

UCLA

UCLA Electronic Theses and Dissertations

Title

Intervention and Cross-Sectional Analysis of the Effects of Resistance Training and Smoking Cessation on Cardiorespiratory Fitness and Muscular Strength in Sedentary Smokers

Permalink

<https://escholarship.org/uc/item/16n3h9tq>

Author

Blythe, Tia Laine

Publication Date

2012

Peer reviewed|Thesis/dissertation

UNIVERSITY OF CALIFORNIA

Los Angeles

Intervention and Cross-Sectional Analysis of the Effects of Resistance
Training and Smoking Cessation on Cardiorespiratory Fitness and
Muscular Strength in Sedentary Smokers.

A thesis submitted in partial satisfaction
of the requirements for the degree Master of Science
in Physiological Science

by

Tia Laine Blythe

2012

ABSTRACT OF THE THESIS

Intervention and Cross-Sectional Analysis of the Effects of Resistance
Training and Smoking Cessation on Cardiorespiratory Fitness and
Muscular Strength in Sedentary Smokers.

by

Tia Laine Blythe

Master of Science in Physiological Science

University of California, Los Angeles, 2012

Professor Peter Narins, Chair

The rising trend in cardiovascular disease is made evident by the drastic increase in health care costs as more and more people seek medical attention for coronary heart disease, atherosclerosis, heart attack, and stroke. This disease is further exacerbated by cigarette smoking which increases inflammation and has been proven to cause cancer. The focus to combat this disease has shifted away from treatment and towards prevention as people are realizing the benefits of exercise on all aspects of health. While the benefits of aerobic exercise are well-documented, resistance training (RT) as a means to counteract the markers of cardiovascular disease is not as well understood. The current study exams the effect of a 12-week periodized RT intervention and nicotine replacement

therapy (NRT) on the fitness level and body composition in a population of young sedentary smokers. The subjects were randomized into four groups: RT and NRT, only RT, only NRT, or into the control group which received neither RT nor NRT. Participants were young (age 24.5 ± 4.6 yr), sedentary smokers. The control group had no significant drop in BMI and weight compared to the RT/NRT and RT groups. The RT/NRT group had a significant decrease in total fat, trunk fat, and fat percentage. The RT group had a significant increase in CRF measures compared to the other groups. Relative maximum aerobic capacity increased from 27.4 ± 3.05 ml/kg/min to 30.8 ± 2.12 ml/kg/min. This was significantly greater than the improvement seen in the NRT group ($P < 0.05$). The improved absolute maximum aerobic capacity and maximum breathing frequency were greatest in the RT group than in the NRT/RT, NRT, and Control groups. There was no significant difference between the changes in maximum heart rate. NRT/RT and RT groups had significantly greater improvements in 1-RM for chest press, leg press, and seated row as well as the composite RM as compared to the NRT group. The body mass index between the healthy cohort (HC) (23.17 ± 3.0) and smokers (25.05 ± 5.60) was not significantly different, neither was the height, weight, nor age. However, the body composition between these two groups was significantly different in all values analyzed. Total fat in the HC was 11.22 ± 10.97 kg while smokers had a total fat of 18.06 ± 10.97 kg. Trunk fat was measured at 4.69 ± 2.22 kg in the HC and 7.90 ± 6.30 kg in the smokers. There was a significant difference between body fat percentage with the smokers having an average of more than 5% higher than the HC and lean body mass was significantly lower for smokers as well.

The Thesis of Tia Laine Blythe is approved.

Rachelle Crosbie Watson

Oscar Scremin

Peter Narins, Committee Chair

University of California, Los Angeles

2012

Table of Contents

	<u>Page</u>
List of Figures	vii
List of Tables	viii
List of Abbreviations	xi
Acknowledgements	x
Chapter 1: Introduction and Background	1
Rationale for Studying Young Adults	2
Rationale for Studying Resistance Training and Smoking Cessation	3
Cardiorespiratory Fitness	5
Defining Measures of Cardiorespiratory Fitness	8
Muscular Strength	10
Cardiorespiratory Fitness and Muscular Strength as Independent Predictors of Cardiovascular Disease	11
Hypothesis	14
Chapter 2: Methods	15
Chapter 3: Results	24
Intervention Results	24
Anthropometric Results	24
Cardiorespiratory Fitness and Muscular Strength Measures	25
Cross Sectional Study Results	28
Anthropometric Results	28
Cardiorespiratory Fitness and Muscular Strength Measures	29

Chapter 4: Discussion	33
Chapter 5: Future Directions	38
Chapter 6: References	39

<u>List of Figures</u>	<u>Page</u>
Figure 1: Example of Maximum Aerobic Capacity Graph	9
Figure 2: The Sliding Filament Theory	11
Figure 3: Fat Percentage in the Intervention Group	25
Figure 4: Lean Body Mass in the Intervention Group	25
Figure 5: Relative Maximum Aerobic Capacity in Intervention Group	26
Figure 6: Absolute Maximum Aerobic Capacity in Intervention Group	27
Figure 7: Maximum Breathing Frequency in the Intervention Group	27
Figure 8: Composite 1-RM in Intervention Group	28
Figure 9: Relative Maximum Aerobic Capacity in Smokers and Nonsmokers	30
Figure 10: Maximum Heart Rate in Smokers and Nonsmokers	30
Figure 11: Maximum Breathing Frequency in Smokers and Nonsmokers	31
Figure 12: Relative 1-RM for Smokers and Nonsmokers	32
Figure 13: Composite 1-RM for Smokers and Nonsmokers	32

<u>List of Tables</u>	<u>Page</u>
Table 1: Study Design	16
Table 2: Resistance Training Intervention Phases	17
Table 3: Resistance Training Intervention Workouts	18
Table 4: Anthropometry and Body Composition in Intervention Group	24
Table 5: Cardiorespiratory and Strength Measures in Intervention Group	24
Table 6: Anthropometry and Body Composition in Cross Sectional Analysis	29
Table 7: Cardiorespiratory and Strength Measures in Cross Sectional Analysis	29

List of Abbreviations

Cardiorespiratory fitness (CRF)

Cardiovascular Disease (CVD)

Flow Mediated Dilation (FMD)

Healthy Cohort (HC)

Nicotine Replacement Therapy (NRT)

One-Repetition Maximum (1RM)

Resistance Training (RT)

Resistance Training and Nicotine Replacement Therapy (RT/NRT)

Type II Diabetes (T2D)

Acknowledgements

I would first like to thank the members of the Exercise and Metabolic Disease Research Laboratory for their unsurpassed hard work and support these past two years. The pilot data presented here was gathered from a study under my mentor Dr. Christian Roberts who put more hours into this project than every member of the lab combined. I would also like to thank Sharon Lee, the dedicated study coordinator; Michael Chronley, a fellow graduate student who helped compile the data for both the CRF and muscular strength measures; and the many undergraduate volunteers who allowed the study to run as efficiently as possible.

Next, I would like to express my gratitude to my family. They do not believe the word “can’t” is even in my vocabulary and it is because of their belief that I make sure to never to use it. My grandmother, Donna, has been there for me from the day I was born and always had faith that I would do something great. I can always count on my mother to be there for me if I ever I need her, and my brother has been calling me “Doctor Tia” since I was in high school. I would also like to acknowledge my father, Johnny, who was the first person to really push me to never quit and always set my goals high. He will forever be in my heart.

Lastly, I would like to thank my committee members: Dr. Peter Narins, Dr. Rachelle Crosbie Watson, and Dr. Oscar Scremin, for their patience and support as I collected data, painstakingly tried to figure out how to work statistical programs, and finally compiled everything I discovered into this thesis. I would like to give a special

thanks to Dr. Peter Narins who advised me on multiple occasions when I found myself contemplating taking on the challenge of finishing the Master's Degree.

Chapter 1: Introduction and Background

This study was driven by the pressing public health need to discover effective and novel ways to prevent and treat the onset of cardiovascular disease (CVD) risk, type 2 diabetes (T2D), and cancer, especially in the young smoking adult population who are at increased risk of these chronic diseases. CVD, T2D, and cancer account for 45% of all deaths in the world and more than 60% of deaths in the United States¹. The annual healthcare costs of CVD alone in the United States have been estimated at more than \$475 billion per year. The costs of T2D is more than \$175 billion, together totaling more than 26% of U.S. annual health care costs^{1,2}. The prevalence of these chronic and often fatal diseases is made even greater by cigarette smoking which harms nearly every tissue of the body with 33.5% of smoking-related deaths being cardiovascular-related³. The unfavorable health effects cause an estimated 443,000 deaths each year in the United States.³ More people die from the effects of tobacco use than immunodeficiency virus (HIV), illegal drug use, alcohol use, motor vehicle injuries, suicides, and murders combined.⁴

With the United States already spending very large sums of money on healthcare, finding a cost effective means of improving the quality of human life has become a priority. In order to do this, it is important to target the younger populations to stop CVD, T2D, and cancer before its onset. More time investigating the benefits of physical activity and smoking cessation as a means of prevention as well as a way to improve the quality of life for those who are already suffering from these diseases, will instill in the younger

populations the importance and benefits are physical activity and smoking cessation, to ensure the health future generations.

It has already been well documented that aerobic exercise acts to decrease CVD risk.⁵ However, there still lies some controversy in the benefits of a pure resistance training exercise program on cardiovascular health markers such as cardiorespiratory and muscular fitness as independent predictors of CVD risk. Many studies have previously shown that more frequent and intense physical activity acts to not only decrease but also to prevent CVD symptoms; however, more evidence on the different physical activity modalities will help motivate people to take part in different training regimens. If a resistance training regimen can be beneficial in preventing CVD, T2D, and cancer, then those individuals who are unlikely to participate in some form of endurance training can still get the required physical activity necessary to maintain a healthy lifestyle.

Proving that smoking cessation also has health benefits may motivate individuals to stop smoking. The physical damage that smoking causes over time has been well-known with the emphasis being placed solely on what will happen if one does not quit. If smokers are presented with the knowledge that smoking cessation will not only prevent future damage but can also reverse some of the damage already done; perhaps people will be more motivated to stop smoking.

Rationale for Studying Young Adults

Atherosclerosis is the underlying cause for CVD worldwide and the atherosclerotic process has been shown to begin in childhood by the Pathobiological Determinants of Atherosclerosis in Youth (PDAY). This study looked at data from 3000

youths between the ages of 15 and 34 who had died from external causes. Even at just 14 years old, teenagers had fatty streaks which are the first sign of atherosclerosis. These fatty streaks appear as early as infancy for those who had mothers who smoked cigarettes, had poor diets, or a lack of physical activity causing them to be overweight, have diabetes, and high cholesterol⁷. Asymptomatic atherosclerosis at a young age is linked to a greater occurrence of CVD in the future and so it is important to make the younger population aware of the consequences of smoking and inactivity⁸. The reason for targeting the specific age group of 18-35 is not only because of the prevalence of the atherosclerotic process already beginning in this age range, but also due to the independence and understanding of this age group. By reaching out to those who are in the beginning process of taking care of themselves and making their own decisions, it is hopeful that they will be educated to make lifelong lifestyle changes that will prevent the onset of CVD, T2D, and cancer. Starting the intervention at this age will hopefully help to ameliorate the prevalence of chronic disease in the future.

Rationale for Studying Resistance Training and Smoking Cessation

Previous studies have shown that maintaining lean body mass into old age counteracts the cardiovascular ailments seen with the onset of obesity and sarcopenia as adults participate in less frequent physical activity with age⁹. It is likely that the maintenance of lean body mass help offset insulin insensitivity since the increased muscle mass allows for an increase in glucose uptake in the form of muscle glycogen. It has been shown that the increase in adipose tissue seen with decreased physical activity increases the likelihood of cardiovascular disease, T2D, and cancer.

Resistance training has also been shown to improve the flow-mediated dilation (considered a reliable measure of endothelial function) which is measured as the percent change in brachial artery diameter after a cuff occluding the artery is removed¹¹. After the cuff is removed, blood flow rushes through the once occluded artery to supply blood to the forearm. This blood flow causes a sheer stress on the intima layer comprised of endothelial cells that line the inside of the artery wall. In response, the endothelial cells produce nitric oxide which then diffuses to the smooth muscle layer called the media, relaxing the artery wall allowing for vasodilation. FMD is considered a reliable measure of endothelial function¹¹. Because resistance training significantly improved the FMD response, it can be considered to induce a protective effect from CVD.

Inflammatory markers such as CRP have also been shown to decrease after a resistance training intervention¹². Markers which provide evidence of chronic low grade inflammation such as this play a crucial role in the development of atherosclerosis and cardiovascular disease.

The negative health effects from cigarette smoking have become more and more evident in recent years as the public health sector has linked more than one-third of smoking-related death to be cardiovascular-related¹³. Cigarette smoking lowers the levels of good HDL cholesterol, thus indirectly causing an increase in the bad LDL cholesterol¹⁴. LDL is phagocytosed by macrophages becoming foam cells which then invade the intima-media layer of the artery wall. When these foam cells build up and die in the artery wall, plaques form which decrease the diameter of the artery leading to atherosclerosis. The same plaque build up in the coronary arteries will lead to coronary

artery disease and places the individual at high risk for plaque ruptures that cause heart attacks and strokes. In addition to the damage done to the vascular system, the toxins in cigarette smoke damage the lung tissue itself causing emphysema and decreasing the efficiency of oxygen exchange. Nicotine itself acts to increase heart rate and, over time, the heart is forced to work harder; ultimately, leading to heart failure. While the damage to the cardiovascular system is widespread, smoking cessation has been shown to reverse some of the damage in as little as a few days as carbon monoxide levels drop to nearly zero¹⁵.

Cardiorespiratory Fitness

Cardiorespiratory fitness is an accepted CVD risk marker and low CVD in the adult population carries a greater risk ratio for all-cause mortality¹⁶. CRF is a measure of the body's ability to exchange oxygen and carbon dioxide in the lung tissue and utilize the oxygen in working muscle tissue. The body's ability to do so is dependent on many aspects of the cardiovascular system making this measure a very good indicator of cardiovascular function. At rest, only a small fraction of the oxygen delivered to the tissues is used. For a healthy individual, the exchange of oxygen and carbon dioxide in the lung is not the limiting factor for exercise. In other words, it is not the oxygen delivery, but the oxygen consumption that limits the work that can be performed by muscle.

Oxygen Delivery

The delivery of oxygen is dependent on the gross cardiovascular system. Beginning in the lung, inspired atmospheric oxygen is taken through the conduction

airways of the mouth, trachea, and bronchi into the respiratory zone where the alveoli are found. The alveolar walls are comprised of a very thin layer of epithelial cells which maximize the diffusion of oxygen into the blood and carbon dioxide out of the blood down their separate concentration gradients. Once oxygen enters the pulmonary capillaries, it is transported in the blood primarily as oxyhemoglobin within the red blood cells. The now oxygenated blood returns to the heart where it is then pumped to the systemic circulation to deliver oxygen to the working tissues. This delivery system can be hampered in many ways by symptoms of CVD. Sedentary smokers are at higher risk for high LDL levels which leads to atherosclerosis¹⁷. Oxygenated blood depends on the arteries to reach its destination and if those arteries have a reduced diameter due to atherosclerosis, the delivery system will no longer be as efficient. Furthermore, if there is a plaque that is not yet stable and calcified, an increase in blood flow can actually rupture the plaque leaving the free-floating embolism to occlude a coronary artery causing a heart attack or a cerebral artery causing a stroke. Thus, an individual with poor CRF, may be suffering from atherosclerosis which would decrease their maximum aerobic capacity through this mechanism. Another aspect of oxygen delivery by the cardiovascular system is the heart itself. The heart acts as the pump which powers blood through the vascular system. As mentioned earlier, nicotine actually causes heart rate to increase and this increase in workload by the heart can lead to heart failure over time. In addition, with atherosclerosis, there is a greater afterload the heart must pump against in order to move blood through the arteries. If the heart must work harder, it cannot work as efficiently

which could explain the decreased oxygen delivery and CRF seen in the sedentary smoking population.

Active individuals actually improve their oxygen delivery system by increasing their cardiac output which is a function of heart rate and stroke volume. The stroke volume, amount of blood ejected per heart beat, is dependent on the heart's contractility and venous return which increases during exercise. Thus, the recreationally-active individuals of the healthy cohort are likely to have a much better oxygen delivery system based on their improved cardiac output and lower incidence of atherosclerosis.

One negative side effect of smoking is the toxins that are inhaled in addition to the addictive nicotine. One such toxin, carbon monoxide, has a very high affinity for hemoglobin, the oxygen binding site of the red blood cell. With less available binding sites for oxygen, delivery to the tissues of the smoking group is also hampered. During rest, this effect is asymptomatic since the percentage of oxygen in the blood far exceeds the oxygen requirements of resting tissues; however, during maximal exercise the decreased carrying capacity for oxygen by the blood can potentially limit the aerobic metabolism of the working muscle tissue¹⁸.

Oxygen Consumption

The utilization of oxygen that is delivered by the heart and vascular system to the tissues is performed through oxidative phosphorylation which is performed at the level of the organelles that reside within the tissues, specifically, the inner membrane of the mitochondria. Oxygen that diffuses down its concentration gradient into the muscle tissue is used to accept the hydrogen ions that are pumped through ATPase to create ATP, the

primary source of energy for the body. These hydrogen ions join oxygen to form water. When the hydrogen ions used to create ATP is generated faster than oxygen can diffuse across the membrane of the mitochondria, the tissue builds up hydrogen ions, the pH of the tissues drops, and the acidic environment that forms causes muscle fatigue.

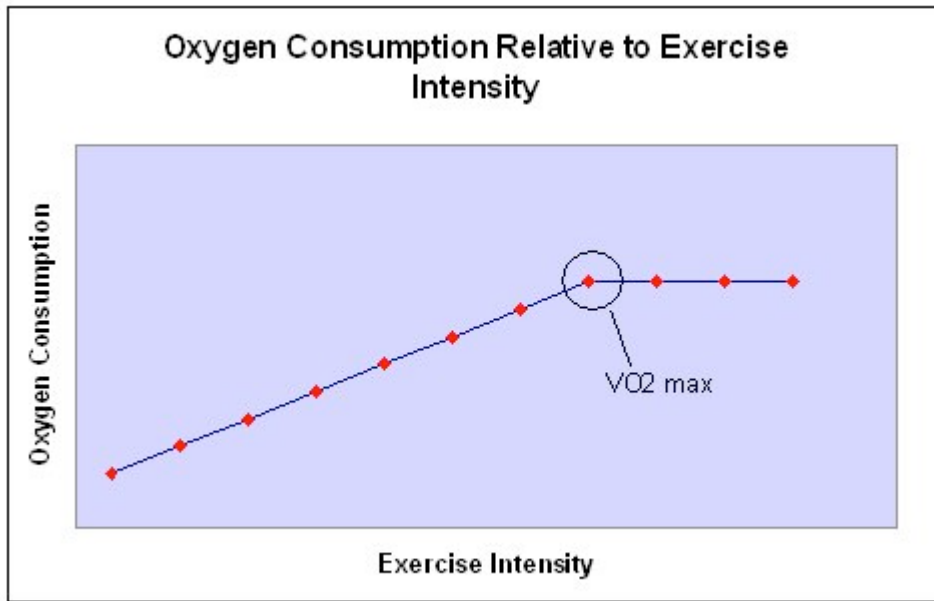
For recreationally-active individuals, there are physiological adaptations made by the tissues as well as by the oxygen delivery system itself. With training, the capillaries undergo a process called angiogenesis. Angiogenesis is the process by which capillaries increase their proliferation into the tissues. More capillaries allow for a greater surface area for oxygen and carbon dioxide exchange; thus, more of the oxygen that is delivered to the tissues can be utilized. Another adaptation to exercise which increases the efficiency of oxygen consumption is an increase in the number of mitochondria and mitochondrial enzymes, such as succinate dehydrogenase, that participate in oxidative phosphorylation. The greater number of mitochondria and enzymes allows for more ions to be pumped along the electron transport chain, more ATP to be synthesized, and more oxygen to be consumed.

Defining Measures of CRF

Cardiorespiratory fitness is a measure of oxygen consumption by the tissues. A greater maximum aerobic capacity is indicative of the adaptation mentioned above, while a poor aerobic capacity predicts CVD risk factors such as atherosclerosis and heart failure. The measures of interest that will be discussed further are relative and absolute maximum aerobic capacity, maximum heart rate, and maximum breathing frequency.

Absolute maximum aerobic capacity is the milliliters (ml) of oxygen consumed per minute during maximal exercise. This value is obtained by subtracting the ml oxygen exhaled from the ml oxygen inhaled as the exercise intensity increases. The difference between these two values is the amount of oxygen consumed. Oxygen consumption increases to match the demands of the muscle which must work harder with increasing exercise intensity. When reaching maximum aerobic capacity, oxygen consumption no longer increases despite increases in exercise intensity (Figure 1). At this point, there is a rapid build up of lactic acid and the muscle quickly fatigues. Relative maximum aerobic capacity is the ml of oxygen consumed per kilogram body weight per minute. This relative value is the common unit used because it normalizes the data based on differences between body weights of different subjects. An individual who simply has more mass will have a higher absolute maximum aerobic capacity because they have more tissue using oxygen and not because of exercise adaptations such as angiogenesis, increased mitochondria, or increased mitochondrial enzymes.

Figure 1: Example of Maximum Aerobic Capacity Graph



Maximum heart rate is another measure of fitness that will be analyzed. Healthy individuals are able to reach a higher maximum heart rate because they have more efficient oxygen consumption so they do not reach muscle fatigue before reaching maximum heart rate.

Maximum breathing frequency is not a typical measure that is used as an indicator of fitness. However, the frequency of breath is an important aspect of the oxygen delivery system that is often impeded in the smoking population. The increased breathing frequency during exercise is necessary to clear more carbon dioxide from the blood and lungs and to bring more oxygen to those same structures. Without the increased clearance of carbon dioxide, the pH of the blood decreases and the muscle fatigues under the acidic conditions. Smokers often suffer from exercise-induced asthma which is just one of the negative effects of cigarette smoking. The toxins in cigarette smoke paralyze the cilia that

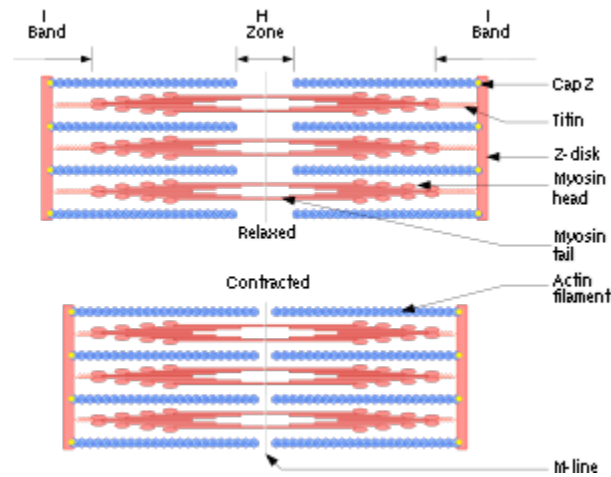
line the respiratory airways so more particulates are able to pass into the respiratory zone. These particulates must be phagocytosed by macrophages which bring with them the inflammatory response. Inflammation in the airways prevents them from dilating fully so there is a decreased frequency of respiration. Without optimal breathing frequency to clear the build-up of carbon dioxide created by the working muscle tissue, the muscle fatigues much faster leading to lower CRF¹⁹.

Muscular Strength

It has been shown that muscular strength, tested as the maximum weight that can be lifted through one repetition (one repetition maximum), is an indicator of CVD risk. Muscle mass permits more storage of glucose as muscle glycogen, instead of glucose storage within adipose tissue. As mentioned earlier, this helps increase insulin sensitivity.

Healthy individuals tend to have greater muscular strength because they are physically active. Adaptations to exercise, such as a greater cross-sectional area of the muscle, allows for a greater one repetition maximum. If a muscle has a greater cross-sectional area, there are more sarcomeres (the functional unit of muscle) in parallel. Each sarcomere has a thick filament made up of myosin and a thin filament made up of actin. In order to contract, these filaments slide across one another as per the sliding-filament theory where myosin heads attach to the actin forming a microscopic muscular connection called a cross-bridge that pull the filaments past each other (Figure 2). A greater number of sarcomeres in parallel allow for more force production by the muscle.

Figure 2: The Sliding Filament Theory



One study showed that there was an inverse relationship between grip strength and metabolic syndrome, a key risk factor for CVD²⁰. Not only does the sedentary smoking population does have this muscular adaptation simply because they lack physical activity, but one study showed that smoking actually impairs muscle protein synthesis and increases the expression of myostatin, a muscle protein synthesis inhibitor²¹. Thus, this population is at greater risk for CVD, T2D, and cancer.

Cardiorespiratory Fitness and Muscular Strength as Independent Predictors of Cardiovascular Disease

Many studies have shown that both CRF and muscular strength are independent predictors of cardiovascular disease. One study called the Coronary Artery Risk Development in Young Adults (CARDIA) examined over 2000 men and women ages 18-30 over 15 years in a population-based longitudinal cohort. This study found that those in the cohort who had a CRF in the bottom 20th percentile were 3 to 6 times more likely to develop T2D, hypertension, and metabolic syndrome than those whose fitness was in the top 60th percentile²². The association between fitness and cardiovascular risk

has been well-documented but what has not been pinpointed is the mechanism behind this effect. The CARDIA study looked at many health factors and determined that obesity was the key link between fitness and CVD risk.

Those who have better CRF tend to engage in regular physical activity and thus have a more favorable caloric balance. If the energy input, or calories consumed, is greater than the energy output, calories burned through exercise, the individual will become overweight with time. Lower body weights actually protect against hypertension, T2D, and metabolic syndrome due to decreased vascular resistance, reduced cardiac output, and decreased plasma noradrenaline concentrations²³. Less vascular resistance is indicative of a healthy oxygen delivery system. Vascular resistance is caused by atherosclerotic plaques and endothelial dysfunction. The endothelial cells synthesize nitric oxide which causes the arterial smooth muscle to relax allowing the arteries to vasodilate. When there is more vascular resistance, the heart must work harder to pump against the greater afterload, thus increasing cardiac output. A greater cardiac output over time can place unnecessary strain on the heart leading to heart failure.

Fitness also decreases the risk of CVD by improving the individual's lipid profile. Physical activity increases the activity of lipoprotein lipase in skeletal muscle which speeds up the clearance of plasma triglycerides and increases transport of lipids to the liver to be metabolized²⁴. Since the development of atherosclerosis is dependent on taking up lipids from the systemic circulation into the arterial wall, less lipids in the blood helps decrease the plaque build up that causes the vascular resistance that leads to hypertension and increased cardiac output.

CRF has also been found to attenuate the increased risk of mortality that is usually associated with obesity. In other words, an improvement in fitness improved their cardiometabolic profile independent of weight loss²⁵.

Muscular strength has been increasingly recognized in the pathogenesis and prevention of cardiovascular disease. It has shown to have an independent protective effect on all cause mortality and has been inversely associated with the CVD risks associated with obesity, hypertension, and metabolic syndrome. A previous study put obese young men through a 12-week resistance training intervention and found that muscular strength was inversely associated with insulin resistance and inflammatory proteins. The increased lean body mass from improved muscular strength provides more storage of glucose as muscle glycogen. The quick uptake of glucose from the blood plasma to be stored in muscle tissues increases insulin sensitivity²⁶.

CRF and muscular strength are two strong independent predictors of CVD. Examined together, they provide a reliable warning of chronic disease in those who are in the lowest quantile of fitness.

HYPOTHESIS

The goal of this study was to determine the effect of nicotine replacement therapy and resistance training on cardiorespiratory fitness and muscular strength in a population of young, sedentary smokers. Using cross-sectional data from a healthy cohort of recreationally-active nonsmokers, the secondary goal was to observe probable differences between these fitness measures between the smokers and nonsmokers. The markers of CRF used were relative maximum aerobic capacity, absolute maximum aerobic capacity, maximum heart rate, and maximum breathing frequency. One repetition maximums for chest press, seated row, and leg press, as well as the relative and composite repetition maximums were used as an index of muscular strength. It was hypothesized that among the four groups, those who received both NRT and RT would have greater CRF and muscular strength improvements than those who received only one form of intervention. In addition, the healthy cohort would have better CRF and muscular strength than the smokers.

Chapter 2: Methods

Study Population

Twenty-nine smokers entered the study and completed their first visit. Smoking status was also verified via breath carbon monoxide (CO) concentration. Sixteen smokers (13 men, 3 women, age 24.5 ± 4.6 yr) and 46 non-smokers (32 men, 14 women, age 22.5 ± 3.7 yr) volunteered for and completed the study. The data from the first visit of those who did not complete the study was used to compare to the non-smokers to compare the two groups at baseline. Subjects were in good health (as indicated by comprehensive history, physical examination, and standard blood tests at their baseline visit) and were untrained, participating in moderate-intensity physical activities ≤ 2 times/wk, and non-smokers were recreationally active. Potential participants who (i) have had documented coronary artery disease (CAD) or cardiac surgery; (ii) have participated in a structured exercise, nutrition, or weight loss program in the past 6 months; (iii) have used medications that influence CV function, body composition, or insulin indices (e.g. prednisone, Ritalin, Adderall, GH); or (iv) have had a known heart arrhythmia and/or abnormalities in an electrocardiogram (ECG) reading were excluded from the study. Prior to any testing procedure, informed written consent was obtained from each participant. This study was approved by the Institutional Review Board of the University of California, Los Angeles.

Randomization

Allocations were concealed from participants until after the first visit of their pre-intervention tests. Participants were randomized into one of four groups as seen in Table

1. All groups were instructed to maintain their normal *ad-libitum* diet, and normal daily activities.

Group Design	Smoking Cessation (NRT)	
	NRT/No RT	No NRT/No RT
Resistance Training	NRT + RT	No NRT + RT

Control Group (C)

Participants randomized to the

Table 1. Study Design.

No NRT/ No RT group served as the control group. These subjects came in for their baseline measures, maintained their normal diet and normal daily activities with no intervention, and then returned for the post-study measures 12 weeks later.

Cross-sectional Participants- Healthy Cohort (HC)

46 recreationally active, nonsmoking subjects total underwent a baseline assessment.

Resistance Training (RT) Group

Participants in the RT group began with a 12-week RT intervention (60 min sessions, 3x/wk). All evaluable participants in the RT group received a minimum of 34 out of the 36 total training sessions within the 12 week period, demonstrating strong adherence to the training program.

Nicotine Replacement Therapy (NRT) Group

The NRT group was given the recommended dosage of Nicoderm CQ patches determined by how much the subjects smoked. Adjustments to this dosage were made if the subject changed their smoking habits or felt a smaller or greater dose was needed in order to feel the appropriate effects of the nicotine replacement therapy.

Both Resistance Training and Nicotine Replacement Therapy (RT/NRT) Group

Participants in the RT/NRT group received both treatments described above simultaneously.

Resistance Training Intervention

All training occurred at the UCLA John Wooden Center. The training overload was modified using a linear periodization model with 3 phases. Phase 1 (wks 1-2) familiarized participants with the training program and proper lifting technique. During this phase, participants completed two sets of 12-15 repetitions for each exercise, at 100% of their approximated 12-15 repetition maximum (RM) (i.e. participants were motivated to reach volitional fatigue/failure within 15 repetitions). During phase 2 (wks 3-7) and phase 3 (wks 8-12) greater intensity and volume modalities of the same exercises were used to overload the musculature and encourage muscular hypertrophy. In phases 2 and 3, participants completed three sets of 8-12 repetitions at 100% of their 8-12RM and 6-8 repetitions at 100% of their 6-8RM, respectively (Table 2). As participants adapted to the training overload, the weight was progressively increased to maintain the prescribed training intensity for each phase. Detailed records regarding attendance, number of repetitions performed, resistance used, and the total amount of weight lifted per session were maintained by the training supervisor. All participants trained on 3 non-consecutive days/wk cycling between two unique workout regimens (Table 3). All subjects in the RT group completed at least 34 of 36 sessions and subjects in the C group completed at least 10 of 12 sessions. All training sessions were led by a certified personal trainer with a maximum 3:1 participant to trainer ratio.

Table 2

--

Table 3

--

Muscular Strength Testing

To evaluate strength changes, participants performed a maximal strength test consisting of 1RM lifts for the barbell bench press, the 45° incline leg press, and the machine seated row. To quantitate subjects overall strength, a strength score was calculated by summing the absolute value of all three 1-RM lifts. Subjects first warmed up each muscle group by doing 8-10 repetitions using a light weight. Next, subjects were prompted to progressively increase the weight while decreasing the repetitions until they

could safely attempt an estimated 1-RM for that lift. A successful 1-RM occurred on the 2nd to last lift attempted by the subject with the last attempt recorded as a failure. Subjects were allowed 3-4 minutes of rest in between all sets. The determination of each subject's 1-RM was achieved within 8 total sets, including the warm-up. For both groups, participants performed a total of 2 maximal strength tests: one immediately preceded their first training session, the second immediately preceded their penultimate training session (RT group) or the pre-assessment visit (C group).

Cardiorespiratory Fitness Testing

Immediately prior to the muscular strength testing, cardiorespiratory fitness was assessed by VO₂max. Subjects were reminded by phone and email to abstain from the consumption of caffeine, alcohol and vitamin supplements for 12 hours prior to testing and not to engage in any vigorous physical activity 72 hours prior to testing. CRF was determined using the MAX –IIa metabolic cart and Lodestone cycle ergometer. Resting data was obtained for a minimum of 2 minutes or until a respiratory exchange ratio (RER) less than 0.9 was achieved. As a warm up, the subject then cycled at 60 rpm for 3 minutes with no resistance. The subject was then instructed to maintain 60-70 rpm for the duration of the test which lasted 8-12 minutes. A ramp protocol was used with the workload (watts/min) determined by the subject's sex, age, height, weight, and physical activity. The subject cycled until 60 rpm could no longer be maintained and then recovery data was taken for 2 minutes following the completion of the test. The Max-IIa software records the maximum absolute and relative aerobic capacity, maximum heart rate, and peak RER obtained during the test.

Nicotine Replacement Therapy

The NRT group was given the recommended dosage of Nicoderm CQ patches determined by how much the subjects smoked. Adjustments to this dosage were made if the subject changed their smoking habits or felt a smaller or greater dose was needed in order to feel the appropriate effects of the nicotine replacement therapy.

Outpatient Visit Procedures

Evaluable participants completed two assessments (designated pre- and post-) over an 12 -week period. Major outcome variables were determined over two outpatient visits per assessment/test. The first visit took place during the week at the Clinical Translational Research Center (CTRC) followed by a Saturday visit that same week at the Gonda (Goldschmied) Diabetes Center. These visits were methodically scheduled at weeks 0 and 13 for all participants to control for any acute effects of the 12-week RT program employed in the RT randomizations group; the first day outpatient visit occurred 72 hours after the final RT session (during wk 13) and the second day of outpatient visits occurred 96-120 hours after the final RT session. Prior to both visits, subjects were reminded by phone and email to abstain from the consumption of all food including caffeine, alcohol and vitamin supplements for 12 hours prior to testing. They were also reminded not to engage in any moderate to vigorous physical activity within 72 hours prior to Day 1 of the outpatient visit or 96 hours prior to Day 2 of the outpatient visit. All within-subject sessions were conducted at approximately the same time of day to reduce possible diurnal variations in physiologic measures. In addition, each participant was

formally escorted to each visit by a member of the study team to obtain verbal confirmation of subject adherence to the aforementioned criteria.

Outpatient Visit, Day 1: The outpatient procedures at the CTRC began at 7:30am and typically lasted 3.5 hours. A 12-lead Electrocardiogram (ECG) was administered as a safety measure and checked by a physician before allowing any participation in exercise testing/ intervention. Height, weight and WC were measured in duplicate in all subjects using the procedures of Lohman et al.⁸⁴. Supine blood pressure and heart rate were measured on the right arm after the subject had rested quietly for 5 min. Two readings of blood pressure and heart rate were obtained and the average was recorded. Resting/basal metabolic rate was then determined using indirect calorimetry. Blood was drawn and processed for various assays and venous blood draw was concluded with the Frequently Sampled Intravenous Glucose Test (FSIGT). During the three hours spanning the course of FSIGT, subjects completed selected smoking questionnaires.

Outpatient Visit, Day 2: Upon arrival, subjects underwent an ordered set of outpatient procedures. First, height and weight were measured in duplicate. Then body composition was determined by dual-energy x-ray absorptiometry (DEXA) scan which was followed by flow-mediated dilation (FMD) arterial stiffness indices testing. Following these acutely sensitive tests, subjects underwent a finger prick to measure glycated hemoglobin (HbA1c) via DCA Vantage® Analyzer (Siemens Medical Solutions Diagnostics, New York, USA), and completed a physical activity questionnaire (International Physical Activity Questionnaire, IPAQ). The muscle and fat tissue biopsy from subjects' left vastus lateralis was the final procedure for the visit.

Body Composition

Height, weight and WC were measured in duplicate. Whole body fat%, total trunk fat mass, and LBM were estimated by DEXA (Hologic QDR4500 Fan Beam X-ray Densitometer, Hologic, Inc. Waltham, MA).

Carbon Monoxide Levels

Carbon monoxide level were measured using the CO monitor brand is Bedfont Micro+ Smokerlyzer.

Statistical Analysis

Between-group comparisons of baseline (pre-test) outcomes were performed for evaluable participants using one-way analysis of variance (ANOVA) to identify possible randomization imbalance. No differences were found. All data were analyzed for homoscedasticity and normality. The overall effects of the intervention were tested for evaluable participants using ANOVA on the post-pre change score (between-group comparisons). Within-group sample mean-comparison analyses were Between-group comparisons of baseline (pre-test) outcomes were performed for evaluable participants using repeated measures ANOVA between pre- and post-test measures. Robust measure of statistical significance was obtained by running a Monte Carlo permutation for each respective test statistic (e.g. F-statistic) 1,000 times, creating a distribution (e.g. F-distribution), from which a test for significance was obtained at an alpha level of 0.05. Figures report mean and 95% confidence intervals (CI) (CI, derived by bias-corrected bootstrap methods) and tables report mean $\pm$ SD. All analyses were performed with the

use of R Development Core Team (2008). (R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. ISBN 3-900051-07-0, URL <http://www.R-project.org>.)

Sample Size and Power Considerations: The sample size and power calculation are based on the primary outcome, cardiorespiratory fitness and muscular strength. Two primary types of comparisons are of interest: within group analysis for intervention post-pre test change, and between group analysis for SRT vs. HC comparing the post-pre test change score. An evaluable sample of 24 subjects was expected to provide 80% power to detect an effect size of at least 0.6 (Cohen's d 'medium' effect size) using a paired t-test with a 0.05 two-sided significance when evaluating the within group effect of the intervention on CRF and muscular strength. For the between group analysis, an evaluable sample of 15 SRT subjects and 22 HC subjects is expected to provide an 80% power to detect an effect size of at least 6 ml/kg/min and 100lbs. Power calculations were measured by G*Power 3 software.

Chapter 3: Results

Intervention Results

At the time the data for this thesis was analyzed, 16 subjects had completed their pre and post visits. The data from these 13 men and 3 women were randomized into one of four groups. 5 subjects were assigned to receive both RT and NRT, 5 received only RT, 3 received only NRT, and 3 served as a control group.

Anthropometric data is summarized in Table 4. Evaluable participants were young (age 24.5 ± 4.6 yr), sedentary (participating in recreational physical activity less than 2 times per week and by baseline fitness assessments) smokers (as determined by breath carbon monoxide levels and a smoking questionnaire). CRF and muscular strength data are summarized in Table 5. The control group had no significant drop in BMI and weight compared to the RT/NRT and RT groups. The RT/NRT group had a significant decrease in total fat, trunk fat, and fat percentage.

Table 4: Anthropometry and Body Composition

Outcomes	RT/NRT (n=5)		RT (n=5)		NRT (n=3)		C (n=3)	
	Pre-test	Post-test	Pre-test	Post-test	Pre-test	Post-test	Pre-Test	Post-Test
Age (yrs)	26.0 (5.5)		28.8 (6.8)		23.5 (2.4)		27.7 (6.0)	
Height (in)	71.7 (2.8)		68.7 (2.5)		69.3 (2.5)		68.9 (2.7)	
BMI (kg/m ²)	25.6 (4.74)	26.3 (4.66)	25.6 (3.87)	25.6 (4.38)	34.7 (6.66)	36.0 (6.90)	24.5 (5.12)	23.7 (4.65)
Weight (kg)	84.1 (14.2)	86.9 (14.5)	78.5 (14.3)	78.3 (15.0)	116.1 (30.7)	118.3 (31.4)	75.1 (14.1)	73.3 (14.3)
Total fat (kg)	15.3 (6.3)	15.9 (6.7)	21.1 (6.5)	20.6 (7.2)	29.2 (14.6)	25.6 (14.9)	21.1 (21.1)	20.0 (11.9)
Total fat (%)	18.6 (4.8)	18.2 (4.7)	26.3 (5.4)	25.1 (4.7)	26.5 (6.5)	26.1 (6.6)	25.0 (9.4)	23.9 (9.9)
Trunk fat (kg)	7.4 (4.2)	7.6 (4.5)	9.7 (3.7)	9.3 (4.6)	15.5 (9.4)	15.9 (9.5)	10.1 (6.2)	9.4 (6.1)
Total Lean (kg)	62.7 (7.8)	66.3 (8.6)	56.1 (11.7)	57.9 (11.7)	74.2 (15.3)	76.9 (15.0)	56.4 (5.9)	56.8 (7.0)

Table 5: Cardiorespiratory and Strength Measurements

Outcomes	RT/NRT (n=5)		RT (n=5)		NRT (n=3)		C (n=3)	
	Pre-test	Post-test	Pre-test	Post-test	Pre-test	Post-test	Pre-test	Post-test
Rel. Max Aerobic Capacity (ml/kg/min)	31.4 (5.3)	34.5 (5.7)	27.4 (3.0)	30.8 (2.1)	29.3 (6.1)	31.6 (6.1)	25.1 (8.0)	25.1 (5.6)
Abs. Max Aerobic Capacity (ml/min)	2784 (257)	3127 (282)	2108 (330)	2394 (461)	2759 (723)	2957 (730)	1900 (292)	1892 (200)
Max Heart Rate (beats/min)	184 (19)	181 (11)	168 (20)	168 (8)	187 (2)	181 (7)	189 (7)	177 (9)
Max Breathing Frequency (breaths/min)	45.2 (3.9)	43.4 (7.1)	36.6 (3.7)	35.0 (4.0)	51 (8.9)	44.3 (2.5)	39.7 (2.9)	39.7 (3.8)
1-RM Chest Press (lbs)	136 (28)	168 (30)	115 (39)	140 (54)	195 (53)	210 (57)	153 (18)	153 (67)
1-RM Leg Press (lbs)	498 (152)	650 (176)	451 (53)	548 (118)	730 (123)	795 (153)	535 (120)	561 (148)
1-RM Seated Row (lbs)	178 (19)	192 (21)	140 (32)	162 (36)	225 (22)	227 (23)	178 (39)	183 (74)
Relative 1-RM (lbs)	3.88 (1.2)	5.60 (0.31)	4.04 (0.65)	4.89 (1.2)	5.04 (1.1)	5.42 (1.3)	4.43 (0.27)	4.6 (0.59)
Composite 1-RM (lbs)	819 (194)	1026 (201)	706 (103)	850 (179)	1150 (195)	1232 (216)	865 (64)	895 (7)

The following figures show the pre-test and post-test data for the control and three intervention groups. Mean data was used to represent each group.

Figure 3: Fat Percentage in the Intervention Group

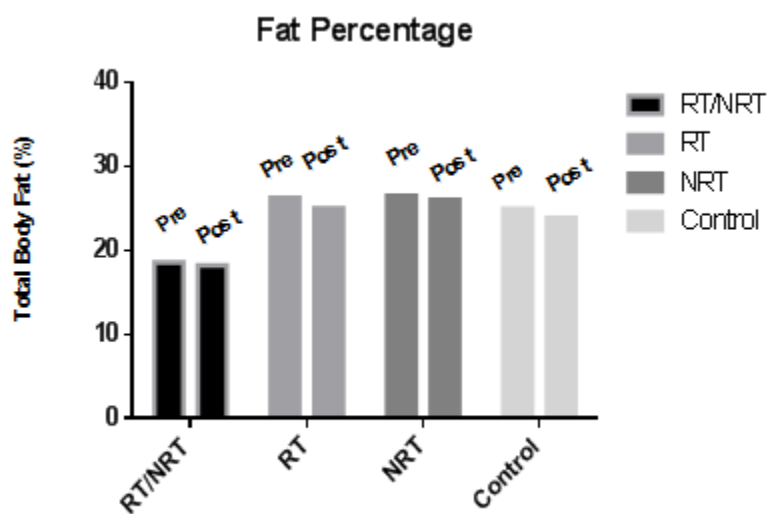
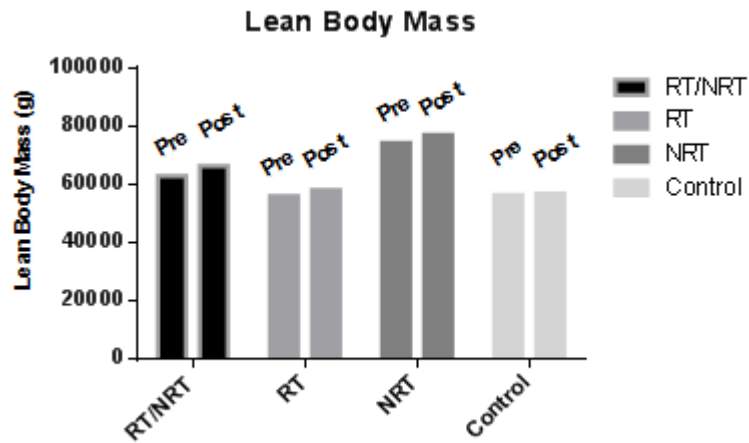


Figure 4: Lean Body Mass in the Intervention Group



Cardiorespiratory Fitness and Muscular Strength in Intervention Study

Data for relative and absolute maximum aerobic capacity, maximum heart rate, maximum breathing frequency, and 1-RM measures are summarized in Figures 5-7. The RT group had a significant increase in CRF measures compared to the other groups. Relative maximum aerobic capacity increased from 27.4 ± 3.05 ml/kg/min to 30.8 ± 2.12 ml/kg/min. This was significantly greater than the improvement seen in the NRT group ($P < 0.05$). The improved absolute maximum aerobic capacity and maximum breathing frequency were greater in the RT group than in the NRT/RT, NRT, and Control groups. There was no significant difference between the changes in maximum heart rate. NRT/RT and RT groups had significantly greater improvements in 1-RM for chest press, leg press, and seated row as well as the composite RM as compared to the NRT group. No significant difference was seen in the change in relative RM measures.

The following figures show the pre-test and post-test data for the control and three intervention groups. Mean data was used to represent each group.

Figure 5: Relative Maximum Aerobic Capacity in the Intervention Group

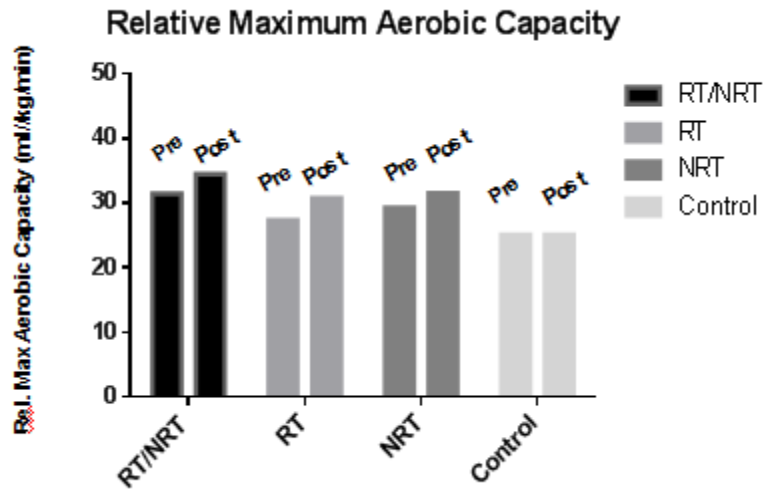


Figure 6: Absolute Maximum Aerobic Capacity in the Intervention Group

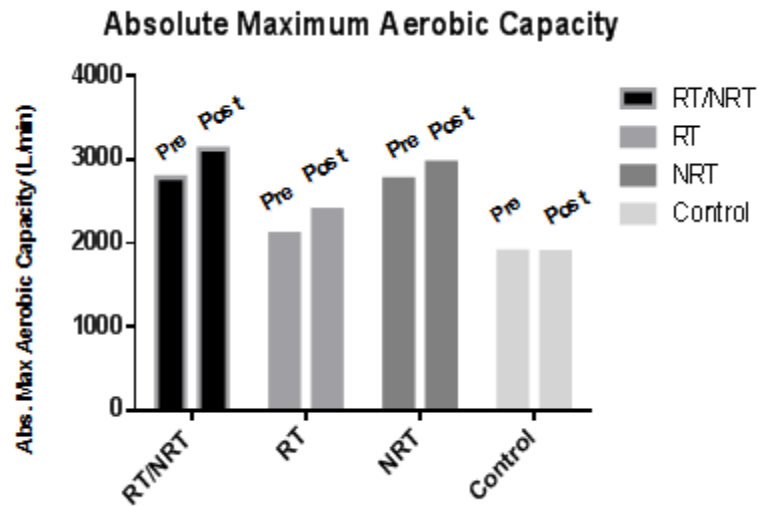


Figure 7: Maximum Breathing Frequency in the Intervention Group

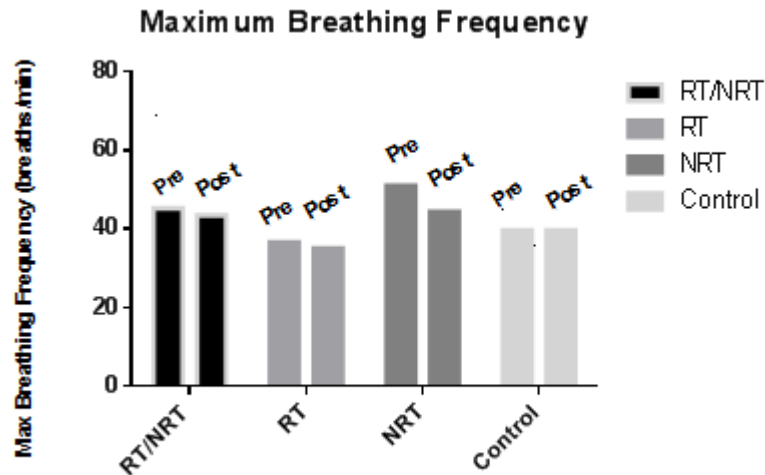
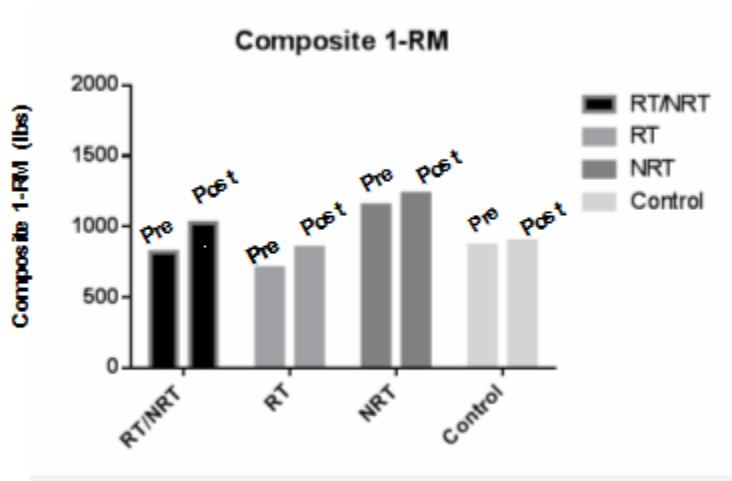


Figure 8: Composite 1-RM in the Intervention Group



Cross-Sectional Study Results

Anthropometric data is summarized in Table 6. Evaluable participants were young (age 22.5 ± 3.7 yr), recreationally-active (participating in recreational physical activity more than 3 times per week and by baseline fitness assessments) non-smokers. The cardiometabolic measures of this population were compared to the sedentary smokers'

baseline data to understand the cardiovascular and metabolic compromises between these two lifestyles. The body mass index between the healthy cohort (HC) (23.17 ± 3.0) and smokers (25.05 ± 5.60) was not significantly different, neither was the height, weight, nor age. However, the body composition between these two groups was significantly different in all values analyzed. Total fat in the HC was $11.22 \pm 10.97\text{kg}$ while smokers had a total fat of $18.06 \pm 10.97\text{kg}$. Trunk fat was measured at $4.69 \pm 2.22\text{kg}$ in the HC and $7.90 \pm 6.30\text{kg}$ in the smokers. There was a significant difference between body fat percentage with the smokers having an average of more than 5% higher than the HC and lean body mass was significantly lower for smokers as well.

Outcomes	Smokers	Healthy Cohort	p-value
Age (yrs)	24 (4.64)	22 (3.74)	0.66
Height (m)	1.8 (0.2)	1.7 (0.1)	0.42
BMI (kg/m ²)	25.1 (5.6)	23.2 (3.0)	0.07
Weight (kg)	75.9 (21.5)	71.3 (12.6)	0.1
Total fat (kg)	18.1 (11.0)	11.2 (4.5)	0.001
Total fat (%)	22.5 (7.0)	17.2 (6.7)	0.033
Trunk fat (kg)	7.9 (6.3)	4.7 (2.2)	0.002
Total Lean (kg)	59.4 (12.11)	60.1 (12.1)	0.36

CRF and muscular strength data are summarized in Table 7. Briefly, smokers had lower aerobic fitness as measured by relative maximum aerobic capacity, maximum heart rate, and maximum breathing frequency. Smokers also had lower muscular strength as measured by the 1RM for chest press, the relative 1RM, and the composite 1RM.

Outcomes	Smokers	Healthy Cohort	p-value
Rel. Max Aerobic Capacity (ml/kg/min)	28.7 (5.8)	37.3 (8.0)	< 0.0001
Abs. Max Aerobic Capacity (ml/min)	2368 (528)	2496 (761)	0.761
Max Heart Rate (beats/min)	172 (22)	183 (22)	0.015
Max Breathing Frequency (breaths/min)	38 (8)	45 (10)	0.002
1-RM Chest Press (lbs)	150 (41)	185 (59)	0.012
1-RM Leg Press (lbs)	520 (146)	600 (153)	0.103
1-RM Seated Row (lbs)	190 (29)	205 (51)	0.126
Relative 1-RM (lbs)	4.62 (0.7)	6.10 (1.1)	<0.0001
Composite 1-RM (lbs)	845 (247)	1015 (247)	0.49

The following figures display the significant differences between the HC and smoking group for both CRF and muscular strength measures. Data is expressed as box plots.

Figure 9: Relative Maximum Aerobic Capacity in Smokers and Nonsmokers

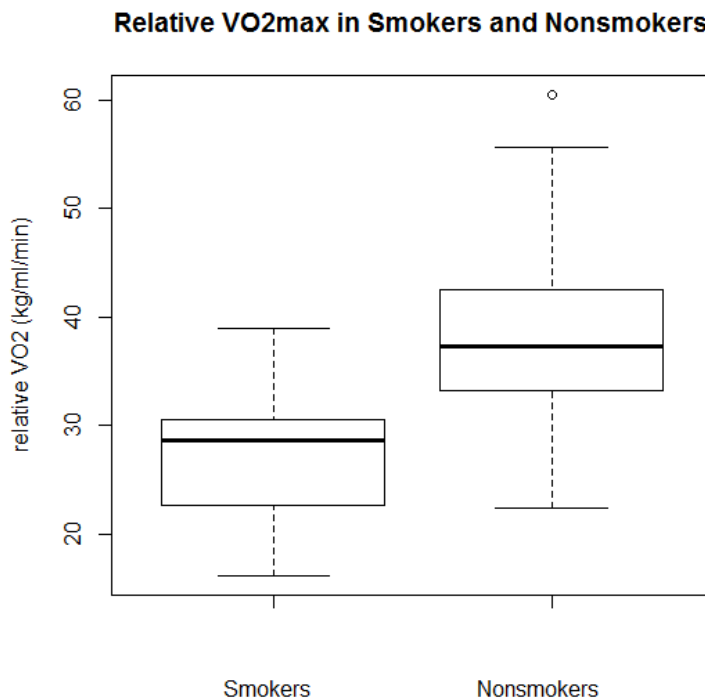


Figure 10: Maximum Heart Rate in Smokers and Nonsmokers

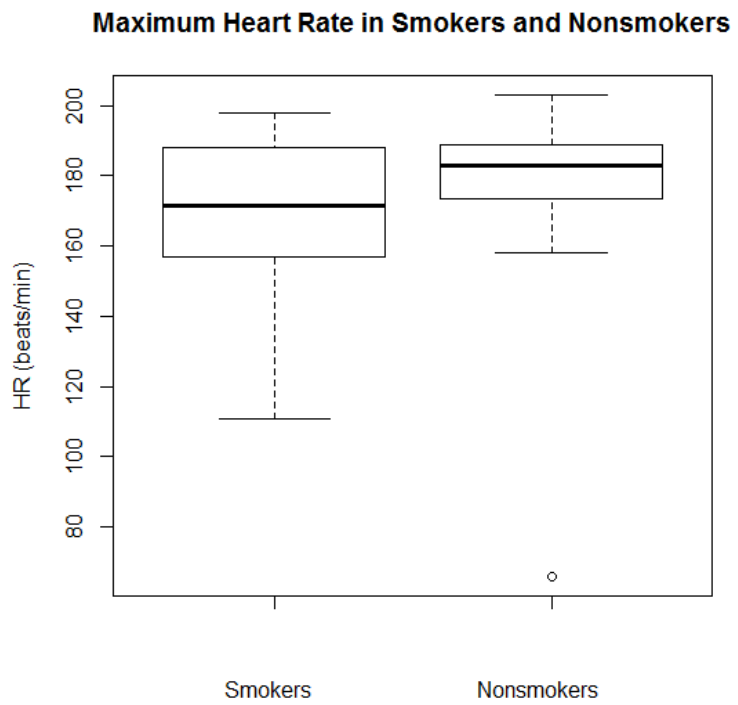


Figure 11: Maximum Breathing Frequency in Smokers and Nonsmokers

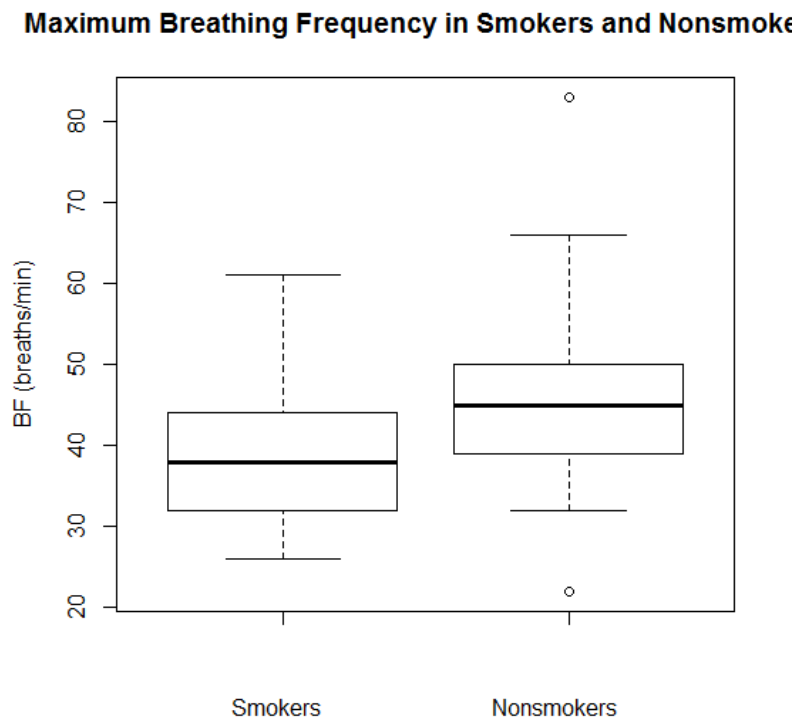


Figure 12: Relative 1-RM for Smokers and Nonsmokers

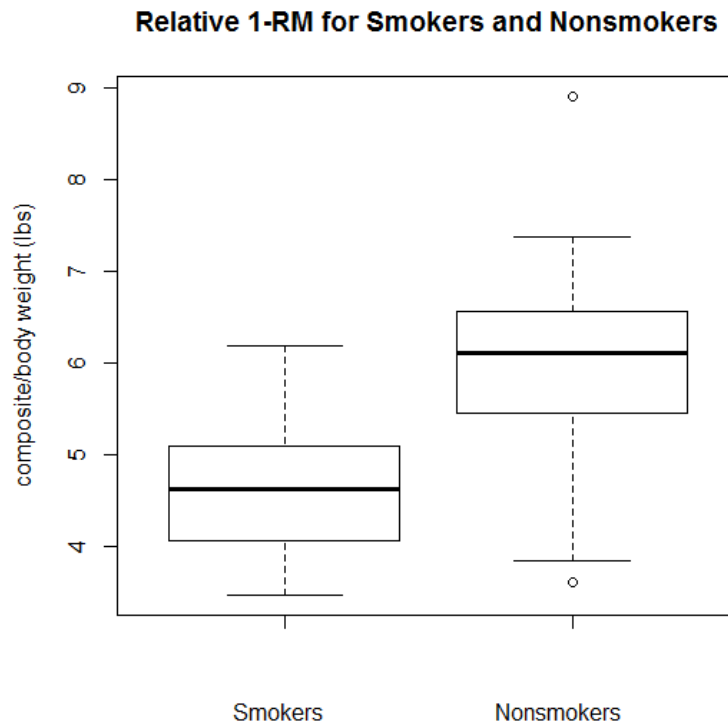
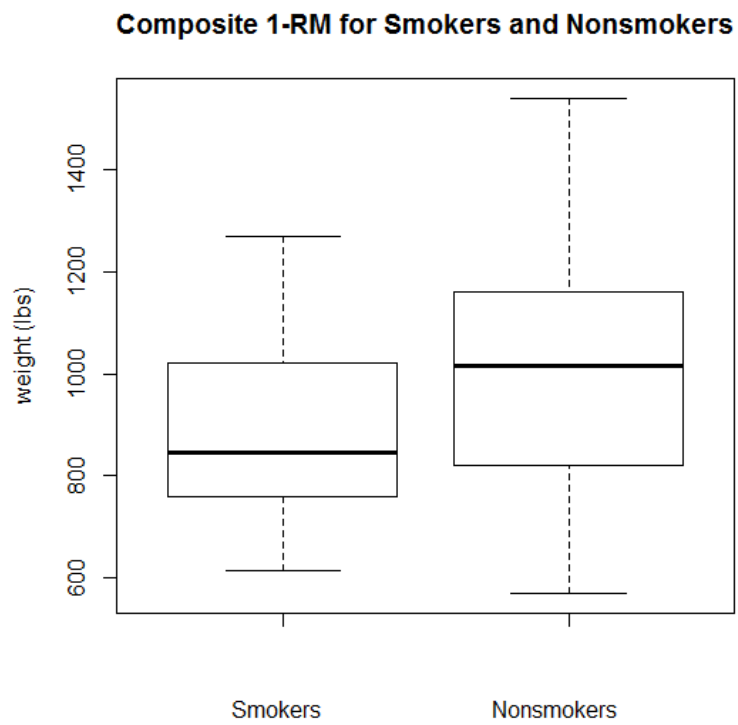


Figure 13: Composite 1-RM for Smokers and Nonsmokers



Chapter 4: Discussion

Cardiovascular disease is the leading cause of death for all males and females in the United States. While the death rate from illnesses related to CVD has decreased as medical knowledge and technology has improved, the direct and indirect cost of disease still remains among the highest in the country with over 280 billion dollars spent in 2008 and the projected cost in 2030 at 1117.6 billion dollars²⁷. The prevalence of CVD remains highest in older individuals. Many of these individuals have maintained a poor lifestyle for much of their life which amplifies the need to instill good lifestyle habits at a young age. Poor diet, smoking, and inactivity all contribute to the development of atherosclerosis. The PDAY study showed that, in America, those as young as their early teens have already developed the fatty streak that grow into raised lesions with a fibrous cap that can rupture causing a clot to form. Because most myocardial infarctions are caused by low-grade stenoses²⁸, which are most common in men between the ages of 45 and 60, intervention must take place early on in atherosclerotic development. Despite the knowledge among the general public that smoking is dangerous to health, the prevalence of cigarette smoking remains high even in high school students. An estimated 22% of non-Hispanic whites, 10% of non-Hispanic blacks, and 19% of Hispanics reported current cigarette use in 2009²⁹. By 2015, the WHO estimates tobacco will cause 6.4 million deaths a year.

Studies implementing either some form of physical activity intervention or a cross-sectional analysis have shown the benefits of starting an exercise regimen. Physical activity has been shown to improved body composition, decrease total cholesterol, LDL,

and triglycerides, and reverse T2D and the metabolic syndrome. This benefit can be seen in all populations regardless of gender, age, or ethnicity. However, many of these studies do not give sole attention to a resistance training regimen. For example, a study determining the intensity of physical activity necessary to improve cardiovascular health focused only on moderate-to-vigorous aerobic physical activity although the conclusions drawn from the study were generalized to all physical activity³⁰. Aerobic training and resistance training vary greatly in the mechanisms they improve fitness and likely in the mechanisms they decrease cardiovascular risk.

While CRF and muscular fitness have become accepted predictors of CVD, some studies disagree on whether or not these are truly independent predictors or must be looked at concurrently. One such study advocates muscular strength as a predictor of CVD but claims that this link is weakened without considering CRF as well³¹. The additive relationship between these two factors needs to be developed further to solidify the results.

Other studies have looked only at the effect of smoking cessation on the risk ratio of non-fatal myocardial infarctions. While studies agree that those who ceased smoking had decreased risk, the effect differed greatly with a study by Johansson et al., 1985 finding a ratio of only 0.79 and another by Sato et al., 1992 seeing a drop to 0.10. A study in Japan found that there was an increased risk of developing diabetes among those who had recently quit smoking compared to those who had never smoked²⁸.

The importance of this intervention study thus far is the finding that there is an additive positive effect on CRF and muscular fitness when both NRT and RT were

implemented. Previous studies looking at smoking cessation and exercise intervention have had a wide range of results. A randomized control trial trying to determine if an exercise program helped individuals quit smoking found no difference between those who received the intervention and those who did not³². It is important to note that this was done in a female population and cognitive behavioral therapy was used in place of NRT. However, studies have found that cognitive behavioral therapy and NRT have comparable efficacy in smoking cessation at 34.8% and 35.3% respectively³³. Also, there was low compliance with the resistance training intervention so it is possible that the true effect of the program was not accurately measured. We found that those who received any intervention decreased the number of cigarettes they smoked with those receiving both forms of intervention having the greatest incidence of smoking cessation. An ongoing study with very similar methods to those presented earlier, looks at the effect of NRT and RT in smokers who suffer from multiple sclerosis³⁴. While the results of that study focusing on smoking cessation, it will be interesting to compare the outcome in an entirely different population.

Cross-sectional analysis of arterial stiffness and muscular strength offer further knowledge and support to the benefits of resistance training and smoking cessation for cardiovascular health. The study by Fahs et al. shows that, even after controlling for CRF, as muscular strength decreases, aortic stiffness increases in a population of young men. Results in this cross-sectional study showed similar data, with the HC group having significantly higher strength and lower arterial stiffness as measured by AIx and PWV compared to the smoking population despite no differences in BMI which was believed

to be an indicator of CVD risk before actually body composition was taken into account. The HC also show decreased aortic pressure, systolic blood pressure, and diastolic blood pressure compared to the smokers, which indicates that fitness likely plays a role in reducing high blood pressure. A nonsmoking status and recreational activity at least 4 times per week were inclusion criteria for the HC group which tells of the benefits of even a moderate exercise modality; however, it is possible that these exercise benefits are due to healthier diets or the participation in aerobic physical activity.

A CRF marker that is surprisingly not often analyzed is the maximum breathing frequency reached during maximal exercise. Studies that tend to look at this marker are interested in special groups such as those with cystic fibrosis or those who have had an ongoing panic disorder. A study looking at the response to physical exercise in those with a panic disorder found that breathing frequency was positively correlated to perceived exertion³⁵. While this was not the primary outcome of the study, it is not an unexpected result since more oxygen must be brought to the tissues and thus to the lungs during exercise. Although the increased breathing frequency is an expected result, we found that the smokers had a significantly lower maximum breathing frequency than the nonsmoking group when testing CRF. Smoking, especially for those who have smoked for many years, causes exercise-induced asthma which prevents the airways from effectively dilating during exercise³⁶. With poor airway dilation and decreased breathing frequency, the body cannot expel carbon dioxide, thus the pH in the tissues drop and the muscle fatigues in the acidic environment. While breathing frequency is not an independent predictor of risk, it contributes to the poor CRF seen in the smoking population.

Some potential limitations to this study include the narrow population observed. This intervention program only targeted young people in the Los Angeles area and so cannot be generalized to the entire population. Also, the subjects were primarily of white or Asian ethnicity and so a more culturally diverse population needs to be explored. Additionally, it is possible that a resistance training program will not have similar benefits for an older population and potential negative effects must be known before being implemented in these individuals. Another limitation to the data analysis was the small group size. Because this study is not yet complete, the small sample size likely affected the statistical significance.

Chapter 5: Future Directions

Only a handful of cardiometabolic profile markers studied in this population of young, sedentary smokers have been analyzed here. This study remains in an early phase with the hopes of analyzing tens more subjects for these along with many other markers such as endothelial progenitor cells, inflammatory markers, lipid profiles, and insulin sensitivity. It has already been determined that there is a significant difference in the aerobic and muscular fitness between sedentary smokers and even just recreationally-active nonsmokers as well as differences in arterial function, endothelial function, and body mass. A previous study examined the results from the same 12-week resistance training intervention in obese young males and found that this intervention alone led to improved body composition with greater lean body mass and less fat mass, increased in insulin sensitivity, and improved lipid profiles.

Future studies on cardiorespiratory fitness and muscular strength should include broader populations. Because this study only looks at the benefit of a resistance training regimen on a young, healthy population, it is impossible to know if it may actually have negative effects on an older unhealthy population. Our laboratory will be assessing this resistance training regimen in both young and old populations of obese men and women while on a low glycemic load diet. If this form of training can be shown to benefit a broad population, it can be implemented in recommended physical activity programs to help prevent or alleviate symptoms of cardiovascular disease.

Chapter 6: References

1. U.S. Department of Health and Human Services. The Health Consequences of Smoking: A Report of the Surgeon General. Atlanta: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health, 2004 [accessed 2012 Jan 10].
2. Centers for Disease Control and Prevention. Annual Smoking-Attributable Mortality, Years of Potential Life Lost, and Productivity Losses—United States, 2000–2004. *Morbidity and Mortality Weekly Report* 2008;57(45):1226–8 [accessed 2012 Jan 10].
3. Centers for Disease Control and Prevention. Health, United States. Hyattsville (MD): Centers for Disease Control and Prevention, National Center for Health Statistics. [accessed 2012 Jan 10].
4. Mokdad AH, Marks JS, Stroup DF, Gerberding JL. Actual Causes of Death in the United States. *JAMA: Journal of the American Medical Association* 2004;291(10):1238–45 [cited 2012 Jan 10].
5. U.S. Department of Health and Human Services. Reducing the Health Consequences of Smoking: 25 Years of Progress. A Report of the Surgeon General. Rockville (MD): U.S. Department of Health and Human Services, Public Health Service, Centers for Disease Control, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health, 1989 [accessed 2012 Jan 10].
6. Ockene IS, Miller NH. Cigarette Smoking, Cardiovascular Disease, and Stroke: A Statement for Healthcare Profession from the American Heart Association. *Circulation* 1997;96(9):3242-7
7. McGill HC, Jr., McMahan CA, Malcom GT, Oalmann MC, Strong JP. Relation of glycohemoglobin and adiposity to atherosclerosis in youth. Pathobiological Determinants of Atherosclerosis in Youth (PDAY) Research Group. *Arterioscler Thromb Vasc Biol.* Apr 1995;15(4):431-440.
8. Institute of Medicine. Secondhand Smoke Exposure and Cardiovascular Effects: Making Sense of the Evidence. Washington: National Academy of Sciences, Institute of Medicine, 2009 [accessed 2012 Jan 10].
9. U.S. Department of Health and Human Services. Women and Smoking: A Report of the Surgeon General. Rockville (MD): U.S. Department of Health and Human

- Services, Public Health Service, Office of the Surgeon General, 2001 [accessed 2012 Jan 10].
10. Lloyd-Jones, D. et al. Executive summary: heart disease and stroke statistics--2010 update: a report from the American Heart Association. *Circulation* 121, 948-954(2010).
 11. Olson TP, Dengel DR, Leon AS, Schmitz KH. Moderate resistance training and vascular health in overweight women. *Med Sci Sports Exerc.* Sep 2006;38(9): 1558-1564.
 12. Kampus P, Kals J, Ristimae T, Fischer K, Zilmer M, Teesalu R. High-sensitivity C-reactive protein affects central haemodynamics and augmentation index in apparently healthy persons. *J Hypertens.* Jun 2004;22(6):1133-1139.
 13. Chen Z, Boreham J. Smoking and cardiovascular disease. *Semin Vasc Med.* 2002 Aug;2(3):243-52. Review
 14. Mustata S, Chan C, Lai V, Miller JA. Impact of an exercise program on arterial stiffness and insulin resistance in hemodialysis patients. *J Am Soc Nephrol.* Oct 2004;15(10):2713-2718.
 15. Kitahara Y, Hattori N, Yokoyama A, Yamane K, Sekikawa K, Inamizu T, Kohno N. Hiroshima. Cigarette smoking decreases dynamic inspiratory capacity during maximal exercise in patients with type 2 diabetes. *J Med Sci.* 2012 Jun;61(2): 29-36.
 16. Song JK, Stebbins CL, Kim TK, Kim HB, Kang HJ, Chai JH.
Effects of 12 weeks of aerobic exercise on body composition and vascular compliance in obese boys. *J Sports Med Phys Fitness.* 2012 Oct;52(5):522-9.
 17. Sanada S, Nishida M, Ishii K, Moriyama T, Komuro I, Yamauchi-Takahara K.
Smoking Promotes Subclinical Atherosclerosis in Apparently Healthy Men.
Circ J. 2012 Aug 29.
 18. Zavorsky GS, Smoliga JM, Longo LD, Uhanowsky KA, Cadman CR, Duffin J, Fisher JA. Increased carbon monoxide clearance during exercise in humans. *Med Sci Sports Exerc.* 2012 May 29.
 19. Chong Do Lee, Steven N Blair, and Andrew S Jackson. Cardiorespiratory fitness, body composition, and all-cause and cardiovascular disease mortality in men. American Society for Clinical Nutrition 1999.
 20. Metter EJ, Talbot LA, Schrager M, Conwit R. Skeletal Muscle Strength as a Predictor of All-Cause Mortality in Healthy Men. *J Gerontol A Biol Sci Med Sci.* October 1, 2002 2002;57(10):B359-365.

21. Petersen AM, Magkos F, Atherton P, Selby A, Smith K, Rennie MJ, Pedersen BK, Mittendorfer B. Smoking impairs muscle protein synthesis and increases the expression of myostatin and MAFbx in muscle. *Am J Physiol Endocrinol Metab*. 2007 Sep;293(3):E843-8.
22. Lee DC, Artero EG, Sui X, Blair SN. Mortality trends in the general population: the importance of cardiorespiratory fitness. *J Psychopharmacol*. 2010 Nov;24(4 Suppl):27-35.
23. Fagard RH. Physical activity in the prevention and treatment of hypertension in the obese. *Med Sci Sports Exerc* 1993; 31 (11 suppl): S624-S630.
24. Artero EG, Lee DC, Lavie CJ, España-Romero V, Sui X, Church TS, Blair SN. Effects of Muscular Strength on Cardiovascular Risk Factors and Prognosis. *J Cardiopulm Rehabil Prev*. 2012 Aug 9. [Epub ahead of print]
25. Farrell SW, Finley CE, Grundy SM. Cardiorespiratory Fitness, LDL Cholesterol, and Coronary Heart Disease Mortality in Men. *Med Sci Sports Exerc*. 2012 Jul 6.
26. Izadpanah A, Barnard RJ, Almeda AJ, Baldwin GC, Bridges SA, Shellman ER, Burant CF, Roberts CK. A short-term diet and exercise intervention ameliorates inflammation and markers of metabolic health in overweight/obese children. *Am J Physiol Endocrinol Metab*. 2012 Aug;303(4):E542-50.
26. Carnethon MR, Gidding SS, Nehgme R, Sidney S, Jacobs DR Jr, Liu K. Cardiorespiratory fitness in young adulthood and the development of cardiovascular disease risk factors. *JAMA*. 2003 Dec 17;290(23):3092-100.
27. Roger VL, Go AS, Lloyd-Jones DM, Adams RJ, Berry JD, Brown TM. Heart disease and stroke statistics--2011 update: a report from the American Heart Association. *Circulation*. 2011 Feb 1;123(4):e18-e209. Epub 2010 Dec 15.
28. Madsen T, Christensen JH, Toft E, Schmidt EB. C-reactive protein is associated with heart rate variability. *Ann Noninvasive Electrocardiol*. 2007 Jul;12(3): 216-22.
29. Eaton DK, Kann L, Kinchen S, Shanklin S, Ross J, Hawkins J, Harris WA, Lowry R, McManus T, Chyen D, Lim C, Whittle L, Brener ND, Wechsler H; Centers for

Disease Control and Prevention (CDC). Youth risk behavior surveillance - United States, 2009. *MMWR Surveill Summ*. 2010 Jun 4;59(5):1-142.

30. Oba S., Noda M., and Kaki K. Smoking cessation increases short-term risk of type 2 diabetes irrespective of weight gain: The Japan public health center-based prospective study. *PLoS One*. 2012;7(2):e17061. Epub Feb 13.
31. Glazer NL. Sustained and shorter bouts of physical activity are related to cardiovascular health. *Med Sci Sports Exerc*. Aug 14 2012.
32. Artero EG. Effects of muscular strength on cardiovascular risk factors and prognosis. *J Cardiopulm Rehabil Prev*. 2012 Aug 17.
33. Whitely JA. YMCA commit to quit: randomized trial outcomes. *Am J Prev Med*. 2012 Sep;43(3):25-62.
34. Ciccolo JT. Rationale and design of a clinical trial investigating resistance training as an aid to smoking cessation in persons with multiple sclerosis. *Contemp Clin Trials*. 2012 Jul;33(4):848-52.
35. Wittchen HU. Smoking cessation in primary care – a randomized controlled trial of bupropione, nicotine replacements, CBT and a minimal intervention. *Int J Methods Psychiatr Res*. 2011 Mar;20(1)28-39.
36. Caldirola D, Namia C. Cardiorespiratory response to physical exercise and psychological variables in panic disorder. *Rev Bras Psiquiatr*. 2011 Dec;33(4):385-9.