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A Comparison of Two Different Types of High Intensity Interval Training on Cardiometabolic Health in Overweight/Obese Women

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UNIVERSITY OF MIAMI

A COMPARISON OF TWO DIFFERENT HIGH INTENSITY INTERVAL TRAINING
PROTOCOLS ON CARDIOMETABOLIC HEALTH
IN OVERWEIGHT/OBESE WOMEN

By

Ozgur Alan

A DISSERTATION

Submitted to the Faculty
of the University of Miami
in partial fulfillment of the requirements for
the degree of Doctor of Philosophy

Coral Gables, Florida

August 2018

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A Comparison of Two Different High Intensity Interval
Training Protocols on Cardiometabolic Health
in Overweight/Obese Women

(August 2018)

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Dissertation supervised by Professor Arlette Perry.

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The purpose of the study was to compare the effects of aerobic high intensity interval training (A-HIIT) and resistance-high intensity interval training (R-HIIT) to that of a control group (CON) on physical characteristics, cardiometabolic health, and self-reported well-being. A total of 48 overweight/obese women met the criteria for possessing one or more metabolic syndrome (MetS) risk factors and were randomly assigned to one of three groups. Following eight weeks of training, a total of 31 women completed the intervention and were included in the statistical analysis: A-HIIT (n=10), R-HIIT (n=10), and CON (n=11). Both experimental groups trained three times a week for 25 minutes throughout the eight-week protocol. Both A-HIIT and R-HIIT groups improved aerobic fitness compared to CON ($p=0.029$ for both groups). Only R-HIIT group showed increases in upper body power over CON ($p=0.002$). R-HIIT group also showed statistically significant reductions in fasting insulin levels ($p=0.036$) and insulin resistance ($p=0.046$) compared to CON. Furthermore, β -cell function scores were lower in R-HIIT compared to CON ($p=0.017$) and A-HIIT ($p=0.002$) groups. R-HIIT also had significantly higher scores on the physical function domain of Patient Reported Outcome Measurement System (PROMIS[®])-57 well-being questionnaire compared to the CON group ($p=0.035$).

Our study showed that R-HIIT can be considered as part of an optimal worksite-wellness strategy for improving physical characteristics, cardiometabolic health, and well-being in women at risk for or possessing MetS seeking an expeditious form of training.

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CHAPTER 1: INTRODUCTION

Many therapeutic interventions have combined moderate intensity continuous training (MICT), 150 minutes per week supplemented with resistance training to improve metabolic variables associated with obesity, metabolic syndrome (MetS) and type 2 diabetes mellitus (T2DM) (Snowling & Hopkins, 2006; Ismail *et al.*, 2012; Sarzynski *et al.*, 2015). Despite the reported benefits of MICT and resistance training for improving these medical conditions, (Yang *et al.*, 2014; Jelleyman *et al.*, 2015; Lin *et al.*, 2015), only 20% of the women meet recommended guidelines for both aerobic and muscle building activities in the United States (US) (Clarke *et al.*, 2017). Interestingly, lack of time is the most frequently reported personal barrier to physical activity participation in both overweight/obese individuals and the general population at large (Andersen & Jakicic, 2009; Borodulin *et al.*, 2016).

MetS is a progressive pathophysiological state evidenced by a cluster of cardiometabolic risk factors associated with cardiovascular disease (CVD) and T2DM (Sperling *et al.*, 2015). This includes high blood pressure, hyperglycemia, dyslipidemia and central obesity (Grundy *et al.*, 2005). Obesity, impaired glucose homeostasis, increased insulin resistance, and alterations in insulin sensitivity appear to lie at the core of the MetS and T2DM risk (Hanley *et al.*, 2002; Muoio & Newgard, 2008; Garvey *et al.*, 2016). These major health concerns are on the rise as the estimated prevalence of T2DM and MetS in women in the United States are 13% and 35% in the US, respectively with a cost of \$115 billion (Control & Prevention, 2017; Moore *et al.*, 2017).

High intensity interval training (HIIT) using short high intensity work bouts, alternated with low intensity recovery intervals, has been shown to be an effective exercise model to promote beneficial changes in cardiometabolic variables (Weston *et al.*, 2014; Lin *et al.*, 2015). By increasing the intensity of a shortened exercise bout and alternating it with low intensity recovery intervals, HIIT can lead to significant cardiometabolic benefits in a reduced time period compared to traditional continuous training methods. Furthermore, HIIT programs have been shown to improve adherence and quality of life in exercise interventions (Molmen-Hansen *et al.*, 2012; Ulbrich *et al.*, 2016; Stavrinou *et al.*, 2018). In the past several years, HIIT has been used for chronic disease prevention in worksite wellness programs (Jay *et al.*, 2011; Dreyer *et al.*, 2012) with significant improvements in employee fitness (Pohjonen & Ranta, 2001; Jay *et al.*, 2011) and personal well-being observed (Cheema *et al.*, 2013; Sjøgaard *et al.*, 2014).

Most of the reported benefits of HIIT studies have been conducted using aerobic activities such as jogging, running, or biking, also called aerobic-high intensity interval training (A-HIIT) (Little *et al.*, 2011; Gillen *et al.*, 2013; Skelly *et al.*, 2014; Weston *et al.*, 2014). However, few HIIT programs have utilized bodily movements, weighted objects, yoga poses, resistance bands incorporating more resistance activities (McRae *et al.*, 2012; Wingfield *et al.*, 2015; Francois *et al.*, 2016; Nieuwoudt *et al.*, 2017; Fealy *et al.*, 2018) known as resistance-high intensity interval training (R-HIIT) (Kilpatrick *et al.*, 2014).

This type of training may be particularly relevant for those who wish to improve strength, balance, power and functionality, as well as aerobic fitness in a shorter time period. Few studies have examined the effects of both HIIT modalities in a single study.

The purpose of this study was to determine whether A-HIIT, R-HIIT and/or a control (CON) group is optimal for improving a) physical characteristics, b) cardiometabolic health and c) well-being in a single study of overweight/obese women at risk for or possessing MetS.

CHAPTER 2: METHODS

Subjects

Subjects were recruited through university-wide newsletters and via physician recommendations at the Healthy Canes Clinic from the University of Miami. A total of 73 women volunteered to participate in the study and completed screening. A Consolidated Standards of Reporting Trials (CONSORT) flow diagram of the MetS study is shown in Fig. 1.

Screening consisted of evaluation of waist circumference, systolic blood pressure (SBP), diastolic blood pressure (DBP) and prescribed medicines. In order to be eligible for the study, subjects had to possess one or more of the following: a) waist circumference >88cm, b) SBP \geq 135mmHg, c) DBP \geq 85 mmHg, and/or d) medicines required to lower blood pressure/lipids according to updated National Cholesterol Education Program-Adult Treatment (Grundy *et al.*, 2005). During screening, subjects also completed the pre-activity readiness questionnaire (PAR-Q) and a detailed medical health questionnaire to determine whether they qualified or needed physician referral and/or approval upon participating in the study. Exclusion criteria included unstable chronic disease status, uncontrolled symptomatic heart failure, acute systemic infection accompanied by fever, body aches, swollen lymph glands, kidney failure, severe musculoskeletal issues, and/or the use of beta-blockers, and thyroid medications.

A total of 48 overweight/obese (BMI>25), sedentary women (not exercising on a regular basis, <2x/ week) with one or more MetS risk factors completed baseline testing and were deemed eligible to participate in the study. There were 25 participants excluded

from the study due to failure to meet baseline criteria (see Fig.1). Following randomization, a total of five participants failed to complete post-testing in the CON group and six participants failed to complete requirements for both A-HIIT and R-HIIT groups leaving a total of 31 subjects available for data analysis in the study. All testing and training procedures were approved by the University of Miami Institutional Review Board.

Study Design

The study was an 8-week randomized control trial. Following the completion of baseline testing and stratification based on the number of MetS risk factors per subject, participants were randomly assigned to one of three groups (A-HIIT, R-HIIT, CON). Allocation sequences were generated using a computer-generated randomization list to allocate subjects across the three groups.

Investigators assigned to physical testing and blood test analyses were blinded to group assignments, however, participants were aware of the group assignment. Trainers and evaluators went through a 2-week workshop to ensure standardization of testing procedures, quality of instruction and accuracy and reliability of the reported data. Inter-rater reliability for physical fitness and body composition measures were completed based on a mean-rating ($k=5$), absolute-agreement, 2-way mixed effect model for each test. Intra-class correlation estimates were >0.89 for all fitness tests indicating good to excellent inter-rater reliability.

Baseline and post-testing measurements were completed before and 24-72 hours after the 8-week program for all participants in the A-HIIT, R-HIIT and CON groups. The CON group did not go through exercise training, however, after the study's completion, four weeks of HIIT were provided to everyone participating in the CON group. All participants

were told to continue their typical dietary and lifestyle behavioral activities as they have in the past with the exception of exercise training for A-HIIT and R-HIIT groups.

Exercise Training

The A-HIIT and R-HIIT groups participated in supervised training sessions three days per week for eight weeks. The protocol used was previously shown to be well tolerated by overweight/obese men with T2DM which included alternating bouts of 10x1-min high-intensity intervals interspersed by 10x1-minute low-intensity recovery intervals with a 3-min warm-up and a 2 -min cool down for a total 25 minutes (Little *et al.*, 2011). Participants in the A-HIIT group were required to exceed 80% of age-predicted maximum heart rate ($\text{pred HR}_{\text{max}}$) for the high intensity interval as previously defined (MacInnis & Gibala, 2017). In order to achieve this intensity, subjects self-selected their resistance on spin bikes (Star Trac Spinner NXT, Irvine, CA, USA) using monitored heart rates (HR) displayed on a visual screen. During the first week of the protocol, there was a familiarization period in which subjects were ramped up to 75% $\text{pred HR}_{\text{max}}$ during the high intensity intervals. During the second week, subjects were ramped up to 80% $\text{pred HR}_{\text{max}}$ to get them accustomed to the high intensity intervals. From week three onward, subjects were allowed to exercise between 80-100 % $\text{pred HR}_{\text{max}}$ providing an expansion of the upper limit of their high intensity interval depending upon how well they could handle the high intensity interval. For the recovery/relief interval, subjects were allowed to drop down to 60-70% of their $\text{pred HR}_{\text{max}}$ by decreasing the speed and resistance of their work on the spin bikes.

The R-HIIT group followed the same frequency (3x/wk), duration (25 min) and intensity (>80 % pred HR_{max} in high intervals) using the same ramp-up procedure as the A-HIIT group. This was done in a functional resistance training mode by using their own bodyweight, dumbbells, fitness bars, medicine balls and resistance bands to perform various functional multi-joint exercises (squats, lunges, pull and push exercises with free-weights and yoga poses) in a group exercise setting.

Proper technique, adequate range of motion and movement efficiency were emphasized during the first two weeks of the intervention. Between weeks three and eight, movement complexity, load and movement speeds were increased to elicit 80-100% pred HR_{max} during high intervals. Warm-up and cool-down procedures for R-HIIT were performed in the same manner as that for A-HIIT. Although modifications (progression and regression) of the exercises were used to make the exercise program more personalized and creative for participants, the same sequence of exercises were executed throughout the study (Appendix A).

Heart Rate Monitoring

All subjects were fitted with HR monitoring transmitters (Polar H7, Kempele, Finland) to obtain simultaneous feedback of their HR values along with colors of their HR zones reflected on the wall/TV utilizing a special software system (Polar Club, Kempele, Finland). This system allowed participants to acquire consistent HR information via instantaneous feedback throughout the entire training program. This feedback system also enabled subjects and trainers to closely monitor HR and avoid any fluctuations in HR and distractions encountered during the training sessions. Subjects were able to make the necessary adjustments to elicit their prescribed target HR by altering the resistance and

cycling speed on the spin bikes during A-HIIT and increasing the movement speed and loads and/or using exercise progressions/regressions during R-HIIT.

Dietary Recall

Total energy intake of the subjects were monitored using the Automated Self-Administered 24-Hour Recall (ASA24) for 1-weekday and 1-weekend day at baseline and at post-testing (Subar *et al.*, 2012). The average 2-day total calorie intake along with macronutrient consumption were evaluated to determine whether dietary intakes remained consistent throughout the program and ensured that no changes in total calorie and macronutrient intake occurred among the three groups throughout the program.

Physical Characteristics

Body composition/Fat Distribution

A noninvasive direct segmental multi-frequency bioelectrical impedance body composition analyzer, InBody 570 (Seoul, Korea), was used to assess fat mass, skeletal muscle mass and %body fat. Age, height, and gender information were entered following body mass measurement. A safe, low-level electrical current in three different frequencies (5, 50, 500kHz) was sent through an electrode system to five segments (right arm, left arm, trunk, right leg, left leg) for a total of 15-electrical measurements. These measurements automatically utilize resistance and reactance of tissue types based on their water and electrolyte content. Fat-free mass and body fat were calculated via the software algorithms of the InBody 570. Waist circumference were measured to assess fat distribution by placing a Gulick spring loaded measuring tape (Dunlee, Aurora, IL) midway between the last rib and the iliac crest while the subjects were standing with their feet shoulder width apart

during a minimal inspiration. Values were recorded to the nearest 0.1 cm (Janssen et al., 2002).

Physical Fitness

Aerobic Fitness: The NIH 2-minute walk test (2MWT) protocol, was used to measure aerobic fitness by instructing subjects to walk back and forth as quickly as possible between two markers on a 15.3 m course. Aerobic fitness was determined by recording the maximum distance covered in two minutes (Reuben *et al.*, 2013).

Upper and Lower Body Strength: Maximal strength for upper and lower body were measured via determination of one repetition maximum (1RM) for arm-curl and leg press, respectively using guidelines from the National Strength and Conditioning Association (Miller & Association, 2012) for the Keiser Pneumatic machines (Keiser A420, Keiser Sports Health Equipment, Fresno, CA).

Upper and Lower Body Power were determined using a previously established protocol (Balachandran *et al.*, 2014). Briefly, 40-50% of 1RM arm-curl and 50-60% of 1RM leg press loads were used to determine peak power for upper and lower body power, respectively. Subjects were given two attempts at each load for a total of four trials with a 60-sec recovery. The highest values attained were included in the analyses.

Cardiometabolic Health

Resting blood pressure was taken in the right arm in a seated position after five-minute rest period using an automated electronic cuff inflated to at least 200 mmHg with a gradual release according to standard procedures (BpTRU BPM-200, BpTRU Medical Devices, Coquitlam, BC, Canada).

Following an overnight 12-hour fast, approximately 10 cc of blood were withdrawn from the antecubital vein by a licensed phlebotomist. All measurements were taken after subjects were seated quietly for five minutes. Post-testing blood samples were collected 24-72 hours following the last training session. Fasting serum glucose (FSG) levels were determined by spectrophotometry at a wavelength of 340 nm using a hexokinase reaction developed by Roche (Roche Diagnostic System, Nutley, NJ). Fasting serum insulin (FSI) levels were determined by radioimmunoassay using a Coat-A-Count insulin procedure (Diagnostic Products, Los Angeles, CA). Insulin resistance was calculated by using the updated homeostasis model assessment 2 (HOMA2) index along with beta cell function (HOMA2-%B) and insulin sensitivity (HOMA2-%S) as derived from HOMA calculator (<https://www.dtu.ox.ac.uk/homacalculator/>). HOMA2-%B and HOMA2-%S are indirect measures of beta cell function and insulin sensitivity, respectively, which use fasting/basal plasma glucose and insulin concentrations for calculations (Wallace *et al.*, 2004).

Total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C) and triglycerides (TG's) were measured by the Diabetes Research Institute at University of Miami whose serum standards used for calibration were developed and calibrated against serum samples from the Centers for Disease and Control Prevention Laboratory, Atlanta, GA.

Very low-density lipoprotein cholesterol (VLDL-C) was estimated by dividing TG's by five while low-density lipoprotein- cholesterol (LDL-C) was obtained by subtracting HDL-C and VLDL-C from TC utilizing Friedewald's equation (Friedewald *et al.*, 1972).

Well-Being

The National Institute of Health (NIH)'s Patient Reported Outcome Measurement Information System (PROMIS[®]) 57 global health questionnaire was used to evaluate subjects' well-being, prior to and following the protocol (Broderick *et al.*, 2013; Lanting *et al.*, 2013). This is comprised of physical health (physical function, fatigue, sleep disturbance, pain intensity, pain interference profile domains), mental health (anxiety, depression profile domains), and social health (ability to participate in social roles and activities profile domain). The internal consistency reliabilities (Cronbach's alpha) of the PROMIS[®]-57 scales were Anxiety=0.95, Depression=0.96, Fatigue= 0.96, Pain Interference=0.96, Physical Functioning=0.89, Satisfaction with Social Roles=0.98, and Sleep Disturbance=0.94 (Lanting *et al.*, 2013). NIH's PROMIS[®] demonstrates significant clinical validity that is effective both in general and clinical populations (n= 1500, cancer, depression, back pain, chronic obstructive pulmonary disease, rheumatoid arthritis) (Cook *et al.*, 2016). PROMIS[®]-57 also showed high convergent validity (Fatigue, Pain Interference, FACT Physical Well-Being all $r \geq 0.68$) and discriminant validity (unrelated domains all $r \leq 0.3$) across survey short forms, age, and race-ethnicity (Jensen *et al.*, 2015). Raw data for each domain of the questionnaire was uploaded to the PROMIS[®] Health Measures Scoring Service and calculated T-scores for all domains were used in the statistical analysis (<https://www.assessmentcenter.net>).

Statistics

A priori power analysis was conducted utilizing the change in MetS z-score in a previous HIIT study (Ramos *et al.*, 2017) to calculate the sample size using G*Power statistical power analysis program (Faul *et al.*, 2009). Based on the statistical power of 0.8

at $\alpha=0.05$, the total sample size needed to detect a 0.5 (medium) effect size difference between groups, was calculated at 42 subjects.

All statistical analyses were performed using SPSS, version 24 statistical package (IBM SPSS Statistics, Armonk, NY). Means and standard error of mean (SEM) are presented for all subject characteristics at baseline. An analysis of variance (ANOVA) was used to compare baseline characteristics (physical, cardiometabolic, well-being) among the three groups. Kolmogorov-Smirnov and Levene's tests were used to determine normal distribution of the data and the homogeneity of variances, respectively. Independent sample t-tests were utilized to compare the weekly average HR between A-HIIT and R-HIIT across the entire 8-week program. An analysis of covariance (ANCOVA) was used to determine differences among A-HIIT, R-HIIT and CON groups on all dependent variables including physical characteristics (body composition/fat distribution, physical fitness), cardiometabolic health (blood pressure, insulin/glucose measures, serum lipids and lipoproteins) and well-being (physical, social, mental) after adjusting for baseline values. Post-hoc analyses were performed using Bonferroni adjustments. Significance level was set at $p<0.05$.

CHAPTER 3: RESULTS

Presented in Tables 1 and 2 are the physical characteristics and cardiometabolic health characteristics of subjects who completed all baseline measurements: 11 CON, 10 A-HIIT, and 10 R-HIIT. There were no significant differences among groups in any of the variables at baseline. Following stratification, there were no significant differences in the number of MetS risk factors per group ($p=0.683$): CON (2.8 ± 0.4), A-HIIT (2.5 ± 0.4) and R-HIIT (2.3 ± 0.4). Furthermore, 14 subjects already met criteria for MetS in CON ($n= 6$, 55%) A-HIIT ($n= 4$, 40%), and R-HIIT ($n= 4$, 40%) groups.

As shown in Fig. 2 are the ANCOVA findings for significant physical fitness variables after controlling for baseline values. Examining aerobic fitness, there was a significant mean difference on the 2MWT distances by group, $F(2, 27) = 5.4$, $p=0.011$, $\eta^2_p = 0.28$, after adjusting for baseline values. Post-hoc analysis indicated that 2MWT distance was higher in both the A-HIIT ($M_{adj}= 214.8$ m, $SEM= 6.3$) $M_{diff}= 23.9$ m, $p=0.029$ and R-HIIT ($M_{adj}=214.7$ m, $SEM= 6.3$) $M_{diff}= 23.8$ m, $p=0.029$, compared to CON (Fig. 2A).

There was a significant mean difference in arm curl power among groups, $F(2, 27) = 7.2$, $p=0.030$, $\eta^2_p = 0.35$, indicating that upper body power significantly differed by group after controlling for baseline values. Post-hoc analysis revealed that arm-curl power increased in R-HIIT ($M_{adj}= 140.2$ W, $SEM=8.6$) vs CON ($M_{adj}= 94.9$ W, $SEM= 8.2$), $M_{diff} = 45.3$ W, $p=0.002$, but not the A-HIIT ($M_{adj}= 120.5$ W, $SEM= 8.5$) $M_{diff}= 25.6$, W, $p=0.343$ (Fig. 2B). There were no other significant differences among groups in any other physical fitness or body composition variables following the program.

As shown in Fig. 3, are the ANCOVA analyses for significant cardiometabolic health variables after controlling for baseline values. There was a significant difference among groups in FSI, $F(2, 27) = 3.9$, $p=0.032$, $\eta^2_p = 0.23$, after controlling for baseline values. Follow-up testing using the Bonferroni adjustment indicated that the R-HIIT ($M_{adj} = 11.8 \mu\text{U/ml}$, $SEM= 1.5$) evidenced lower FSI levels than the CON ($M_{adj}= 17.4 \mu\text{U/ml}$, $SEM= 1.4$), $M_{diff}= - 5.6 \mu\text{U/ml}$, $p=0.036$ but not the A-HIIT ($M_{adj} = 16.3 \mu\text{U/ml}$, $SEM= 1.5$) $M_{diff}= -4.5 \mu\text{U/ml}$, $p=0.149$ (Fig. 3A).

There was a significant mean difference in HOMA2-IR across groups, $F(2, 27) = 3.6$, $p=0.043$, $\eta^2_p = 0.21$, after adjusting for baseline values. Following post-hoc analysis, insulin resistance in the R-HIIT ($M_{adj}= 1.5$, $SEM= 0.2$) was lower than the CON group ($M_{adj} = 2.2$ $SEM=0.2$), $M_{diff}= - 0.7$, $p=0.046$, but not the A-HIIT ($M_{adj}= 2.0$, $SEM= 0.2$), $M_{diff}= - 0.53$, $p=0.214$ (Fig. 3B).

There was a significant difference among groups for HOMA2-%B, $F(2, 27) = 8.1$, $p<0.01$, $\eta^2_p = 0.37$, after adjusting for baseline values. Post-hoc analysis indicated that HOMA2-%B was lower in R-HIIT ($M_{adj}= 120.8\%$ $SEM=9.3$) compared to both CON ($M_{adj}= 159.3\%$, $SEM= 8.8$), $M_{diff}= - 38.5\%$, $p=0.017$, and A-HIIT ($M_{adj}= 172.2\%$, $SEM= 9.4$) $M_{diff}= - 51.4\%$, $p=0.002$, when controlling for the baseline values (Fig. 3C). There were no other significant between group differences in other cardiometabolic health variables ($p>0.05$).

As shown in Fig. 4 there was a statistically significant difference among groups in the physical function domain using the PROMIS®-57 $F(2, 27) = 3.8$, $p=0.036$, $\eta^2_p = 0.22$. The R-HIIT group ($M_{adj}= 57.5$, $SEM= 1.5$) possessed higher physical function levels at

post-testing compared to CON ($M_{adj}= 51.8$ $SEM=1.4$), $M_{diff}= 5.7$, $p=0.035$, after adjustment for baseline values. There were no significant differences among groups in any other domains for the PROMIS® -57 including fatigue, anxiety, depression, pain intensity, pain interference, sleep disturbance, social interactions ($p> 0.05$ for all).

Presented in Fig. 5 is the average weekly training intensity for each 20-minute exercise protocol during the 8-week program in experimental groups. There were no significant differences between A-HIIT (81.0 ± 1 % pred HR_{max}) and R-HIIT (81.9 ± 1 % pred HR_{max}) throughout the 8-week intervention. However, upon comparison of the weekly average % pred HR_{max} , R-HIIT was 3.6% higher than A-HIIT at baseline ($t=-3.36$, $p=0.001$) and 3.5% higher than A-HIIT at week-4 ($t=-3.38$, $p=0.001$). There were no HR differences at any other time points for the rest of the program.

Not presented in the data analyses, were the dietary recall values among groups after controlling for baseline values. There were no significant differences across groups for macronutrients or average total energy intake per kg bodyweight. Similarly, there were also no significant differences among groups at baseline in calorie and macronutrient intake using dietary recall analyses.

CHAPTER 4: DISCUSSION

Brief Key findings: The present study was unique in that two different types of interval training, A-HIIT and R-HIIT, were evaluated in a single study compared to a CON group. Key findings of the study were; both A-HIIT and R-HIIT groups demonstrated higher aerobic fitness compared to CON, however, only R-HIIT showed significant benefits in upper body power and the physical function domain compared to the CON group. Upon examination of cardiometabolic variables, the R-HIIT evidenced significantly lower FSI and HOMA2-IR compared to the CON group. Furthermore, R-HIIT group showed a lower mean HOMA2-%B compared to both CON and A-HIIT groups indicating that insulin sensitivity increased in the group that underwent R-HIIT. These data show that a supervised HIIT program can serve as a practical worksite wellness program to improve physical characteristics, cardiometabolic health, and well-being in overweight/obese women at risk for or possessing MetS.

Physical Characteristics

HIIT has been extensively studied and shown to improve aerobic fitness. Consistent with previous meta-analyses on HIIT (Weston *et al.*, 2013; Batacan *et al.*, 2017), aerobic fitness was improved in both A-HIIT (11%) and R-HIIT (11%) groups compared to CON. Given the fact that our subjects demonstrated grade 1 and 2 obesity, averaged more than 40% body fat, and had one or more MetS components, our findings add to the growing body of evidence showing that HIIT can be safely followed and well-tolerated in high risk individuals while leading to improved aerobic fitness. This is particularly desirable since training can be completed in one-half the time of standard aerobic training protocols while reaping positive benefits in aerobic fitness.

Training programs that focus on resistance exercise are generally expected to demonstrate improvements in strength and power, however, traditional programs also tend to last longer. A high-speed low load resistance training resulted in a 20% increase in upper body power in women however; the program was 70 minutes in duration (Ramírez-Campillo *et al.*, 2014). Another study that utilized a combination of strength/power and aerobic fitness and showed a 32% improvement in upper body power, however, that program was 40 minutes in duration (Kraemer *et al.*, 2001). The R-HIIT program showed a 48% increase in upper body power compared to CON along with changes in aerobic fitness in only 25 minutes. We know of no other programs showing improvements in upper body power using HIIT. Since A-HIIT did not result in significant improvements in upper body power above CON, our findings demonstrate the superiority of R-HIIT for improving power in addition to aerobic fitness.

Cardiometabolic Health

Reductions in FSI of approximately 8% are generally observed in HIIT programs lasting two-16 weeks (Jelleyman, 2015). Compared to CON, R-HIIT showed a 32% reduction in FSI levels amounting to an almost 3-fold greater reduction than that observed for A-HIIT, at 12% compared to CON. Elevated fasting insulin is associated with hypertension (Wang *et al.*, 2017), increases in serum lipids/lipoproteins (Samuel & Shulman, 2016), certain forms of cancer (Pisani, 2008; Hernandez *et al.*, 2015), obesity (Kahn *et al.*, 2006), and MetS (Sperling *et al.*, 2015). Although there were no differences in MetS risk factors across groups, the significant reduction in fasting insulin in the R-HIIT might be helpful in mitigating the pathogenesis of aforementioned diseases.

Chronic elevations in fasting insulin can also lead to insulin resistance characterized by the resistance of cells to the action of insulin, reduced glucose uptake, and reduced insulin sensitivity (Kahn *et al.*, 2006). Insulin resistance is associated with obesity (Kahn *et al.*, 2006), hypertension (Wang *et al.*, 2017), dyslipidemia (Samuel & Shulman, 2016), and various cancers (Pisani, 2008; Hernandez *et al.*, 2015). In our study, there was a 32% reduction in HOMA2-IR, a measure of insulin resistance, in the R-HIIT group only compared to CON. This reduction was also clinically significant since R-HIIT HOMA2-IR score dropped to 1.5, the insulin resistance cut-off point (Bird & Hawley, 2017). Studies examining the effect of A-HIIT on reducing insulin resistance have been significant and actually better than that reported for continuous aerobic training (Jelleyman, 2015). Therefore, the improvement in HOMA2-IR in R-HIIT only, was unexpected. Faster glycogen depletion leading to an upregulation of enzymes involved in elevated GLUT4 transporter activity and content along with mitochondrial biogenesis (Roberts *et al.*, 2013; Weston *et al.*, 2014) may explain, in part, the benefits of HIIT. Furthermore, upregulation of various local factors related to musculoskeletal contraction may also be responsible for the enhanced action of insulin with R-HIIT (Holten *et al.*, 2004). Growing evidence to indicate that combined resistance and aerobic training may be more efficient compared to either training method alone (Mann *et al.*, 2014). Although R-HIIT included weight-bearing, ballistic maneuvers using medicine balls, free weights and elastic bands, it also utilized novel forms of functional resistance exercise to keep heart rates and work intensity elevated throughout the training protocol. Therefore, R-HIIT may be considered a hybrid model of exercise that can lead to benefits in both aerobic fitness and power.

Chronically elevated insulin resistance can also lead to overwork and exhaustion of β -cells in their general function marked by increases in HOMA-2B%. It is thought that β -cells tend to increase insulin release to offset the reductions in insulin sensitivity and maintain glucose homeostasis (Kahn *et al.*, 2006). Obese non-diabetic individuals similar to participants in our study, appear to compensate for their insulin resistance with higher HOMA2-B%. The lower HOMA2-%B observed in the R-HIIT group compared to CON (-24%) and A-HIIT (-32%) groups concomitant with lower FSI and HOMA-2IR scores, suggest an improvement in insulin sensitivity and a decrease in insulin secretion of β -cells. It is unknown why R-HIIT was superior to both A-HIIT and CON groups. There were no differences in skeletal muscle mass at baseline or post-testing among groups however, the R-HIIT utilized more eccentric contractions during higher impact activities and multiplanar movement patterns which are known to enhance muscle protein synthesis more so than concentric contractions commonly associated with cycling. These different contraction characteristics may be responsible for the improved insulin sensitivity, insulin action or glucoregulatory mechanisms found in the R-HIIT group. These findings tend to support R-HIIT as an optimal training strategy in those at risk for or possessing MetS.

Well-being

Given significant improvements in some physical and cardiometabolic variables, it is not surprising that the physical domain portion of our global health questionnaire improved. Using NIH guidelines for evaluating PROMIS-57 showed that the R-HIIT group evidenced both statistically and clinically significant t-scores in the physical function domain of approximately 10% above that of the CON group.

Our R-HIIT protocol, offered as a part of a worksite-wellness program, can be considered a practical, low-cost method of improving well-being. The American Heart Association (AHA) policy statement on worksite wellness solicits innovative employers “to provide convenient time and location for exercise and wellness programs during the workday” (Carnethon et al., 2009). On-site exercise programs were one of the most preferred worksite health promotion services provided while the most reported barrier was no time before, during, and after the workday in the same report. Time constraints was the most highly reported barrier to exercise (Kruger *et al.*, 2007).

Limitations

One of the major limitations was the duration of the study, which was eight weeks. Most of the other HIIT programs reporting significant benefits in cardiometabolic variables used longer duration studies of 12 weeks or longer (Batacan et al., 2017). Unfortunately, there was a mandatory 2-week break after the third week of the intervention due to Hurricane Irma, which had negative effects on study duration, adherence and morale, and may have influenced the results.

Another limitation was the use of a single fasting serum sample instead of multiple samples to identify insulin sensitivity and glycemic control. Although the HOMA model has been validated against the gold standard, hyperinsulinemic-euglycemic clamp technique (Wallace et al., 2004), it remains a single static measure of insulin sensitivity and β -cell function and may not be viewed as strong a measure of insulin/glucose status.

Adherence to the study was 65%, which was surprisingly low due to unforeseen factors such as high number of job changes, schedules and after effects of Hurricane Irma. However, no injuries or complications occurred during the exercise or testing protocols.

Moreover, among the subjects who completed the study, the attendance rates were $89 \pm 6\%$ for the A-HIIT group and $86 \pm 6\%$ for the R-HIIT group which are similar to the attendance rates reported in previous HIIT studies (Weston *et al.*, 2014).

Both HIIT protocols were well tolerated by subjects as training occurred without incident. The biggest complaint was discomfort using spin bikes reported by participants in the A-HIIT group. Therefore, extra seat pads were provided after the first week of training and there were no further complaints. Moreover, make-up sessions were provided during each week of the program and more than 150 sessions in total were provided throughout the program to facilitate compliance.

Conclusion

Our study shows that worksite wellness programs using HIIT can be well tolerated in sedentary, overweight and obese women employees possessing risk factors for the MetS. Furthermore, R-HIIT appears to be the optimal training method for improving physical variables, cardiometabolic health, and well-being in overweight/obese employees at risk for or possessing MetS and related medical conditions. For employees looking to improve their general health and well-being, R-HIIT may be a suitable training alternative for worksite wellness programs.

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FIGURES

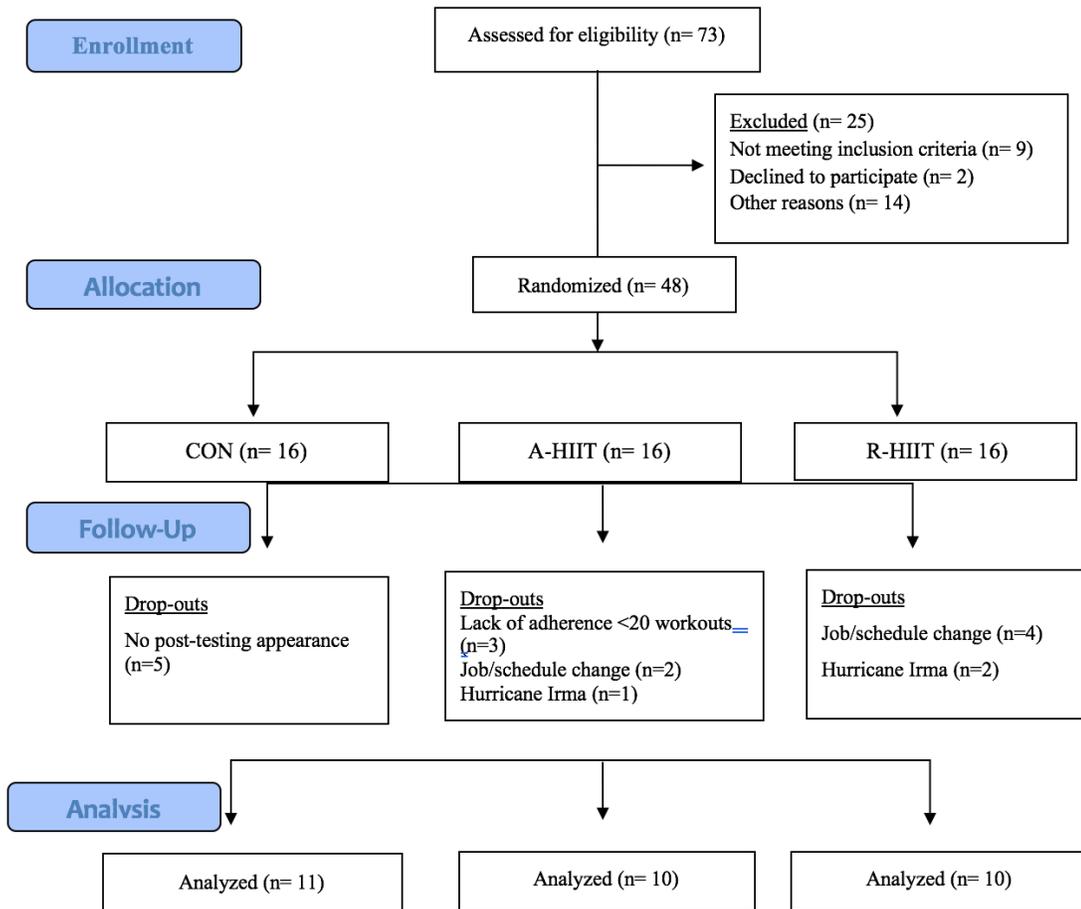


Figure 1. CONSORT flow diagram

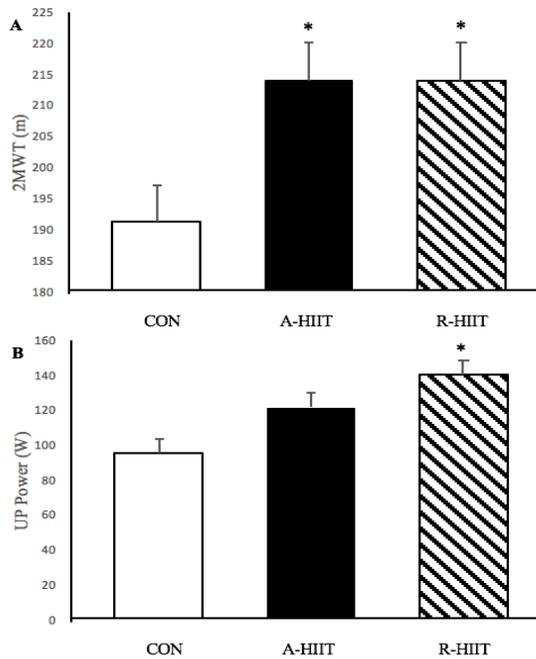


Figure 2. A comparison of significant physical fitness variables at post-testing.

A. Aerobic fitness measured using a 2-minute walk test (2MWT), **B.** Upper body power (UB Power) measured using pneumatic machines at 40-50% 1RM. Control (CON) (n=11), aerobic-high intensity interval training (A-HIIT) (n=10), Resistance-high intensity interval training (R-HIIT) (n=10). Values are means \pm SEM adjusted for baseline scores.

* $p < 0.05$, significantly different from CON.

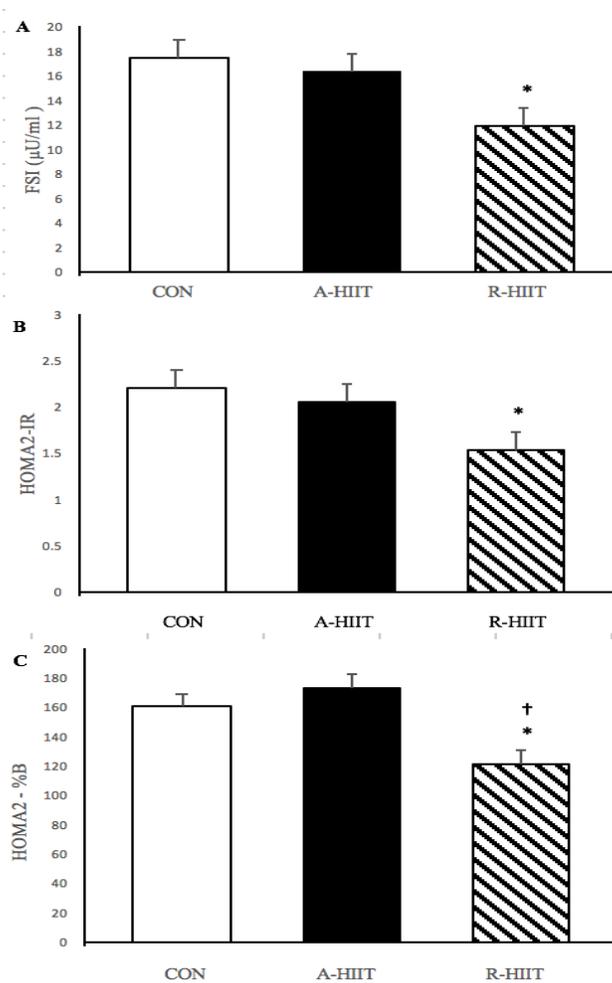


Figure 3. A comparison of significant metabolic variables at post-testing. A. Fasting serum insulin (FSI), B. Modified homeostatic model assessment for insulin resistance (HOMA2-IR) and C Modified homeostatic model assessment for % β -cell function (HOMA2-%B) for control (CON), aerobic-high intensity interval training (A-HIIT), resistance-high intensity interval training (R-HIIT) groups. Values are means \pm SEM after adjustment for baseline values. * $p < 0.05$, different than CON, † $p < 0.05$, different than A-HIIT.

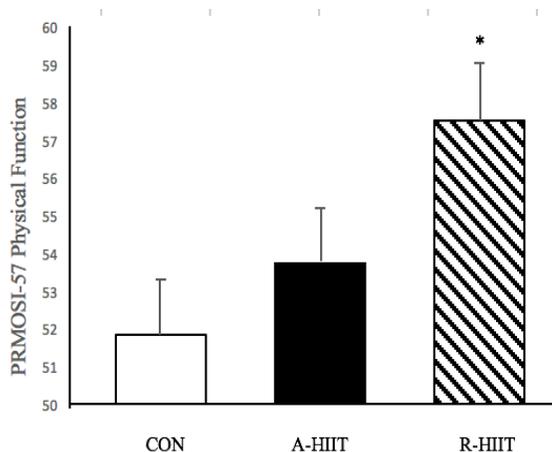


Figure 4. A comparison of physical function scores using the PROMIS®-57. Patient Reported Outcome Measurement Information System (PROMIS®)-57 physical function t-score for control (CON), aerobic-high intensity interval training (A-HIIT), resistance-high intensity interval training (R-HIIT) groups. Values are means \pm SEM after adjustment for baseline values.
* $p < 0.05$, different than CON

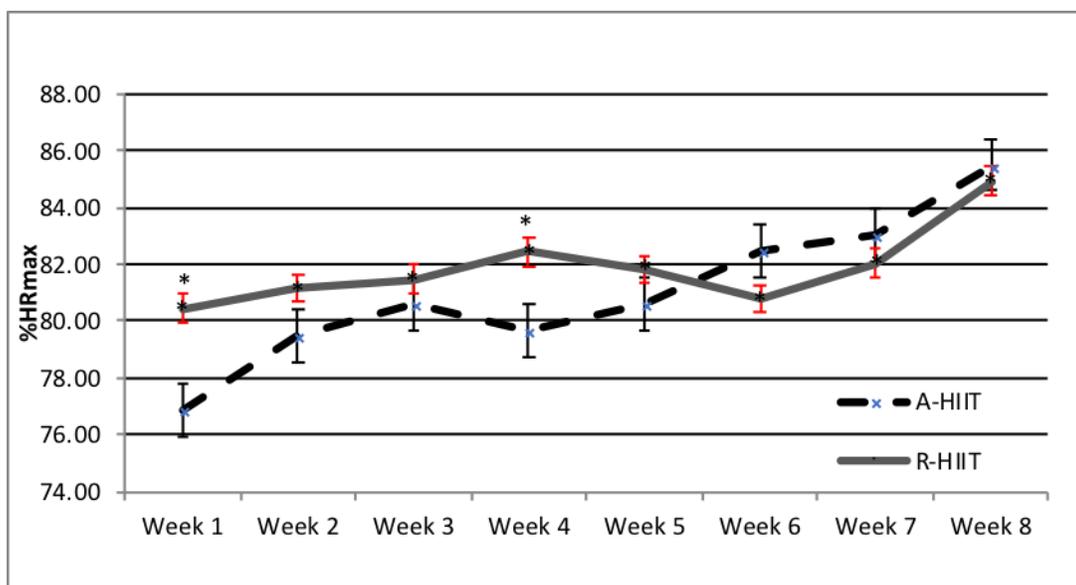


Figure 5. Weekly average training intensities for experimental groups across the training program Aerobic-high intensity interval training (A-HIIT), resistance-high intensity interval training (R-HIIT). Percent heart rate (%HR_{max}) values are presented as mean \pm SEM *Different from A-HIIT, $p < 0.05$

TABLES

Table 1. Physical characteristics at baseline

	CON (n=11)	A-HIIT (n=10)	R-HIIT (n=10)	<i>p</i>
<u>Subject Characteristics</u>				
Age (years)	53.2 ±2.9	43.9 ±3.0	47.2 ±3.0	.093
Height (cm)	161.1 ±2.1	162.3 ±2.2	166.6 ±2.2	.201
Weight (kg)	91.2 ±4.6	90.2 ±4.8	88.7 ±4.8	.931
BMI	35.1 ±1.9	34.3 ±2.0	32.2 ±2.0	.573
<u>Body Composition/Fat Distribution</u>				
Body Fat (%)	47.5 ±1.9	44.8 ±2.0	41.4 ±2.0	.109
Fat Mass (kg)	44.2 ±3.5	40.8±3.7	37.5±3.7	.429
SMM (kg)	25.6 ±1.1	27.4 ±1.1	28.1 ±1.1	.259
Waist (cm)	105.5 ±3.5	102.0 ±3.7	99.1 ±3.7	.456
<u>Physical Fitness</u>				
2MWT	192.9 ±9.5	188.8 ±10.0	202.8 ±10.0	.523
UB Strength(kg)	11.4 ±0.9	13.5 ± 1.0	14.6 ±1.0	.053
LB Strength(kg)	174.4 ±11.0	209.8 ±11.5	209.3 ±11.5	.050
UB Power (W)	102.1 ±42.6	110.9 ±35.5	121.4 ±22.2	.499
LB Power (W)	905.9 ±92.3	1041.8 ±96.8	1113.6 ±96.8	.300

Values are means ±SEM. BMI, Body mass index; SMM, skeletal muscle mass; waist, waist circumference; 2MWT, 2-minute walk test for aerobic fitness; UB, upper body; LB, lower body.

Table 2. Cardiometabolic characteristics at baseline

	CON n=11	A-HIIT n=10	R-HIIT n=10	<i>p</i>
<u>Blood Pressure</u>				
SBP (mmHg)	134.2 ±4.7	122.5 ±4.9	128.2 ±4.9	.099
DBP (mmHg)	86.5 ±2.2	80.6 ±2.3	81.1 ±2.3	.136
MAP (mmHg)	102.4 ±2.6	94.6 ±2.8	96.8 ±2.8	.064
<u>Insulin/glucose</u>				
FSG (mg/dl)	89.4 ±6.6	91.9 ±10.7	91.4 ±14.5	.887
FSI (μU/ml)	17.4 ±2.8	20.8 ±2.9	15.6 ±2.9	.456
HOMA2-IR	2.2 ±0.4	2.7 ±0.4	2.1 ±0.4	.460
HOMA2-%B	157.3 ±15.5	172.9 ±16.3	147.1±16.0	.554
HOMA2-%S	64.5 ±10.8	46.7 ±11.3	65.0 ±11.3	.447
<u>Serum lipids and lipoproteins</u>				
TC (mg/dl)	174.2 ±9.5	189.0 ±10.0	190.6 ±10.0	.435
HDL-C (mg/dl)	51.3 ±8.0	59.1 ±13.6	53.8 ±14.0	.343
LDL-C (mg/dl)	98.0 ±7.8	103.4 ±8.1	111.4 ±8.1	.506
TG (mg/dl)	124.1 ±21.3	132.4 ±22.3	127.0 ±22.3	.971
VLDL-C(mg/dl)	24.9 ±4.3	26.5 ±4.5	25.4 ±4.5	.968

Values are means ±SEM. SBP, systolic blood pressure; DBP, diastolic blood pressure; MAP, mean arterial pressure; FSG, fasting serum glucose; FSI, fasting serum insulin; HOMA2-IR, modified homeostatic model assessment insulin resistance, HOMA2-%B, β-cell function; HOMA2-%S, insulin sensitivity; TC, total cholesterol; HDL-C, high density lipoprotein-cholesterol; LDL-C, low density lipoprotein-cholesterol; TG, triglycerides; VLDL-C, very low-density lipoprotein-cholesterol.

APPENDIX

R-HIIT Exercise List

Warm-up

Multi directional step
Good morning with IYTs **X 2 sets**
Step back rotation
Side progressive squats

- 1- H: Goblet squats
L: Downward dog
- 2- H: Reverse lunge with chop
L: Kneeling lunge with reach
- 3- H: Push-up
L: Child pose, cat cow and downward dog
- 4- H: Single Leg Romanian Deadlift with DB
Dancer pose and kneeling lunge with contralateral reach
- 5- H: DB Flies, DB swings
L: Upward facing dog and kneeling TA stretch
- 6- H: Forward lunge with lean
L: Pigeon pose
- 7- H: DB curl to Arnold Press
L: Triceps and shoulder stretches
- 8- H: MB toss
L: Glute bridges
- 9- H: Band row
L: eagle pose, crisscross arms
- 10- H: MB Reaching Crunch, MB Oblique Twist
L: External, internal oblique stretch, QL stretch

H: High interval, L: Low interval, DB: Dumbbell, MB: Medicine ball. Each high and low interval exercises were executed for one-minute. Unilateral exercises were done for 30 seconds for both sides for a total of one minute.