Spring 2015

The effect of run sprint interval training on diabetic metabolic markers in prediabetic adults

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The Effect of Run Sprint Interval Training on Diabetic Metabolic Markers in Prediabetic Adults

Kathryn L. Hilovsky

A thesis submitted to the Graduate Faculty of
JAMES MADISON UNIVERSITY
In
Partial Fulfillment of the Requirements
for the degree of
Master of Science

Department of Kinesiology

May 2015
Dedication

This thesis project is dedicated to the men and women of the City of Savannah, GA diabetes management program, GoStrong!. It was through your individual journeys that I found my professional purpose. By allowing me into your lives, I learned some of my greatest lessons. Thank you for teaching me!

This thesis project is also dedicated to my wonderful and loving family, especially my parents Dr. Jeffrey and Marcia Hilovsky. At a very young age you both taught me the value of hard work and always striving for excellence. You also demonstrated how to be loving, kind and compassionate. Thank you for leading by example and teaching me how to reach my professional goals and for showing me how to be a good person. To my brothers Tim and Brad, my sister-in-law Melissa, and my sweet Natalie, your support and love always provided me with a motivational boost! Thank you for always being by my side. Finally, to Josh. You challenge me every single day to wake up and be better than I was the day before. Thank you for always believing my abilities!
Acknowledgements

I would like to express my sincere gratitude to my committee chair Dr. Elizabeth S. Edwards for guiding me through all of the stages of this project. Your expertise, strong statistical skills, and moral support enhanced the outcome of this project as well as my academic and personal growth. Thank you for your personal dedication to my success.

I would also like to thank my mentor and committee member, Dr. David Wenos. I will never be able to fully thank you for all of the ways in which you have challenged me to grow. I will forever be indebted to you for the opportunities you have given to me. Your personal investment in my future is directly related to my success. Thank you for everything, I will cherish HAP and this research project for the rest of my life.

This thesis project would not have been possible without Dr. Jeremy Akers. As one of my committee members and leaders of this project, I want to thank you for all of your efforts in making this project a success. Your support, encouragement and rapid communication skills allowed the Team to overcome obstacles quickly and effectively. Your kindness and helpful demeanor is contagious. Thank you for being such a positive advisor! We couldn’t have done this without you!

I would also like to thank Dr. M. Kent Todd and Dr. Trent Hargens for their guidance throughout all stages of this project. It has been a pleasure and an honor to work under your clinical expertise and extensive research knowledge. Thank you for challenging me.
Finally, I would like to thank my research team Nicole Gilbertson and Joan Mandelson. Your support and encouragement, as well as your friendship, made this experience enjoyable and memorable. Thank you for being such good teammates, I will cherish our time together forever.
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Abstract

Purpose: The primary purpose of this study was to compare the effects of an 8-week run-sprint interval training (R-SIT) and continuous moderate-intensity training (MIT) on fasting blood glucose, HbA1c, insulin sensitivity, and β-cell function in sedentary, prediabetic adults. Secondary outcomes of the study included anthropometric, body composition variables, and aerobic capacity.

Methods: Sedentary, physician diagnosed prediabetic individuals were randomized into R-SIT (n=7, BMI 36.76 ± 9.79) or MIT (n=8, BMI 40.59 ± 12.49) interventions. Subjects participated in supervised exercise three times a week and attended a Diabetes Prevention Program course, once weekly. R-SIT participants performed 4-6 x 30-second “all-out” treadmill sprints, interspersed with a 4-minute active recovery at 2-2.5 mph. MIT participants performed 30-40 minutes of continuous moderate-intensity exercise at 45-55% HRR. Analysis of fasting blood glucose, HbA1c, and fasting insulin were obtained at baseline and 8-weeks. Insulin sensitivity (%) and β-cell function (%) were assessed via HOMA2-IR. Body composition, assessed via dual x-ray absorptiometry, and aerobic capacity assessed during a treadmill ramp protocol, were also obtained before and after 8-weeks of training.

Results: Across groups, HbA1c improved across time (p = 0.042). There were no significant changes in fasting blood glucose, insulin sensitivity, or β-cell function in either group. Relative VO\textsubscript{2max} significantly improved in the R-SIT participants (+1.63 ± 1.75mL*kg\textsuperscript{-1}*min\textsuperscript{-1}), whereas no change in relative VO\textsubscript{2max} occurred in the MIT participants. Significant differences in body composition following 8-weeks of exercise occurred only in the MIT group, as measured by body weight (-9.35 ± 6.21 lb.), BMI (-1.21 ± 1.07 kg/m\textsuperscript{2}), BF% (-2.02 ± 1.88%), and LM% (+2.05 ± 1.84%).

Conclusion: Eight weeks of exercise improved HbA1c in prediabetic participants. Although no other improvements in glycemic control were demonstrated in either group, R-SIT participants demonstrated improvements in aerobic capacity, despite exercising at maximal intensities for only two to three minutes per session. In contrast, body composition significantly improved in the MIT group only. These findings suggest that 8-weeks of R-SIT training may be an effective strategy for improving cardiorespiratory fitness levels in overweight and obese prediabetic individuals, but is not effective in improving body composition.
Chapter I: Introduction

The prevalence of Type 2 Diabetes (T2D) and the associated clinical manifestations, are at a record high. In 2010, the Center for Disease Control (CDC) estimated that 25.8 million Americans were affected by T2D (CDC, 2014), a number that is expected to reach 29.6 million by 2030 (Whiting et al., 2011). Furthermore, secondary complications resulting from chronic hyperglycemia are among the leading causes of cardiovascular disease, blindness, kidney disease, and nontraumatic amputations (CDC, 2014). Fortunately, indisputable evidence supports exercise therapy as an effective strategy for glucose management and treatment in T2D patients (Church et al., 2010; Giannopoulou et al., 2005; Hansen et al., 2009; Kang et al., 1996; Kjaer et al., 1990; Michishita et al., 2008; Mourier et al., 1997; Segerstrom et al., 2010; Senechal et al., 2013; Sigal et al., 2007). Currently, continuous low–moderate intensity aerobic exercise, defined as \( \leq 65\% \) VO2max, performed for a minimum of 150 minutes a week on nonconsecutive days (Colberg et al., 2010), has shown to be effective in reducing plasma glucose values and improving insulin sensitivity (Michishita et al., 2008). However, many individuals, do not meet the daily physical activity recommendations stating “lack of time” as a common barrier (Trost et al., 2002). Physical inactivity and adiposity are highly modifiable risk factors for diabetes, specifically for individuals who are considered “high risk for diabetes”, or prediabetic (Tabak et al., 2012).

Sedentary behavior and obesity, especially abdominal obesity, can cause insulin resistance resulting in the reduction of glucose disposal after a glucose challenge. Obesity can directly influence the reduction of insulin-mediated glucose uptake by the muscle cells resulting in impaired fasting glucose (IFG) values, (blood glucose of 100-125
mg/dL after an eight hour fast), impaired glucose tolerance IGT) (blood glucose of 140-199 mg/dL two hours after consuming 75g of glucose), or both (Colberg et al., 2010; Tabak et al., 2012). In fact, the pathophysiology of prediabetes results in increases in glucose values, and reductions in insulin sensitivity and beta-cell function, years before the development of diabetes (Tabak et al., 2012). IFG and IGT are indicative criterion of prediabetes, a condition that affects approximately 79 million Americans over the age of 20 (CDC, 2014). Furthermore, 15-30% of individuals with IFG and/or IGF (CDC, 2014) will develop T2D in five years if lifestyle remains unchanged (Colberg et al., 2010; Grundy et al., 2005; Bird and Hawley, 2012). Fortunately though, research in diabetes prevention and management over the past few decades has been extensive. Examining the effects of diet only, diet plus exercise, and exercise only interventions in preventing or delaying the incidence of diabetes revealed that a combination of diet and exercise improved weight loss, metabolic and cardiovascular risk factors, as well as, reduced the risk of developing diabetes by 39-46% (Eriksson et al., 1999; Pan et al., 1996; Ramachandran et al., 2005).

The Diabetes Prevention Program (DPP), demonstrated the enhanced effectiveness of a lifestyle intervention in lowering the risk of developing T2D when compared to a pharmacological intervention (Knowler et al., 2002). Participants with IFG and IGT were randomly assigned to into a control group, diet and exercise group, or Metformin group. The diet and exercise group were encouraged to obtain a 7% weight loss goal and engage in at least 150 minutes of physical activity, whereas the drug intervention group was instructed to ingest 850mg of Metformin twice daily. When compared to the placebo, the lifestyle group reduced the incidence of T2D by 58%,
whereas the Metformin group reduced the incidence by 31% (Knowler et al., 2002). Furthermore, an analysis of the effects of changes in weight, diet, and physical activity on the risk of developing T2D in a cohort of the DPP participants revealed on average, a 16% reduction in the risk of developing diabetes occurs with every kilogram of weight loss. Of equal importance, participants who did not meet their weight loss goal of 7%, but met or exceeded the minimum physical activity requirements of 150 minutes per week, reduced their incidence by 44% (Hamman et al, 2006). Similarly, participants of the Finnish Diabetes Prevention Study who did not meet their weight loss goals, but were successful in meeting the physical activity goals of > 4 h · week$^{-1}$ experienced a reduction of diabetes incidence by 70% (Tuomilehto et al, 2001). Based on the findings of these pioneer prevention studies, overwhelming evidence supports lifestyle interventions, specifically daily moderately-intense physical activity, as an appropriate prevention method in reducing the incidence of T2D.

Few diabetes prevention studies have examined exercise interventions above moderate-intensity levels, however those studies involving high-intensity exercise interventions ($\geq 65\% \text{ VO}_{2\text{max}}$) in T2D management studies have revealed reductions in visceral fat, in addition to traditional adaptations to aerobic training (Church et al., 2010; Giannopoulou et al., 2005; Hansen et al., 2009; Kang et al., 1996; Senechal et al., 2010; Sigal et al., 2007). The reduction of visceral fat has been linked to the improvements in insulin action and HbA1C, as well as other cardiovascular risk factors (Church et al., 2010; Segerstrom et al., 2010; Sigal et al., 2007). Furthermore, combinations of continuous high-intensity exercise and intermittent sprints have been shown to substantially increase glucose disposal for up to 24 hours post-exercise, as well as
improve cardiorespiratory fitness levels, improve insulin sensitivity, and elicit significant reductions in abdominal adipose tissue (Kjaer et al., 1990; Mourier et al., 1997).

The association of greater glucose control in response to higher-intensity exercise seems to challenge the practicality and effectiveness of traditional moderate-intensity aerobic exercise interventions for T2D patients. A growing body of knowledge on low-volume exercise protocols involving a high-intensity bout of exercise followed by rest or active recovery is classified as High-Intensity Interval Training (HIIT). HIIT protocols usually consist of repeated bouts of exercise performed at intensities ≥90% VO\(_2\)peak. High-intensity intervals can last between a few seconds to up to several minutes and are separated by an equal or greater amount of rest or active recovery (Gibala and McGee, 2008). The results of recent HIIT studies, mostly performed on a cycle ergometer or by running, have demonstrated similar effects on body fat and metabolic parameters to that of traditional endurance training in both healthy, sedentary obese individuals and T2D patients, despite a lower time commitment (Gibala et al., 2012; Hood et al., 2011; Little et al., 2011; Metcalfe et al., 2011; Terada et al., 2013; Trapp et al., 2008). Trapp et al. (2008), compared the effects of an eight week cycle interval training to steady-state exercise in young healthy women and reported a 31% reduction in fasting insulin levels in the interval group. They further identified a correlation between the central abdominal fat loss and the decrease in insulin concentrations. Hood et al. (2011) examined the effects of two weeks of cycle HIIT on healthy, but sedentary middle-aged adults. The subjects in this study performed 10 x 60- second intervals at 80-95% HRR, three times a week. The researchers reported an increase in GLUT 4 content by 260%, a reduction in fasting insulin levels, and an increase in insulin sensitivity by 35%. Additionally, longer
duration cycle HIIT studies, ranging from six to 15 weeks, in healthy sedentary populations illustrated a significant increase in relative VO\textsubscript{2}\text{peak} (Heydari et al., 2012; Metcalfe et al., 2011) and decreases in total body fat, abdominal fat, and visceral fat (Heydari et al., 2012; Terada et al., 2013; Trapp et al., 2008). Additionally, cycle HIIT interventions on T2D patients revealed similar health benefits as did the studies evaluating healthy subjects. Gillen et al. (2012), investigated the acute effects of a single cycle ergometer HIIT exercise session in seven T2D patients. Following the HIIT session of 10 X 60-second intervals at 90% VO\textsubscript{2}\text{peak}, a significant reduction in postprandial hyperglycemia was reported. Studies lasting two weeks, utilizing the 10 X 60-second protocol, three times a week, also illustrated improvements in postprandial glucose. Additionally, GLUT 4 protein content increased by 369%, as well as increases in insulin sensitivity, skeletal muscle oxidative capacity, and a reduction in fasting insulin concentrations (Hood et al., 201; Little et al., 2011).

The attractiveness of a small time commitment during HIIT protocols and the associated benefits on body composition, cardiorespiratory fitness, and glucose parameters has influenced the emergence of an even higher-intensity interval protocol, Sprint Interval Training. SIT protocols are similar to the Wingate test which is defined as an “all-out” 30-second sprint performed on a cycle ergometer at a fixed resistance, followed by an active recovery (Gibala et al., 2012; Gibala and Little, 2010; Hazell et al., 2014). Generally, SIT protocols progressively increase from four- to-six sprints throughout six-weeks of training. Each 30-second sprint is separated by a four to four-and-a-half minute active recovery period, totaling two to three minutes of intense exercise, and approximately 12 minutes of low-intensity exercise per SIT session (Babraj
et al., 2009, Burgomaster et al., 2007; Nie et al., 2012; Richards et al., 2010; Whyte et al., 2010, 2012). In contrast to cycle HIIT, cycle SIT studies have primarily evaluated the health benefits of sprint intervals on healthy, young men and women. Although a limited amount of evidence exists, the acute effects of a single SIT session may suggest improvements in glucose tolerance in obese sedentary men immediately, and up to 24 hours after exercise (Nie et al., 2012). In a six week study consisting of only six SIT sessions involving 25 sedentary or recreationally active men, Babraj et al. (2009), found a significant increase in insulin sensitivity and ~6% increase in aerobic cycling performance. Additionally, a 12% reduction in AUC plasma glucose, a 37% reduction in AUC plasma insulin levels, and a 26% reduction in plasma NEFA values were also reported. In a similar SIT study, sedentary overweight/obese men, improved their insulin sensitivity index by 23.3% after the 24 hour post-intervention, as well as an 8.4% increase in VO_2max (Whyte et al., 2010). Lower fasting insulin and insulin AUC levels were also reported (Whyte et al., 2010).

Traditional six-week SIT protocols comprised of young, healthy, normal-to-slightly overweight subjects, have demonstrated improvements in skeletal muscle adaptations and insulin sensitivity (Burgomaster et al., 2007; Richards et al., 2010). Burgomaster et al., (2007) studied the effects of a six-week SIT protocol on metabolite transport proteins. The results of this study revealed a ~25% increase in muscle GLUT 4 protein content. Following the training however, the same subjects entered a six-week detraining period. GLUT 4 content was measured following the six-week detraining period, and interestingly, GLUT 4 content remained ~20% above the baseline values. Thus, the rapid improvements in insulin sensitivity and cardiorespiratory fitness levels
demonstrated in euglycemic young, healthy individuals warrants the need to extend SIT research into populations who may benefit from improving glucose tolerance and lowering their risk for other chronic morbidities.

Although cycle HIIT and SIT studies have clearly demonstrated the effectiveness of high-intensity intervals on blood glucose parameters, cardiorespiratory fitness, and body composition, less documentation is available on the effects of running interval protocols. Running may be considered a more universal mode of exercise due to the lack of equipment and familiarization needed to perform. Additionally, running is a form of exercise that is commonly applied to many recreational or exercise programs (MacPherson et al., 2010). Unfortunately, the physiological adaptations that occurred as a result of cycle HIIT and SIT studies cannot be assumed for running interval protocols, R-HIIT and R-SIT. Running, elicits both concentric and eccentric muscle contractions in which the eccentric muscle contraction not only cause muscle damage, but may also cause insulin resistance (Costill et al., 1990). However, recent R-HIIT studies have discovered promising health improvements and cardiorespiratory fitness benefits similar to those found in cycle HIIT and cycle SIT studies (Earnest et al., 2013; Nybo et al., 2010; Sijie et al., 2012; Tjonna et al., 2008). Sijie et al. (2012) compared the effects of a 12 week R-HIIT protocol to a continuous moderate-intensity protocol on body composition, cardiac function, and aerobic capacity in young overweight women. The R-HIIT protocol consisted of five 3-minute intervals performed at 85% VO2max, separated by three minutes of active recovery at 50% VO2max. The moderate-intensity protocol consisted of 40-minutes of continuous walking/jogging at 50% VO2max. Post-testing results revealed the women in the R-HIIT reduced their body fat percentage by 9.9%
whereas the moderate-intensity group only reduced their body fat percentage by 5.2%. Additionally, women who completed the R-HIIT protocol also saw significantly greater cardiorespiratory improvements demonstrated as increases in VO$_{2max}$, stroke volume, left ventricular ejection fraction, ventilatory threshold, and a reduction in resting heart rate more than the women who completed the moderate intensity protocol. Nybo et al., (2010) also reported superior increases in VO$_{2max}$ values in untrained men who completed a R-HIIT program as opposed to untrained men who completed a moderate-intensity training program.

R-HIIT protocols have also demonstrated health benefits in clinical populations. Tjonna et al., (2008) examined the effects of an R-HIIT protocol on individuals diagnosed with metabolic syndrome. At the conclusion of the 16 weeks, post-testing results revealed significant improvements in insulin sensitivity, beta cell function, insulin receptor phosphorylation and activation, and maximal oxygen uptake, as well as significant reductions in body weight and waist circumference in in participants who completed the R-HIIT program. Furthermore, 46% of the participants in the R-HIIT group reversed their metabolic syndrome diagnosis as opposed to 37% in the moderately-intense exercise group. Earnest et al., (2013) compared the effects of a 12 week R-HIIT protocol to a steady state eucaloric energy expenditure protocol on previously sedentary men who were “at risk” for developing prediabetes. The results revealed similar reductions in fasting glucose and fasting insulin levels between the two groups, however, only participants who completed the R-HIIT program experienced improvements in HOMA-IR. R-HIIT, although effective in reducing metabolic risk factors, often requires as much time commitment as moderately-intense protocols. Therefore, running HIIT
protocols with less time commitment, such as running-SIT protocols, may be more appealing to individuals struggling to meet the exercise guidelines, specifically those who are at risk for chronic conditions, such as T2D.

Run sprint interval training, R-SIT, may be more accessible than cycle interval protocols that are performed on braked cycle ergometers (Macpherson et al., 2010). Additionally, R-SIT protocols may require less time than the traditional HIIT protocols. Unfortunately, only three R-SIT studies have reported the benefits of multiple 30-second “all-out” sprints performed outside or on a treadmill. Macpherson et al., (2010) was the first to conduct a six week study on the effects of R-SIT in comparison to a continuous running protocol. The study was performed on young, healthy men and women with aerobic performance and body composition defined as their major outcomes. Initially, the R-SIT protocol started with four 30-second “all-out” sprints, separated by four minutes of active recovery, three times per week. The number of sprints progressed by one sprint, every two weeks, until six sprints were performed. The moderate-intensity protocol initially started at 30 minutes of continuous running at 65% \( \text{VO}_{2\text{max}} \) and progressed to 60 minutes of continuous running by week six. The major findings of the study showed similar increases in \( \text{VO}_{2\text{max}} \) and body composition between the two groups. However, the individuals that completed the moderate intensity protocol demonstrated a 9.5% improvement in maximal cardiac output, and the R-SIT participants demonstrated a 7.1% increased in \( \text{a-VO}_{2} \) difference. In addition, Hazell et al., 2014, most recently reported the effects of six weeks of R-SIT on body composition, waist circumference, \( \text{VO}_{2\text{max}} \), and lipid profile in young, recreationally active women following the same protocol as MacPherson et al (Hazell et al., 2014). At the conclusion of the study, significant
reductions in body fat and waist circumference were demonstrated. Additionally, VO$_{2\text{max}}$ increased by 8.7%. Similarly, Sandvei et al., (2012) compared the effects of R-SIT to continuous moderately-intense running on insulin sensitivity and cholesterol in young, healthy males and females. The R-SIT participants in this study performed five 30-second sprints on an outside terrain at a 5-8% grade, three sessions a week. By the end of the eight weeks, participants in the R-SIT group had progressed to 10 sprints each session. In the moderate group, however, participants ran continuously for 30 minutes in week one, but progressed to 60 minutes by the end of week eight. The results at the end of the study revealed similar reductions in fasting blood glucose between the two groups, but greater improvements in glucose AUC, HOMA beta-cell index, insulin sensitivity and plasma LDL- cholesterol associated with the R-SIT protocol.

Recent R-SIT studies have solely involved young, healthy men and women. While these findings show promise regarding improvements in insulin sensitivity, cardiorespiratory fitness, and body composition, it is necessary to examine these effects in a pre-clinical, middle-aged population at high risk for diabetes. Given the cost, both economic and physiologic, of T2D, and the proven efficacy of exercise in improving insulin sensitivity and glucose control, it is imperative that we identify exercise protocols that are quick, effective, and easily accessible to a wide-range of participants, particularly those at high risk for the development of T2D.
**Purpose**
The purpose of this study is to determine if fasting blood glucose, insulin sensitivity, HbA1c, body composition, and aerobic capacity are improved to a greater extent in R-SIT participants compared to a moderate-intensity (MIT) group and a control group receiving nutrition and exercise counseling, in prediabetic men and women, following a 16-week intervention.

**Hypotheses**
It is hypothesized that fasting blood glucose, insulin sensitivity, and HbA1c will improve to a greater extent in the R-SIT participants than the MIT participants and the control participants, following a 16-week intervention.

It is hypothesized that reductions in fat and improvements in lean muscle mass will be greater in the R-SIT participants than in the MIT participants and the control participants, following a 16-week intervention.

It is hypothesized that improvements in aerobic capacity will be greater in the R-SIT participants than the MIT participants and the control participants, following a 16-week intervention.

**Assumptions**
It will be assumed that the participants in this study will be able to run on the treadmill as well as reach their maximal capacity during each R-SIT session. It will also be assumed that the participants in this study will maintain their normal dietary habits and activity levels.
Limitations

The results of this study will only be representative to middle-aged prediabetic men and women, not generalized to other populations.

Delimitations

A potential delimitation will be that we are only studying middle-aged individuals. Older individuals, ≥ 65 years or post-menopausal women, will not be included.

Definition of Terms

Prediabetes, as defined by the American Diabetes Association:

Individuals presenting with Impaired Fasting Glucose: 100-125 mg/dL, and/or Impaired Glucose Tolerance: 140-199 mg/dL following 2-h OGTT, and/or HbA1c: 5.7-6.4%

Sedentary:

Exercising less than the ACSM minimum guidelines of 30-60 minutes of moderate to vigorous physical activity three to five days per week, or 150 minutes of physical activity, for the previous six months.
Chapter II: Methodology

Research Design:

The study will be a 16-week, randomly controlled experimental intervention to compare the effects of run sprint interval training (R-SIT) to a moderate-intensity (MIT) aerobic exercise program, and to the Diabetes Prevention Program (DPP) control group in sedentary, prediabetic men and women, diagnosed according to American Diabetes Association standards. The study will be approved by the Institutional Review Board of James Madison University (Harrisonburg, VA). Primary outcomes will be assessed at baseline, eight weeks, and 16 weeks and include fasting blood glucose, plasma insulin concentration, HbA1c, insulin sensitivity and β-cell function via HOMA-IR.

Participants:

The initial recruitment of forty-five participants will be conducted by Rockingham Memorial Hospital (RMH) in Harrisonburg, VA. Inclusion criteria from the participants who are recruited are: (1) adult men and women; (2) sedentary; (3) diagnosis of prediabetes as defined by an elevated HbA1c (5.7%-6.4%), and/or impaired glucose tolerance by 2-h OGTT (140mg/dL-200mg/dL), and/or impaired fasting glucose values (100-125 mg/dL) as indicated by the American Diabetes Association (ADA, 2014). Sedentary is defined as not meeting the ACSM minimum guidelines of 150 minutes per week of moderately-intense physical activity for the previous six months (Pescatello, 2014). Participants will be given PAR-Q to identify other potential CVD risk factors. Following a detailed description of the study, informed consent will be obtained by all
participants. Participants will then be randomly assigned to either the R-SIT, MIT, or DPP control groups.

Participants were excluded from the study for Type 2 diabetes, Type I diabetes, any medication for prediabetes, women who are currently pregnant, and any individuals experiencing any ACSM relative or absolute contraindications to exercise. Additional exclusion criteria include any factors that may limit their adherence to the intervention such as lack of time or physical limitations or conditions.

**Individual Education Session, Familiarization, and Baseline Measures:**

After the initial screening, all participants, regardless of treatment, will receive an individual educational session with one of the researchers on the importance of a healthy lifestyle for the prevention of T2D. The educational session will include information on nutrition and exercise. Following the education session, each participant will be familiarized with the study procedures and the informed consent will be obtained. Additionally, questionnaires including: medical history and medication use, the CDC’s Health Related Quality of Life, perceived enjoyment (PACES) questionnaire, IPAQ, and sleep apnea screening questionnaire, and a three-day food intake record will be obtained. Also in this first meeting, we will obtain resting heart rate and blood pressure measurements, body composition and anthropometric measurements, a maximal exercise test, and heart rate variability measures. On a subsequent day, the participants will travel to RMH outpatient laboratory for baseline blood analyses including a complete lipid panel, fasting glucose, plasma insulin, and HbA1C.
**Anthropometric Measures:**

During the familiarization meeting, body mass will be assessed with a balance scale and height will be measured by a stadiometer (without shoes). BMI will then be calculated by dividing body mass (kg) by height in meters squared (m$^2$). A waist to hip ratio will be determined by circumference measurements. A horizontal measurement will be taken at the height of the iliac crest, without clothing. The hip measurement will be determined by measuring the widest circumference of the buttocks. The waist to hip ratio will then be calculated by dividing the waist circumference by the hip circumference. Each measurement will be taken by the same researcher and the average of three measurements will be recorded.

**Body Composition:**

The body composition of each participant will be measured after a 12-hour fast by the GE Lunar Prodigy dual-X-ray absorptiometry (DEXA). The subject will be instructed to remove all metal objects from their person and lay in a supine position on the DEXA bed. A full body soft tissue analysis will be performed. Total fat-free tissue (lb), fat tissue (lb), and body fat percentage will be recorded.

**Heart Rate and Blood Pressure Measurements:**

Following the body composition assessment, each participant will secure a Polar Heart Rate monitor around their chest and remain in a supine position on the DEXA bed for an additional five minutes. The resting heart rate value will be determined by the monitor and recorded in beats per minute. Additionally, a resting blood pressure
measurement will be performed by the auscultation method and measured at the brachial artery. The first Korotkoff sound will identify the systolic blood pressure reading and the last Korotkoff sound will identify the diastolic blood pressure. Two blood pressure measurements will be taken at least one minute apart; the average of the two will be recorded.

**Cardiorespiratory testing:**

During the second visit, participants will perform a maximal cardiorespiratory exercise test on a treadmill to determine maximal oxygen consumption and cardiovascular fitness, assessed by Cosmed Quark metabolic cart. The graded exercise test will be initiated by a three to five minute warm-up at a self-selected walking speed and 0% grade. After the warm-up, the first stage of a modified ramp protocol will start and will last for three minutes. The grade will remain at 0%, but the participant will increase the speed to a comfortable running speed that will remain constant throughout the duration of the test. Heart rate values will be recorded after every minute and RPE values will be recorded at the end of each stage. At the end of three minutes, the treadmill will increase to 2.5% for three minutes. The grade will be increased every three minutes by 2.5% until volitional exhaustion. An oxygen plateau in response to an increase in workload and an RER of $\geq 1.1$, or a maximal HR value within 10 beats of expected max will serve the criteria used to determine $\text{VO}_{2\text{max}}$, determined by COSMED metabolic cart. Exercise intensities for both the R-SIT and MIT exercise interventions will be determined using percentages of obtained $\text{VO}_{2\text{max}}$. Strong verbal encouragement will be provided throughout the test.
Insulin Sensitivity, Fasting Blood Glucose [BG] and HbA1c:

Participants will be instructed to fast for at least 10 hours (ADA, 2014) and refrain from strenuous exercise for 48 hours before baseline, eight week, and 16-week blood analyses. Samples will be taken from the antecubital vein, and will include fasting blood glucose, plasma insulin concentration, and HbA1c. Insulin sensitivity and β-cell function will be determined via the homeostatic model assessment computer model (HOMA2) from fasting plasma glucose and insulin values, and expressed as HOMA2-%S, and is the reciprocal of HOMA2-IR (Wallace et al., 2004). Insulin sensitivity, determined by the HOMA model, demonstrates a strong correlation when compared to the gold standard, hyperinsulinemic-euglycemic clamp (r = -0.820, P< 0.0001) (Bonora et al., 2000).

Exercise Training:

Subjects will be randomly assigned into either R-SIT, MIT, or DPP control group. R-SIT and MIT supervised training sessions will be completed in Godwin Hall, three days a week, for a 16 week duration. Both the R-SIT and the MIT protocols will progress in four week increments. The exercise session will begin with a five minute warm-up followed by a five minute walking warm-up on the treadmill with a speed of 2.5 mph and 0% grade. Supervised meetings for the DPP control group will take place at the RMH Wellness Center.

R-SIT Protocol:

For the first four weeks of the study, participants will complete four 30-second “all-out” running sprints. In order to prevent orthopedic injuries, participants will perform the sprints at a 3-5% grade (Ehlen et al., 2011). Verbal encouragement will be given to
each participant and heart rate and RPE will be recorded immediately following each sprint. Progression of the sprints increased every four weeks by two, until 10 sprints will be performed during the last four weeks of the study. Treadmill speed and grade will be adjusted throughout the study so maximal HR and RPE values can be obtained.

**MIT Protocol:**

For the first four weeks of the study, the participants in the moderate intensity group will exercise on a treadmill at an intensity level ranging between 45-55% of their heart rate reserve (HRR) for 30 minutes. The treadmill grade will be set between 3-5%. Progression of the moderate intensity protocol increased every four weeks by 10 minutes, until 60 minutes will be performed during the last four weeks of the study. A five minute cool down at 2.5 mph and 0% grade.

<table>
<thead>
<tr>
<th>Weeks</th>
<th>R-SIT</th>
<th>MIT</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-4</td>
<td>4 sprints X 30 seconds</td>
<td>30 minutes at 45-55% VO$_{2\text{max}}$</td>
</tr>
<tr>
<td>5-8</td>
<td>6 sprints X 30 seconds</td>
<td>40 minutes at 45-55% VO$_{2\text{max}}$</td>
</tr>
<tr>
<td>9-12</td>
<td>8 sprints X 30 seconds</td>
<td>50 minutes at 45-55% VO$_{2\text{max}}$</td>
</tr>
<tr>
<td>13-16</td>
<td>10 sprints X 30 seconds</td>
<td>60 minutes at 45-55% VO$_{2\text{max}}$</td>
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**DPP Control Group:**

The DPP control group will receive a 16 week intensive lifestyle intervention which includes general information classes on diet, exercise, and health behavior strategies. All participants in this group will be encouraged to achieve a 7% weight-loss goal through a reduction in dietary fat intake and maintaining at least 150 minutes of moderate-intensity physical activity per week, equivalent to ~700 kcal/week. Furthermore, two supervised exercise sessions per week will be implemented by trained RMH Wellness Center staff members. Descriptive methodology about the DPP intensive lifestyle intervention have been previously described (Bray et al., 1999).
Statistical Analysis:

HOMA2-IR indices, Fasting Blood Glucose, HbA1c, body fat percentages, and VO$_{2\text{max}}$ will be analyzed using a two-way repeated measures ANOVA. Significance will be set *a priori* at $p < 0.05$. 
Chapter III : Manuscript

Abstract

Purpose: The primary purpose of this study was to compare the effects of an 8-week run-sprint interval training (R-SIT) and continuous moderate-intensity training (MIT) on fasting blood glucose, HbA1c, insulin sensitivity, and β-cell function in sedentary, prediabetic adults. Secondary outcomes of the study included anthropometric, body composition variables, and aerobic capacity.

Methods: Sedentary, physician diagnosed prediabetic individuals were randomized into R-SIT (n=7, BMI 36.76 ± 9.79) or MIT (n=8, BMI 40.59 ± 12.49) interventions. Subjects participated in supervised exercise three times a week and attended a Diabetes Prevention Program course, once weekly. R-SIT participants performed 4-6 x 30-second “all-out” treadmill sprints, interspersed with a 4-minute active recovery at 2-2.5 mph. MIT participants performed 30-40 minutes of continuous moderate-intensity exercise at 45-55% HRR. Analysis of fasting blood glucose, HbA1c, and fasting insulin were obtained at baseline and 8-weeks. Insulin sensitivity (%) and β-cell function (%) were assessed via HOMA2-IR. Body composition, assessed via dual x-ray absorptiometry, and aerobic capacity assessed during a treadmill ramp protocol, were also obtained before and after 8-weeks of training.

Results: Across groups, HbA1c improved across time (p = 0.042). There were no significant changes in fasting blood glucose, insulin sensitivity, or β-cell function in either group. Relative VO$_{2\text{max}}$ significantly improved in the R-SIT participants (+1.63 ± 1.75mL*kg$^{-1}$*min$^{-1}$), whereas no change in relative VO$_{2\text{max}}$ occurred in the MIT participants. Significant differences in body composition following 8-weeks of exercise occurred only in the MIT group, as measured by body weight (-9.35 ± 6.21 lb.), BMI (-1.21 ± 1.07 kg/m$^2$), BF% (-2.02 ± 1.88%), and LM% (+2.05 ± 1.84%).

Conclusion: Eight weeks of exercise improved HbA1c in prediabetic participants. Although no other improvements in glycemic control were demonstrated in either group, R-SIT participants demonstrated improvements in aerobic capacity, despite exercising at maximal intensities for only two to three minutes per session. In contrast, body composition significantly improved in the MIT group only. These findings suggest that 8-weeks of R-SIT training may be an effective strategy for improving cardiorespiratory fitness levels in overweight and obese prediabetic individuals, but is not effective in improving body composition.
Introduction

The prevalence of Type 2 Diabetes (T2D) and the associated clinical manifestations, are at a record high (CDC, 2014). In 2014, the Center for Disease Control (CDC) released the National Diabetes Statistics Report estimating that 29 million Americans are affected by T2D (CDC, 2014). Furthermore, secondary complications resulting from chronic hyperglycemia are among the leading causes of cardiovascular disease (CVD), blindness, kidney disease, and non-traumatic amputations (CDC, 2014). Fortunately, indisputable evidence supports exercise therapy as an effective strategy for glucose management and treatment in T2D patients (Church et al., 2010; Giannopoulou et al., 2005; Hansen et al., 2009; Kang et al., 1996; Kjaer et al., 1990; Michishita et al., 2008; Mourier et al., 1997; Segerstrom et al., 2010; Senechal et al., 2013). Currently, continuous low-to-moderate intensity aerobic exercise, $\leq 65\% \text{ VO}_2\text{max}$, performed for a minimum of 150 minutes a week on nonconsecutive days (Colberg et al., 2010), has shown to be effective in reducing plasma glucose values and improving insulin sensitivity (Michishita et al., 2008). However, many individuals do not meet the weekly physical activity recommendations stating, “lack of time” as a common barrier (Trost et al., 2002). Physical inactivity and adiposity are highly modifiable risk factors for diabetes, specifically for individuals who are considered “high risk for diabetes”, or prediabetic (Tabak et al., 2012).

Sedentary behavior and obesity, especially abdominal obesity, contributes to insulin resistance resulting in the reduction of glucose disposal after a glucose challenge (Colberg et al., 2010). Obesity can directly influence the reduction of insulin-mediated glucose uptake by the muscle cells contributing to impaired fasting glucose (IFG) values, 100-125 mg/dL, impaired glucose tolerance (IGT) 140-199 mg/dL, or both (Colberg et al., 2010; Tabak et al., 2012). The pathophysiology of prediabetes identifies increases in glucose values, and reductions in insulin sensitivity and beta-cell function, years before the development of diabetes (Tabak et al., 2012). IFG and IGT are indicative criterion of prediabetes, a condition that affects approximately 86 million Americans over the age of 20 (CDC, 2014). Furthermore, 15-30% of individuals with IFG and/or IGT (CDC, 2014) will develop T2D within five years if lifestyle remains unchanged (Bird and Hawley,
Prevention studies have demonstrated that lifestyle interventions, specifically those in which the participants have met their physical activity goals, can reduce the risk of developing T2D by 44% (Hamman et al., 2006) to 70% (Tuomilehto et al., 2001), independent of weight loss. Thus, overwhelming evidence supports lifestyle interventions, specifically daily moderate-intensity exercise, as an effective strategy in reducing the incidence of T2D.

Although very few traditional diabetes prevention studies have examined the effects of high-intensity exercise interventions, ≥ 65% VO2max, as a prophylactic therapy for T2D, high-intensity exercise interventions for T2D management have revealed improvements in insulin action and HbA1c, as well as other cardiovascular risk factors (Church et al., 2010; Segerstrom et al., 2010; Sigal et al., 2007). Furthermore, combinations of continuous high-intensity exercise and intermittent sprints have been shown to significantly increase insulin sensitivity (Mourier et al., 1997) and glucose disposal for up to 24-hours post-exercise (Kjaer et al., 1990). Thus, the association of greater glucose control in response to higher-intensity exercise seems to challenge the practicality and effectiveness of traditional moderate-intensity aerobic exercise interventions for T2D patients.

A growing body of knowledge on low-volume exercise protocols involving a high-intensity bout of exercise followed by rest or active recovery is classified as high-intensity interval training (HIIT). HIIT protocols usually consist of repeated bouts of exercise performed at intensities ≥90% VO2peak. Cycle HIIT studies lasting two weeks, utilizing a 10 X 60- second protocol at an intensity of 90% HRmax, three times a week, illustrated improvements in postprandial glucose, insulin sensitivity, and skeletal muscle oxidative capacity. Additionally, GLUT 4 protein content increased by 369%, and a reduction in fasting insulin concentrations was also reported (Hood et al., 2011; Little et al., 2011).

The attractiveness of a shorter time commitment during HIIT protocols and the associated benefits on glucose parameters and cardiorespiratory fitness has influenced the emergence of an even higher-intensity interval protocol, Sprint Interval Training (SIT). SIT protocols are similar to the Wingate test which is defined as an “all-out” 30-second sprint performed on a cycle ergometer at a fixed resistance, followed by an active
recovery (Gibala et al., 2010; Gibala et al., 2012; Hazell et al., 2014). Traditional cycle SIT protocols have primarily evaluated the health benefits on young, healthy, normal-to-slightly overweight subjects following six weeks of training. The results of these studies have demonstrated significant improvements in insulin sensitivity, improvements in plasma glucose and plasma insulin following an OGTT, plasma non-esterified fatty acid (NEFA) values, and aerobic cycling performance (Babraj et al., 2009), as well as increases in skeletal muscle adaptations (Burgomaster et al., 2007; Richards et al., 2010). The rapid improvements in insulin sensitivity and cardiorespiratory fitness levels demonstrated in euglycemic young, healthy individuals warrants the need to extend SIT research into populations that may benefit from improving glucose tolerance and lowering their risk for other chronic morbidities.

Although cycle HIIT and SIT studies have clearly demonstrated the effectiveness of high-intensity intervals on blood glucose parameters and cardiorespiratory fitness, less documentation is available on the effects of running interval protocols. Running may be considered a more universal mode of exercise due to the lack of equipment and familiarization needed to perform it. Additionally, running is a form of exercise that is commonly applied to many recreational or exercise programs (Macpherson et al., 2011). Unfortunately, the physiological adaptations that occur as a result of cycle HIIT and SIT studies cannot be assumed for running interval protocols, R-HIIT and R-SIT. However, recent studies have discovered that participants who completed the R-HIIT protocols experienced significant fat loss and cardiorespiratory fitness benefits similar to those found in cycle HIIT and cycle SIT studies (Earnest et al., 2013; Nybo et al., 2010; Sijie et al., 2012; Tjonna et al., 2008).

R-HIIT protocols have also demonstrated health benefits in clinical populations. Tjonna et al. (2008) compared the effects of an R-HIIT versus continuous moderate-intensity exercise in individuals diagnosed with metabolic syndrome. At the conclusion of the 16-week intervention, post-testing results revealed significantly greater improvements in insulin sensitivity, β-cell function, and insulin receptor phosphorylation and activation in the participants that completed the R-HIIT intervention. Furthermore, 46% of the participants in the R-HIIT group reversed their metabolic syndrome risk
factors as compared to 37% in the moderate intensity exercise group (Tjonna et al., 2008).

Run sprint interval training, R-SIT, may be more accessible than cycle interval protocols that are performed on braked cycle ergometers. Additionally, R-SIT protocols may require less time than the traditional HIIT protocols. Unfortunately, only three R-SIT studies have reported the benefits of multiple 30-second “all-out” sprints performed outside, or on a treadmill (Hazell et al., 2014; Macpherson et al., 2011; Sandvei et al., 2012). The major findings of the R-SIT studies showed similar improvements in VO$_{2\text{max}}$, body composition (Macpherson et al., 2011), and fasting glucose improvements (Sandvei et al., 2012) between the continuous moderate-intensity group and the R-SIT groups, despite less time spent in exercise. However, individuals that completed the R-SIT protocol decreased glucose AUC, increased HOMA $\beta$-cell index, increased insulin sensitivity and reduced plasma LDL-cholesterol to a greater extent than those in the moderate-intensity protocol (Sandvei et al., 2012).

Unfortunately, the recent R-SIT studies have solely involved young, healthy men and women. While these findings show promise regarding improvements in insulin sensitivity, cardiorespiratory fitness, and body composition, it is necessary to examine the effects in a pre-clinical population at high risk for diabetes. Given the cost, both economically and physiologically, of T2D, and the proven efficacy of exercise in improving insulin sensitivity and glucose control, it is imperative that we identify exercise protocols that are quick, effective, and easily accessible to a wide-range of participants, particularly those at high risk for the development of T2D.

**Methods**

**Research Design**

The present study was an 8-week, randomly controlled experimental intervention comparing the effects of R-SIT to a continuous moderate intensity aerobic exercise program in sedentary, prediabetic men and women diagnosed with American Diabetes
Association (ADA) standards. The study was approved by James Madison University (Harrisonburg, VA) according to ethical standards of the Institutional Review Boards. Prior to randomization and baseline measurements, informed consent was completed by all participants. Primary outcomes were assessed at baseline and 8 weeks and included fasting blood glucose, fasting plasma insulin, and HbA1c. Secondary outcomes were also assessed at baseline and 8 weeks and included body composition variables and aerobic capacity (VO$_{2\text{max}}$).

**Subjects**

The sample size of the study was 15 participants. Participants were recruited by local news media, posting flyers and advertisements throughout the community and on the JMU website, as well as referrals from local physicians. Inclusion criteria from the participants who were recruited were: (1) men and women between 20 and 70 years of age; (2) sedentary; (3) had an elevated HbA1C (5.7%-6.4%), and/or impaired glucose tolerance by 2-h OGTT (140mg/dL-200mg/dL), impaired fasting glucose values (100-125 mg/dL) as indicated by the American Diabetes Association (ADA, 2014), and/or by physician diagnosis. Participants were given a PAR-Q to identify other potential CVD risk factors. The participants were randomized into the R-SIT or moderate intensity (MIT) protocol by age, gender, and BMI. Exclusion criteria included a Type I or Type 2 diabetes diagnosis, women who were pregnant, and individuals experiencing any ACSM relative or absolute contraindications to exercise. Additional exclusion criteria included any factors that limited their adherence to the intervention such as lack of time or physical disabilities.
**Familiarization and Baseline Measures**

Participants attended a familiarization session which informed them of the study protocol and requirements. Additionally, initial paperwork, including the informed consent, medical history, and other baseline questionnaires were completed. Familiarization of the treadmill protocol included determination of test walking/running speed, review of safety hand signals and explanation of RPE scale. Baseline measurements were also performed during the familiarization session and included resting heart rate and blood pressure measurements, body composition and anthropometric measurements, a maximal exercise test, and heart rate variability measures. At the conclusion of the familiarization session, participants were provided with a lab voucher and instructed to visit a Sentara-RMH outpatient laboratory for baseline blood values.

**Anthropometric Measures and Body Composition**

Body mass was assessed with a Seca balance scale and height was measured by a Chorder stadiometer (without shoes). A waist to hip ratio was determined by circumference measurements. A horizontal measurement was taken one-inch above the height of the iliac crest, without clothing. The hip measurement was determined by measuring the widest circumference of the buttocks, under the gluteal fold. Additionally, a full body soft-tissue analysis was performed by GE Lunar Prodigy dual-X-ray absorptiometry (DEXA). Total fat-free tissue (lb), fat tissue (lb), body fat and lean muscle mass percentages were recorded.
Cardiorespiratory testing

In a meeting separate from the familiarization session, participants performed a maximal cardiorespiratory exercise test on a Quinton Club Track 612 Plus treadmill to determine maximal oxygen consumption and cardiovascular fitness, assessed by a ParvoMed metabolic cart. An oxygen plateau in response to an increase in workload, or an RER of $\geq 1.1$, or a maximal HR value within 10 beats of expected max served as the criteria to determine $\text{VO}_{2\text{max}}$.

Insulin Sensitivity, $\beta$-cell Function, Fasting Blood Glucose [BG] and HbA1c

Participants were instructed to fast for at least 10-hours (ADA, 2014) and refrain from strenuous exercise for 48 hours before baseline and eight week blood analyses. Samples were taken from the antecubital vein by certified phlebotomists at Sentara-RMH Outpatient Laboratory, and included fasting blood glucose, plasma insulin concentration, and HbA1C. Insulin sensitivity (HOMA- %S) and $\beta$-cell function ($\%\beta$) was determined via the homeostatic model assessment computer model (HOMA2) from fasting plasma glucose and insulin values (Wallace et al., 2004). Insulin sensitivity, determined by the HOMA2 model, demonstrates a strong correlation when compared to the gold standard, hyperinsulinemic-euglycemic clamp ($r = -0.820, P< 0.0001$) (Bonora et al., 2000).

Exercise Training

Subjects were randomly assigned into either a run-sprint interval training (RSIT) experimental group or a moderate intensity training (MIT) control group. Supervised training sessions were completed in Godwin Hall, three days a week, for 8-weeks duration. Both the R-SIT and the MIT protocols progressed in four week increments. The
exercise session began with a five-minute body weight exercise warm-up followed by a five-minute walking warm-up on the treadmill with a speed of 2.5 mph and 0% grade. A five-minute cool-down at 2.5mph and 0% grade followed each exercise session.

**R-SIT Protocol**

For the first four weeks of the study, participants completed four 30-second “all-out” running sprints, followed by 4-minutes of active recovery at 2.0 mph and 0% grade. In order to prevent orthopedic injuries, participants performed the sprints at a 3-5% grade (Ehlen et al., 2011). Verbal encouragement was given to each participant and heart rate and RPE was recorded immediately following each sprint. Progression of the sprints increased by two, following the first four weeks of the study. Treadmill speed and grade were adjusted throughout the study so maximal HR and RPE values could be obtained.

**MIT Protocol**

For the first four weeks of the study, participants in the moderate-intensity group exercised on a treadmill at an intensity level ranging between 45-55% of their VO$_{2\text{max}}$ for 30 minutes. The treadmill grade was set between 0-5%. Progression of the moderate-intensity protocol increased by 10 minutes, following the first four weeks of the study.

**Statistical Analysis**

Mixed design (Time x Group) ANOVA’s were used to determine potential significant differences between the means of dependent measures between groups. Post hoc analyses included paired student $t$-tests for within group comparisons and independent samples $t$-tests for between group differences at baseline and follow-up. A level of $p < 0.05$ will be considered statistical significance. All results will be expressed as mean ± SD.
**DPP Education:**

All participants received an eight week intensive lifestyle intervention which included general information classes on diet, exercise, and health behavior strategies. All participants were encouraged to achieve a 7% weight-loss goal through reductions in dietary fat intake and maintaining at least 150 minutes of moderate-intensity physical activity per week, equivalent to ~700 kcal/week. Descriptive methodology about the DPP intensive lifestyle intervention have been previously described (Bray et al., 1999).

**Results**

**Sample Characteristics**

Twenty individuals were randomized into either the R-SIT group or the MIT group; 15 participants maintained at least 80% adherence to their exercise training sessions and were used in the data analysis. Independent sample *t*-tests were used for the comparison of baseline characteristics between the two exercise groups and are illustrated in (Table 1). No significant differences in age, BMI, fasting blood glucose, HbA1c, or aerobic capacity were present between the two groups at the start of the study. Normality was assessed by the Shapiro-Wilk test.

**Glycemic Control and Maximal Oxygen Uptake**

Paired samples *t*-tests were conducted to evaluate differences within and between each exercise group. HbA1c values were significantly reduced in all individuals over the eight week training period, however there were no observed differences between groups (Figure 1). In contrast, no significant changes within groups or differences between groups in fasting blood glucose, insulin sensitivity, β-cell function, or HOMA-IR values
were demonstrated over the 8-week intervention period (Table 2). Despite no significant biochemical findings, the R-SIT exercise group significantly improved their relative VO$_{2\text{max}}$ after 8-weeks of progressive sprint interval training ($1.84 \pm 1.70; p = 0.028$) whereas the MIT exercise group maintained their relative VO$_{2\text{max}}$ value (Figure 2). There were no significant improvements in VO$_{2\text{max}}$ in either the R-SIT or MIT groups when expressed in absolute terms (L/min).

**Body Composition**

Following 8-weeks of continuous moderate intensity exercise, significant improvements in body composition were identified (Table 3). Mean body weight ($9.35 \pm 6.21$ lbs; $p = 0.004$) (Figure 3), BMI ($1.21 \pm 1.07$ kg/m$^2$; $p = 0.015$) (Figure 4), body fat percentage ($2.02 \pm 1.88\%$; $p = 0.019$), and percentage of lean muscle mass ($2.05 \pm 1.84\%$; $p = 0.016$) (Figure 5) were significantly improved in the MIT group. No observed significant differences in body weight or body composition were identified in the R-SIT group.

**Discussion**

The present study examined the effects of progressive run sprint interval training versus continuous moderate intensity exercise on reducing hyperglycemia and improving insulin sensitivity in prediabetic adults. Despite the small sample size, the major finding in this investigation was that R-SIT can be used as an effective training intervention for improving cardiorespiratory fitness levels in prediabetic adults. To our knowledge, the present study is the first study that has examined the effects of run sprint interval training on glycemic control in adult prediabetic men and women.
**Glycemic Control**

All individuals demonstrated significant improvements in HbA1c following 8-weeks of exercise training. Surprisingly, no previous HIIT or SIT interventions have reported significant improvements in HbA1c. In fact, previous evidence suggests that greater reductions in HbA1c are associated with structured exercise programs that require more than 150-minutes of exercise per week for at least 12-weeks in duration (Umpierre et al., 2011). Therefore, the significant reduction in HbA1c values in all participants suggests that 8-weeks of R-SIT training may be just as effective in reducing HbA1c as continuous moderate intensity exercise, despite the lower time commitment and exercise volume.

Despite the improvements in HbA1c, average fasting blood glucose, β-cell function, or insulin sensitivity values did not significantly improve in either the R-SIT or MIT participants, following 8-weeks of exercise training. The results in the present study contrast observations following a similar 8-week comparison study of R-SIT versus continuous moderate-intensity exercise. Sandvei et al. reported that both sprint interval and continuous moderate-intensity training participants reduced fasting glucose values (Sandvei et al., 2012). In addition, Sandvei and colleagues reported improvements in insulin sensitivity and β-cell function only in the R-SIT group, whereas in the present study, no improvements in insulin sensitivity or β-cell function occurred in either group. Differences in the outcomes of these studies may be due to the differences in participant characteristics. The present study evaluated sedentary, physician diagnosed prediabetic adult men and women; whereas, the aforementioned study evaluated young, non-obese sedentary to moderately active men and women, with no history of cardiovascular or
metabolic disease. However, our results also differed from previous studies comparing the effects of running HIIT and continuous moderate-intensity exercise on glycemic control in individuals with metabolic syndrome. Superior improvements in insulin sensitivity (Tjonna et al., 2009) and HOMA-IR values (Earnest et al., 2013) were observed in the running HIIT group when compared to the participants who completed the continuous moderate-intensity exercise. These improvements however, were observed in exercise interventions of longer duration, 12-weeks (Earnest et al., 2013) and 16-weeks (Tjonna et al., 2009).

Exercise mode may also influence improvements in glycemic control following a SIT exercise intervention in individuals with prediabetes. Many previous cycle SIT studies evaluating the effects on glycemic control in young, healthy participants also contradict our findings and have demonstrated improvements in insulin sensitivity (Babraj et al., 2009; Richards et al., 2010; Whyte et al., 2012) and reductions in blood glucose AUC (Babraj et al., 2009) in as little as two weeks of training. To our knowledge, only one cycle SIT intervention demonstrated improvements in insulin sensitivity following a two week cycle SIT intervention in sedentary obese men (Whyte et al., 2012). The differences in outcomes regarding improvements in insulin sensitivity and blood glucose AUC may be attributed to the differences in power output between the two in exercise modes, (i.e. cycling versus running). The power output during a 30-second supra-maximal sprint on a cycle ergometer is much higher than the power output produced during a 30-second running sprint on a treadmill; therefore exercise modes that elicit greater power outputs than running may be more beneficial in improving glycemic control in previously sedentary, obese individuals (Sandvei et al., 2012). Furthermore, it
is well established that many factors negatively affect glucose homeostasis, and among the most noteworthy are obesity and physical inactivity. Obese individuals are often also physically inactive and have demonstrated mitochondrial dysfunction and reduced skeletal muscle oxidative capacity as a result (Kelley et al., 2002; Lowell and Shulman, 2005; Simoneau and Kelley, 1997). Not only does reduced skeletal muscle oxidative capacity adversely impact cardiorespiratory health, but it has also been highly correlated with insulin resistance in both prediabetic and Type 2 Diabetic patients (Earnest, 2008; Simoneau and Kelley, 1997). Therefore, individuals presenting with evidence of metabolic dysfunction may require an exercise intervention of longer duration and/or with a more powerful exercise stimulus than young, healthy individuals to improve variables of glycemic control.

**Cardiorespiratory Fitness**

Significant improvements in relative VO$_{2\text{max}}$ were observed in the R-SIT group, whereas VO$_{2\text{max}}$ did not improve in the MIT group. This study supports existing evidence that R-SIT elicits improvements in aerobic capacity (Hazell et al., 2013) and to a greater extent than continuous moderate-intensity exercise (Macpherson et al., 2010; Sandvei et al., 2012). Interestingly, the improvements in relative VO$_{2\text{max}}$ values in the R-SIT group occurred despite exercising at maximal intensity for only 2-3 minutes per exercise session. Additionally, these values improved in the absence of weight loss indicating that central O$_2$ delivery and peripheral physiological adaptations are likely the source of this improvement. Although stroke volume and cardiac output have been shown to improve in response to high-intensity interval training in previous studies (Daussin et al., 2007; Daussin et al., 2008; Tjonna et al., 2009), Macpherson and colleagues reported that the
30-second sprint interval used in recent R-SIT investigations appears to be too short to elicit a change in central \( O_2 \) delivery (Macpherson et al., 2010). However, peripheral adaptations in skeletal muscles, such as increased enzymatic markers for glycolysis and mitochondrial biogenesis, have been demonstrated in many recent running interval studies (Macpherson et al., 2009; Tjonna et al., 2009; Earnest et al., 2013) and cycle interval studies (Burgomaster et al., 2007; Hood et al., 2011; Gibala et al., 2008; Little et al., 2011). Although skeletal muscle biopsies were not performed at the beginning of this study, the aforementioned skeletal muscle adaptations resulting from repeated maximal-intensity exercise intervals, likely represent the increased \( VO_{2\text{max}} \) values in the R-SIT group versus no change in \( VO_{2\text{max}} \) in the MIT group. Some running comparison studies have reported similar improvements in \( VO_{2\text{max}} \) values in both R-SIT and MIT groups; however, the continuous moderate-intensity groups in those interventions were running, thus exercising at higher intensities than the MIT group in the present study (Macpherson et al., 2010; Sandvei et al., 2012). Improvements in \( VO_{2\text{max}} \) in individuals diagnosed with prediabetes is of clinical importance because higher cardiorespiratory fitness values are associated with decreased risk of all-cause mortality (Blair et al., 1995).

**Body Composition**

Another secondary measure of the present study was to compare the effects of R-SIT and MIT on body composition. After 8-weeks of exercising, only the MIT participants demonstrated reductions in body weight and BMI whereas the R-SIT participants did not see significant reductions. Furthermore, only the MIT group significantly improved body fat and lean muscle mass percentages. Although caloric expenditure was not measured during each training session, differences in training
volume and duration between the two interventions may explain the significant improvements in body composition in the MIT group versus the R-SIT group. In one treadmill HIIT comparison study by Tjonna et al., patients with metabolic syndrome demonstrated similar improvements in body weight when the caloric expenditure was equalized between the aerobic interval training sessions and the continuous moderate intensity training sessions (Tjonna et al., 2008). In contrast, another treadmill HIIT and continuous moderate exercise comparison study only showed significant improvements in body mass and body fat percentage in the interval group following three months of eucaloric training (Earnest et al., 2013). Despite these contrasting results in previous HIIT interventions, only one study has compared the effects of R-SIT and MIT on body composition, to date. Macpherson et al. reported reductions in fat mass in both R-SIT and MIT groups, but differences between the groups were not significant (Macpherson et al., 2010). Another R-SIT study reported significant reductions in fat mass, body fat percentage and waist circumference, as well as significant increases in FFM following six weeks of R-SIT; however, this investigation did not compare these findings to a MIT exercise group (Hazell et al., 2014). Although these findings may suggest that R-SIT protocols may be effective in improving body composition, it is well known within the scientific community that the generalization of significant findings can only suggest plausible outcomes for comparable populations under similar conditions. It should also be noted, that the previously reported R-SIT studies were performed on recreationally active, young men and women (Hazell et al., 2014; Macpherson et al., 2010), whereas the present study included sedentary, overweight and obese participants varying in age, ranging from 20-70 years. With no previous studies comparing interval training and
continuous aerobic exercise to a placebo-control, Keating et al. was the first to report that
continuous aerobic exercise, rather than HIIT, reduced total body fat and android fat in
previously inactive, overweight adults (Keating et al., 2014). Thus, these findings may
suggest that overweight adults, specifically overweight adults with prediabetes, may
benefit more from the current moderate-intensity exercise recommendations in order to
achieve the health-related benefits associated with weight loss.

Although the present study is the first to report on the health-related effects of 8-
weeks of R-SIT in comparison to MIT in individuals diagnosed with prediabetes, it is
important to consider our small sample size when evaluating our results. Furthermore, it
is important to note that the participants recruited for this study were approved for
participation by a physician diagnosis of prediabetes. Upon receiving baseline blood
values, it was observed that some of the participants had FBG values and/or HbA1c
values there were not considered to be within the ADA prediabetes classification. The
individuals presenting with baseline values outside the ADA criterion remained in the
study as other laboratory measures, such as an OGTT, have been reported to be better
predictors of identifying overweight and obese individuals with prediabetes or T2D
(Cosson et al., 2009). Therefore, a physician diagnosis of prediabetes, rather than
baseline blood values, were used for accepting participants for this study.

It is also relevant to point out that many of our R-SIT participants found it
challenging to reach their target maximal heart rate within a 30-second interval. Many of
the participants indicated that they had a “fear of falling off of the treadmill” when
increasing the speed or elevation of the treadmill to high levels. This limitation alone may
have influenced the results as failure to reach the target maximum heart rate negates
following our SIT protocol requirements. Although many of our participants anecdotally
identified challenges in maintaining protocol standards, another study reported high-
intensity interval running was just as feasible for participants with T2DM to perform than
continuous moderate-intensity exercise (Terada et al., 2012). Thus, more studies
evaluating the feasibility of treadmill R-SIT protocols are warranted.

Finally, the timing of the present study presented dietary challenges to many of
our participants. Although no formal dietary instruction was provided to the participants,
weekly educational lectures on preventing diabetes included information on the
importance of healthy eating. Many of the participants that were recruited for this study
started their exercise training and diabetes prevention lectures in mid-November which
extended through the prime holiday season in North America. While some participants
reported that the structure of the program provided assistance in making healthy lifestyle
choices, many participants identified challenges in regards to maintaining healthy dietary
habits during the holidays. Even though dietary intake was not evaluated in our study,
evidence reporting that many Americans gain weight over the holiday season may have
impacted our results more so than if the study had been conducted during a different time
of the year (Yanovski et al., 2000). Despite this limitation, the lack of improvements in
glycemic control in either R-SIT or MIT group suggest that a formal dietary intervention
may be necessary to supplement the exercise training in order to achieve improvements
in glycemic control and body composition in this population, during this time period.

In conclusion, 8-weeks of structured aerobic exercise improved HbA1c values in
prediabetic individuals. In addition, running sprint interval training increased relative
\( \text{VO}_{2\text{max}} \) values in prediabetic adults more so than continuous moderate-intensity exercise,
despite exercising at maximal levels for only 2-3 minutes per session. In contrast, continuous moderate-intensity exercise demonstrated to be a better stimulus for improving body composition. Although a substantial amount of evidence identifies high-intensity interval training as a time-saving exercise strategy in achieving similar health benefits associated with moderate-intensity exercise, no previous R-SIT evidence serves as a comparison for our results. Additionally, varying exercise modes, protocol type, intervention duration, and differences in population characteristics make it impossible to evaluate if interval training is as effective for overweight and obese individuals, specifically those using exercise as a prophylactic treatment for T2DM. However, our results indicate that R-SIT may be as effective in reducing HbA1c values as the current exercise recommendations in individuals with prediabetes. While the concept of repeatedly challenging the anaerobic system to produce positive fitness and health gains in a shorter amount of time may propose a solution to a common exercise barrier, larger studies of longer duration are necessary in order evaluate the effectiveness, feasibility, and safety for this population.
Table 1. Participant Characteristics at Baseline

<table>
<thead>
<tr>
<th></th>
<th>RSIT (n = 7)</th>
<th>MIT (n = 8)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>42.71 ± 7.53</td>
<td>48.88 ± 5.29</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>164.19 ± 5.82</td>
<td>162.56 ± 8.43</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>100.1 ± 31.67</td>
<td>107.27 ± 33.73</td>
</tr>
<tr>
<td>BMI (kg/m^2)</td>
<td>36.76 ± 9.79</td>
<td>40.59 ± 12.49</td>
</tr>
<tr>
<td>Fasting Glucose (mg/dL)</td>
<td>95.71 ± 9.34</td>
<td>105.88 ± 16.08</td>
</tr>
<tr>
<td>HbA1c (%) *</td>
<td>5.54 ± 0.25</td>
<td>5.91 ± 0.26</td>
</tr>
<tr>
<td>VO_{2}max (ml/kg/min)</td>
<td>24.27 ± 7.14</td>
<td>29.93 ± 7.55</td>
</tr>
</tbody>
</table>

Values are presented as means ± SD. *Significantly different between groups (p < 0.05).
<table>
<thead>
<tr>
<th>Blood Measures</th>
<th>Baseline</th>
<th>8-weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fasting Blood Glucose</td>
<td>94.71 ± 9.34</td>
<td>94.29 ± 5.15</td>
</tr>
<tr>
<td>(mg/dL)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>RSIT</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fasting Insulin (uU/IU)</td>
<td>11.90 ± 6.58</td>
<td>11.39 ± 6.22</td>
</tr>
<tr>
<td>HbA1c (%)</td>
<td>5.54 ± 0.25</td>
<td>5.34 ± 0.55</td>
</tr>
<tr>
<td>Insulin Sensitivity (%)</td>
<td>80.49 ± 42.47</td>
<td>104.73 ± 87.28</td>
</tr>
<tr>
<td>B-cell Function (%)</td>
<td>115.40 ± 59.81</td>
<td>108.30 ± 42.43</td>
</tr>
<tr>
<td>HOMA-IR (%)</td>
<td>1.54 ± 0.80</td>
<td>1.82 ± 0.84</td>
</tr>
<tr>
<td>MIT</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fasting Blood Glucose</td>
<td>105.88 ± 16.08</td>
<td>103.63 ± 14.83</td>
</tr>
<tr>
<td>(mg/dL)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fasting Insulin (uU/IU)</td>
<td>13.31 ± 9.94</td>
<td>12.93 ± 6.41</td>
</tr>
<tr>
<td>HbA1c (%)</td>
<td>5.91 ± 0.26</td>
<td>5.75 ± 0.39</td>
</tr>
<tr>
<td>Insulin Sensitivity (%)</td>
<td>71.64 ± 36.26</td>
<td>71.38 ± 33.51</td>
</tr>
<tr>
<td>B-cell Function (%)</td>
<td>96.24 ± 35.48</td>
<td>99.05 ± 14.29</td>
</tr>
<tr>
<td>HOMA-IR (%)</td>
<td>1.78 ± 1.34</td>
<td>1.73 ± 0.89</td>
</tr>
</tbody>
</table>

Values are presented as means ± SD. There are no significant differences between groups or within groups.
Figure 1. Main effect for time in HbA1c (%) for all participants after eight weeks of exercise training. HbA1c values obtained following 10 hour fast. *Significantly different from baseline ($p < 0.05$).
Figure 2. Changes in relative VO$_{2\text{max}}$ values after 8-weeks of exercise training. VO$_{2\text{max}}$ values achieved during a treadmill ramp protocol via open-circuit spirometry. *Significantly different from baseline ($p < 0.05$).
Figure 3. Changes in body weight after 8-weeks of exercise training. *Significantly different from baseline ($p < 0.05$).
Figure 4. Changes in body mass index after 8-weeks of exercise training. *Significantly different from baseline ($p < 0.05$).
Figure 5. Changes in body fat percentage after 8-weeks of exercise training. Percent body fat values were obtained via DEXA. *Significantly different from baseline ($p < 0.05$). BF = Body Fat
Figure 6. Changes in lean muscle mass after 8-weeks of exercise training. Percent lean muscle mass values were obtained via DEXA. *Significantly different from baseline ($p < 0.05$). LMM = Lean Muscle Mass
Manuscript References


Intensity Interval Training Improves Fat Distribution in Overweight Adults.  
*Journal of Obesity, Volume 14.*


insulin sensitivity in women with T2D. *European Journal of Internal Medicine*, 21, 404-408.


**Appendix A**

**James Madison University**

**Departments of Kinesiology and Health Sciences**

**Consent for Investigative Procedure**

*(Informed Consent)*

You are being asked to participate in a research study conducted by Drs. Elizabeth Edwards, Jeremy Akers, Trent Hargens, David Wenos, and graduate students Katie Hilovsky, Jo Mandelson, and Nicole Gilbertson from the Departments of Kinesiology and Health Sciences at James Madison University. The purpose of this study is to determine the effect of low volume, high intensity training on physical fitness, physical activity enjoyment, and physical activity adherence, along with factors known to increase risk for chronic disease (blood lipids, etc.) by conducting an experimental study in a cohort of prediabetic men and women.

**Research Procedures.** The study will consist of a 16-week supervised exercise program. The research study will consist of three groups. Each participant will be randomized to a control, low volume, high intensity training, or moderate intensity training group. Prior to beginning the study, at the mid-point of the study (8 weeks), upon completion of the study (16 weeks), and at three-month and six-month follow-up, you will complete various supervised tests and questionnaires to measure the physical fitness, health status, lifestyle behaviors, body composition, blood lipids, insulin, and blood glucose levels.

**Note:** In the event you discover that any of the following information is not clear, please ask one of the researchers to explain immediately.

**Blood Pressure.** Blood pressure measurements will be taken using a sphygmomanometer and stethoscope. A blood pressure cuff will be placed over the upper portion of your right arm, slightly above the elbow. The cuff will be inflated to approximately 200mmHg and then slowly released, while a researcher uses a stethoscope to listen to sounds of blood flow through the vein on this inside of your elbow.

**Blood Draws.** A fasted (8-10 hour) blood sample will be obtained by a butterfly needle in a vein in your mid arm. All blood draws will be taken from Sentara Rockingham Memorial Hospital.
(SRMH). In order to minimize the transfer of blood-borne pathogens, the trained person taking your blood will wear latex gloves at all times during blood sampling and testing. All values will be sent to researchers in a sealed envelope. Per SRMH protocol you will be required to provide a medical provider’s information at each blood draw session. If blood values are outside normal/optimal ranges the blood values will be sent to your primary medical provider. For each blood draw, we will be measuring several different substances in the blood related to health and disease risk.

**Preparation for Blood Draw.** You will be asked to fast for 8-10 hours before the session. This includes coffee, tea, alcohol, or tobacco products.

**Body Composition and Bone Mineral Density.** Your height and weight will be measured and used to calculate body mass index BMI (kg/m$^2$). Additionally, the size of your waist and hips will be measured with a cloth tape measure. Your waist measurement is important in determining your risk for cardiovascular disease and diabetes. Dual-energy x-ray absorptiometry (DXA) will be used to estimate body composition data and bone mineral density through the whole body scan. For the DXA scan, you’ll be asked to lie on your back and remain still for the whole scan; the scan will last approximately 6-10 minutes.

**Maximal Exercise Test.** The purpose of the maximal graded exercise test, also known as the VO$_2$max test, is to measure cardiorespiratory fitness. Cardiorespiratory fitness is the ability to engage in dynamic moderate- to high-intensity exercise for a prolonged period of time. Cardiorespiratory fitness is an important consideration when health risks and overall exercise capability are assessed. High levels of cardiorespiratory fitness are correlated with reduced risk coronary artery disease.

**Preparation for Exercise Testing.** Prior to exercise testing, we will ask you to not eat or drink anything, except water for three hours prior to the test. Please note that this includes caffeinated beverages – such as coffee or tea! Use of tobacco products should be avoided at least three hours prior to testing as well. Please avoid heavy exercise on the testing day. Try to get to get at least six hours of sleep the night before, to ensure that you are well rested. Wear clothing that is comfortable and allows you to move freely, such as shorts, a t-shirt, and comfortable running shoes. Be aware that the test is fatiguing, so you may wish to be fully hydrated before the test.

**Procedure for Exercise Testing.** Resting heart rate and blood pressure will be taken prior to testing. The treadmill test follows a predetermined protocol to obtain a maximal oxygen uptake. You will run on a treadmill, with the speed and/or grade increasing as the test progresses, until you’re working as hard as you can. You will be fitted with a heart rate monitor chest strap and a pulmonary facemask. Nonverbal cues will be used to communicate during the test. Hand signals include “yes,” “no,” and/or “stop the test.” It is important to realize that you may stop the test when you wish because of feelings of fatigue or any other discomfort. Additionally, we may stop the test at any time due to signs of fatigue or abnormal physiological responses. These may include failure for heart rate increase with increased workload, dizziness, chest pains, or muscular fatigue. Please note that both protocols and procedures are in adherence with the guidelines set forth by the American College of Sports Medicine for exercise testing.
You will be permitted to leave once post exercise heart rate drops below 100 beats per minute or resting heart rate levels. Avoid a hot shower and a heavy meal for at least an hour after the exercise test.

**At-Home Sleep Assessment:** The at-home sleep assessment will be utilized to screen for possible obstructive sleep apnea (OSA), a frequent co-morbid condition with diabetes, and a condition that may confound data analysis without accounting for. Research staff will instruct the you on the proper setup and use of the ApneaLink™ at-home screening device. The ApneaLink device is composed of a pulse oximeter, which is worn on the end of an index finger, and a nasal cannula, which is worn over the face, and into the nose to measure airflow. The ApneaLink device is harmless and painless to wear. You will be wearing this device one night while you sleep only at the beginning of the study.

**Heart rate variability (HRV):** HRV will be utilized to assess autonomic function, which is another proposed mechanism linking obstructive sleep apnea and cardio vascular disease. You will be asked to complete a resting HRV and heart rate measurement using a monitor that is strapped on your chest. You will be asked to lie flat on your back in a darkened room, while heart rate and HRV are measured over a 15 minute time period. You will be asked to breathe in rhythm with an instrument that is set at 12 beats per minute, thus representing 12 breaths per minute which is considered to be the average respiration rate for a healthy adult.

**Health Status.** Your health status will be determined via questionnaires and ACSM’s Risk Stratification for Cardiovascular Disease Risk (ACSM, 2010). Assessment of your risk for cardiovascular disease will be made using the ACSM’s Coronary Artery Disease Risk Factor Thresholds along with the ACSM Risk Stratification. Risk stratification is based upon age, family history, smoking habits, blood lipid levels, and fasted blood glucose values, resting blood pressure, body mass index and physical activity habits. We will also be asking about current and previous conditions, surgeries, and medications, so that we may ensure that you are healthy enough to participate in this study.

**Lifestyle Behaviors**
You will be asked to complete the following questionnaires:

a. **Exercise Behavior** – The International Physical Activity Questionnaire (IPAQ) estimates how much activity you have participated in over the previous seven days. It will ask about your physical activity as part of your daily life, including work, as well as leisure time activity.

b. **Perceived Enjoyment** – The Physical Activity Enjoyment Scale (PACES) asks you about your perceptions and feelings about physical activity.

c. **Dietary Behavior** – A 3-day dietary record, where you will record what you consumed for 3 nonconsecutive days.

d. **Sleepiness** - The Epworth Sleepiness Scale is a measure of a person’s general level of daytime sleepiness, or their average sleep propensity in daily life.

e. **Health Related Quality of Life**– The Health Related Quality of Life Scale is a measure of a person’s physical and mental health and function.
Time Required. If you are randomized to the training group then you will be asked to commit to up to three hours per week, for sixteen weeks for the training segment of this project. Additionally, you will be asked to commit to ten testing and informational sessions that will each last up to two hours. Testing and training will take place as follows:

- **Familiarization Session (Pre):** This is the familiarization session. During this session, all tests and procedures will be explained, after which we’ll ask you to complete the appropriate health and medical status questionnaires and an Informed Consent Form. Additionally, participants will be asked to complete the questionnaires pertaining physical activity levels, health behavior, sleepiness, and perceived enjoyment. This session is estimated to last approximately 1 ½ -2 hours. You will also be given dietary record forms to be completed and returned to the researchers at the next meeting. After this session, future questionnaires will be completed during the clinical testing sessions.

- **Clinical Testing (Pre, Mid, Post, 3M FU, 6M FU):** In this session we measure your blood pressure and heart rate and complete a dual x-ray absorptiometry (DXA) scan for the assessment of body composition and bone mineral (hip) density. Diet records will also be collected. This session is estimated to last approximately 1 ½ -2 hours: 1 ½ hours for testing, 20 minutes for dietary records. All clinical testing will take place in the Kinesiology Human Performance Lab. For the mid-point, post-training, follow-up sessions, you will also be asked to complete the study questionnaires at this session. This is expected to add approximately 15 minutes to the session.

- **Fitness Testing (Pre, Mid, Post, 3M FU, 6M FU):** You will be asked to come to complete a maximal exercise test ($VO_{2max}$ test) the same day as your clinical testing. Maximal testing will be completed in the Kinesiology Human Performance Lab.

- **Blood Values (Pre, Mid, Post, 3M FU, 6M FU):** In this session you will be asked to visit the Sentara RMH Outpatient Center located with the Sentara RMH Occupational Health Center at 1790-64B to have blood taken. Researchers will provide all documentation for you to take to each session. You will be required to fast for 8-10 hours. Please note that per SRMH protocol you will be required to provide a medical provider’s information at each blood draw session. If blood values are outside normal/optimal ranges the blood values will be sent to your primary medical provider. This session should last 15 minutes.

- **Training Protocol:** As the main portion of the study, you will participate in a training session 3 days per week that will progress from 30 minutes per session, to 60 minutes per session for the next 16 weeks. Your group assignment will determine exactly what these exercise sessions will consist of. In brief, you will either be participating in moderate-intensity training, which consists of a continuous bout of exercise performed at a moderate intensity (moderate intensity is described as a 5 or 6 on a scale of 1 to 10); short high-intensity interval training, which consists of short bouts (30 seconds) of maximal effort exercise followed by longer recovery periods (4 minutes); or a combination of the two, which consists of one day of the continuous moderate intensity training session and two days of the high intensity interval training. You will be
asked to come into the Marilyn Crawford Fitness Center (Godwin Hall) to complete all training sessions. Training groups are expected to see improvements in fitness.

Risks. There is minimal risk associated with submaximal exercise testing in individuals who are “low” or “moderate” risk according to guidelines established by the American College of Sports Medicine. There is a minimal level of discomfort that may be experienced during the exercise testing, which includes muscle soreness and fatigue. Muscle soreness may be felt 24-48 hours following the testing.

The risks of venipuncture blood sampling include possible mild bruising and the risk of transfer of blood-borne pathogens. This risk is considered to be minimal and all safety precautions for handing blood samples will be followed according to OSHA protocols and SRMH.

According to the manufacture’s specifications (i.e., GE Healthcare), whole body DXA analysis exposes participants to 1.5 mrem of radiation. The exposure to radiation during a single chest x-ray (i.e., 5 mrem) is more than 3 times greater than radiation from DXA. Also, background radiation from DXA is about equal to the amount of radiation one experiences during a flight from New York to London. Please note that the effects of the DXA scan are cumulative depending on your prior exposure to radiation. If you have questions regarding your risk from the scan please consult with the researchers.

Benefits. Potential benefits from participation in this study include free testing of cardiorespiratory fitness, body composition, lipid profile, and bone mineral density. You will receive the results from your individual tests, including a rating of how you compare to individuals within your age category. Along with these results, you’ll receive information regarding the importance and meaning of measure, as well as what steps you could take to improve these measures if you would like to. You will also have the opportunity to learn about habitual dietary intake and your percentages of energy nutrients and total caloric intake. Participation in this study will also help researchers understand metabolic responses and adherence to long-term exercise. Finally, if you complete the study, you’ll receive a free dietary consultation.

If you are randomized to the two training groups you will also receive free monitored workout sessions and motivation from the researchers. The researchers expect to see positive metabolic changes for participants in all training protocols that may result in improved health and general well-being.

Confidentiality. All data and results will be kept confidential. You will be assigned an identification code. All of your questionnaires and other results will be filed only according to your identification code, with your full name not located in that file. For the duration of the study, your first name will be stored with this data, so that research staff may address you, but this will be removed at the completion of the study. These results will be stored in a locked cabinet in a locked office. Electronic copies of the data will be password protected and kept only on secure servers. Only research personnel, who may include students, will have access to this data in either hard or electronic format. Any forms that link your name with your identification number, including this form, will be kept in a different file, which will be located in the office of one of the head researchers on this study. Additionally, any electronic formats of this information will be kept by one of the head researchers and will be password protected with a
different password than the data. None of your test results or data will be located in this file. Access to these files will be limited to the head researchers on this staff and will only be used for the purposes of matching up your data to previous results and to contact you for the follow-up measures. After the second follow-up measure, any form that links your name to your identification number will be destroyed. The data collected will be analyzed and used to complete three graduate student research theses, a national presentation, and submission for publication in a professional journal.

Participation and Withdrawal. Your participation is entirely voluntary. You are free to choose not to participate. Should you choose to participate, you can withdraw at any time without consequences of any kind. If at any time you choose to withdraw from the study, any identifying information that links your name to your data will be destroyed at that time.

Reporting Procedures. You will be provided health and fitness tests data at the completion of each test and will receive the results of your blood tests after they have been processed. The findings of the study will be presented at regional and national organizations conferences and submitted for publication in professional journals.

Questions about the Study. If you have questions or concerns during the time of your participation in this study, or after its completion or you would like to receive a copy of the final aggregate results of this study, please contact:

Dr. Elizabeth Skidmore Edwards  
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edwardes@jmu.edu  
mailto:edwardes@jmu.edu  
540-568-5220

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Appendix B

Health Status Questionnaire

Part I: Medical History

1. Has anyone in your family had a heart attack, heart surgery, or sudden death due to cardiovascular disease prior to the age of 65? (Circle one) Yes No

If yes, who? ____________________

How old were they? (Circle one) 54 or younger 55-59 60-64

2. Date of last medical exam: ________________ Last physical fitness test: ________________

3. Please list any operations that you have had:

______________________________________________________________________________________
______________________________________________________________________________________
______________________________________________________________________________________

4. Please list any condition for which you have been diagnosed or are being treated for by a physician or health professional:

______________________________________________________________________________________
______________________________________________________________________________________
______________________________________________________________________________________

5. Please list all medications taken in the last six months:

______________________________________________________________________________________
______________________________________________________________________________________
______________________________________________________________________________________

6. The occurrence of any of these health symptoms frequently is the basis for medical attention. Please check how often you have each of the following:

<table>
<thead>
<tr>
<th>Symptom</th>
<th>1 Rarely</th>
<th>2 Infrequently</th>
<th>3 Sometimes</th>
<th>4 Fairly Often</th>
<th>5 Very Often</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cough up blood</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Abdominal pain</td>
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<tr>
<td>Low back pain</td>
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<td>Leg pain</td>
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<tr>
<td>Arm or shoulder pain</td>
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<tr>
<td>Chest pain</td>
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<tr>
<td>Swollen joints</td>
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<td>---</td>
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<td></td>
</tr>
<tr>
<td>Feel faint</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Dizziness</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Breathless on slight exertion</td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

7. Do you smoke? (Circle one)       Yes       No

If yes, how many per day: Cigarettes: 40 or more  20-39  10-19  1-9

Cigars or pipes only: 5 or more or any inhaled less than 5, none inhaled

Appendix C

INTERNATIONAL PHYSICAL ACTIVITY QUESTIONNAIRE

We are interested in finding out about the kinds of physical activities that people do as part of their everyday lives. The questions will ask you about the time you spent being physically active in the last 7 days. Please answer each question even if you do not consider yourself to be an active person. Please think about the activities you do at work, as part of your house and yard work, to get from place to place, and in your spare time for recreation, exercise or sport.

Think about all the vigorous and moderate activities that you did in the last 7 days. Vigorous physical activities refer to activities that take hard physical effort and make you breathe much harder than normal. Moderate activities refer to activities that take moderate physical effort and make you breathe somewhat harder than normal.

PART 1: JOB-RELATED PHYSICAL ACTIVITY

The first section is about your work. This includes paid jobs, farming, volunteer work, course work, and any other unpaid work that you did outside your home. Do not include unpaid work you might do around your home, like housework, yard work, general maintenance, and caring for your family. These are asked in Part 3.

1. Do you currently have a job or do any unpaid work outside your home?
   Yes
   No
   
   Skip to PART 2: TRANSPORTATION

The next questions are about all the physical activity you did in the last 7 days as part of your paid or unpaid work. This does not include traveling to and from work.

2. During the last 7 days, on how many days did you do vigorous physical activities like heavy lifting, digging, heavy construction, or climbing up stairs as part of your work? Think about only those physical activities that you did for at least 10 minutes at a time.

   _____ days per week

   No vigorous job-related physical activity
   
   Skip to question 4

3. How much time did you usually spend on one of those days doing vigorous physical activities as part of your work?
   _____ hours per day
   _____ minutes per day
4. Again, think about only those physical activities that you did for at least 10 minutes at a time. During the last 7 days, on how many days did you do moderate physical activities like carrying light loads as part of your work? Please do not include walking.

_____ days per week

No moderate job-related physical activity  

5. How much time did you usually spend on one of those days doing moderate physical activities as part of your work?

_____ hours per day  
_____ minutes per day

6. During the last 7 days, on how many days did you walk for at least 10 minutes at a time as part of your work? Please do not count any walking you did to travel to or from work.

_____ days per week

No job-related walking  

7. How much time did you usually spend on one of those days walking as part of your work?

_____ hours per day  
_____ minutes per day

PART 2: TRANSPORTATION PHYSICAL ACTIVITY

These questions are about how you traveled from place to place, including to places like work, stores, movies, and so on.

8. During the last 7 days, on how many days did you travel in a motor vehicle like a train, bus, car, or tram?

_____ days per week

No traveling in a motor vehicle  

9. How much time did you usually spend on one of those days traveling in a train, bus, car, tram, or other kind of motor vehicle?

_____ hours per day  
_____ minutes per day

Now think only about the bicycling and walking you might have done to travel to and from work, to do errands, or to go from place to place.

10. During the last 7 days, on how many days did you bicycle for at least 10 minutes at a time to go from place to place?

_____ days per week

No bicycling from place to place  

Skip to question 6

Skip to PART 2: TRANSPORTATION

Skip to question 10

Skip to question 12
11. How much time did you usually spend on one of those days to bicycle from place to place?
   _____ hours per day
   _____ minutes per day

12. During the last 7 days, on how many days did you walk for at least 10 minutes at a time to go from place to place?
   _____ days per week

   No walking from place to place

   Skip to PART 3: HOUSEWORK, HOUSE MAINTENANCE, AND CARING FOR FAMILY

13. How much time did you usually spend on one of those days walking from place to place?
   _____ hours per day
   _____ minutes per day

PART 3: HOUSEWORK, HOUSE MAINTENANCE, AND CARING FOR FAMILY

This section is about some of the physical activities you might have done in the last 7 days in and around your home, like housework, gardening, yard work, general maintenance work, and caring for your family.

14. Think about only those physical activities that you did for at least 10 minutes at a time. During the last 7 days, on how many days did you do vigorous physical activities like heavy lifting, chopping wood, shoveling snow, or digging in the garden or yard?
   _____ days per week

   No vigorous activity in garden or yard

   Skip to question 16

15. How much time did you usually spend on one of those days doing vigorous physical activities in the garden or yard?
   _____ hours per day
   _____ minutes per day

16. Again, think about only those physical activities that you did for at least 10 minutes at a time. During the last 7 days, on how many days did you do moderate activities like carrying light loads, sweeping, washing windows, and raking in the garden or yard?
   _____ days per week

   No moderate activity in garden or yard

   Skip to question 18

17. How much time did you usually spend on one of those days doing moderate physical activities in the garden or yard?
   _____ hours per day
18. Once again, think about only those physical activities that you did for at least 10 minutes at a time. During the last 7 days, on how many days did you do moderate activities like carrying light loads, washing windows, scrubbing floors and sweeping inside your home? _____ days per week

No moderate activity inside home

19. How much time did you usually spend on one of those days doing moderate physical activities inside your home?

_____ hours per day
_____ minutes per day

PART 4: RECREATION, SPORT, AND LEISURE-TIME PHYSICAL ACTIVITY

This section is about all the physical activities that you did in the last 7 days solely for recreation, sport, exercise or leisure. Please do not include any activities you have already mentioned.

20. Not counting any walking you have already mentioned, during the last 7 days, on how many days did you walk for at least 10 minutes at a time in your leisure time? _____ days per week

No walking in leisure time

21. How much time did you usually spend on one of those days walking in your leisure time?

_____ hours per day
_____ minutes per day

22. Think about only those physical activities that you did for at least 10 minutes at a time. During the last 7 days, on how many days did you do vigorous physical activities like aerobics, running, fast bicycling, or fast swimming in your leisure time? _____ days per week

No vigorous activity in leisure time

23. How much time did you usually spend on one of those days doing vigorous physical activities in your leisure time?

_____ hours per day
_____ minutes per day

24. Again, think about only those physical activities that you did for at least 10 minutes at a time. During the last 7 days, on how many days did you do moderate physical activities like
bicycling at a regular pace, swimming at a regular pace, and doubles tennis in your leisure time?

_____ days per week

No moderate activity in leisure time

25. How much time did you usually spend on one of those days doing moderate physical activities in your leisure time?

_____ hours per day

_____ minutes per day

PART 5: TIME SPENT SITTING

The last questions are about the time you spend sitting while at work, at home, while doing course work and during leisure time. This may include time spent sitting at a desk, visiting friends, reading or sitting or lying down to watch television. Do not include any time spent sitting in a motor vehicle that you have already told me about.

26. During the last 7 days, how much time did you usually spend sitting on a weekday?

_____ hours per day

_____ minutes per day

27. During the last 7 days, how much time did you usually spend sitting on a weekend day?

_____ hours per day

_____ minutes per day

This is the end of the questionnaire, thank you for participating.
Appendix D

PAR-Q & YOU

(A Questionnaire for People Aged 15 to 69)

Regular physical activity is fun and healthy, and increasingly more people are starting to become more active every day. Being more active is very safe for most people. However, some people should check with their doctor before they start becoming much more physically active.

If you are planning to become much more physically active than you are now, start by answering the seven questions in the box below. If you are between the ages of 15 and 69, the PAR-Q will tell you if you should check with your doctor before you start. If you are over 69 years of age, and you are not used to being very active, check with your doctor.

Common sense is your best guide when you answer these questions. Please read the questions carefully and answer each one honestly: check YES or NO.

YES NO
1. Has your doctor ever said that you have a heart condition and that you should only do physical activity recommended by a doctor?
2. Do you feel pain in your chest when you do physical activity?
3. In the past month, have you had chest pain when you were not doing physical activity?
4. Do you lose your balance because of dizziness or do you ever lose consciousness?
5. Do you have a bone or joint problem (for example, back, knee or hip) that could be made worse by a change in your physical activity?
6. Is your doctor currently prescribing drugs (for example, water pills) for your blood pressure or heart condition?
7. Do you know of any other reason why you should not do physical activity?

If you answered YES to one or more questions
Talk with your doctor by phone or in person BEFORE you start becoming much more physically active or BEFORE you have a fitness appraisal. Tell your doctor about the PAR-Q and which questions you answered YES.
• You may be able to do any activity you want — as long as you start slowly and build up gradually. Or, you may need to restrict your activities to those which are safe for you. Talk with your doctor about the kinds of activities you wish to participate in and follow his/her advice.
• Find out which community programs are safe and helpful for you.

NO to all questions
If you answered NO honestly to all PAR-Q questions, you can be reasonably sure that you can:
• start becoming much more physically active — begin slowly and build up gradually. This is the safest and easiest way to go.
• take part in a fitness appraisal — this is an excellent way to determine your basic fitness so that you can plan the best way for you to live actively. It is also highly recommended that you have your blood pressure evaluated. If your reading is over 144/94, talk with your doctor before you start becoming much more physically active.

DELAY BECOMING MUCH MORE ACTIVE:
• if you are not feeling well because of a temporary illness such as a cold or a fever — wait until you feel better; or
• if you are or may be pregnant — talk to your doctor before you start becoming more active.

PLEASE NOTE: If your health changes so that you then answer YES to any of the above questions, tell your fitness or health professional. Ask whether you should change your physical activity plan.

Important Use of the PAR-Q. The Canadian Society for Exercise Physiology, Health Canada, and their agents assume no liability for persons who undertake physical activity, and if in doubt after completing this questionnaire, consult your doctor prior to physical activity.

No changes permitted. You are encouraged to photocopy the PAR-Q but only if you use the entire form.

NOTE: If the PAR-Q is being given to a person before he or she participates in a physical activity program or a fitness appraisal, this section may be used for legal or administrative purposes.

"I have read, understood and completed this questionnaire. Any questions I had were answered to my full satisfaction."

NAME

SIGNATURE

DATE

SIGNATURE OF PARENT or GUARDIAN (for participants under the age of majority)

DATE

WITNESS

Note: This physical activity clearance is valid for a maximum of 12 months from the date it is completed and becomes invalid if your condition changes so that you would answer YES to any of the seven questions.
Appendix E

Physician Approval Form

Patient Name: ________________

1. Is the patient prediabetic, diagnosed by one of the following?
   a. HbA1C ______
   b. Fasting Blood Glucose ______
   c. OGTT ______

   Date of diagnosis ________

2. Are there specific concerns or conditions we should be aware of before this individual engages in the physical fitness assessment for this study??
   _______________________________________________________________________
   _______________________________________________________________________

3. If this individual has completed a graded exercise test (stress test) please provide the following:
   a. Date of Test: __________________________________________________________

   b. A copy of the final exercise report and interpretation.

4. Please provide the following information so that we may contact you if we have any further questions:
   ___ I AGREE to the participation of this individual in the herein described study.
   ___ I DO NOT AGREE that this individual is a candidate for this study.

Physician’s Signature
   _______________________________________________________________________


References


