FITNESS NON-RESPONSE FOLLOWING AEROBIC EXERCISE TRAINING IN OBESE AFRICAN AMERICANS

by

Macon Travis Hammond

December, 2019

Director of Thesis: Damon Swift, Ph.D.

Major Department: Kinesiology

Cardiorespiratory fitness (CRF) has been closely associated with cardiovascular disease (CVD) and all-cause mortality. An inverse relationship between CRF, and CVD and all-cause mortality has been well-established. To decrease the risk of developing CVD and all-cause mortality, aerobic exercise is prescribed as a preventative measure. Most individuals exhibit increases in CRF, and subsequent CVD and mortality risk reduction, following engagement in aerobic exercise in accordance with current physical activity guidelines. However, a percentage of individuals have been shown to exhibit an atypical response to exercise when considering CRF. This group of individuals demonstrate attenuated responses or adverse responses to exercise even after following aerobic exercise prescribed in concert with current physical activity guidelines. Additionally, CRF non-response has been reported to be a possible health disparity between African Americans and other races when comparing non-response prevalence following aerobic exercise. As a result, these individuals do not reap the well-documented benefits of aerobic exercise, specifically CVD and all-cause mortality risk reduction. The objective of this study was to examine the prevalence of CRF non-response following moderate and high intensity aerobic exercise in obese African Americans.

We examined obese African American participants as part of the High Intensity exercise to Promote Accelerated improvements in Cardiorespiratory fitness (HI-PACE) study. Participants were randomized to a control group or one of two supervised exercise intervention groups for 24 weeks. CRF non-response was defined as a VO_2 response of ≤ 0 L/min or ml/kg/min following aerobic exercise, while CRF response was defined as a VO_2 response of > 0 L/min or ml/kg/min following aerobic exercise. Participants were further classified into responders or non-responders based on follow-up measures at the 12-week mid-intervention mark.

A total of 33 participants (mean age=48.8 ± 7.6 years; 75.8% females) were examined for the purpose of this study. When comparing the exercise training groups, both the moderate and high intensity groups demonstrated increases in overall CRF levels. When comparing follow-up values to baseline values within the CRF responder group, significant improvements were elicited in systolic and diastolic blood pressures, and in estimated metabolic equivalents (METs). Additionally, the data trends indicated that high intensity exercise elicited higher CRF increases and clinically significant MET increases when compared to the moderate intensity group although statistical significance was not achieved. No significant differences were observed when comparing follow-up values and change scores between responder and non-responder groups.

Based on the results, it may be concluded that both moderate and high intensity aerobic exercise training is effective at increasing overall CRF levels. Additionally, high intensity exercise may be slightly more effective at increasing CRF and eliciting clinically significant MET increases.

FITNESS NON-RESPONSE FOLLOWING AEROBIC EXERCISE TRAINING IN OBESE AFRICAN AMERICANS

A Thesis

Presented To The Faculty of the Department of Kinesiology

East Carolina University

In Partial Fulfillment of the Requirements for the Degree

Master of Science in Kinesiology

Exercise Physiology

by

Macon Travis Hammond

December, 2019

FITNESS NON-RESPONSE FOLLOWING AEROBIC EXERCISE TRAINING IN OBESE AFRICAN AMERICANS

by

Macon Travis Hammond

APPROVED BY:

DIRECTOR OF THESIS: ____
Damon Swift, Ph.D.

COMMITTEE MEMBER: ____
Joseph Houmard, Ph.D.

COMMITTEE MEMBER: ____
Katrina Dubose, Ph.D.

CHAIR OF THE DEPARTMENT OF KINESIOLOGY: _________________________
Joonkoo Yun, Ph.D.

DEAN OF THE GRADUATE SCHOOL: ______________________________
Paul J. Gemperline, PhD

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF ABBREVIATIONS

CVD	Cardiovascular Disease	1
CRF	Cardiorespiratory Fitness	1
VO_{2max}	Maximal Oxygen Consumption	6
VO_{2peak}	Peak Oxygen Consumption	24
PA	Physical Activity	1

CHAPTER 1: INTRODUCTION

The association between cardiorespiratory fitness (CRF) levels, and cardiovascular disease (CVD) and all-cause mortality has been well-established (Laukkanen et al., 2004; Blair et al., 1989; Sui et al., 2007). Fortunately, the benefits of physical activity (PA) and structured exercise training on CRF levels are also numerous and well-documented (Garber et al., 2011; Barlow et al., 2006). The various benefits of regular PA and exercise include risk reduction for type 2 diabetes, various forms of cancer, CVD, and an increase in overall fitness levels, longevity, and quality of daily living (Garber et al., 2011; Kohl et al., 2012; Naci & Ioannidis, 2013).

Low CRF levels have been associated with an increased CVD and all-cause mortality risk (Blair et al., 2001), while increasing fitness levels are associated with a decreased CVD and mortality risk (Blair et al., 1996; Blair et al., 1995, Blair et al., 1989; Stevens et al., 2004; Myers et al., 2002; Gulati et al., 2003; Mora et al., 2003). When engaged in appropriate frequency and volumes of cardiorespiratory endurance exercise, the expected response is that CRF should increase with sustained exercise training (Sisson et al., 2009). However, there is much heterogeneity in CRF response as a substantial number of individuals have been reported to exhibit non-response following staff supervised moderate and vigorous aerobic exercise training (Bouchard & Rankinen, 2001; Hautala et al., 2003; Sisson et al., 2009, Swift et al., 2013). Based on previous exercise training studies, non-response rates following aerobic exercise training range from 15-32% (Hautala et al., 2003; Kohrt et al., 1991; Wilmore et al., 2001) indicating a possible major problem for non-responders.

Existing literature has examined CVD risk, associated morbidity and mortality, and modifiable CVD risk factors (Powell et al., 1987; USDHHS, 1989; Manson et al., 1991; NCEP, 1993; Stamler et al., 1993; Willet et al., 1995; CDC, 2004) among differing races. Substantial differences have been reported in the incidence and prevalence of CVD and its associated risk factors when comparing African Americans to Caucasians (Cooper et al., 2000; LaPorte et al., 1995; Kenny et al., 1995; Tull et al., 1995; Stern et al., 1995). In African Americans and Caucasians, the leading cause of all-cause mortality is attributed to CVD; however, African Americans have a higher rate of CVD-associated mortality when compared to Caucasians (Gillum, 1996). Underlying factors for the higher rate of CVD in African Americans is associated with the higher prevalence of hypertension, including other CVD comorbidities such as diabetes, obesity, and lower CRF levels (Lavie et al., 2004; Zeno et al., 2010; Ceaser et al., 2013) when compared to Caucasians (AHA, 2002). Because aerobic exercise is commonly prescribed as a treatment modality for CVD and its risk factors, and all-cause mortality risk reduction (Lee et al., 2012), CRF non-response following aerobic exercise training is a growing major public issue, especially for African Americans (Swift et al., 2013).

Previous studies have indicated that individuals' age, gender, race, and baseline CRF levels do not accurately predict levels of response to exercise training (Bouchard & Rankinen, 2001; Kohrt et al., 1991; Skinner et al., 2001); however, other studies have reported opposing results (Hautala et al., 2003; Sisson et al., 2009). To our knowledge, little data are available that have examined the incidence, extent, and specific predictors of CRF non-response in African Americans. Due to inconsistency and a minimal volume of literature in this research area, the purpose of this study is two-fold: 1) to compare CRF non-response following moderate and vigorous aerobic exercise training in obese African Americans and 2) to determine potential predictors of fitness non-response in African Americans.

For the purpose of the present study, we utilized data collected from the High Intensity exercise to Promote Accelerated improvements in Cardiorespiratory fitness (HI-PACE) study which examined the effects of moderate and high intensity aerobic exercise training over 24 weeks on CRF in obese African Americans. Current literature suggests that fitness non-response decreases following higher amounts and intensities of aerobic exercise (Ross et al., 2015; Sisson et al., 2009), and possible racial CRF differences are present following aerobic exercise training (Swift et al., 2013); therefore, we hypothesize that CRF non-response in African Americans will be lower following high intensity aerobic exercise when compared to moderate intensity aerobic exercise. This study will expand the knowledge regarding fitness response to specific amounts and intensities of aerobic exercise, which will allow for exercise prescription adjustments to be made, specifically in African Americans.

Purpose

The purpose of this study was to compare CRF non-response following moderate and high intensity aerobic exercise training in obese African Americans.

Hypothesis

Fitness non-response in African Americans would be lower following high intensity aerobic exercise when compared to moderate intensity aerobic exercise.

Delimitations

The present study included the use of sedentary, obese African Americans aged 45-60 years, moderate and vigorous aerobic exercise training on a treadmill, and retrospective data.

Limitations

The use of sedentary, obese African Americans aged 45-60 years limited the generalizability of results to other races, age groups, and BMI classifications. Since the exercise intervention consisted of a moderate and vigorous nature, results cannot be inferred regarding other intensities of exercise. The use of a treadmill also limited generalizability to other exercise modalities. Lastly, since retrospective data was used, the HI-PACE study design was not initially developed with the main purpose of evaluating CRF non-response in African Americans following aerobic exercise training.

CHAPTER 2: REVIEW OF LITERATURE

The purpose of this study was to compare fitness non-response following moderate and vigorous aerobic exercise training in obese African Americans. The following review of literature will examine the following topics: 1) African American CVD Risk, 2) CRF as a CVD and Mortality Risk Factor, 3) CRF in African Americans, 4) Potential Causation for Low CRF in African Americans, 5) and CRF Non-Response.

African American CVD Risk

When compared to Caucasians, African Americans have a significantly greater risk for the development of CVD and CVD-associated mortality (Thomas et al., 2005; Kalinowski et al., 2004; Loehr et al., 2004; Kodama et al., 2013; Swift et al., 2013). The American Heart Association reported CVD mortality rates in the 2016 Heart Disease and Stroke Statistics stating that for every 100,000 Americans, approximately 220 Americans died due to CVD. When comparing CVD mortality rates between African Americans and Caucasians, approximately 352 African American males and 241 African American females died per 100,000 individuals, while 268 Caucasian males and 182 Caucasian females died per 100,000 individuals. Additional statistics also indicate that 37.4% and 33.8% of Caucasian men and women, respectively, are affected by CVD, while 44.8% and 47.3% of African American men and women, respectively, are affected by CVD (Lloyd-Jones, Hong et al., 2010). These reports support the significantly greater risk in CVD-associated mortality rate previously reported when comparing African Americans to Caucasians indicating a concerning racial health disparity (Benjamin et al., 2017).

Associated with CVD are risk factors including obesity, diabetes, dyslipidemia, cigarette smoking, physical inactivity, and hypertension (Flack et al., 2003). African Americans have been reported to have a higher prevalence of type 2 diabetes, obesity, and hypertension when compared to Caucasians (Lloyd-Jones, Hong et al., 2010). Hypertension among African Americans leads statistically across the globe with a rate of 44% (Lloyd-Jones, Adams et al., 2010). Another possible underlying causation for the development of CVD is sedentary behavior. African Americans have also been reported to have a higher prevalence of insufficient PA levels when compared to Caucasians (Appel et al., 2002; Sundquist et al., 2001). The American Heart Association classifies sedentary behavior as a major risk factor in the development of CVD, specifically coronary heart disease (Roger et al., 2012). The associated risk of these CVD risk factors may be diminished, or greatly reduced, by engagement in regular aerobic exercise (Jacobson et al., 2015; Garcia et al., 2001).

CRF as a CVD and Mortality Risk Factor

Cardiorespiratory fitness can be objectively measured in terms of METs (metabolic equivalents) or maximal aerobic capacity (VO_{2max}) (Swift et al., 2013; Ross et al., 2016). Various research studies have established an inverse relationship between CRF and CVD mortality (Gulati et al., 2003; Mora et al., 2003; Blair et al., 1989). Since lower CRF levels predispose individuals to CVD development, it is imperative for CRF to be improved for CVD risk reduction. Blair et al. (Blair et al., 1989) concluded that moderate-to-high fitness levels provided protection from CVD and its associated risks when compared to individuals with low CRF. Because CVD is the leading cause of mortality across the United States, exercise is prescribed by many healthcare/public health agencies (e.g., American College of Sports Medicine; American Heart Association) with the intent of combatting CVD and its associated risks by increasing CRF (Haskell et al., 2007; Garber et al., 2011; USDHHS, 2008).

CRF has been classified as a risk factor for CVD development independent of other various CVD risk factors such as hypertension and dyslipidemia (Ross et al., 2016; Blair et al., 1995; Myers et al., 2002; Church et al., 2005). Utilizing data from approximately 33,000 subjects associated with the Aerobics Center Longitudinal Study (ACLS), Blair et al. (Blair et al., 1996) reported that a low CRF is a strong predictor for CVD and all-cause mortality. In men, low CRF resulted in a relative risk of 1.70 for CVD mortality. Additionally, a relative risk of 1.52 for all-cause mortality due to low CRF was reported in men, while a relative risk of approximately 2.00 was reported in women further validating the inverse relationship between low CRF and all-cause mortality. Blair et al. (Blair et al., 1989), in a previous longitudinal study examining 10,224 men and 3,120 women, also reported a strong inverse relationship between all-cause mortality and CRF levels. The results indicated that the lowest CRF quintile (lowest 20% of sample) placed women and men at a 94% and 58% increased risk of all-cause mortality, respectively, when compared to other quintiles after age and traditional CVD risk factor adjustments were made. When comparing the lowest CRF quintile to the next lowest CRF quintile after age adjustments were made, significant reductions were reported in all-cause mortality in women and men (women 4.7 vs. 2.4; men 3.4 vs 1.4). Lee et al. (Lee et al., 2012), after examining 3,148 participants, also supported this finding by reporting that a 1 MET increase in CRF was associated with a 15% decrease in all-cause mortality and a 19% decrease in CVD risk. As a result, the inverse relationship between elevated CRF levels and the decreased risk for CVD development and all-cause mortality was again validated.

An additional study including data from 27,055 women, Mora et al. (Mora et al., 2007) supported the inverse relationship in women by reporting that elevated CRF levels decrease CVD risk among apparently healthy women after a follow-up period of 6 and 12 months. The results indicated that CVD risk reduction increased from 30% to 50% following engagement in PA. When participating in moderate intensity PA, CVD relative risk reduction improved from 30% to 40%. Church et al. (Church et al., 2005), also utilizing data from the Aerobics Center Longitudinal Study, validated the inverse relationship between CRF and CVD mortality risk among obese individuals with type 2 diabetes. A sample of 2,316 men, aged 50 years, were compared across fitness and fatness levels. The findings reported that fitness levels of participants, regardless of weight status (normal, overweight, class 1 obese), was an accurate predictor of CVD mortality risk. Participants classified as overweight and class 1 obese with high fitness levels experienced no significant increases in CVD mortality risk when compared to participants classified as normal weight with high fitness levels. These findings are notable considering that type 2 diabetes and obesity are well-established health disparities in African Americans when compared to Caucasians (Wang et al., 2007; CDC, 2014). Both type 2 diabetes and obesity are possible CVD comorbidities and are more prevalent in African Americans when compared to Caucasians (Wang et al., 2007; CDC, 2014).

Kodama et al. (Kodama et al., 2009) performed a meta-analysis of 33 studies examining CRF levels, measured in METs, and its association with CVD and all-cause mortality in healthy men and women. The meta-analysis included a total of 102,980 subjects with 6,910 all-cause fatalities, and 84,323 subjects with CVD-associated events. The minimum CRF level required to achieve significant CVD risk reduction in women was 8 METs in men and 6 METs in women. The results indicated that an increase of 1 MET in CRF was correlated with a 13% decrease in all-cause mortality and a 15% decrease in CVD risk (Kodama et al., 2009). The above studies and results indicate that increased CRF is a preventative measure utilized to combat and protect against CVD, its associated risks, and morbidity and mortality (Swift et al., 2013), and should be included in CVD risk stratification (Lee et al., 2010). Due to its cardioprotective measures, engagement in appropriate amounts and intensities of aerobic exercise is critical for all individuals, but especially for African Americans.

CRF in African Americans

When comparing African Americans and Caucasians, there is a notable difference in CRF levels; however, a similar relationship exists between CRF levels and all-cause and CVD-associated mortality regardless of ethnicity (Kokkinos et al., 2008; Al-Mallah et al., 2016). African Americans have been reported to exhibit lower baseline CRF levels and less adherence to public health guidelines leading to increases in CVD risk and CVD-associated mortality when compared to Caucasians (Swift et al., 2017; Pandey et al., 2016). Based on results from various epidemiological studies, CRF has been reported to be a predictor and risk factor for the development of CVD independent of other CVD comorbidities such as hypertension and dyslipidemia (Blair et al., 1995; Myers et al., 2002; Church et al., 2005).

In a study of 53,876 participants, Al-Mallah et al. (Al-Mallah et al., 2016) determined that African Americans, when compared to Caucasians, achieved lower CRF levels following analysis of maximal exercise testing. The results also indicated an inverse relationship between CRF and mortality risk when analyzing African Americans and Caucasians. Lastly, the authors concluded that although CRF was a strong predictor of all-cause mortality in both African Americans and Caucasians, no significant differences were observed in all-cause mortality and CRF levels between ethnicities. Kokkinos et al. (Kokkinos et al., 2008), after examining 15,660 males from two Veterans Affairs Medical Centers, reported post-maximal graded exercise testing data indicating that CRF was a more accurate predictor of all-cause mortality than already established CVD risk factors. Increasing CRF by 1 MET was reported to result in a 13%

decrease in mortality rate. For participants classified as moderately fit (5-7 METs), a decrease of approximately 20% was observed when compared to participants achieving <5 METs. When comparing moderately fit African Americans and Caucasians relative risk of mortality, African Americans only gained a significant reduction when achieving CRF levels >7 METs. Opposingly, Caucasians received significant reductions in mortality rate when achieving CRF levels of 5-7 METs. This information suggests that African Americans affected by CVD may require higher doses of exercise when compared to Caucasians to receive identical protective cardiovascular mechanisms associated with regular exercise engagement. Zeno et al. (Zeno et al., 2010) reported that low CRF could possibly place apparently healthy African Americans at a higher risk for CVD development. The study also validated that including CRF in CVD risk stratification (Lee et al., 2010), in addition to already established CVD risk factors, may aid in prevention by allowing for early identification of CVD in high-risk African Americans.

Utilizing data from 8,457 subjects included in the National Health and Nutrition Examination Survey (NHANES), Carnethon et al. (Carnethon et al., 2005) reported that low CRF in African Americans was more prevalent across various age groups when compared to Caucasians following submaximal cycle ergometer testing. Although NHANES does not use maximal exercise testing for CRF measurement, the results indicate that African Americans exhibited lower CRF than Caucasians. Lower CRF levels were even more exaggerated when comparing African American women to Caucasian women (Ceaser et al., 2013; Wang et al., 2010; Duncan et al., 2005).

After analyzing NHANES data from 1999-2002, Duncan et al. (Duncan et al., 2005) reported that lower CRF levels were observed in African American adults (33.0 ml/kg/min) when compared to Caucasian adults (34.9 ml/kg/min). CRF levels in African American women

(33.1 ml/kg/min) were also significantly lower when compared to CRF levels in Caucasian women (36.4 ml/kg/min), but CRF levels were not significantly different when comparing men. Ceasar et al. (Ceasar et al., 2013) examined a total of 3,115 subjects from 1999-2004 NHANES data reporting that lower CRF levels were observed in 18-49-year-old African Americans (37.9 ml/kg/min) when compared to Caucasians (40.2 ml/kg/min) of an identical age group. Additionally, Wang et al. (Wang et al., 2010) examined 4,860 subjects, in terms of body mass index and age (20-49 years old), from 1999-2004 NHANES data observing that CRF levels in African American men aged 30-39 years were lower when compared to Caucasians aged 30-39 years. It should be reiterated that two major limitations of NHANES data includes the measurement of CRF through utilization of submaximal testing and exclusion of participants exhibiting any CVD risk factors. Despite these limitations, there is compelling evidence that African Americans are associated with lower CRF levels when compared to Caucasians (Swift et al., 2013).

Since NHANES data was collected and analyzed, additional studies have examined the ethnic differences in CRF. Swift et al. (Swift et al., 2013) concluded that African Americans undoubtedly exhibit lower CRF when compared to Caucasians despite submaximal or maximal measurement methods. Utilizing data from 633 subjects included in the Health, Risk Factors, Exercise Training, and Genetics (HERITAGE) Family study, Skinner et al. (Skinner et al., 2001) reported a 1.1 MET difference between African American and Caucasian men, while a 1.5 MET difference was observed between African American women and Caucasian women following maximal aerobic capacity testing.

Based on the current literature, it is well-established that African Americans are observed to have a higher prevalence of low CRF than Caucasians. Unfortunately, a higher rate of low

CRF prevalence results in a higher risk for CVD development and CVD-associated mortality (Swift et al., 2017). In terms of clinical relevance, early identification of decreased CRF levels and subsequent prescription of CRF-focused PA may greatly reduce CVD health disparities between African Americans and Caucasians, and may play a vital role in decreasing and/or preventing CVD development, especially in African Americans (Swift et al., 2017; Zeno et al., 2010).

Potential Causation for Low CRF in African Americans

There are various reasons possibly explaining why African Americans exhibit lower CRF levels when compared to Caucasians ranging from physiological to behavioral to socioeconomic influences. Behaviorally, African Americans have been reported to exhibit less adherence to PA guidelines set forth by the ACSM and CDC when compared to Caucasians (Haskell et al., 2007; Marshall et al., 2007). Physiologically, possible reasons include a lower percentage of type 1 oxidative muscle fibers and reduced hemoglobin levels stunting the amount of oxygen carried in blood (Swift et al., 2017). The combination of these mechanisms may possibly explain why African Americans have categorically defined lower CRF levels, therefore predisposing African Americans to a higher CVD development and all-cause mortality risk. Although, lower CRF in African Americans may be associated with less PA adherence, type 1 muscle fiber type, and hemoglobin levels, ethnic differences in CRF cannot be solely explained by these possible mechanisms (Swift et al., 2013).

In terms of PA guideline adherence, Haskell et al. (Haskell et al., 2007) reported that 41.8% of African Americans achieved the recommended level of PA, while 51.1% of Caucasians adhered to PA guidelines indicating a significant ethnic difference. Tucker et al. (Tucker et al., 2011) also reported that African Americans were less engaged (58.9%) in moderate-to-vigorous

PA when compared to Caucasians (52.5%). The 2017 Heart Disease and Stroke Statistics (Benjamin et al., 2017) report indicated that African Americans exhibited a 39% rate of physical inactivity when compared to a 27% rate of physical inactivity in Caucasians. Opposingly, Swift et al. (Swift et al., 2013) reported no significant differences in African American and Caucasian postmenopausal women pedometer-determined step counts. Another study utilizing accelerometer measurements supported Swift et al. that no significant differences in PA adherence between African Americans and Caucasians were present (Matthews et al., 2008). Based on these studies, there is much heterogeneity among results; therefore, there is not enough conclusive evidence to establish causation and/or a relationship between low CRF levels and adherence to PA guidelines when comparing African Americans to Caucasians (Swift et al., 2017).

Physiologically, a lower percentage of type 1 muscle fibers indicates less oxidative capacity and less mitochondria, possibly decreasing the ability to perform PA purposed with improving CRF. When comparing matched age, weight, and body mass index of sedentary African Americans and Caucasians, Ama et al. (Ama et al., 1986) indicated that type 1 muscle fiber percentage in African Americans was significantly lower. Similarly, when comparing type 1 muscle fiber percentage in obese African Americans and Caucasians, African Americans exhibited 35%, while Caucasians exhibited 45% (Tanner et al., 2002). Hunter et al. (Hunter et al., 2001), following magnetic resonance spectrometry, reported lower muscular oxidative capacity in premenopausal African American women when compared to premenopausal Caucasian women. Lower muscular oxidative capacity was present and was a VO_{2max} predictor, but differing CRF among ethnicities could not be solely attributed to differing muscle fiber types. Based on these results, it is possible that lower type 1 muscle fiber percentage is, in part, a reason for reduced CRF levels in African Americans when compared to Caucasians.

In addition to a lower percentage of less type 1 muscle fibers, decreased amounts of hemoglobin have been reported in African Americans when compared to Caucasians. Decreased hemoglobin accounts for a lowered ability of the body to circulate oxygen throughout arterial blood and has been reported to be present in African Americans when compared to Caucasians (Hunter et al., 2001; Pivarnik et al., 1995; Beutler & West, 2005; Williams, 1981). Lower hemoglobin in African Americans has also been associated with lower CRF levels in African Americans as evidenced in the Hunter et al. (Hunter et al., 2001) study that reported lower CRF in African Americans when compared to Caucasians following VO_{2max} assessment (Hunter et al., 2001). African Americans exhibited average VO_{2max} values of 29.3 $ml/kg^{-1}/min^{-1}$, while Caucasians achieved average values of 33.6 $ml/kg^{-1}/min^{-1}$. In African Americans, hemoglobin levels were reported as 11.9 $g.dL^{-1}$, while Caucasians were reported to have hemoglobin levels of 12.9 $g.dL^{-1}$. Swift et al. (Swift et al., 2013), in the Dose Response to Exercise in Women (DREW) study, concurrently reported lower hemoglobin levels in postmenopausal African American women (12.6 $g.dL^{-1}$) when compared to postmenopausal Caucasian women (13.2 $g.dL^{-1}$). Although both studies reported lower hemoglobin levels in African Americans, the conclusion that CRF is lower in African Americans due to lower hemoglobin levels does not seem to fully explain the racial differences in CRF (Swift et al., 2017).

Fitness Non-Response

Because CRF is strongly associated with a decreased relative risk of CVD development, CVD mortality, and all-cause mortality, aerobic exercise is prescribed to effectively improve CRF to combat the previously listed risks (Haskell et al., 2007; Blair et al., 1995; Garber et al., 2011; USDHHS, 2008; Lee et al., 2011; Erikssen et al., 1998). Previous literature has further reported that aerobic training is effective in improving CRF in sedentary individuals (Garber et al., 2011), and especially in African Americans (Skinner et al., 2001; Duey et al., 1998; Stephens et al., 2007). However, within groups of exercisers, some individuals experience an attenuated fitness response, no fitness response, or even an adverse fitness response. These three responses to exercise are classified as fitness non-response. Fitness non-response is measured by a technical error which accounts for assessor error and individual CRF variations from day-to-day (Ross et al., 2015).

Based on current literature and available data, only a few studies have examined African American and Caucasian fitness response following a standardized aerobic exercise training regimen. The HERITAGE Family Study examined fitness improvement following 20 weeks of aerobic training in 198 African Americans and 435 Caucasians. The results reported that an attenuated relative CRF response was observed in African Americans (4.9 ml/kg^{-1}/min^{-1}) when compared to Caucasians (5.5 ml/kg^{-1}/min^{-1}), but did not reach statistical significance. However, the ethnic difference was reported to account for approximately 1% of fitness response heterogeneity (Bouchard & Rankinen, 2001).

Swift et al. (Swift et al., 2013), in the DREW study, measured fitness response in a total of 244 postmenopausal Caucasian women and 122 postmenopausal African American women following aerobic training conducted on a cycle ergometer. Participants were randomly assigned to either a control, 4 kcal/kg/body weight^{-1}/week^{-13} (KKW), 8 KKW, or 12 KKW group for a period of 6 months. Participants in the 4, 8, and 12 KKW groups were engaged in exercise at 50% of peak VO_2 for 3-4 sessions per week. Prior to the aerobic exercise training, African American women exhibited lower baseline CRF when compared to Caucasian women.

Following aerobic exercise training, the results indicated a greater relative CRF improvement in Caucasian women compared to African Americans in the 4 (CA=1.00, AA=0.35 ml/kg^{-1}/min^{-1}), 8 (CA=1.59, AA=0.82 ml/kg^{-1}/min^{-1}), and 12 (CA=1.98, AA= 0.50 ml/kg^{-1}/min^{-1}) KKW groups. In terms of absolute CRF improvement, similar significant results were reported in the 8 (CA= 0.10 l O_2/min^{-1}, AA=0.04 l O_2/min^{-1}) and 12 (CA= 0.13 l O_2/min^{-1}, AA=0.04 l O_2/min^{-1}) KKW groups excluding the 4 (CA= 0.04 l O_2/min^{-1}, AA=0.02 l O_2/min^{-1}) KKW group. An overall attenuated mean CRF response was exhibited in African American women when compared to Caucasian women when exercising at a 100% level (AA=0.041, CA=0.105 l O_2/min^{-1}) and 150% level (AA=0.039, CA=0.128 l O_2/min^{-1}) of public health PA guidelines. Overall, the study emphasized the decreased baseline CRF of African Americans when compared to Caucasians and the attenuated fitness response of African Americans to increasing exercise doses. However, despite the incidence of fitness non-response associated with the DREW study exercise training intervention, the percentage of fitness responders to the exercise training protocol among both ethnicities was similar.

To further examine fitness non-response associated with the DREW study, Sisson et al. (Sisson et al., 2009) focused on determining predictors of fitness non-response following aerobic exercise training for 6 months in 310 sedentary, post-menopausal women. The results reported similar findings to those of the DREW study indicating that with increasing exercise an attenuated fitness response was observed. In the 4 KKW group, 44.9% of participants were classified as non-responders, while the 8 KKW and 12 KKW groups included a total non-responder percentage of 23.8% and 19.3%, respectively. Following exercise training, individual response to exercise training ranged from -33.2% to 76.0% indicating a large heterogeneric response to aerobic exercise among participants. When combining training groups, the average percentage of non-responders resulted in 32% of all participants. The results also reported that ethnicity was a significant predictor of baseline values. Despite the large amount of heterogeneity in response to aerobic exercise, this study supported previous DREW study results indicating that with increasing doses of exercise, the percentage of non-responders decreased.

Ross et al. (Ross et al., 2015) further expanded the literature regarding non-response following aerobic exercise training focused on improving CRF. The study analyzed 121 participants classified as sedentary and abdominally obese over a period of 24 weeks. Participants were randomly assigned to three different treatment groups: 1) low amount, low intensity (LALI), 2) high amount, low intensity (HALI), or 3) high amount, high intensity (HAHI). The participants included in the LALI and HALI groups were engaged in supervised aerobic exercise 5 days per week at an intensity of 50% of maximum heart rate. The HAHI group participants were also engaged in aerobic exercise 5 days per week, but intensity was increased to 75% of maximum heart rate. The LALI group energy expenditure was set at 180 and 300 kilocalories per week for men and women, respectively. The energy expenditure for the HALI and HAHI groups was set at 360 kilocalories per week for women and 600 kilocalories per week for men. Following the exercise intervention, 38.5% of LALI participants, 17.6% of HALI participants, and 0.0% of HAHI participants were classified as CRF non-responders according to the CRF error measurement. Overall, CRF non-response rates decreased over the course of the study’s exercise training protocol indicating that CRF non-response rates decrease with increasing amount and intensity of aerobic exercise training.

Summary

Cardiorespiratory fitness is inversely associated with CVD and all-cause mortality. As a result, aerobic exercise is prescribed to elicit higher CRF levels to sharply decrease the risk for

CVD development and all-cause mortality in all ethnicities. Because of this strong relationship, CRF can effectively be utilized in CVD risk stratification processes. Organizations including the ACSM and AHA recommend appropriate exercise amounts and intensities for CRF improvement. Unfortunately, a small group of individuals within the larger population experience fitness non-response following an aerobic exercise training program. African Americans have been reported to exhibit lower baseline CRF and elicit lower CRF when compared to other ethnicities, specifically Caucasians. Because African Americans have higher fitness non-response rates, CVD and all-cause mortality risk are not reduced indicating a major public health concern, and a possible major health disparity between African Americans and other ethnicities. Current literature indicates that with higher amounts and intensities of exercise, the disparity between African American CRF and CRF of other ethnicities may be reduced; therefore, CVD and all-cause mortality rates should inevitably be reduced. Due to current knowledge and limited literature in this area of study, the purpose of this study is to compare fitness non-response in obese African Americans following moderate and high intensity aerobic exercise, and to determine accurate predictors of fitness non-response in obese African Americans. We hypothesize that the rate of fitness non-response will be lower following high intensity aerobic exercise when compared to moderate intensity aerobic exercise.

CHAPTER 3: METHODS

The purpose of this present study was to compare CRF non-response in sedentary, obese African Americans following moderate and high intensity aerobic exercise. Data for this present study was obtained from the High Intensity exercise to Promote Accelerated improvements in Cardiorespiratory fitness (HI-PACE) study database. The primary purpose of the HI-PACE study was to determine the effect of exercise intensity on CRF and insulin sensitivity in obese African Americans. The HI-PACE methodology was accepted, reviewed, and approved by the East Carolina University Institutional Review Board. Written informed consent was obtained from each participant prior to study enrollment.

Participants

Utilizing flyers, website advertisement, and e-mail distributions, 60 participants were recruited. Inclusion criteria included African American participants, 40-65 years of age, classified as obese (30.0-45.0 kg/m^2) and sedentary (step count ≤ 6,500 steps/day and not exercising ≥ 20 minutes on ≥ 3 days/week for the last 3 months). African American race was established by self-report. Exclusion criteria included diagnosis of type 2 diabetes (blood glucose value > 125 mg/dL), known cardiovascular diseases, unsafe high resting blood pressure (systolic > 180 mmHg; diastolic > 100 mmHg), significant medical conditions/diseases, life threatening conditions, pregnancy or planned pregnancies, current engagement in dietary or weight loss interventions, and non-adherence to study protocols.

Participant Screening

Screening was initiated with a telephone interview where study staff screened individuals based on the HI-PACE inclusion/exclusion criteria and provided information about the study.

Following the telephone interview, eligible participants were invited to a one-on-one orientation session with the research coordinator to further discuss study design, procedures, and associated risks and benefits. A barriers interview was conducted to assess participant study availability and adherence. Participants interested in enrolling provided written informed consent. At the screening visit, participant medical/medication history and screening measurements (i.e. resting blood pressure measurements, BMI, and waist circumference) were performed for inclusion/exclusion purposes. Additionally, blood was drawn and sent to a clinical laboratory for lipid, glucose, and insulin analyses, and a comprehensive metabolic panel. Physical activity levels were assessed using accelerometry measured by a Fitbit Flex (Fitbit Inc., San Francisco, CA) for 7 days.

Baseline and Follow-Up Assessment

For the HI-PACE study, baseline measurements including the primary outcome measure (CRF) and secondary outcome measures (BMI, DEXA, waist circumference) were assessed. These measures were re-assessed at the end of the 24-week intervention. At the 12-week, mid-intervention point, CRF, body weight, and other anthropometric measures were assessed. For the purpose of this study, baseline values and 12-week, mid-intervention values will be utilized.

To determine body mass index (BMI in kg/m^2), body weight was measured using a Digi Tol calibrated scale (Mettler Toledo, Columbus, OH), while height was measured by utilization of a height rod on a balanced scale. Body composition was measured by utilization of dual energy x-ray absorptiometry (DEXA). Participants gave written informed consent prior to testing. Participants were asked to remove all jewelry and shoes and lie motionless on the DEXA machine until scan completion. Waist circumference was measured at the natural waist (inferior border of the rib cage, superior aspect of the iliac crest) via a Gulick tape measure.

Maximal oxygen consumption (VO_{2max}) data was collected utilizing a modified Balke treadmill (Trackmaster 425, Carefusion, Newton, KS) protocol to measure CRF, and to determine heart rate range for appropriate intensity. Participants began walking at 2.0 mph with 0% grade for the first 2 minutes of the test. The treadmill speed was then increased to 3.0 mph for the remainder of the test. Treadmill incline was increased by 2.5% every two minutes until participants reached volitional exhaustion. Ventilation and respiratory gas (VO_2, CO_2) measures were collected continuously utilizing a True Max 2400 Metabolic Measurement Cart (Parvomedics, Salt Lake City, UT).

Study Procedures

Participants were randomized to the moderate intensity (MOD-INT; n = 20), high intensity (HIGH-INT; n = 20), or non-exercise control group (n = 20) for a period of 24 weeks. Participants were engaged in supervised exercise 3-4 days per week (varied based on the division of MET minutes over the course of a week) on a treadmill to maintain close control of energy expenditure.

The MOD-INT group exercised at a heart rate associated with 50% VO_{2max}, while the HIGH-INT group exercised at a heart rate associated with 75% VO_{2max}. Both groups accrued 600 MET-minutes/week which corresponds with current PA guidelines (500-1,000 MET-minutes/week). Because participants were sedentary, both groups exercised at 300 MET-minutes during week 1. Each week, the volume of exercise was increased by 50 MET-minutes until the 600 MET-minute level was achieved by week 7. MET-minutes were calculated via ACSM equations based on treadmill speed and grade, and participant weight.

Every two weeks for the first month of exercise, indirect calorimetry was utilized to directly measure energy expenditure and control for exercise economy variability at the participants' steady state exercise prescription. Thereafter, participants were reassessed monthly. The MET-minutes determined by indirect calorimetry during steady state exercise at the prescribed exercise was divided by the MET-minutes determined by ACSM equations to develop a correction factor. This correction factor was utilized with ACSM equations to determine the estimated time to meet the necessary amount of exercise for a given week.

Participant heart rate was continuously monitored by use of Zephyr Bioharness 3 monitors (Annapolis, MD) to monitor and ensure appropriate exercise intensities for each group. Following exercise, heart rate data was downloaded to a computer. The start and end of an exercise session was timestamped to determine average heart rate for the entire exercise session.

Statistical Analysis

Based on previous studies (Sisson et al., 2009; Pandey et al., 2016), CRF response was defined as > 0 L/min VO_2, while CRF non-response was defined as ≤ 0 L/min VO_2 following aerobic exercise training when compared to VO_{2max} baseline values. Baseline values for continuous variables including age, anthropometric measures, resting systolic and diastolic blood pressures, blood panel measurements, CRF values, maximum respiratory exchange ratio (RER), and estimated METs were accumulated and reported in mean and standard deviation. These values were analyzed using a 2x3 analysis of variance (ANOVA) to determine the presence of any significant differences in baseline characteristics prior to the intervention. Baseline differences in categorical variables including gender and intervention group were analyzed with a chi square. When comparing responders to non-responders a 2x2 ANOVA was utilized to determine significant main effects between groups. To analyze CRF non-response differences among groups, a chi square analysis was utilized with an alpha level of <0.05. If a significant main effect was found to be present, a Tukey pairwise comparison tests were then utilized.

CHAPTER 4: RESULTS

A total of 33 participants were included as part of this study. Baseline demographic and anthropometric data are presented in Table 1. Females comprised 75.8% of participants, while males comprised the remaining 24.2% of participants. Average age of all participants was 48.9 ± 7.5 years, BMI was 34.8 ± 5.4 kg/m^2, resting SBP was 126.9 ± 12.9 mmHg, and resting DBP was 78.6 ± 9.7 mmHg. Baseline exercise data indicated an average absolute VO_{2peak} of 1.9 ± 0.5 L/min, a relative VO_{2peak} of 19.2 ± 4.0 ml/kg/min, and estimated METs of 7.6 ± 1.6. Additional anthropometric, blood panel, and pre-exercise data are included in the table. Baseline characteristics were similar across exercise intervention groups ($p>0.05$ for all).

Table 1. Baseline characteristics among intervention groups.

	ALL	Control	Moderate	High
n	33	12	10	10
Female	25 (75.8)	9 (75.0)	8 (80.0)	8 (72.7)
Age (years)	48.8 ± 7.6	48.8 ± 6.3	49.8 ± 6.6	47.8 ± 10.0
BMI (kg/m^2)	34.6 ± 5.7	31.9 ± 5.7	36.3 ± 4.5	35.7 ± 6.0
Body Fat Mass (%)	41.8 ± 7.8	40.0 ± 8.6	43.7 ± 7.8	42.5 ± 6.9
Weight (kg)	97.0 ± 17.3	90.0 ± 17.9	101.8 ± 12.1	100.3 ± 19.3
Waist Circumference (cm)	98.1 ± 12.0	92.5 ± 12.3	100.3 ± 6.8	102.2 ± 13.8
Resting SBP (mmHg)	126.4 ± 14.1	122.0 ± 14.6	125.0 ± 14.5	132.4 ± 11.6
Resting DBP (mmHg)	78.7 ± 9.7	79.2 ± 10.4	78.0 ± 7.1	78.7 ± 11.7
Total Cholesterol (mg/dL)	179.6 ± 34.6	182.9 ± 29.1	184.6 ± 46.0	171.4 ± 29.9
LDL (mg/dL)	107.4 ± 31.3	110.2 ± 25.0	113.1 ± 44.9	99.1 ± 22.4
HDL (mg/dL)	53.7 ± 13.7	54.2 ± 11.4	54.1 ± 14.1	52.7 ± 16.5
Insulin (ulU/mL)	15.5 ± 8.7	12.8 ± 8.4	18.1 ± 10.2	16.1 ± 7.5
Glucose (mg/dL)	93.4 ± 7.4	91.1 ± 7.6	95.3 ± 5.9	93.7 ± 8.7
Absolute VO_{2peak} (L/min)	1.9 ± 0.5	1.9 ± 0.5	1.9 ± 0.5	2.0 ± 0.6
Relative VO_{2peak} (ml/kg/min)	19.9 ± 5.0	21.4 ± 5.5	18.9 ± 5.1	19.4 ± 4.4
Total Time to Exhaustion (min)	9.7 ± 3.0	10.5 ± 3.1	8.6 ± 2.7	10.0 ± 2.9
Maximum Heart Rate (bpm)	169.3 ± 16.0	170.4 ± 11.5	166.4 ± 23.7	170.7 ± 12.5
Maximum RER (VCO_2/VO_2)	1.2 ± 0.1	1.2 ± 0.1	1.1 ± 0.1	1.2 ± 0.1
Estimated METs	7.6 ± 1.6	8.1 ± 1.5	6.9 ± 1.6	7.7 ± 1.6

Data are *n* (%) or mean ± standard deviation.

Table 2 presents 3-month intervention follow-up data with corresponding change scores and *P*-values when compared to baseline data. When comparing systolic blood pressure follow-up measurements to baseline measurements, statistical significance ($p<0.05$) was observed in both the moderate and high intensity groups, although the high intensity group elicited a greater reduction when compared to the moderate intensity group. Additionally, statistical significance was observed in the high intensity group when comparing follow-up diastolic blood pressure measurements to the baseline value. Although not reaching statistical significance, the moderate intensity group did demonstrate a reduction in diastolic blood pressure as significance was approached ($p=0.0749$). Additionally, both the moderate and high intensity group exhibited increases in absolute and relative VO_{2peak}, total time to exhaustion, and estimated METs as statistical significance was approached but not reached.

Table 2. Twelve-week follow-up values compared to baseline values.

	Control	Moderate	High	*P*-value
BMI (kg/m^2)				
Baseline	31.9 ± 5.7	36.3 ± 4.5	35.7 ± 6.0	
Follow-up	32.1 ± 6.1	36.3 ± 4.5	35.8 ± 6.2	
Change Score	+0.2	0	+0.1	0.5011
Weight (kg)				
Baseline	90.0 ± 17.9	101.8 ± 12.1	100.3 ± 19.3	
Follow-up	90.0 ± 18.7	101.7 ± 12.2	100.4 ± 19.1	
Change Score	0	-0.1	+.0.1	0.3907
Waist Circumference (cm)				
Baseline	92.5 ± 12.3	100.3 ± 6.8	102.2 ± 13.8	
Follow-up	94.0 ± 14.2	101.4 ± 9.7	104.3 ± 14.6	
Change Score	+1.5	+1.1	+1.9	0.3748
Resting SBP (mmHg)				
Baseline	122.0 ± 14.6	125.0 ± 14.5	132.4 ± 11.6	
Follow-up	121.7 ± 15.9	123.2 ± 19.8	127.1 ± 14.6	
Change Score	-0.3	-1.8*	-5.3**	0.0184
Resting DBP (mmHg)				
Baseline	79.2 ± 10.4	78.0 ± 7.1	78.7 ± 11.7	
Follow-up	75.7 ± 10.3	75.2 ± 12.5	72.0 ± 8.9	
Change Score	-3.3	-2.8	-6.7*	0.0394
Absolute VO_{2peak} (L/min)				
Baseline	1.9 ± 0.5	1.9 ± 0.5	2.0 ± 0.6	

Follow-up	1.8 ± 0.6	2.0 ± 0.5	2.2 ± 0.6	
Change Score	-0.1	+0.1	+0.2	0.2349
Relative VO_{2peak} (ml/kg/min)				
Baseline	21.4 ± 5.5	18.9 ± 5.1	19.4 ± 4.4	
Follow-up	21.1 ± 6.3	19.8 ± 4.5	21.7 ± 5.1	
Change Score	-0.3	+0.9	+2.3	0.1914
Total Time to Exhaustion (min)				
Baseline	10.5 ± 3.1	8.6 ± 2.7	10.0 ± 2.9	
Follow-up	10.2 ± 3.1	9.8 ± 2.7	11.1 ± 2.6	
Change Score	-0.3	+1.2	+1.1	0.4257
Maximum HR (bpm)				
Baseline	170.4 ± 11.5	166.4 ± 23.7	170.7 ± 12.5	
Follow-up	168.7 ± 9.3	171.5 ± 14.5	170.7 ± 13.0	
Change Score	-1.7	+5.1	0	0.2834
Maximum RER (VCO_2/VO_2)				
Baseline	1.2 ± 0.1	1.1 ± 0.1	1.2 ± 0.1	
Follow-up	1.2 ± 0.1	1.1 ± 0.1	1.1 ± 0.1	
Change Score	0	0	-0.1	0.9996
Estimated METs				
Baseline	8.1 ± 1.5	6.9 ± 1.6	7.7 ± 1.6	
Follow-up	8.1 ± 1.7	7.8 ± 1.5	8.3 ± 1.5	
Change Score	0	+0.9	+0.6	0.1487

Data are presented in mean ± SD.

Figure 1 depicts the mean change in estimated METs after exercise training in the moderate and high intensity groups. No statistical significance was observed, although the moderate and high intensity groups both increased estimated MET levels following the 3-month exercise intervention. Additionally, Figure 2 depicts the change in relative and absolute VO_{2peak} when compared to baseline values. Like estimated METs, the change in relative VO_{2peak} did not reach statistical significance; however, these values did increase in both the moderate and high intensity groups when compared to baseline values.

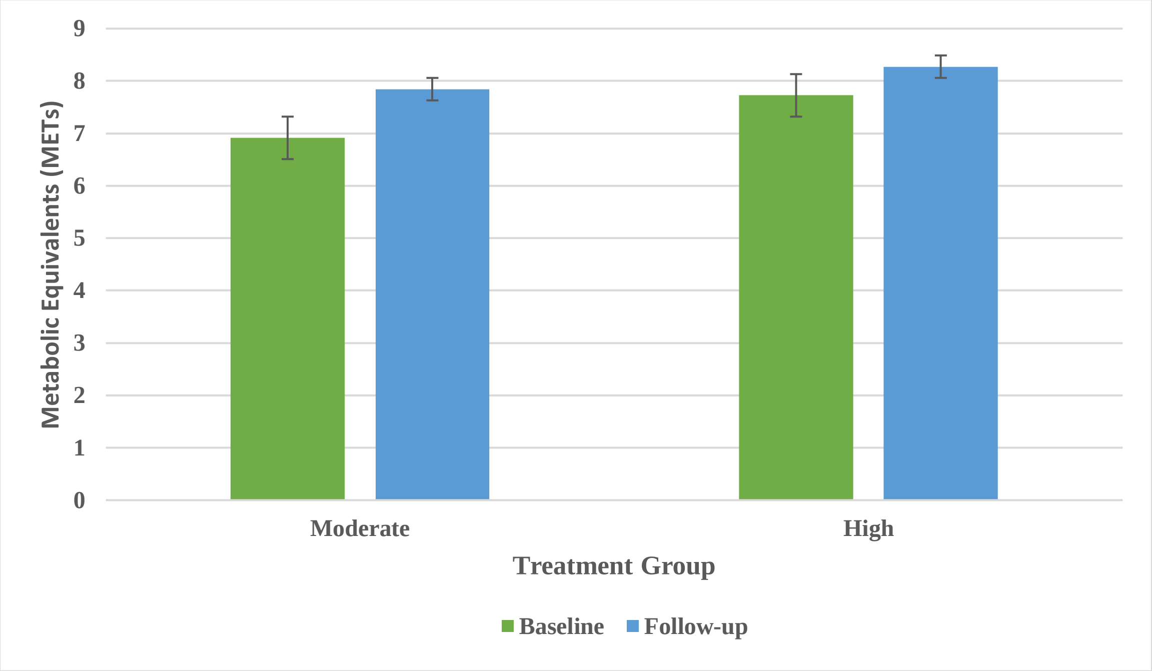


Figure 1. Fitness response by estimated METs.

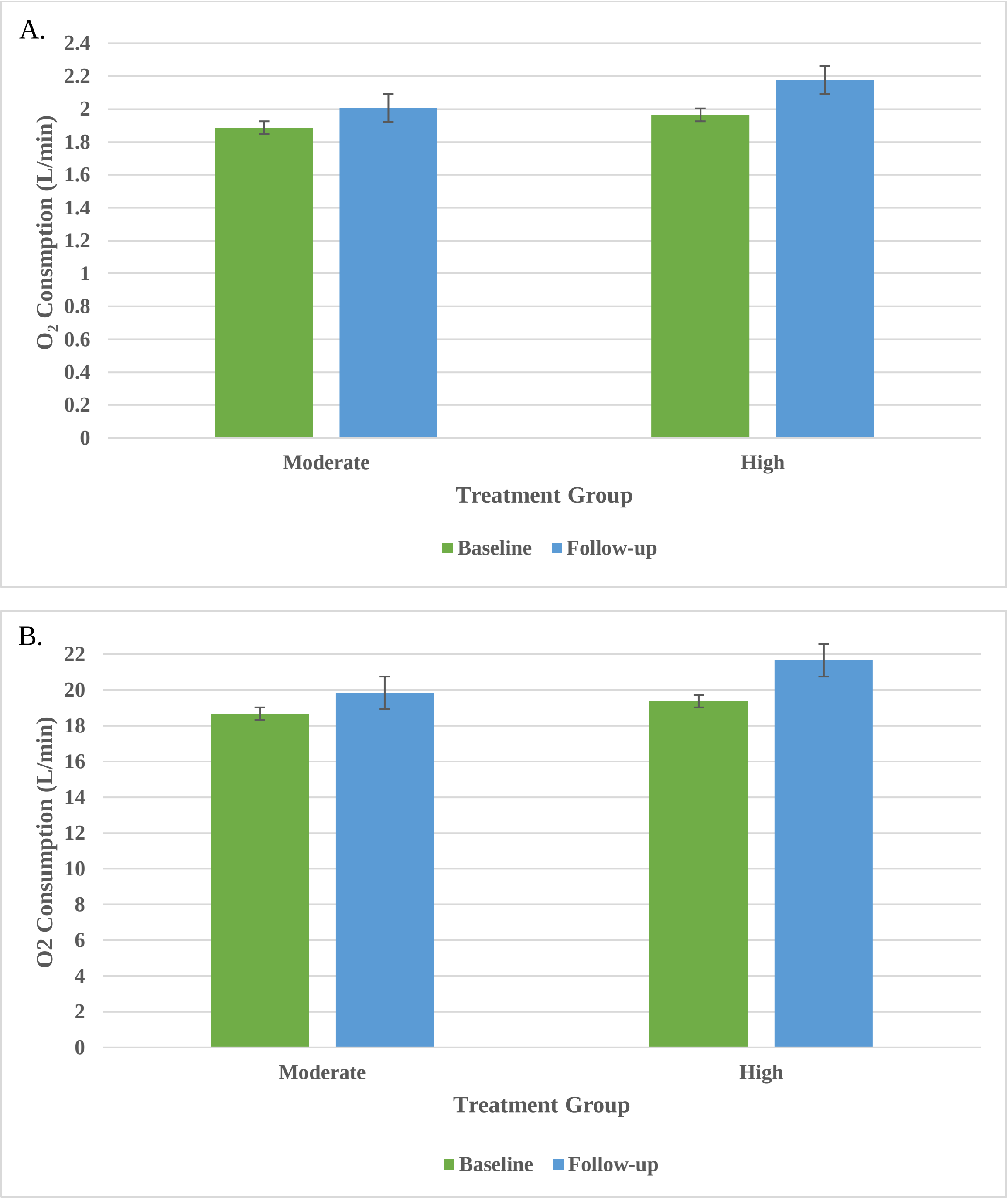


Figure 2. Fitness response by absolute VO$_{2peak}$ (A) and relative VO$_{2peak}$ (B).

Figure 3 illustrates the change in estimated METs for each participant included in the moderate and high intensity groups. For the purpose of this study, a clinically significant change in estimated METs was an increase of 0.5 METs or higher. As depicted in the waterfall graph, 30% of participants in the moderate intensity group exhibited a clinically significant change in estimated METS, while 54.6% of participants in the high intensity group exhibited a clinically significant change in estimated METs. Directly correlated with figure 3, figure 4 depicts the change in relative VO_{2peak} for each participant in both intervention groups following the exercise treatment. When observing the moderate intensity group, 70% of participants demonstrated increases in relative VO_{2peak}, while 74% of participants in the high intensity group demonstrated increases in relative VO_{2peak} despite not reaching statistical significance (p=0.1983).

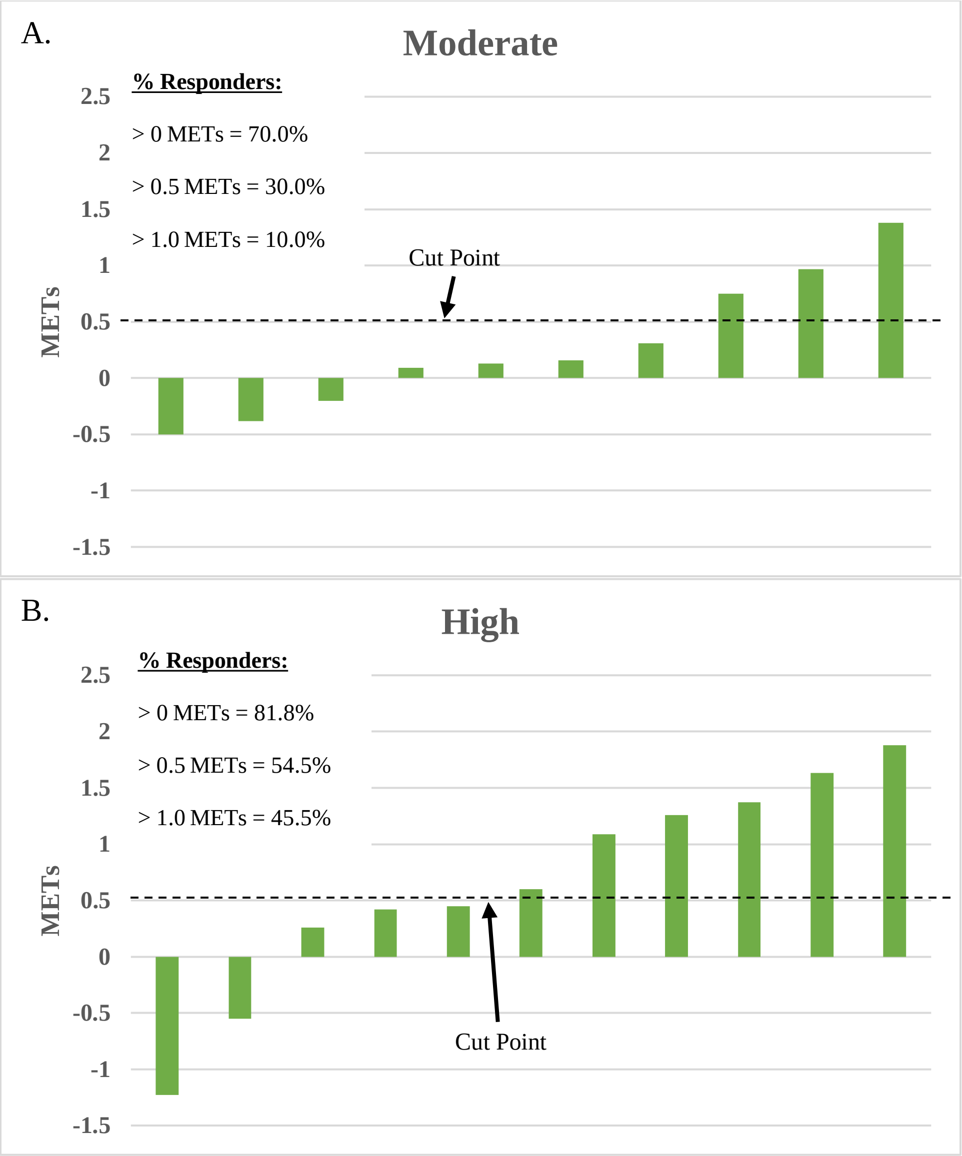


Figure 3. Participant change in estimated METs among moderate (A) and high (B) intensity groups.

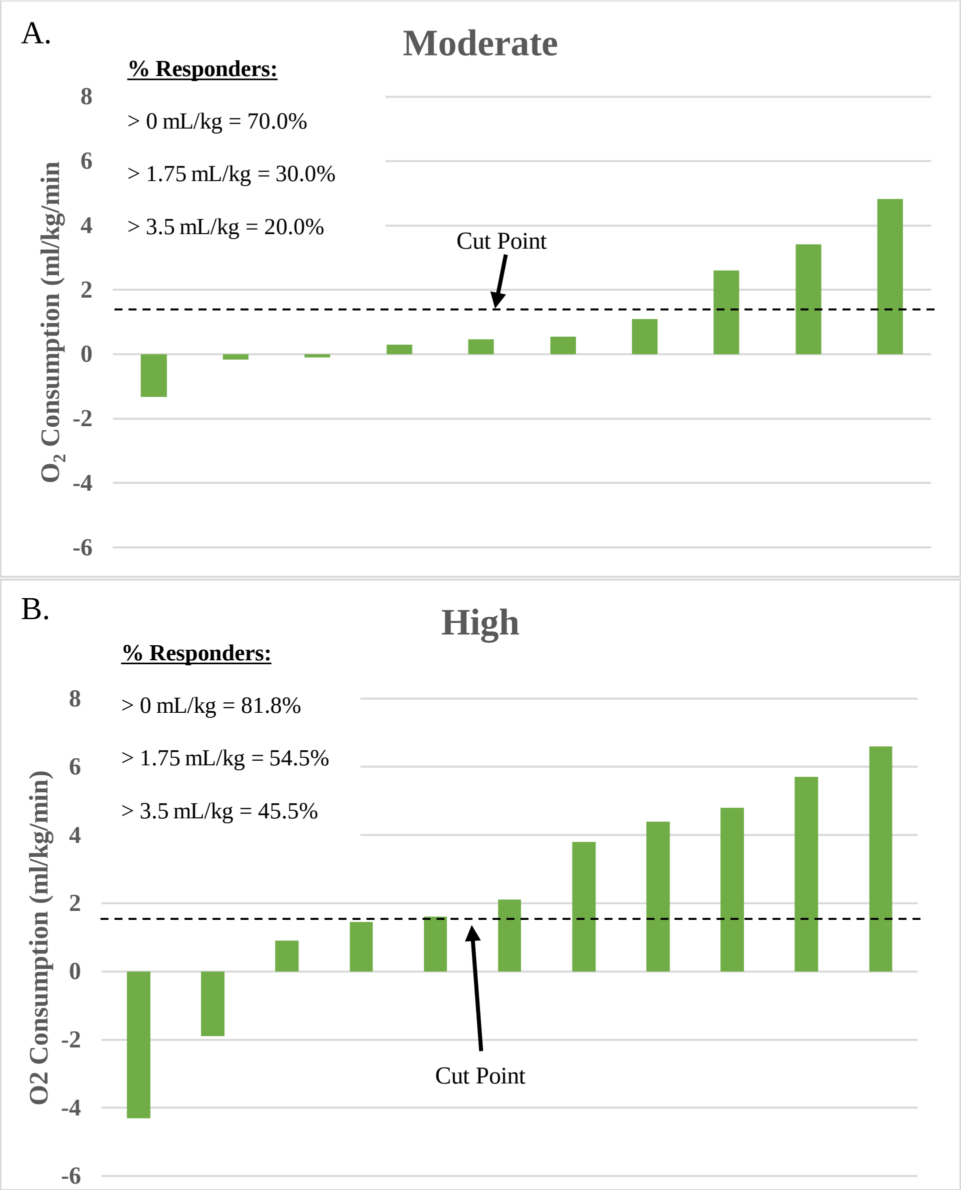


Figure 4. Participant change in relative VO_{2peak} among moderate (A) and high (B) intensity groups.

Figure 5 depicts the fitness response and non-response rate when controlling for measurement error using a technical error of measurement formula ($\sum D^2/2N$). D represents the difference in follow-up and baseline measurements, while N is the total number of measurements made on each participant. When controlling for measurement error, 50% of the moderate intensity group participants were responders, while 63.6% of high intensity participants were classified as responders.

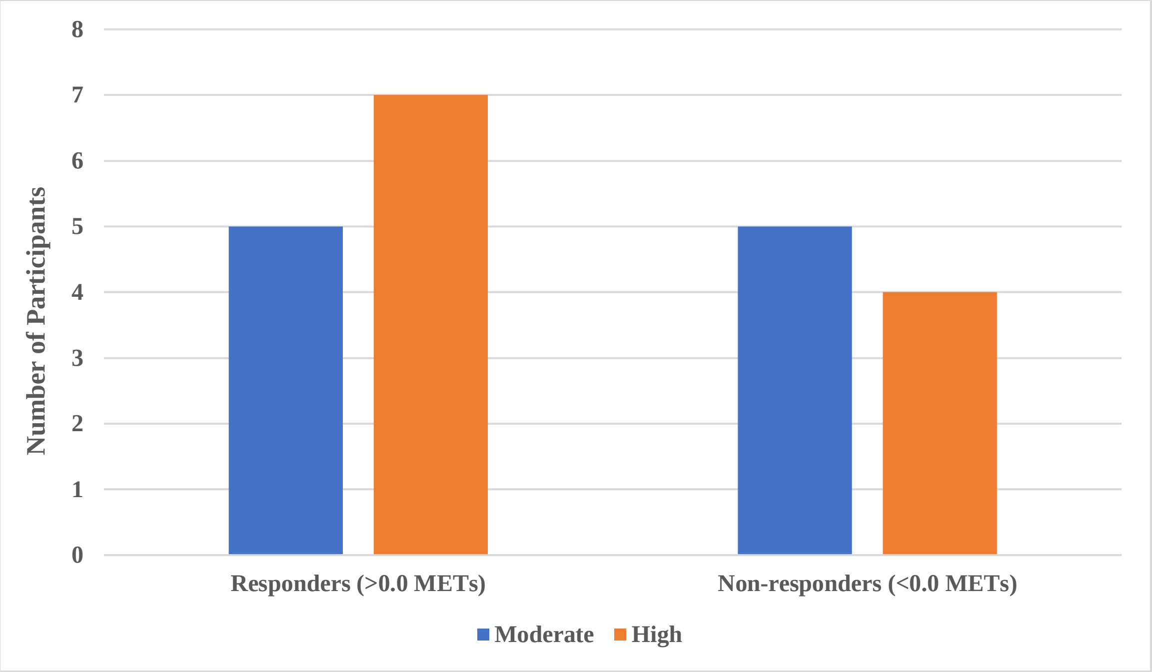


Figure 5. Fitness response adjusted for technical error.

When comparing measured fitness response and technical error fitness response, fewer responders were observed in both the moderate intensity and high intensity groups. When comparing the moderate intensity group, 70% of participants were classified as responders, but when including technical error measurement, 50% of participants were deemed responders. In the high intensity group, 81.8% of participants exhibited positive fitness response rates. When including technical error measurement, 63.6% of participants were found to be responders. No statistical significance was observed despite fewer responders when considering technical error measurement fitness response (p=0.2741).

Table 3 illustrates the baseline characteristics of responders versus non-responders, respectively. When comparing the group means of each intervention group, no statistically significant baseline differences were observed in any of the characteristics.

Table 3. Responder baseline values compared to non-responder baseline values.

	Responders	Non-Responders	p-value
n	17	5	
Female	14 (82.4)	3 (60.0)	
Age (years)	47.7 ± 8.3	55.2 ± 8.6	0.0930
BMI (kg/m^2)	36.2 ± 5.5	35.4 ± 3.8	0.7597
Body Fat Mass (%)	45.8 ± 5.8	40.2 ± 7.7	0.5113
Weight (kg)	100.1 ± 15.8	105.1 ± 17.0	0.2982
Waist Circumference (cm)	100.0 ± 10.9	105.4 ± 9.9	0.2971
Resting SBP (mmHg)	129.3 ± 12.3	130.0 ± 17.7	0.9196
Resting DBP (mmHg)	79.6 ± 9.2	72.0 ± 9.3	0.1185
Total Cholesterol (mg/dL)	173.7 ± 39.8	185.4 ± 23.3	0.4415
LDL (mg/dL)	102.1 ± 35.9	104.0 ± 14.5	0.6408
HDL (mg/dL)	53.2 ± 10.9	61.8 ± 23.4	0.3840
Insulin (ulU/mL)	14.6 ± 5.9	20.8 ± 13.6	0.5072
Absolute VO$_{2peak}$ (L/min)	1.8 ± 0.5	2.4 ± 0.6	0.3830
Relative VO$_{2peak}$ (ml/kg/min)	18.0 ± 3.3	22.9 ± 6.1	0.6061
Total Time to Exhaustion (min)	8.8 ± 2.5	11.3 ± 3.2	0.9117
Maximum Heart Rate (bpm)	171.6 ± 13.2	173.8 ± 19.9	0.1822
Maximum RER (VCO$_2$/VO$_2$)	1.1 ± 0.1	1.2 ± 0.1	0.1969
Estimated METs	7.0 ± 1.5	8.5 ± 1.6	0.8059

Data are *n* (%) or mean ± standard deviation.

Table 4 depicts the change scores with corresponding values for baseline and follow-up measurements between responders and non-responders. Within the responder group, participants elicited a statistically significant decrease in systolic and diastolic blood pressure when comparing follow-up values to baseline values. Systolic blood pressure decreased an average of 5.4 mmHg (p=0.0335) while diastolic blood pressure decreased an average of 5.8 mmHg (p=0.0146). When comparing the baseline and follow-up values of the non-responder group, no statistically significant differences were observed. Additionally, when comparing follow-up values of responders to follow-up values of non-responders no statistically significant differences were observed; however, waist circumference (p=0.1619), resting systolic blood pressure (p=0.2104), and weight (p=0.2244) began to approach statistical significance.

Table 4. Twelve-week responder follow-up values compared to non-responder follow-up values.

	Responders	Non-Responders	p-value	Effect Size
BMI (kg/m^2)				
Baseline	36.2 ± 5.5	35.4 ± 3.8		
Follow-up	36.1 ± 5.7	35.9 ± 3.6	0.9764	0.04
Change Score	-0.1	+0.4		
p-value	>0.9999	>0.9999		
Weight (kg)				
Baseline	100.9 ± 16.1	105.1 ± 17.0		
Follow-up	100.5 ± 15.9	106.8 ± 16.8	0.2244	0.39
Change Score	-0.4	+1.7		
p-value	0.9097	0.9999		
Waist Circumference (cm)				
Baseline	100.7 ± 11.1	105.4 ± 9.9		
Follow-up	102.2 ± 12.7	109.4 ± 12.4	0.1619	0.57
Change Score	+1.5	+4.0		
p-value	0.6646	0.5868		
Resting SBP (mmHg)				
Baseline	129.3 ± 12.3	130.0 ± 17.7		
Follow-up	123.9 ± 19.0*	130.4 ± 18.8	0.2104	0.34
Change Score	-5.4	+0.4		
p-value	0.0335	0.9733		
Resting DBP (mmHg)				
Baseline	79.6 ± 9.2	72.0 ± 9.3		
Follow-up	73.8 ± 8.0*	70.8 ± 17.2	0.5683	0.22
Change Score	-5.8	-1.2		
p-value	0.0146	0.8941		
Absolute VO$_{2peak}$ (L/min)				
Baseline	1.8 ± 0.5	2.3 ± 0.6		
Follow-up	2.0 ± 0.5	2.3 ± 0.6	0.9604	0.54
Change Score	+0.2	0.0		
p-value	>0.9999	>0.9999		
Relative VO$_{2peak}$ (ml/kg/min)				
Baseline	17.7 ± 3.4	22.9 ± 6.1		
Follow-up	20.4 ± 4.7	21.4 ± 5.5	0.8486	0.20
Change Score	+2.7	-1.5		

p-value	0.8292	>0.9999		
Total Time to Exhaustion				
Baseline	8.6 ± 2.5	11.3 ± 3.2		
Follow-up	10.1 ± 2.4	11.0 ± 3.7	0.8480	0.29
Change Score	+1.5	-0.3		
p-value	0.9980	>0.9999		
Maximum HR (bpm)				
Baseline	166.4 ± 17.8	173.8 ± 19.9		
Follow-up	171.2 ± 11.8	168.0 ± 19.4	0.5410	0.20
Change Score	+4.8	-5.8		
p-value	0.0866	0.4156		
Maximum RER (VCO_2/VO_2)				
Baseline	1.1 ± 0.5	1.2 ± 0.1		
Follow-up	1.1 ± 0.1	1.1 ± 0.1	0.9998	0.00
Change Score	0.0	-0.1		
p-value	>0.9999	>0.9999		
Estimated METs				
Baseline	7.0 ± 1.5	8.5 ± 1.6		
Follow-up	7.9 ± 1.3	8.5 ± 1.9	0.9065	0.37
Change Score	+0.9	0.0		
p-value	>0.9999	>0.9999		

Data are *n* (%) or mean ± standard deviation; *p≤0.05 between trials: **p≤ between groups.

CHAPTER 5: DISCUSSION

The primary finding of this investigation indicated that both the moderate and high intensity groups increased overall fitness levels when comparing post-intervention data to pre-intervention data. This finding reinforces well-established knowledge regarding the importance of engaging in moderate-to-high intensity aerobic exercise to increase fitness levels. When comparing the percentage of fitness non-response between the moderate and high intensity groups, no statistically significant differences were observed (p=0.6351). However, when comparing clinically significant MET increases across treatment groups, although statistical significance was not achieved, the data seem to be suggestive that the high intensity group exhibited a greater increase in fitness levels from a clinically significant perspective when compared to the moderate intensity group (p=0.2563; effect size=0.51). This trend may possibly indicate that engaging in high intensity aerobic exercise may be more effective at increasing clinically significant fitness levels than engaging in moderate intensity aerobic exercise alone. If the data would continue this trend in a larger sample size, this finding could be especially important to populations, such as African Americans, who are predisposed to higher CVD risk and associated mortality. It should be noted, however, that moderate intensity aerobic exercise is effective at improving overall fitness levels despite the suggestion that high intensity aerobic exercise may be more effective at improving clinically significant fitness levels.

An extensive body of research has solidified the association of CRF with CVD risk (Laukkanen et al., 2004; Blair et al., 1989; Sui et al., 2007). More recently, researchers have observed small groups of study participants who have experienced fitness non-response following adherence to current physical activity guidelines (Bouchard & Rankinen, 2001; Hautala et al., 2003; Sisson et al., 2009; Ross et al., 2015; Swift et al., 2013). As a result, current literature has recently highlighted the issue of fitness non-response and its associated health risks, especially in the African American population. African Americans, when compared to Caucasians, have been observed to have a significantly greater risk of developing CVD (Thomas et al., 2005; Kalinowski et al., 2004; Loehr et al., 2004; Kodama et al., 2013; Swift et al., 2013). To support this claim, an additional research study was conducted indicating a glaring racial health disparity between African Americans and Caucasians when comparing CVD development and CVD-associated mortality (Benjamin et al., 2017). To reduce CVD development and associated mortality, aerobic exercise is prescribed as a preventative measure. The literature well establishes that increasing CRF elicits a decreased risk of CVD development (Gulati et al., 2003; Mora et al., 2003; Blair et al., 1989); therefore, a typical response to aerobic exercise should result in increased CRF and decreased CVD risk (Blair et al., 1989). A recent meta-analysis by Kodama et al. (2009) indicated that a 1 MET increase in CRF was associated a 13% decrease in all-cause mortality risk and a 15% decrease in CVD risk. To support the findings of the above studies, most participants in our study elicited the typical response to exercise by increasing CRF following aerobic exercise training, although a percentage of individuals were classified as non-responders (23.8%).

As previously stated, our data indicated that when comparing the high and moderate intensity groups, a greater percentage of individuals in the high intensity group elicited clinically significant MET increases of 0.5 METs or more when compared to the moderate intensity group (54.6% vs. 30%) although statistical significance was not achieved. In the moderate intensity group, 20% of individuals increased by ≥0.5 METs, while 10% increased by ≥1 MET; however, 30% were classified as non-responders. In the high intensity group, 9.1% increased by ≥0.5 METs, while 45.5% increased by ≥1 MET. In addition, 18.2% were classified as non-responders.

Achieving an increase of 1 MET is clinically important due to the 13% decrease in all-cause mortality risk and 15% decrease in CVD risk (Kodama et al., 2009). These data appear to agree with the literature suggesting that both moderate and high intensity aerobic exercise is effective at increasing fitness levels; however, high intensity aerobic exercise may be more effective at achieving clinically significant MET increases. As a result, high intensity aerobic exercise may possibly be associated with even greater decreases in CVD development risk and associated mortality. Regarding the non-responders, these data suggest that not all individuals elicit a typical response following prescribed aerobic exercise.

The most similar study to the present study was performed by Ross et al. (2015). This study further examined the effect of exercise intensity on fitness non-response levels. His study randomized participants into a low amount, low intensity group (LALI), high amount, low intensity group (HALI), and a high amount, high intensity group (HAHI). All participants increased overall CRF ($p<0.001$), but non-response results were varied based on exercise intensity. Following a 24-week intervention, the LALI group included 38.5%, the HALI group 17.6%, and the HAHI group 0% non-responders indicating that fitness response levels are directly correlated with exercise intensity ($p=0.02$). The current study differs from the aforementioned study regarding intervention methodology and participant demographics. Our study maintained the amount of aerobic exercise training but varied intensity (600 MET minutes/week), while Ross et al. (2015) varied both exercise amount and intensity. Additionally, the Ross et al. (2015) study utilized participants from various races, whereas the current study exclusively utilized African Americans. From the current study findings, the data did not support that increasing the intensity of aerobic exercise results in lower fitness non-response between groups ($p=0.6351$) (possibly limited by a small sample size). Additionally, Ross et al. (2015)

examined participant data for a duration of 24 weeks, while the current study utilized 12-week mid-intervention data. A data trend was present that suggested that increasing exercise intensity may possibly result in greater clinically significant MET increases (p=0.2563).

Sisson et al. (2009) indicated that increasing doses of aerobic exercise resulted in greater increases in fitness levels and lower rates of fitness non-response. In her study, 44.9% of participants in the 4 kilocalorie/kilogram/week (KKW) were non-responders, while the 8 KKW and 12 KKW participants demonstrated non-response rates of 23.8% and 19.3%, respectively (p<0.0001). The current study maintained exercise dosage (MET minutes were identical across groups), but increased exercise intensity suggesting higher intensity may result in greater overall CRF increases and clinically significant MET increases. Additionally, Sisson et al. (2009) concluded that both age and race were accurate predictors of fitness non-response (p<0.05). Earnest et al. (2010) supported this finding regarding age by concluding that with increasing age, fitness non-response became more prevalent. In the Earnest et al. (2010) study, despite increasing exercise dosage, the results indicated that as age increased, response to exercise was attenuated (p=0.001). From the current study, while not a primary aim, it may possibly be extrapolated that race and age may be potential predictors of fitness non-response. In our study, the age of the responders was 47.7 ± 8.3 years while the high intensity group was 55.2 ± years 8.6. This characteristic did not reach statistical significance; however, statistical significance was approached (p=0.0903) suggesting a trend in the data (possibly limited by the small sample size).

An additional study by Pandey et al. (2015) examined exercise effects on metabolic parameters on participants with type 2 diabetes mellitus who were classified as fitness non-responders. The study concluded that participants, regardless of improvement in CRF, exhibited significant improvements in metabolic parameters including waist circumference (-3.7 to -1.5).

As a result, Pandey et al. (2015) suggested de-emphasizing CRF as the exclusive indicator for responsiveness to aerobic exercise and emphasized including metabolic measurements as an additional indicator. Our current study findings contradicted this conclusion as participants who were classified as non-responders did not significantly improve metabolic parameters. Waist circumference of non-responders exhibited an increase of 4.0 cm from pre-intervention to post-intervention. Additionally, metabolic parameters such as BMI (+0.4 kg/m^2) and weight (+1.7 kg) both increased from pre-intervention to post-intervention. At baseline, non-responders also appeared to have higher total cholesterol values (+11.7 mg/dL), LDL (+1.9 mg/dL), and insulin (+6.2 ulU/mL) when compared to responders. Although no significant differences were observed between groups, the current study did, however, suggest that when comparing values within groups, responders significantly reduced resting SBP (-5.4 mmHg; p=0.0335) and resting DBP (-5.8 mmHg; p=0.0146) at follow-up when compared to baseline values.

Current PA recommendations from numerous organizations (e.g., ACSM, AHA) emphasize the need for engagement in regular aerobic exercise to combat CVD risk and CVD-associated mortality; however, these recommendations are not population-specific regarding race. African Americans have been reported to be predisposed to higher rates of fitness non-response following adherence to current PA recommendations further resulting in higher risk for CVD development and associated mortality (Sisson et al., 2009, Swift et al., 2013). Because our study exclusively utilized African Americans, no comparisons could be made to other races disallowing our data to support the above studies. However, our study did include a group of participants (23.8%) who experienced CRF non-response following aerobic exercise training highlighting the importance of determining appropriate amount and intensity of aerobic exercise to reduce CVD risk and associated mortality. When comparing the moderate and high intensity groups, there was a slight reduction in CRF non-response rates in the high-intensity group when compared to the moderate-intensity group possibly indicating that African Americans may need higher amounts and intensities of exercise to reduce CVD risk and CVD-associated mortality. Additionally, CRF responders exhibited clinically significant, positive health benefits in characteristics such as systolic blood pressure (-5.4 mmHg), diastolic blood pressure (-5.8 mmHg), and estimated METs (+0.9) following the aerobic exercise intervention. Each of these characteristics are strongly associated with CVD risk and CVD-associated mortality. These findings are encouraging due to the well-known predisposition of African Americans to fitness non-response and CVD. The overall results of the study suggest that African Americans may require higher intensities of aerobic exercise doses to ensure CVD risk and associated mortality risk is reduced.

As part of the study, there were a few limitations decreasing the applicability and generalizability to real-world scenarios. To begin, the study has limited generalizability due to the exclusive use of a treadmill modality. As a result, future studies should consider examining the effects of differing modalities (e.g., elliptical). The study also exclusively utilized aerobic exercise. Because of the well-known predisposition of African Americans to conditions such as diabetes mellitus and the suggestion that resistance training aids in controlling blood glucose levels, research is warranted that includes aerobic training combined with resistance. In addition, high intensity interval training (HIIT) may be an additional exercise type to incorporate in exercise interventions. This study also included an overwhelming majority of African American women when compared to men. Prospective research studies may consider placing an emphasis on having an approximate balance regarding participant gender. Lastly, due to the extensive staff exercise session supervision, real-world applicability is reduced.

Despite the few limitations associated with the study, many strengths are also present. Aerobic exercise amounts and intensities were designed in concert with current PA recommendations. All participants were blindly randomized to treatment groups ensuring no researcher bias was present. Although listed as a limitation in the previous paragraph, extensive exercise session supervision (e.g., continuous HR monitoring) was also a major strength of the study. Extensive staff supervision ensured that all data was valid and reliable for the entirety of the intervention. Lastly, and as previously mentioned, African Americans are predisposed to CVD and CVD-associated risk factors; therefore, a primary focus of the study was to closely examine at-risk, overweight and obese African American male and female populations. To further expand on reducing prevalence of CRF non-response and reducing CVD risk in this population, prospective research studies needs to focus on determining predictors of CRF non-response to ensure that an appropriate amount and intensity of exercise is prescribed to effectively combat CVD and mortality risks. Aside from age, additional causative factors of CRF non-response may be due to previously reported data that suggests that African Americans have a lower percentage of type 1 oxidative muscle fibers and reduced hemoglobin levels (Swift et al., 2017). Additional studies have also suggested that African Americans demonstrate lower adherence to current PA recommendations when compared to other races, specifically Caucasians (Haskell et al., 2007; Marshall et al., 2007). Future research may need to focus on determinants of why African Americans exhibit lower PA adherence. Researchers may also need to focus on mitochondrial functionality and muscle fiber type in the African American population to determine possible physiological predictors of CRF non-response.

In conclusion, among obese, sedentary African Americans, both moderate and high intensity aerobic exercise was associated with improvements in overall fitness levels. Results also suggested that with increasing exercise intensity, clinically significant MET increases may become more prevalent. Additionally, within the responder group, statistically significant decreases in CVD risk factors (e.g., SBP, DBP) were observed when comparing follow-up values to baseline values. When considering that aerobic exercise is prescribed to decrease CVD risk and CVD-associated mortality, research should be increased regarding the fitness non-response issue in African Americans due to their already well-established predisposition to CVD. In addition, further research may consider more closely examining the appropriate dosage and intensity of exercise to enhance fitness response; therefore, decreasing CVD risk and associated mortality.

CHAPTER 6: BIBLIOGRAPHY

Al-Mallah, M.H., Qureshi, W.T., Keteyian, S.J., et al. (2016). Racial differences in the prognostic value of cardiorespiratory fitness (results from the Henry Ford exercise testing project). *Am J Cardiol*. **117**:1449–1454.

Ama, P.F., Simoneau, J.A., Boulay, M.R., et al. (1986). Skeletal muscle characteristics in sedentary black and Caucasian males. *J Appl Physiol*. **61**:1758–1761

American Heart Association. 2003 Heart Disease and Stroke Statistics-Update. Dallas, TX: American Heart Association; 2002.

Appel, S.J., Harrel, J.S., Deng, S. (2002). Racial and socioeconomic differences in risk factors for cardiovascular disease among southern rural women. *Nurs Res*. **51**(3).

Barlow, C.E., LaMonte, M.J., FitzGerald, S.J., et al. (2006). Cardiorespiratory fitness is an independent predictor of hypertension incidence among initially normotensive healthy women. *Am J Epidemiol*. **163**(2):142–50.

Benjamin, E.J., Blaha, M.J., Chiuve, S.E., et al. (2017). Heart disease and stroke statistics—2017 update: a report from the American Heart Association. *Circulation*.

Beutler, E. & West, C. (2005). Hematologic differences between African-Americans and whites: the roles of iron deficiency and α-thalassemia on hemoglobin levels and mean corpuscular volume. *Blood*. **106**(2), pp. 740-745.

Blair, S. N., & Jackson, A. S. (2001). Physical fitness and activity as separate heart disease risk factors: a meta-analysis. *Med Sci Sports Exerc*. **33**(5):762.

Blair, S.N., Kampert, J.B., Kohl, H.W., Barlow, C.E., Macera, C.A., Paffenbarger, R.S., Gibbons, L.W. (1996). Influences of cardiorespiratory fitness and other precursors on cardiovascular disease and all-cause mortality in men and women. *JAMA*. **276**:205-210.

Blair, S.N., Kohl, H.W., Barlow, C.E., Paffenbarger, R.S., Gibbons, L.W., Macera, C.A. (1995). Changes in physical fitness and all-cause mortality. A prospective study of healthy and unhealthy men. *JAMA*. **273**:1093-1098.

Blair, S.N., Kohl, H.W., Paffenbarger, R.S., Clark, D.G., Cooper, K.H., Gibbons, L.W. (1989). Physical fitness and all-cause mortality: a prospective study of healthy men and women. *JAMA*. **262**:2395-2401.

Bouchard, C. (1983). Human adaptability may have a genetic basis. In: F. Landry, editor. *Health Risk Estimation, Risk Reduction and Health Promotion. Proceedings of the 18th Annual Meeting of the Society of Prospective Medicine*. Ottawa: Canadian Public Health Association. p. 463-476.

Bouchard, C. & Rankinen, T. (2001). Individual differences in response to regular physical activity. *Med Sci Sports Exerc*. **33**(6 Suppl): S446-451; discussion S452-453.

Ceaser, T.G., Fitzhugh, E.C., Thompson, D.L., et al. (2013). Association of physical activity, fitness, and race: NHANES 1999–2004. *Med Sci Sports Exerc*. **45**(2):286–93.

Carnethon, M.R., Gulati, M., & Greenland, P. (2005). Prevalence and cardiovascular disease correlates of low cardiorespiratory fitness in adolescents and adults. *JAMA*. **294**(23): 2981-2988.

Centers for Disease Control and Prevention CfDCa. (2014). National diabetes statistics report.

Centers for Disease Control and Prevention. (2004). Racial/ethnic disparities in prevalence, treatment, and control of hypertension–United States, 1999–2002. *Nutr Cancer*. **50**(2):111–119.

Centers for Disease Control and Prevention. (2004). The Burden of Chronic Diseases and Their Risk Factors: National and State Perspectives 2004.

Church, T.S., LaMonte, M.J., Barlow, C.E. et al. (2005). Cardiorespiratory fitness and body mass index as predictors of cardiovascular disease mortality among men with diabetes. *Arch Intern Med*. **165**:2114–2120

Cooper, R., Cutler, J., Desvigne-Nickens, P., et al. (2000). Trends and disparities in coronary heart disease, stroke, and other cardiovascular diseases in the United States: findings of the National Conference on Cardiovascular Disease Prevention. *Circulation*. **102**:3137–3147.

Duey, W.J., O'Brien, W.L., Crutchfield, A.B., Brown, L.A., Williford, H.N., Sharff-Olson, M. (1998). Effects of exercise training on aerobic fitness in African-American females. *Ethnicity & Disease*. **8**(3):306-311.

Duncan, G.E., Li, S.M., Zhou, X.H. (2005). Cardiovascular fitness among US adults: NHANES 1999–2000 and 2001–2002. *Med Sci Sports Exerc*. **37**(8):1324–8.

Earnest, C.P., Blair, S.N., & Church, T.S. (2010). Age attenuated response to aerobic conditioning in postmenopausal women. *European Journal of Applied Physiology*, **110**(1):75-82.

Erikssen, G., Liestol, K., Bjornholt, J., et al. (1998). Changes in physical fitness and changes in mortality. *Lancet*. **352**(9130):759–62.

Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. (1993). Summary of the second report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel II). *JAMA*. **269**:3015–3023.

Flack, J.M., Ferdinand, K.C. & Nasser, S.A. (2003). Epidemiology of Hypertension and Cardiovascular Disease in African Americans. *The Journal of Clinical Hypertension*. **5**: 5–11.

Garber, C.E., Blissmer, B., Deschenes, M.R., Franklin, B.A., Lamonte, M.J., Lee, I.M., Nieman, D.C., & Swain, D.P. (2011). American College of Sports Medicine position stand. Quantity and quality of exercise for developing and maintaining cardiorespiratory, musculoskeletal, and neuromotor fitness in apparently healthy adults: guidance for prescribing exercise. *Med Sci Sports Exerc*. **43**:1334-1359.

Garcia, M.M. (2001). Cardiovascular disease in women: Clinical perspectives. *Circ Res*. **118**(8):1273-1293.

Gillum, R.F. (1996). The epidemiology of cardiovascular disease in black Americans [editorial]. *N Engl J Med*. **335**:1597–1598.

Gulati, M., Pandey, D.K., Arnsdorf, M.F., et al. (2003). Exercise capacity and the risk of death in women: the St James Women Take Heart Project. *Circulation*. **108**:1554-1559.

Haskell, W.L., Lee, I.M., Pate, R.R., et al. (2007). Physical activity and public health: Updated recommendation for adults from the American College of Sports Medicine and the American Heart Association. *Med Sci Sports Exerc*. **39**(8):1423–34.

Hautala, A.J., Makikallio, T.H., Kiviniemi, A., et al. (2003). Cardiovascular autonomic function correlates with the response to aerobic training in healthy sedentary subjects. *Am J Physiol Heart Circ Physiol*. **285**:H1747-1752.

Hunter, G.R., Weinsier, R.L., Mccarthy, J.P., et al. (2001). Hemoglobin, muscle oxidative capacity, and VO_2 max in African-American and Caucasian women. *Med Sci Sports Exerc*, **33**(10): pp. 1739-1743

Jacobson, T.A., Ito, M.K., Maki, K.C., et al. (2015). National lipid association recommendations for patient-centered management of dyslipidemia: Part 1—Full report. *Journal of Clinical Lipidology*. **9**(2):129-169.

Kalinowski, L., Dobrucki, I.T., Malinski, T. (2004). Race-specific differences in endothelial function: predisposition of African Americans to vascular diseases. *Circulation*. **109**(21): pp. 2511-2517.

Kenny, S.J., Aubert, R.E., Geiss, L.S. (1995). Prevalence and incidence of non-insulin-dependent diabetes. In: Harris, M.I., Cowie, C.C., Stern, M.P., et al. *Diabetes in America*. Bethesda, Md: National Institute of Health, National Institute of Diabetes, and Digestive and Kidney Diseases; pp. 47–67.

Kodama, S., Saito, K., Tanaka, S., et al. (2009). Cardiorespiratory fitness as a quantitative predictor of all-cause mortality and cardiovascular events in healthy men and women. *JAMA*. **301**(19):2024–35.

Kodama, K., Tojjar, D., Yamada, S., et al. (2013). Ethnic differences in the relationship between insulin sensitivity and insulin response: a systematic review and meta-analysis. *Diabetes Care*. **36**(6): pp. 1789-1796.

Kohl, H.W., Craig, C.L., Lambert, E.V., Inoue, S., Alkandari, J.R., Leetongin, G., Kahlmeier, S. (2012). The pandemic of physical inactivity: global action for public health. *Lancet* **380**:294-305.

Kohrt, W.M., Malley, M.T., Coggan, A.R., et al. (1991). Effects of gender, age, and fitness level on response of VO_{2max} to training in 60-71 yr. olds. *J Appl Physiol*. **71**:2004-2011.

Kokkinos, P., Myers, J., Kokkinos, J.P. et al. (2008). Exercise capacity and mortality in black and white men. Circulation. **117**:614–622.

LaPorte, R.E., Matsushima, M., Chang, Y.F. (1995). Prevalence and incidence of insulin-dependent diabetes. In: Harris, M.I., Cowie, C.C., Stern, M.P., et al. *Diabetes in America*. Bethesda, Md: National Institute of Health, National Institute of Diabetes, and Digestive and Kidney Diseases. pp: 37–46.

Laukkanen, J.A., Kurl, S., Salonen, R., Rauramaa, R., Salonen, J.T. (2004). The predictive value of cardiorespiratory fitness for cardiovascular events in men with various risk profiles: a prospective population-based cohort study. *Eur Heart J*. **25**:1428–1437

Lavie CJ, Kuruvanka T, Milani RV, et al. (2004). Exercise capacity in adult african-americans referred for exercise stress testing: Is fitness affected by race? *Chest*. **126**(6):1962–8.

Lee, D.C., Artero, E.G., Sui, X., S.N. Blair. (2010). Mortality trends in the general population: the importance of cardiorespiratory fitness. *J Psychopharm*. **24**(11) Suppl 4:27-35.

Lee, D.C., Blair, S.N., Jackson, A.S. (1999). Cardiorespiratory fitness, body composition, and all-cause and cardiovascular disease mortality in men. *Am J Clin Nutr*. **69**:373–380.

Lee, D.C., Sui, X., Church, T.S., Lavie, C.J., Jackson, A.S., Blair, S.N. (2012). Changes in fitness and fatness on the development of cardiovascular disease risk factors hypertension, metabolic syndrome, and hypercholesterolemia. *J Am Coll Cardiol*. **59**:665–672.

Lloyd-Jones, D., Adams, R.J., Brown, T.M., et al. (2010). Heart disease and stroke statistics—2010 update. *Circulation*. **121**(7): e46–e215.

Lloyd-Jones, D.M., Hong, Y., Labarthe, D., et al. (2010). Defining and setting national goals for cardiovascular health promotion and disease reduction: The American Heart Association’s strategic impact goal through 2020 and beyond. *Circulation*. **121**(4):586–613.

Loehr, L.R., Espeland, M.A., Sutton-Tyrrell, K., et al. (2004). Racial differences in endothelial function in postmenopausal women. *Am Heart J*. **148**(4): pp. 606-611.

Lortie, G., Simoneau, J.A., Hamel, P., Boulay, M.R., Landry, F., Bouchard, C. (1984). Responses of maximal aerobic power and capacity to aerobic training. *Int J Sports Med*. **5**:232-236.

Lynch, J., Helmrich, S.P., Lakka, T.A., et al. (1996). Moderately intense physical activities and high levels of cardiorespiratory fitness reduce the risk of non-insulin-dependent diabetes mellitus in middle-aged men. *Arch Intern Med*. **156**(12):1307–14.

Manson, J.E., Colditz, G.A., Stampfer, M.J., et al. (1991). A prospective study of maturity-onset diabetes mellitus and risk of coronary heart disease and stroke in women. *Arch Intern Med*. **151**:1141–1147.

Marshall, S.J., Jones, D.A., Ainsworth, B.E., Reis, J.P., Levy, S.S., Macera, C.A. (2007). Race/ethnicity, social class, and leisure-time physical inactivity. *Med Sci Sports Exerc*. **39**(1):44-51.

Matthews, C.E., Chen, K.Y., Freedson, F.S., et al. (2008). Amount of time spent in sedentary behaviors in the United States, 2003–2004. *Am J Epidemiol*. **167**(7): pp. 875-881.

Mora, S., Cook, N., Buring, J. E., Ridker, P. M., Lee, I. M. (2007). Physical activity and reduced risk of cardiovascular events. *Circulation*. **116**(19):2110-2118.

Mora S., Redberg, R.F., Cui, Y., et al. (2003). Ability of exercise testing to predict cardiovascular and all-cause death in asymptomatic women: a 20-year follow-up of the lipid research clinics prevalence study. *JAMA*. **290**:1600-1607.

Myers, J., Prakash, M., Froelicher, V., Do, D., Partington, S., Atwood, J.E. (2002). Exercise capacity and mortality among men referred for exercise testing. *N Engl J Med*. **346**:793-801.

Naci, H. & Ioannidis, J.P. (2013). Comparative effectiveness of exercise and drug interventions on mortality outcomes: metaepidemiological study. *BMJ*. **347**:f5577.

O'Donovan, G., Owen, A., Bird, S.R. et al. (1985). Changes in cardiorespiratory fitness and coronary heart disease risk factors following 24 wk of moderate-or high-intensity exercise of equal energy cost. *J Appl Physiol*. **98**:1619–1625.

Pandey, A., Park, B.D., Ayers, C., et al. (2016). Determinants of racial/ethnic differences in cardiorespiratory fitness (from the Dallas heart study). *Am J Cardiol*. **118**(4): pp. 499-503.

Pandey, A., Swift, D.L., McGuire, D.K., Ayers, C.R., Neeland, I.J., Blair, S.N., Church, T.S. (2015). Metabolic effects of exercise training among fitness-nonresponsive patients with type 2 diabetes: the HART-D study. *Diabetes Care*. **38**(8):1494–1501.

Pivarnik, J.M., Bray, M.S., Hergenroeder, A.C., et al. (1995). Ethnicity affects aerobic fitness in U.S. adolescent girls. *Med Sci Sports Exerc*. **27**(12): pp. 1635-1638.

Powell, K.E., Thompson, P.D., Caspersen, C.J., Kendrick, J.S. (1987). Physical activity and the incidence of coronary heart disease. *Annu Rev Public Health*. **8**:253–287.

Rankinen, T., Church, T.S., Rice, T., et al. (2007). Cardiorespiratory fitness, BMI, and risk of hypertension: The hypgene study. *Med Sci Sports Exerc*. **39**(10):1687–92.

Roger, V.L., Go, A.S., Lloyd-Jones, D.M., et al. (2012). Heart disease and stroke statistics—2012 update: a report from the American Heart Association. *Circulation*. **125**(1):e2–220.

Ross, R., Blair, S.N., Arena, R. et al. (2016). Importance of assessing cardiorespiratory fitness in clinical practice: a case for fitness as a clinical vital sign: a scientific statement from the American Heart Association. *Circulation*. **134**:e653–e699

Ross, R. & Katzmarzyk, P.T. (2003). Cardiorespiratory fitness is associated with diminished total and abdominal obesity independent of body mass index. *Int J Obes Relat Metab Disord*. **27**(2):204.

Ross, R., de Lannoy, L., Stotz, P. (2015). Separate effects of intensity and amount of exercise on interindividual cardiorespiratory fitness response. *Elsevier*. **90**(11):1506-1514.

Sawada, S.S., Lee, I.M., Muto, T., et al. (2003). Cardiorespiratory fitness and the incidence of type 2 diabetes. *Diabetes Care*. **26**(10):2918–22.

Sieverdes, J.C., Sui, X., Lee, D.C., et al. (2010). Physical activity, cardiorespiratory fitness and the incidence of type 2 diabetes in a prospective study of men. *Br J Sports Med*. **44**(4):238–44.

Sisson, S. B., Katzmarzyk, P. T., Earnest, C. P., Bouchard, C., Blair, S. N., Church, T. S. (2009). Volume of exercise and fitness non-response in sedentary, post-menopausal women. *Med Sci Sports Exerc*. **41**(3):539.

Skinner, J.S., Jaskolski, A., Jaskolska, A., et al. (2001). Age, sex, race, initial fitness, and response to training: the HERITAGE Family Study. *J Appl Physiol*. **90**:1770-1776.

Stamler, J., Stamler, R., Neaton, J.D. (1993). Blood pressure, systolic and diastolic and cardiovascular risks. *Arch Intern Med*. **153**:598–615.

Stephens, Q., Kirby, T., Buckworth, J., Devor, S., Hamlin, R. (2007). Aerobic exercise improves cardiorespiratory fitness but does not reduce blood pressure in prehypertensive African American women. *Ethnicity and Disease*. **17**(1):55.

Stern, M.P. & Mitchell, B.D. Diabetes in Hispanic Americans. In: Harris, M.I., Cowie, C.C., Stern, M.P., et al. *Diabetes in America*. Bethesda, Md: National Institute of Health, National Institute of Diabetes, and Digestive and Kidney Diseases. pp:613–660.

Stevens, J., Evenson, K.R., Thomas, O., Cai, J., Thomas, R. (2004). Associations of fitness and fatness with mortality in Russian and American men in the lipids research clinics study. *Int J Obes Relat Metab Disord*. **28**:1463-1470.

Sui, X., LaMonte, M.J., Blair, S.N. (2007). Cardiorespiratory fitness as a predictor of nonfatal cardiovascular events in asymptomatic women and men. *Am J Epidemiol*. **165**:1413–1423.

Sundquist, J., Winkleby, M.A., Pudaric, S. (2001). Cardiovascular disease risk factors among older Black, Mexican American and White women and men: an analysis of NHANES III, 1988–1994. *Am Geriatrics Society*. **49**:109–116.

Swift, D. L., Johannsen, N. M., Earnest, C. P., Newton, R. L., McGee, J. E., Church, T. S. (2017). Cardiorespiratory Fitness and Exercise Training in African Americans. *Progress in Cardiovascular Diseases*.

Swift, D. L., Johannsen, N. M., Lavie, C. J., Earnest, C. P., Johnson, W. D., Blair, S. N., Newton, R. L. (2013). Racial differences in the response of cardiorespiratory fitness to aerobic exercise training in Caucasian and African American postmenopausal women. *J Appl Physiol*. **114**(10): 1375-1382.

Swift, D. L., Staiano, A. E., Johannsen, N. M., Lavie, C. J., Earnest, C. P., Katzmarzyk, P. T., Church, T. S. (2013). Low cardiorespiratory fitness in African Americans: a health disparity risk factor?. *Sports Medicine*, **43**(12):1301-1313.

Tanner, C.J., Barakat, H.A., Dohm, G.L. et al. (2002). Muscle fiber type is associated with obesity and weight loss. *Am J Physiol Endocrinol Metab*. **282**:e1191–e1196.

Thom, T., Hasse, N., Rosamond, W., Howard, V.J., et al. (2006). Heart disease and stroke statistics–2006 update: a report from the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. *Circulation*. **113**(14):e696.

Thomas, A.J., Eberly, L.E., Davey Smith, G., et al. (2005). Race/ethnicity, income, major risk factors, and cardiovascular disease mortality. *Am J Public Health*. **95**(8): pp. 1417-1423.

Tucker, J.M., Welk, G.J., Beyler, N.K. (2011). Physical activity in US adults: compliance with the physical activity guidelines for Americans. *Am J Prev Med*. **40**(4):454–61.

Tull, E.S. & Roseman, J.M. (1995). Diabetes in African Americans. In: Harris, M.I., Cowie, C.C., Stern, M.P., et al. *Diabetes in America*. Bethesda, Md: National Institute of Health, National Institute of Diabetes, and Digestive and Kidney Diseases. pp: 613–630.

US Department of Health and Human Services, Cessation, and Advocacy Activities. (1989). Reducing the Health Consequences of Smoking: 25 Years of Progress: A Report of the Surgeon General. Washington, DC: USDHHS. Chap 6. *DHHS publication* 89-8411.

U.S. Department of Health and Human Services. (2008). 2008 physical activity guidelines for Americans. pp. 1–3.

Wang, Y. & Beydoun, M.A. (2007). The obesity epidemic in the united states—gender, age, socioeconomic, racial/ethnic, and geographic characteristics: a systematic review and meta-regression analysis. *Epidemiol Rev*. **29**:6–28.

Wang, C.Y., Haskell, W.L., Farrell, S.W., et al. (2010). Cardiorespiratory fitness levels among us adults 20–49 years of age: findings from the 1999–2004 National Health and Nutrition Examination Survey. *Am J Epidemiol*. **171**(4):426–35.

Willet, W.C., Manson, J.E., Stampfer, M.J., et al. (1995). Weight, weight change, and coronary heart disease in women. *JAMA*. **273**:461–465.

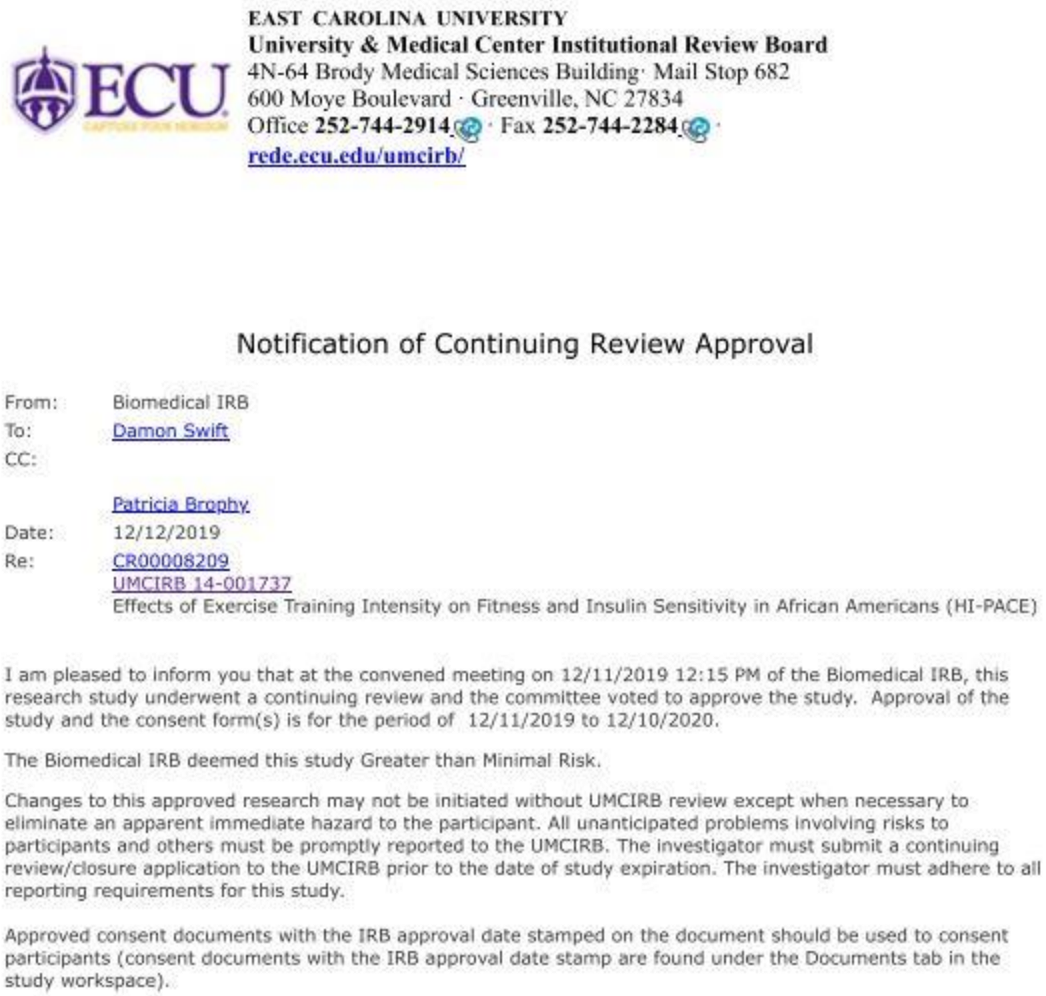
Williams, D.M. (1981). Racial differences of hemoglobin concentration: measurements of iron, copper, and zinc. *Am J Clin Nutr*. **34**(9): pp. 1694-1700.

Wilmore, J. H., Green, J. S., Stanforth, P. R., Gagnon, J., Rankinen, T., Leon, A. S., Bouchard, C. (2001). Relationship of changes in maximal and submaximal aerobic fitness to changes in cardiovascular disease and non-insulin-dependent diabetes mellitus risk factors with endurance training: The HERITAGE Family Study. *Metabolism*. ***50***(11): 1255-1263.

Wong, S.L., Katzmarzyk, P.T., Nichaman, M.Z., et al. (2004). Cardiorespiratory fitness is associated with lower abdominal fat independent of body mass index. *Med Sci Sports Exerc*. **36**(2):286–91.

Zeno, S.A., Kim-Dorner, S.J., Deuster, P.A., Davis, J.L., Remaley, A.T., Poth, M. (2010). Cardiovascular fitness and risk factors of healthy African Americans and Caucasians. *Journal of the National Medical Association*. **102**(1):28-35.

APPENDIX: INSTITUTIONAL REVIEW BOARD LETTER



EAST CAROLINA UNIVERSITY
University & Medical Center Institutional Review Board
4N-64 Brody Medical Sciences Building· Mail Stop 682
600 Moye Boulevard · Greenville, NC 27834
Office **252-744-2914** · Fax **252-744-2284** ·
rede.ecu.edu/umcirb/

Notification of Continuing Review Approval

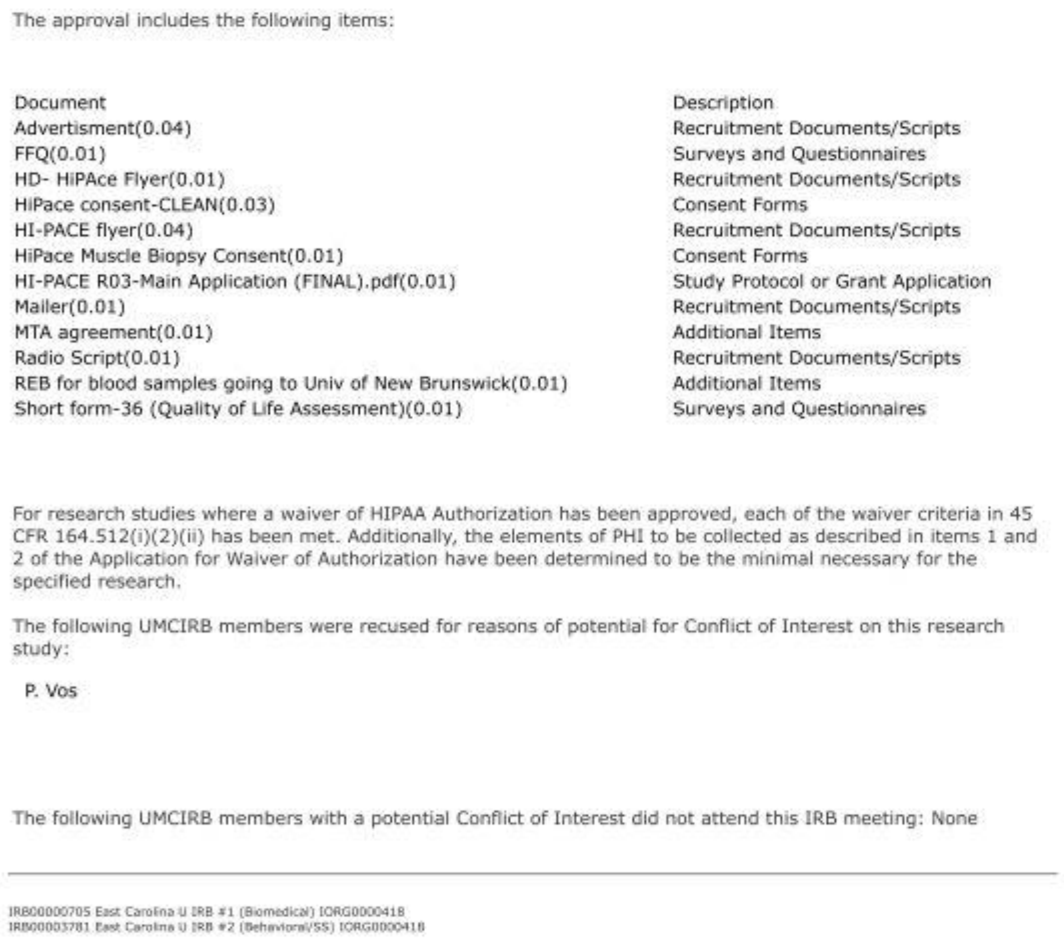
From:	Biomedical IRB
To:	Damon Swift
CC:	
	Patricia Brophy
Date:	12/12/2019
Re:	CR00008209 UMCIRB 14-001737 Effects of Exercise Training Intensity on Fitness and Insulin Sensitivity in African Americans (HI-PACE)

I am pleased to inform you that at the convened meeting on 12/11/2019 12:15 PM of the Biomedical IRB, this research study underwent a continuing review and the committee voted to approve the study. Approval of the study and the consent form(s) is for the period of 12/11/2019 to 12/10/2020.

The Biomedical IRB deemed this study Greater than Minimal Risk.

Changes to this approved research may not be initiated without UMCIRB review except when necessary to eliminate an apparent immediate hazard to the participant. All unanticipated problems involving risks to participants and others must be promptly reported to the UMCIRB. The investigator must submit a continuing review/closure application to the UMCIRB prior to the date of study expiration. The investigator must adhere to all reporting requirements for this study.

Approved consent documents with the IRB approval date stamped on the document should be used to consent participants (consent documents with the IRB approval date stamp are found under the Documents tab in the study workspace).



The approval includes the following items:

Document	Description
Advertisment(0.04)	Recruitment Documents/Scripts
FFQ(0.01)	Surveys and Questionnaires
HD- HiPAce Flyer(0.01)	Recruitment Documents/Scripts
HiPace consent-CLEAN(0.03)	Consent Forms
HI-PACE flyer(0.04)	Recruitment Documents/Scripts
HiPace Muscle Biopsy Consent(0.01)	Consent Forms
HI-PACE R03-Main Application (FINAL).pdf(0.01)	Study Protocol or Grant Application
Mailer(0.01)	Recruitment Documents/Scripts
MTA agreement(0.01)	Additional Items
Radio Script(0.01)	Recruitment Documents/Scripts
REB for blood samples going to Univ of New Brunswick(0.01)	Additional Items
Short form-36 (Quality of Life Assessment)(0.01)	Surveys and Questionnaires

For research studies where a waiver of HIPAA Authorization has been approved, each of the waiver criteria in 45 CFR 164.512(i)(2)(ii) has been met. Additionally, the elements of PHI to be collected as described in items 1 and 2 of the Application for Waiver of Authorization have been determined to be the minimal necessary for the specified research.

The following UMCIRB members were recused for reasons of potential for Conflict of Interest on this research study:

P. Vos

The following UMCIRB members with a potential Conflict of Interest did not attend this IRB meeting: None

IRB00000705 East Carolina U IRB #1 (Biomedical) IORG0000418
IRB00003781 East Carolina U IRB #2 (Behavioral/SS) IORG0000418