Supervised, Vigorous Intensity Exercise Intervention for Depressed Female Smokers: A Pilot Study

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Clinical Trials Registration: NCT01860924

Text word count: 3,480

Tables: 2

Figures: 3

Supplemental Material: intervention manual

Abstract

Introduction. Few studies have evaluated exercise interventions for smokers with depression or other psychiatric comorbidities. This pilot study evaluated the potential role of supervised vigorous exercise as a smoking cessation intervention for depressed females.

Methods. Thirty adult women with moderate-severe depressive symptoms were enrolled and randomly assigned to 12 weeks of thrice weekly, in person sessions of vigorous intensity supervised exercise at a YMCA setting (EX; n=15) or health education (HE; n=15). All participants received behavioral smoking cessation counseling and nicotine patch therapy. Assessments were done in person at baseline, at the end of 12 weeks of treatment, and at 6 months post target-quit-date. Primary endpoints were exercise adherence (proportion of 36 sessions attended) and biochemically confirmed 7-day point prevalence abstinence at Week 12. Biomarkers of inflammation were explored for differences between treatment groups and between women continuing to smoke and those who quit at Week 12.

Results. Treatment adherence was high for both groups (66% for HE and 72% for EX; p=0.55). The week 123 smoking abstinence rate was higher for EX than HE (11/15 [73%] vs. 5/15 [33%]; p=0.028), but no significant differences emerged at 6-month follow-up. Interlukin (IL6) levels increased more for smokers compared with those abstinent at Week 12 (p=0.040).

Conclusions. Vigorous intensity supervised exercise is feasible and enhances smoking cessation among depressed female smokers. Innovative and cost-effective strategies to bolster long-term exercise adherence and smoking cessation need evaluation in this population. Inflammatory biomarkers could be examined in future research as mediators of treatment efficacy.

Implications

This preliminary study found that vigorous intensity supervised exercise is feasible and enhances smoking cessation among depressed female smokers. This research addressed an important gap in the field. Despite decades of research examining exercise interventions for smoking cessation, few studies were done among depressed smokers or those with comorbid psychiatric disorders. A novel finding was increases in levels of a pro-inflammatory biomarker observed among women who continued to smoke after the intervention compared to those who did not.

Introduction

In 2014, the prevalence of cigarette smoking among United States women was 14.8%.[1] Women have lower quit rates than men.[2,3] Also, women smokers tend to have higher levels of depression than non-smokers[4] and smokers with elevated depressive symptoms have poorer smoking treatment outcomes.[5-7] Thus, designing effective smoking cessation interventions for women with depression – a tobacco use disparity group – is a public health priority.[8,9] Few studies have targeted smokers with current depression and, aside from our pilot study,[10] none of these targeted women specifically.[11-15] This pilot study evaluated the potential role of supervised vigorous exercise as a smoking cessation intervention for depressed females.

A recent Cochrane review of 20 randomized trials concluded there was little evidence that exercise was effective as a smoking cessation intervention.[16] These trials were limited by small sample sizes, inadequate control groups, interventions of insufficient exercise intensity, and a lack of support being provided to ensure adherence to the exercise intervention. The only trial to show a long-term effect on smoking abstinence targeted women using 12-weeks of thrice weekly, supervised vigorous intensity exercise;[17] an intervention also effective for treating depression.[18] When this treatment was translated to a community YMCA setting and streamlined to four supervised exercise sessions, it was not effective for smoking cessation and there was poor adherence to exercise.[19] Similarly, two studies of exercise counseling encouraging home-based exercise for depressed smokers found no effect on smoking abstinence compared with a health education contact control group.[10,11]

A supervised exercise program has the potential to benefit depressed smokers by providing reinforcement, guidance, and support for exercise; thus improving adherence.[16] In this study we piloted the feasibility, acceptability and potential efficacy of a supervised, vigorous

intensity exercise intervention for smoking cessation in a community YMCA setting among depressed females. An exploratory aim was to examine potential biological impact of treatment response, through assessment of the intervention (exercise), and smoking cessation outcome on biomarkers of inflammation.

Methods

The study was approved by the Mayo Clinic Institutional Review Board, and registered with clinicaltrials.gov (NCT01860924). Data were collected from September, 2013-April, 2015.

Participants

A sample size of 30 was deemed sufficient to determine the intervention's feasibility with respect to adherence to the exercise treatment protocol.[20-22] The study was not powered to detect significant differences in smoking abstinence rates, but we sought to obtain estimates of the intervention effect towards planning a definitive trial. A doubling of the abstinence rate for the intervention vs. control condition at end-of-treatment was considered to be of clinical significance and warrant proceeding to an efficacy trial.[23]

Participants were recruited by provider referrals and flyers posted in the clinic, and radio and newspaper advertisements. Initial screening was completed by telephone. Eligible women were asked to complete an in-person screening assessment. After obtaining written informed consent, the study coordinator administered the MINI International Neuropsychiatric Interview,[24] to rule out bipolar and thought disorders. Participants then completed a urine pregnancy test and provided height and weight.

If eligible, individuals completed a baseline self-report questionnaire and exercise testing.[25] Potential participants received the Modular Signal Recorder (MSR) accelerometer to

wear for at least four days and return in a pre-paid envelope. If the MSR was returned, the participant was enrolled.

Eligibility criteria were: female, aged 18-55 years, smoked ≥ 10 cigarettes a day for at least the past year, willing to make a quit attempt, currently depressed defined by a clinical cut-off score of ≥16 on the 10-item Center for Epidemiological Studies Depression Scale corresponding to moderate-severe depression (CES-D),[26] not currently meeting the ACSM guidelines for exercise,[27] willing and able to participate in all aspects of the study, provide written informed consent, and if using antidepressant medication, no changes in dose or type of medication during the past three months. Exclusionary criteria were: positive pregnancy test (urine dipstick test), currently breastfeeding, or planning to become pregnant during the nicotine patch study phase, physical limitations to participate in vigorous intensity exercise or sub-maximal exercise testing (PAR-Q),[28] current use (past three months) of smokeless tobacco products, or stop smoking medications or behavioral treatments, any medical condition precluding nicotine patch use, current or lifetime DSM-IV diagnosis of bipolar disorder, schizophrenia/other major thought disorder, and another person from the same household had enrolled. There was no upper cutoff for body mass index (BMI) if no other cardiovascular risk factors were present if BMI was ≥30.

One hundred five individuals were screened by telephone, of which 30 (29%) were enrolled (Figure 1). Sixty-two of those not enrolled did not meet the study eligibility criteria and the primary reason was a CES-D score <16 (38/62, 61%). Others were medical exclusions (n=8), smoked infrequently (n=6), recent change in antidepressant medication (n=2), age (n=5), too physically active (n=1), or distance from exercise facility (n=2). Women not enrolled were given referral resources.

Procedures

We used a randomized, two-group design with assessments completed at baseline, after 12 weeks of treatment, and at six months post-target quit date (TQD). Participants were stratified according to current depression severity (baseline Patient Health Questionnaire [PHQ-9][29] score: mild/moderate vs. severe) and antidepressant medication use (yes/no) and randomly assigned to the exercise intervention group (EX, N=15) or to the health education contact control group (HE, N=15). The conditions were matched for wellness coach contact time and duration of treatment. Allocation to treatment conditions was unknown to the study staff or investigators prior to assignment, and participants completed baseline assessments prior to being informed of their allocation to treatment condition. A study coordinator blinded to allocation group conducted all follow-ups in-person. Participants received $25 for completing the baseline assessment and $50 after completing each follow-up. All participants received a free 6-month YMCA membership (HE participants received this after the final assessment).

For the biomarker analysis, participants were also asked for their written informed consent to provide a blood sample during the baseline visit and again at Week 12. A participant's decision to participate in this aspect of the study did not affect enrollment in the pilot trial. All 30 enrolled women provided consent to participate. They received an additional $25 for providing a blood sample at baseline and $50 for providing the Week 12 sample.

Interventions

For both conditions, the 12-week program comprised three 30-40 minutes individual-based sessions per week delivered by wellness coaches.[30-32] At one session each week, participants received 15-20 minutes of smoking cessation counseling.

Smoking cessation counseling and pharmacotherapy

The cessation counseling[33] was identical for both conditions, except that for HE participants the use of exercise was not discussed as a strategy for managing depression, craving, or withdrawal symptoms. At Weeks 2 and 6, participants were mailed a 4-week supply of nicotine patches. The TQD was the first session of Week 3. At this visit, participants received instructions on using the patch. Patch dosing consisted of 21 mg/24 hours for four weeks, 14 mg/24hrs for two weeks, then 7 mg/24 hours for two weeks.[33] Dosing was tailored based on cigarette consumption. Each week during the treatment phase, the coach assessed participants for side effects and adverse events associated with patch therapy, depressive symptoms and suicidality.

HE

Lectures, handouts, films, and discussions covered various women's health and lifestyle issues, as used in previous trials.[10,17] Attendance was recorded and missed appointments were re-scheduled.

EX

The intervention was identical on exercise duration and intensity to that of Marcus and colleagues.[17] The intervention manual (see supplemental material) incorporated language based on a study of consumer preferences for exercise interventions conducted among adults with a depression history.[34]

All EX sessions were held at the YMCA, with the exception of four sessions which were conducted at a worksite fitness center. Participants engaged in exercise during each session and were encouraged to attend the YMCA on other days and/or to exercise at home. Attendance was documented and missed appointments were re-scheduled.

Exercise was gradually progressed from moderate to vigorous intensity.[27] Target heart rates (using heart rate reserve) were determined from the baseline VO2 maximal exercise test.[25] Participants were instructed to work at a Rating of Perceived Exertion (RPE)[35] of somewhat hard to hard, corresponding to moderate-vigorous intensity;[25] RPE was monitored.

Participants exercised on cardiovascular equipment of their choice and received supervision, reinforcement, and counseling from the coach. Sessions comprised of a 5-minute warm-up, 20-30 minutes of aerobic activity, and a 5-minute cool down with stretching.[17] To reduce the time, the coach delivered the exercise counseling while the participant was engaged in exercise.[36] The counseling included social cognitive theory-based[37] assessment and problem-solving of exercise barriers, reinforcement (shaping) of exercise, and methods to enhance exercise self-efficacy – including guidance on exercise technique, intensity, and positive feedback[30,38,39] delivered using a motivational interviewing counseling style. At the first session, participants were given a Kinetic Activity Monitor (KAM®).[40] The KAM® is worn on the waist and provided feedback to participants on activity increases above resting metabolic rate, activity duration, and number of calories expended.

Wellness coaches, training, and treatment fidelity

The interventions were delivered by female ACSM-certified wellness coaches with a master's degree in clinical psychology (HE) or bachelors' degree in health education (EX). Coaches received six hours of training on the treatment protocols. Coaches used a written treatment manual containing an outline/script and checklist of critical topics to be covered.[41] All sessions were audiotaped and reviewed with the coaches during weekly meetings to reinforce treatment fidelity, provide feedback, and conduct additional training. Fifteen percent of the sessions were randomly selected to be checked for the proportion of intended topics that were delivered.[42]

Coach adherence to the HE and EX manuals was 90% and 95% respectively, indicating high fidelity.

Biomarker Methodology

Laboratory analysis of inflammatory markers was conducted at the Mayo Clinic Translational Neuroscience Laboratory (Tye). Peripheral blood samples (5 mL) were collected from participants at the CRU and centrifuged immediately at 2,500 rpm for ten minutes. Serum was stored at -80˚ C for analysis. Serum levels of pro-inflammatory cytokines interleukin-6 (IL-6), tumor necrosis TNF-α and CRP serum levels were determined using commercially available enzyme-linked immunosorbent assays (ELISAs) in accordance with manufacture instructions (Life Technologies, NY).

Measures

Baseline characteristics

A baseline questionnaire documented age, race/ethnicity, marital status, and education as well as Fagerström Test for Cigarette Dependence score.[43]

Feasibility

Data related to participant recruitment were collected, including the number of potential participants screened, and the number excluded for each of the specific inclusion/exclusion criteria. Study retention was based on the proportion of enrolled women completing follow-up assessments. Treatment adherence was based on the proportion of 36 sessions completed.

Treatment acceptability

At Week 12, participants completed the 10-item validated Consultation and Relational Empathy (CARE) measure to assess satisfaction with the coach.[44] Each item was rated on a 5-point scale ranging from poor to excellent (range 10-50). At six months, participants were asked if they

would recommend the program to depressed women interested in quitting smoking (options: definitely would, probably would, unsure, probably would not, and definitely would not).

Smoking status

Seven-day point-prevalence, self-reported cigarette smoking status was obtained at Week 12 and at six month follow-up.[33] A saliva sample was collected at each time point for cotinine analysis[45] using NicAlert test strips. We assessed use of nicotine replacement therapy because use would elevate the cotinine concentrations. At each time point, participants who self-reported no cigarette smoking (not even a puff) in the last seven days confirmed with a cotinine test strip value of 0 or 1 were classified as non-smokers.[45,46]

Cardiorespiratory fitness

Changes in cardio-respiratory fitness by treatment group served as a manipulation check. At baseline and Week 12, all participants underwent a symptom limited incremental treadmill test using the Bruce protocol.[25] Participants were encouraged to continue the exercise protocol to maximal exertion, confirmed by a RPE of $\geq$17 on the Borg (6-20) scale or a respiratory exchange ratio (RER) of $\geq$1.10. Oxygen consumed (VO_2), carbon dioxide produced (VCO_2), and minute ventilation (V_E) were measured by mouth piece and pneumotachograph (MedGraphics, St. Paul, MN) throughout exercise.[47,48] The RER was calculated as VCO_2/VO_2. Manual volume calibration was performed with a 3 L syringe and gas calibration was performed with manufacturer-recommended gases of known concentration. All calibration procedures were accomplished immediately prior to each test. Data were averaged over the last 30 seconds of each stage. Peak VO_2 was defined as the mean of the last 30 seconds of the exercise test.

Physical activity

At baseline and the week after the last (Week 12) intervention session participants were asked to wear the MSR (model 145) accelerometer, a miniature universal data logger validated for objective physical activity assessment.[49] Participants were asked to wear the device on a belt placed on their lower back during waking hours; four days of at least ten hours of wear was required for a valid assessment. Participants returned the device using a postage-paid envelope. MSR counts of total physical activity and sedentary time were summarized.

Body mass index (BMI)

Height and weight were recorded at baseline and at Week 12 using a calibrated scale.

Depressive symptoms

The PHQ-9 was used to assess depressive symptoms at baseline and at Week 12. This brief self-report measure has been extensively validated[29,50] and has excellent test-retest reliability (r=0.96) over a one-week period among samples of untreated patients.[51,52]

Non-study treatments

At Week 12 and six month follow-up, the study coordinator assessed participant use of concomitant stop smoking medication, antidepressant medication, and other depression treatment.

Statistical Methods

To assess the adequacy of the randomization, demographics were compared between treatment groups using the chi-square test for categorical variables or the two-sample t-test/rank sum test for continuous variables. The percentage of enrolled participants who completed the six month follow-up assessment (i.e., study retention) was compared between treatment conditions using the chi-square test (Fisher's exact test). The mean number of treatment sessions attended was

compared across treatment conditions using a two-sample t-test (rank-sum). Indices of treatment acceptability were compared across treatment conditions using the chi-square test for program recommendation and the two-sample t-test (rank-sum) for CARE scores. The effect of treatment group on PHQ-9 score, BMI, cardiorespiratory fitness, and MSR total physical activity and sedentary time at Week 12 was evaluated using ANCOVA with the baseline score/value as a covariate.

The biochemically confirmed seven-day point prevalence smoking abstinence rate at Week 12 and six month follow-up was summarized for each group (point estimate and 95% CI) and compared between treatment groups using a chi-square test (Fisher's exact test). Using an intent-to-treat approach,[53] missing data were classified as smoking. Analyses also controlled for the stratification variables (PHQ-9 depression severity, antidepressant medication use).

A two-way ANOVA was used to determine the impact of the exercise intervention and participants' Week 12 smoking status on CRP, TNF-α and IL6 levels. Outliers >2 SD from the mean were excluded and significance was set as $p<0.05$.

Results

Participants

Tables 1 and 2 show the baseline characteristics by study condition. Participants were primarily White, college-educated, middle-aged women with obesity and about half were taking antidepressant medication. Baseline characteristics were comparable across treatment groups.

Feasibility

Figure 1 summarizes treatment completion and follow-up information. Treatment adherence was high in both groups. HE participants completed a mean (SD)=24.0 (10.0) sessions (range 5-36) and EX participants completed a mean of 26.0 (10.0) sessions (range 5-36), p=0.55. The average

proportion of sessions attended was 66% for HE participants and 72% for EX. Retention was also good, with 87% (13/15) of participants in both groups completing the six-month assessment.

Treatment acceptability

Satisfaction with the counseling provided by the coach was high for both treatment groups (mean CARE score = 38.0 ± 4.0 [range 30-40] for HE vs. 39.0 ± 3.0 [range 30-41] for EX, p=0.52). All participants in HE and 92% of participants in EX indicated they would "definitely" recommend the program to another female smoker with depression, p=0.31.

Smoking status

Based on intent-to-treat analysis, as expected, the EX condition was associated with significantly higher biochemically verified smoking abstinence rates (73% [11/15]) compared to HE (33% [5/15]) at Week 12; $\chi 2=4.821$, $df=1$, $p=0.028$ (Figure 2). No statistically significant differences between groups were detected at six-month follow-up (27% [4/15] for EX vs. 40% [6/15] for HE); $\chi 2=0.600$, $df=1$, p=0.439. When adjusted for PHQ-9 score and antidepressant medication use, $p=0.035$ at Week 12 and $p=0.48$ at six-month follow-up.

No participants reported engaging in non-study depression or smoking cessation treatments or changes in their medical or psychological depression treatment at Week 12. At six-months, two participants in each group reported change in their depression treatment.

Cardiorespiratory fitness

After adjusting for baseline assessment, cardio-respiratory fitness (V02 max) was, as expected, greater for EX than HE participants at Week 12 (p=0.002; see Table 2).

BMI, physical activity, and depression

None of the additional outcome measures were significantly different for EX compared with HE Week 12 (Table 2).

Inflammation biomarkers

No significant group or interaction effect was observed for CRP, TNF-α or IL6 for intervention and smoking status pre- and post-intervention (data not shown). When individual differences in biomarkers were compared (Week 12 minus baseline level), a significant group effect was observed for IL6 dependent on smoking status. As illustrated in Figure 3, IL6 levels increased significantly more ($F [1, 9] = 5.631$; $p = 0.04$) for smokers compared with those who quit at Week 12. A small portion of subjects had levels below detectable limits (no difference between groups).

Discussion

Vigorous intensity supervised exercise is feasible and enhances smoking cessation among depressed female smokers. This study addressed an important gap in the field. Little previous work[10,11] evaluated exercise interventions for smoking cessation among depressed smokers or those with comorbid psychiatric disorders.[16] Observed increases in cardiorespiratory fitness for EX participants compared with HE confirmed the study conditions were implemented as intended. Strengths of the study are developing the intervention with advice from community women, use of an experimental design with a credible active contact-control group, and inclusion of pharmacotherapy for both groups. The interventions were well-specified in treatment manuals and delivered with high fidelity. Also, the exercise intervention was implemented in a community YMCA setting, enhancing external validity.

The exercise intervention appeared to benefit women only as long as it was active. YMCA data indicated that only two women in the exercise condition attended that facility after Week 12; of these, one exercised twice, another exercised 47 times. Thus, a key challenge for the field is to discover innovative and cost effective strategies to bolster long-term adherence, while

considering that supervised exercise is associated with better outcomes in studies of both depression[54] and smoking cessation (see also Ussher et al.[16] for review).[55,56] Possible strategies include utilizing fitness trainers at the YMCA to reinforce participants for attendance and provide some level of supervised exercise, providing coach feedback and support via mobile technology such as text messaging or through newly available accelerometers that connect users,[57,58] or tapping into natural support networks such as asking participants to bring someone with them to exercise.

The reasons why the intervention did not differentially impact depressive symptoms are unclear especially given that exercise adherence was high and increase in cardiorespiratory fitness was achieved. However, over half of the sample was already being treated for depression with an antidepressant medication, limiting potential impact of exercise on depression severity. Additionally, we did not assess mood/depressive symptoms prior to enrollment, or if the women had treatment resistant depression. Over a 12-week intervention period, no participants reported changes in their depression treatment and only four reported such changes at six months, which could indicate they were functioning well despite ongoing or stable depressive symptoms.

A novel finding indicates that IL6 levels were significantly elevated at Week 12, relative to baseline, for those women who continued smoking compared with those who quit. This preliminary evidence for increases in IL6 could be explored further in larger samples as a potential biological mediator of treatment efficacy.[59,60] Although an interaction effect for smoking status by treatment was not observed, given the small sample size and with only one individual in EX continuing to smoke it is not possible to draw any clear conclusions at this stage.

This pilot has a number of shortcomings that should be noted. Like most pilot trials, the study findings are limited by the small sample size; however, considering the statistically significant results in some of our key variables, the findings are encouraging. Moreover, characteristics of our sample: women only, primarily Caucasian race and more severe depressive symptomatology, limit the generalizability. We inadvertently missed a substantial number of women who would have been eligible to participate if we used a less conservative CESD-10 cutoff score of 10 recommended for general population samples. Two-thirds (38/62) of those screened but not eligible had a score of at least 10 but not as high as 16. Thus, in our definitive study which we plan, increasing the range of depressive symptoms among enrolled women and inclusion of a more diverse sample could substantially extend the reach of the exercise intervention.[61] Despite these limitations, there is potential benefit of sustained, supportive, supervised exercise intervention for smoking cessation in depressed women, and this study points to new directions for future research.

Funding

This study was supported by CTSA Grant Number **UL1 TR000135** from the National Center for Advancing Translational Sciences (NCATS), a component of the National Institutes of Health (NIH). Its contents are solely the responsibility of the authors and do not necessarily represent the official view of NIH. Funding for this study was also provided by a Mayo Clinic NIH-relief award, and a small grant award from the Department of Psychiatry and Psychology.

Declaration of Interests

None declared.

Acknowledgements

From Mayo Clinic, we acknowledge Julie Hathoway, Debi Judy, Marcelo Hanza, Christina Smith, Keagan McPherson, and Devika Basu for assistance with implementation of the study; Gabriel Koepp and Graham Moore for analysis of the accelerometer data; and Katheryn Wininger, J. Blair Price, and Shari Sutor for assistance with biospecimen sample processing and data analysis; and the Center for Clinical and Translational Science Clinical Research Unit staff for assistance with exercise testing and other measures. We also acknowledge the YMCA staff for assistance with implementing the exercise intervention. We would also like to thank the women who participated in the study.

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Figure Legends

Fig. 1: Participant flow.

Fig. 2: Percentage of participants with biochemically confirmed, 7-day point prevalence smoking abstinence at the end of 12 weeks of treatment and six month follow-up by treatment group.

Fig. 3: Change in levels of IL-6 from baseline to end of treatment by study group.

Table 1. Participant Baseline Characteristics by Treatment Group (N=30)

	Health Education Control (N=15)	Exercise Intervention (N=15)	p value*
Age	38.0 ± 11.0	37.0 ± 10.0	0.77
Range	21-53	25-53	
Married/lives with partner	7 (47)	5 (34)	0.72
White	14 (93)	13 (87)	0.54
Education			0.72
High school	1 (7)	2 (13)	
College	12 (80)	12 (80)	
Graduate school	2 (13)	1 (7)	
Employed	13 (87)	9 (60)	0.10
Time to first cigarette ≤ 5 minutes (FTCD)	6 (40)	7 (47)	0.84
FTCD total score	4.2 ± 2.0	4.7 ± 2.2	0.55
Range	1-7	0-8	
Taking antidepressant medication	8 (53)	9 (60)	0.71
Current psychiatric diagnosis (e.g., anxiety or depressive disorder)	5 (33)	6 (40)	0.70

FTCD = Fagerström Test for Cigarette Dependence. Possible scores range from 0-10.

*Two sample t-test or chi-square test as appropriate. Data are reported as n (%) or mean ± SD as appropriate.

Table 2. Baseline and End of Treatment (Week 12) Outcomes by Treatment Group

	Baseline[a]		Week 12		
Measure	Health Education Control	Exercise Intervention	Health Education Control	Exercise Intervention	p value[b]
PHQ-9 score					
(depression)	11.6 ± 4.0	11.7 ± 5.4	7.0 ± 5.1	7.4 ± 4.5	0.90
Range	3-18	4-22	0-17	3-17	
Body Mass Index	30.0 ± 9.0	31.0 ± 7.0	30.0 ± 9.0	31.0 ± 8.0	0.77
Range	19-45	21-42	19-48	21-44	
V02 max[c]	25.0 ± 5.0	24.0 ± 5.0	24.0 ± 4.0	29.0 ± 6.0	0.002
Range	17-37	13-33	20-32	20-39	
V02 max predicted[d]	98.0 ± 14.0	95.0 ± 19.0	97.0 ± 15.0	110.0 ± 16.0	0.002
Range	74-125	49-122	66-123	74-129	
Overall physical					0.94
activity[e]	11452 ± 1687	12133 ± 3581	10924 ± 2057	11459 ± 4545	
Range	9192-13016	7784-20304	8013-15127	7338-23664	

	Baseline[a]		Week 12		
Measure	Health Education Control	Exercise Intervention	Health Education Control	Exercise Intervention	p value[b]
Sedentary time[e]	327.2 ± 92.6	319.6 ± 131.6	286.6 ± 96.7	257.4 ± 114.0	0.56
Range	202-469	146-513	154-477	92-435	

Note. For each treatment group N=15 at Baseline and N=13 at Week 12. Data are reported as mean ± SD.

[a]P values ≥ 0.05 for all variables when comparing health education and exercise interventions on the baseline assessment using a two sample t-test.

[b]Analysis of Covariance (ANCOVA) assessing change in measures. For these analyses, the week 12 assessment was the dependent variable and treatment group and the baseline assessment were the independent variables.

[c]Volume of oxygen consumed in mLs of oxygen per kilogram of body weight per minute.

[d]The prediction equation accounts for participant age.

[e]Data generated from Modular Signal Recorder (MSR) accelerometer.