this manner, those studies that have do not show such a large proportion of non-responsive individuals (5,9). This phenomenon may be due to the uniqueness of the study design and training protocol. All DREW participants exercised at a heart rate established intensity corresponding to 50% of baseline $\text{VO}_{2\text{max}}$. Participants in other trials exercised between 70–85% $\text{VO}_{2\text{max}}$ (6,9,11). The higher intensity of these other trials may partially explain the discrepancy in the proportion of non-responders between our trial and previous studies. Nonetheless, while the exercise prescription in our current study was lower than in other studies, it was of a significant intensity to increase $\text{VO}_{2\text{max}}$ in most participants. The increase in $\text{VO}_{2\text{max}}$ was especially strong in the group that exercised 50% above the current recommendation (i.e., 192 minutes/week (8)).

In contrast to our findings, the HERITAGE Family Study (7) did not find initial $\text{VO}_{2\text{max}}$ to be a significant predictor of heterogeneity of response. A trend towards the significance of initial $\text{VO}_{2\text{max}}$ was reported in another trial of older adults (11) and 30 to 40 year old men (16) however, the HERITAGE Family Study had the largest sample size of the trials examining non-response to training. Volume of exercise was a significant predictor in the DREW trial meaning that those exercising at a level of 8 kcal/kg per week were 55% more likely to increase their $\text{VO}_{2\text{max}}$ than participants exercising at 4 kcal/kg per week. Furthermore, those in the 12 kcal/kg per week were 87% more likely to increase their $\text{VO}_{2\text{max}}$ than the 4 kcal/kg per week group. These findings are in contrast to an 8 week aerobic exercise trial in men where no difference was found between moderate and high volume treatment groups (10). Specifically, Hautala et al. (n=39), the men in the moderate group engaged in 180 minutes of exercise at 70–80% heart rate max per week. This level of exercise corresponds well with the highest dose group in our current cohort who exercised approximately 192 minutes per week or exercise at 50% $\text{VO}_{2\text{max}}$ (8). Kohrt et al. (11) also examined this issue by separating participants into quartiles based on percent improvement in $\text{VO}_{2\text{max}}$. 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 non-response 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 $\text{VO}_{2\text{max}}$ 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 post-test and the differences between test 1 and 2 were significantly smaller than the difference between baseline and post test (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 12 kcal/kg per week groups spent less time, five and four months rather than six, 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, post-menopausal 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 non-response to exercise training in three different treatment groups.

In conclusion, initial levels of $\text{VO}_{2\text{max}}$, volume of training, and age were significant predictors of $\text{VO}_{2\text{max}}$ non-response following a training program in this sample of sedentary, overweight, post-menopausal women. Those women that were younger, less fit initially or exercised more during the trial had greater odds of improving their $\text{VO}_{2\text{max}}$ 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 $\text{VO}_{2\text{max}}$. 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 in order to better examine why some profiles of women appear to not respond to cardiorespiratory endurance training.

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References

1. Blair SN, Haskell WL, Ho P, Paffenbarger RS Jr, Vranizan KM, Farquhar JW, Wood PD. Assessment of habitual physical activity by a seven-day recall in a community survey and controlled experiments. *Am J Epidemiol* 1985;122:794–804. [PubMed: 3876763]
2. Blair SN, Kampert JB, Kohl HW 3rd, Barlow CE, Macera CA, Paffenbarger RS Jr, Gibbons LW. Influences of cardiorespiratory fitness and other precursors on cardiovascular disease and all-cause mortality in men and women. *Jama* 1996;276:205–210. [PubMed: 8667564]
3. Blair SN, Kohl HW 3rd, Barlow CE, Paffenbarger RS Jr, Gibbons LW, Macera CA. Changes in physical fitness and all-cause mortality. A prospective study of healthy and unhealthy men. *Jama* 1995;273:1093–1098. [PubMed: 7707596]
4. Bouchard, C. Human adaptability may have a genetic basis. In: Landry, F., editor. Health risk estimation, risk reduction and health promotion; Proceedings of the 18th annual meeting of the Society of Prospective Medicine; Ottawa: Canadian Public Health Association; 1983. p. 463–476.
5. Bouchard C, An P, Rice T, Skinner JS, Wilmore JH, Gagnon J, Perusse L, Leon AS, Rao DC. Familial aggregation of $\text{VO}_{2\text{max}}$ response to exercise training: results from the HERITAGE Family Study. *J Appl Physiol* 1999;87:1003–1008. [PubMed: 10484570]
6. 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;27:721–729. [PubMed: 7674877]
7. Bouchard C, Rankinen T. Individual differences in response to regular physical activity. *Med Sci Sports Exerc* 2001;33:S446–S451. [PubMed: 11427769]discussion S452–443
8. Church TS, Earnest CP, Skinner JS, Blair SN. Effects of different doses of physical activity on cardiorespiratory fitness among sedentary, overweight or obese postmenopausal women with elevated blood pressure: a randomized controlled trial. *Jama* 2007;297:2081–2091. [PubMed: 17507344]
9. Hautala AJ, Kiviniemi AM, Makikallio TH, Kinnunen H, Nissila S, Huikuri HV, Tulppo MP. Individual differences in the responses to endurance and resistance training. *Eur J Appl Physiol* 2006;96:535–542. [PubMed: 16369817]

10. Hautala AJ, Makikallio TH, Kiviniemi A, Laukkanen RT, Nissila S, Huikuri HV, Tulppo MP. Cardiovascular autonomic function correlates with the response to aerobic training in healthy sedentary subjects. *Am J Physiol Heart Circ Physiol* 2003;285:H1747–H1752. [PubMed: 12816748]
11. Kohrt WM, Malley MT, Coggan AR, Spina RJ, Ogawa T, Ehsani AA, Bourey RE, Martin WH 3rd, Holloszy JO. Effects of gender, age, and fitness level on response of VO₂max to training in 60–71 yr olds. *J Appl Physiol* 1991;71:2004–2011. [PubMed: 1761503]
12. Lortie G, JA S, Hamel P, Boulay MR, Landry F, Bouchard C. Responses of maximal aerobic power and capacity to aerobic training. *Int J Sports Med* 1984;5:232–236. [PubMed: 6500788]
13. Mikus CR, Earnest CP, Blair SN, Church TS. Heart Rate Response to Prolonged Exercise in Post-Menopausal Women: The DREW Study. *British Journal of Sports Medicine*. 2008in press
14. Morss GM, Jordan AN, Skinner JS, Dunn AL, Church TS, Earnest CP, Kampert JB, Jurca R, Blair SN. Dose Response to Exercise in Women aged 45–75 yr (DREW): design and rationale. *Med Sci Sports Exerc* 2004;36:336–344. [PubMed: 14767260]
15. NIH. Physical activity and cardiovascular health. NIH Consensus Development Panel on Physical Activity and Cardiovascular Health. *Jama* 1996;276:241–246. [PubMed: 8667571]
16. Pollock ML, Ward A, Ayres JJ. Cardiorespiratory fitness: response to differing intensities and durations of training. *Arch Phys Med Rehabil* 1977;58:467–473. [PubMed: 931584]
17. Skinner JS, Jaskolski A, Jaskolska A, Krasnoff J, Gagnon J, Leon AS, Rao DC, Wilmore JH, Bouchard C. Age, sex, race, initial fitness, and response to training: the HERITAGE Family Study. *J Appl Physiol* 2001;90:1770–1776. [PubMed: 11299267]
18. Wilmore JH, Green JS, Stanforth PR, Gagnon J, Rankinen T, Leon AS, Rao DC, Skinner JS, Bouchard C. Relationship of changes in maximal and submaximal aerobic fitness to changes in cardiovascular disease and non-insulin-dependent diabetes mellitus risk factors with endurance training: the HERITAGE Family Study. *Metabolism* 2001;50:1255–1263. [PubMed: 11699041]

A) 4 kcal/kg per week treatment group

B) 8 kcal/kg per week treatment group

C) 12 kcal/kg per week treatment group

Figure 1. Individual variability in absolute VO₂ response to exercise training by treatment group

Table 1

Baseline characteristics of study participants (N = 310) by treatment group

Variables	4 kcal/kg per week (n=138)	8 kcal/kg per week (n=84)	12 kcal/kg per week (n=88)
Age (yrs)	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 non-response ($\Delta \leq 0$ L/min)	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/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
VO _{2max} (L/min)	1.3 ± 0.3	1.3 ± 0.2	1.3 ± 0.2
VO _{2max} (mL/kg/min)	15.4 ± 3.0	14.9 ± 2.3 [§]	16.1 ± 3.0 [§]
Resting Heart Rate (BMP)	65.0 ± 7.7	67.1 ± 8.9	65.0 ± 7.3
Steps/day	4792 ± 1870	4787 ± 1881	5095 ± 1830
Energy intake (kcal/day)	2186 ± 978	2304 ± 959	2287 ± 1073
Beers/week (12 oz)	0.8 ± 1.1	0.7 ± 0.8	1.0 ± 1.4
Wine/week (5oz)	2.2 ± 2.1	1.6 ± 2.1	2.7 ± 2.8
Shots/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%

ns

Data presented as mean ± SD or frequency (%)

[§]Significant differences between groups (p<0.05)

Table 2

Odds ratios for predictors of non-response with all continuous variables standardized to mean of zero and unit standard deviation.

Variable	SD unit	Model 1		Model 2	
		OR	95% CI	OR	95% CI
Baseline VO _{2max}	0.24 L/min	2.01	(1.47, 2.74) [§]	2.10	(1.52, 2.91) [§]
Age	6.4 yrs	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/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 KKW vs. 4 KKW)				0.43	(0.23, 0.80) [§]
Treatment (12 KKW vs. 4 KKW)				0.26	(0.13, 0.51) [§]

Significant predictors (p<0.05) are noted with

[§] Predictors included in Model 1: age, baseline VO_{2max}, age of menopause, ethnicity, BMI, and smoking status. Predictors included in Model 2: age, baseline VO_{2max}, age of menopause, ethnicity, BMI, smoking status, and treatment group assignment. 4 KKW Group was the referent group in Model 2. KKW = kcal/kg per week.