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The Impact of Muscular Strength on Cardiovascular Disease Risk Factors

Joel Ernest Harden
Old Dominion University, jeharden1@gmail.com

THE IMPACT OF MUSCULAR STRENGTH ON

CARDIOVASCULAR DISEASE RISK FACTORS

By

Joel Ernest Harden
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Approved by:

—————————————————
Gena Gerstner (Director)

—————————————————
Patrick B. Wilson (Member)

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Leryn Reynolds (Member)

ABSTRACT

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Joel Ernest Harden
Old Dominion University, 2021
Director: Dr. Gena Gerstner

The purpose of this study was to determine the associations between isokinetic leg muscular strength and cardiovascular disease (CVD) risk factor characterizations in Americans aged 50 and older. Using a publicly available dataset from the National Health and Nutrition Examination Survey (NHANES), a secondary analysis was conducted on participants (males $\geq$50 yrs; females $\geq$55 yrs; N=10,858) pooled from 1999 to 2002. CVD risk factors were determined using the American College of Sports Medicine (ACSM) cutoff values, with all nine ACSM risk factors analyzed. CVD risk factor characterization was determined by creating CVD risk factor profiles (i.e., the total number of CVD risk factors an individual possesses), then separating participants into low (0-2 CVD risk factors), moderate (3-5 CVD risk factors), and high (6-8 CVD risk factors) risk factor characterizations. Muscular strength was determined by isokinetic maximal peak force (PF) of the leg extensors, both raw and normalized to body mass. Normalized, but not raw, muscular strength was shown to be significantly inversely associated with CVD risk factor characterization for both males and females (P<0.001). Additionally, when adjusting for all other CVD risk factors, age (males: OR: 1.13, 95% CI: 1.11-1.15; females: OR: 1.12; 95% CI: 1.10-1.15) obesity (males: OR: 0.54; 95% CI: 0.40-0.72; females: OR: 0.58; 95% CI: 0.41-0.82), and smoking status (males: OR: 1.72; 95% CI: 1.31-2.26; females: OR: 1.39; 95% CI: 1.04-1.86) were significantly associated with isokinetic leg extensor muscular strength in both males and females, while blood glucose (OR: 1.41; 95% CI: 1.07-1.86) was only

associated with muscular strength in males. Evidence from the present study supports the notion that muscular strength may have a protective effect against CVD. However, this association must be shown independent of cardiorespiratory fitness (CRF) and in clinical trials before any causative link can be established.

NOMENCLATURE

ACSM	The American College of Sports Medicine
BMI	Body Mass Index
BP	Blood Pressure
CI	Confidence Interval
CRF	Cardiorespiratory Fitness
CVD	Cardiovascular Disease
DXA	Dual X-Ray Absorptiometry
HDL	High-Density Lipoprotein
LDL	Low-Density Lipoprotein
NHANES	National Health and Nutrition Examination Survey
nPF	Normalized Peak Force (N/Kg)
OR	Odds Ratio
PF	Peak Force (N)
PIR	Poverty Income Ratio

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CHAPTER I

INTRODUCTION

Problem Description

CVD is the number one cause of death in Americans, accounting for more than 600,000 deaths annually (1). Among those deaths, more than 90% are from individuals over the age of 55 (2). The risk of CVD can usually be identified for certain individuals or groups based on several risk factors. The ACSM identifies eight risk factors (1-8) that increase and one risk factor (9) that decreases the likelihood of cardiovascular events. They are: (1) age, (2) family history, (3) smoking habits, (4) sedentary lifestyle, (5) body mass index (BMI), (6) high blood pressure (BP), (7) high cholesterol, (8) high blood glucose, and (9) elevated high-density lipoprotein (HDL) levels (3). As men over the age of 45 and women over the age of 55 are already at risk for CVD (3), it is important for this population to have as few risk factors as possible to reduce incidents of CVD. The NHANES data set provides an ideal sample of this population within the United States.

Muscular strength has been demonstrated by several studies to have an inverse relationship with all-cause mortality (4-7). Additionally, it has been suggested that muscular strength may protect against key CVD risk factors specifically, including hypertension (4). Several studies have examined clustered CVD risk factors, now known as CVD risk profiles, and their relationship to cardiorespiratory fitness (CRF) (8-10); however, few have examined these CVD risk profiles regarding muscular strength. Although some studies have found inverse relationships between muscular strength and metabolic syndrome (11), obesity (12), and risk of hypertension (13), research has been generally inconclusive or contradictory regarding muscular strength and CVD risk factors. For instance, a study by Vaara et al. in 2014 (14) found no

correlation of CVD risk factors with muscular strength. However, Vaara et al. had several limitations in their study that are addressed in the present study, including a lower mean age of participants (25 yrs.) and no female participants included. Examining muscular strength compared to CVD risk factors in an older population than was used by Vaara et al. is especially important because muscular strength has been shown to decrease with age (i.e., dynapenia) (15), putting this population at higher risk of low muscular strength (15). Low muscular strength within this population due to their age, in addition to their higher susceptibility to CVD risk factors, provides a strong rationale for further examination and study.

An inverse correlation between leg isokinetic muscular strength and CVD risk factors in older American populations would give further basis for research to find evidence of a potential protective role of muscular strength in CVD risk management on a population-wide scale. Results of this paper may indicate the potential protective nature of muscular strength against CVD risk factors, without inferring causation. Thus, the overall objective of this project is to determine the relationship between leg isokinetic muscular strength and CVD risk factors in males over 50 and females over 55 years in the United States. Our study is unique in that we used all nine ACSM risk factors to build/create NHANES participant CVD risk factor profiles, which is the first study to have done so in relation to measures of raw and normalized muscular strength.

Statement of Purpose

To determine the associations between isokinetic leg muscular strength and cardiovascular disease risk factor characterization in Americans aged 50 and older within the NHANES 1999-2002 data set.

Significance of Study

The proposed project sought to fill a void in the CVD risk factor research regarding NHANES, providing novel insight into the potential role of isokinetic leg muscular strength as protective against CVD risk factors in older American populations.

Research Hypothesis

Older American individuals within the NHANES data set with higher muscular strength will exhibit a lower CVD risk factor characterization.

Variables

Independent Variables

The independent variables in this study were considered the CVD risk factors as defined by the ACSM: (1) age, (2) family history of CVD, (3) smoking status, (4) sedentary lifestyle, (5) obesity, (6) hypertension, (7) blood glucose/diabetes, (8) total cholesterol, (9) high-density lipoprotein (HDL) cholesterol.

Dependent Variables

The dependent variables in this study include isokinetic maximal strength as measured by PF and normalized PF (to body mass).

Limitations

The NHANES data set only has the leg isokinetic muscular strength test during a 4-year period (1999-2002), limiting the number of possible participants. Additionally, the NHANES data set does not include measures of CRF in this 4-year period for adults 50 and older, making it impossible to determine the impact of muscular strength independent of CRF. Several CVD risk factor variables were defined in the present study using survey data (i.e., family history, sedentary lifestyle) or a mix of survey data and physiological data (i.e., hypertension, blood glucose/diabetes, and total cholesterol).

Delimitations

Only subjects aged 50 years and older were included in the data set. Individuals with incidence of myocardial infarction within the past 6 weeks, chest or abdominal surgery in the past three weeks, severe back pain, knee or knee replacement surgery, or a history of brain aneurysm or stroke were excluded from the muscular strength test by the NHANES protocol.

Operational Definitions

- Muscular strength: maximal isokinetic leg muscular strength as measured by peak force in Newtons of the leg extensors.

- CVD risk factor profile: the total number of CVD risk factors that an individual has (i.e., an individual with 6 CVD risk factors has a CVD risk factor profile of 6).

- CVD risk factor characterization: a delineation of low (0-2), moderate (3-5), or high (6-8) based on the individuals CVD risk factor profile (i.e., an individual with 6 CVD risk factors would have a CVD risk factor profile of 6 and be in the "high" characterization).

- Sedentary lifestyle: a score of one out of four on the NHANES physical activity questionnaire ([you sit/he/she sits] during the day and [do/does] not walk about very much).

- Hypertension: above the blood pressure threshold for hypertension ($\geq$130 systolic or $\geq$80 diastolic) OR prescribed hypertensive medication (i.e., answered yes in the NHANES blood pressure and cholesterol questionnaire to the question "Taking prescription for hypertension".

- Diabetes/blood glucose: above the fasted blood glucose threshold for diabetes (125 mg/dL) OR told they have diabetes by a doctor (i.e., answered yes in the NHANES diabetes questionnaire to the question "Doctor told you have diabetes".

- Total cholesterol: low HDL cholesterol (≤ 40 mg/dL) OR high low-density lipoprotein (LDL) cholesterol (≥ 130 mg/dL) OR taking cholesterol medication (i.e., answered yes in the NHANES blood pressure and cholesterol questionnaire to the question "Now taking prescribed medication)".

CHAPTER II

LITERATURE REVIEW

Throughout the literature regarding the development of CVD, nine main risk factors have been identified and were reviewed within this paper. These risk factors include age, family history, smoking status, sedentary lifestyle, obesity, hypertension, blood glucose/diabetes status, cholesterol levels, and elevated HDL levels. All of these risk factors are also identified by the ACSM CVD risk factor screening, and the values for each risk factor are listed in **Table 1** (3). Additionally, muscular strength has been suggested to have a protective effect against certain CVD risk factors (4), demonstrating an inverse relationship with metabolic syndrome (11), obesity (12), and risk of hypertension (13). The literature surrounding to what extent these inverse relationships exist, what type of muscular strength may exhibit this protective effect, and what CVD risk factors are affected by this protective effect were examined in this literature review.

CVD Risk Factors

CVD risk factors refer to any behaviors, conditions, or habits that can increase an individual's chances of developing CVD. As previously mentioned, ACSM lays out a list of CVD risk factors, including family history, sedentary lifestyle status, and smoking habits (3). Other studies, however, commonly use risk factor profiles (16, 17), such as one by Yusuf et al. (1998) comprised of (BP), blood cholesterol, body mass index (BMI), diabetes, and smoking habits. Yusuf et al. (1998) specifically examined whether a CVD risk profile, and the measures within one, can predict CVD. The researchers (17) designed the profile on a zero to five scale – participants exhibiting no risk factors were given a profile score of zero, while those exhibiting all five were given a profile score of five. The authors (17) examined these variables as they

related to coronary heart disease, stroke, and all-cause mortality within 12,932 participants from

the first NHANES data set from 1971-1975 and their subsequent follow up in 1992. The

individuals were between 25 and 75 years old when they were first recorded in the NHANES

data set (17). Each individual risk factor was found to be significantly associated with

developing coronary heart disease (17). Additionally, high BP, high cholesterol, diabetes, and

current smoking were all significantly associated with risk of stroke, and high BP, diabetes, and

smoking were all significantly associated with all-cause mortality (17). Individuals with higher

risk profiles (multiple risk factors) were significantly more likely to develop coronary heart

disease, have a stroke, or die, and each risk significantly increased as more risk factors were

added. The results of the Yusuf et al. (1988) study demonstrated the ability of risk factor profiles

to predict development of CVD and even death, and cemented these 5 specific factors (BP,

cholesterol, diabetes, overweight, and smoking) as relevant risk factors when building a profile.

Table 1: CVD Risk Factors

CVD Risk Factors	Criteria	Used as a Risk Factor in These Studies	Score
Age	Men >45 years, women >55 years *	Dhingra and Vasan, 2012	(+1)
Family History	Heart attack, heart surgery, sudden death for immediate relative*	Carnethon et al., 2003, Lloyd-Jones et al., 2004	(+1)
Smoking	Current smoker or have quit <6 months ago, exposure to environmental smoke*	Carnethon et al., 2003, Paisible et al., 2015, Saydah et al., 2014, Yusuf et al., 1998	(+1)
Sedentary Lifestyle	<3 days/week of exercise for <3 months*	Mainous et al., 2019	(+1)
Obesity	Body Fat Percent: 25% for men and 35% for women[†] BMI: BMI ≥30 or 25 kg/m^2 is defined as obese or overweight[†] Waist Circumference: >40 inches in men and >35 inches in women*	Body Fat Percent: Anderssen et al., 2007, Christou et al., 2005 BMI: Carnethon et al., 2003, Li et al., 2017, Yang et al., 2003, Yusuf et al., 1998	(+1)
Hypertension/ High BP	Systolic 140 and higher, diastolic 90 and higher*	Anderssen et al., 2007, Carnethon et al., 2003, Paisible et al., 2015, Saydah	(+1)

		et al., 2014, Vaara et al., 2014, Yang et al., 2003, Yusuf et al., 1998	
Blood Glucose	>100 mg/dl*	Carnethon et al., 2003, Christou et al., 2005, Li et al., 2017 ; Vaara et al., 2014, Yang et al., 2003	(+1)
High Cholesterol	LDL >130 or HDL <40 or taking medication for cholesterol*	Anderson et al., 1987, Anderssen et al., 2007, Carnethon et al., 2003, Christou et al., 2005, Paisible et al., 2015, Yusuf et al., 1998	(+1)
Elevated HDL	>60*	Anderssen et al., 2007, Carnethon et al., 2003, Christou et al., 2005, Cooney et al., 2009; Li et al., 2017, Saydah et al., 2014, Vaara et al., 2014, Yang et al., 2003	(-1)

*(3); †(18)

The first column, "CVD Risk Factors", contains the CVD risk factors identified by the ACSM (3), while the second column, "Criteria", contains the measurements qualifying the risk factor. Column 3, "Used as a Risk Factor in These Studies", indicates which risk factors were included in the risk factor profiles of each study cited in this paper. The final column, "Score", references which risk factors increase the likelihood for CVD and which decrease its likelihood. Elevated HDL is the only factor that decreases the likelihood of CVD and is thus denoted with "-1" rather than "+1".

Age

Age is significantly associated with the development of CVD, even listed as its own

baseline risk factor for CVD by the ACSM (3). Heart failure, usually caused by aspects of CVD

such as hypertension and coronary heart disease, is so uncommon in younger individuals that its

prevalence within 20-39-year-old people is only 0.1-0.2% (2). This number increases

dramatically as age does, with a 5-10% prevalence in 60-79-year-old people, and as high as 14%

in those 80 and older (2). Coronary heart disease, which itself makes up more than half of all

deaths from CVD, also increases with age, and nearly 82% of deaths attributable to coronary

heart disease come from individuals aged 65 or older (2).

Family History

A family history of CVD is well known as a risk factor for CVD, as noted by the ACSM

(3). When examining the participants in the Framingham heart study, which included over 5,000

residents of Framingham, Massachusetts and additionally more than 5,000 of the original

participants' offspring in follow-up examinations years down the line, a history of at least one parent suffering premature CVD is associated with doubling the risk of CVD in men (19). It was also reported that having at least one parent who had suffered premature CVD was associated with a 70% higher incidence of CVD in women, although this result was non-significant (19).

Smoking

Smoking, especially cigarette smoking, is responsible for roughly one third of all CVD deaths in the United States (20). CVD risk and smoking have a strong relationship, as the more cigarettes one smokes, the longer they have been a smoker, and the younger the age of smoking onset, the greater the chances of CVD developing (20). Environmental smoke, also sometimes known as secondhand smoke, may increase risk of CVD in those who do not smoke at all by 20-30% (20).

Sedentary Lifestyle

Sedentary lifestyle habits may be as harmful regarding CVD as obesity (21). Mainous et al. (2019) examined individuals of a healthy BMI (BMI: 18.5-24.9) within the NHANES regarding how much time they spent sitting per day and whether they met the ACSM recommendations for weekly exercise (150 minutes or more of light-moderate exercise or 75 minutes of vigorous exercise per week). This was then compared to their risk for CVD based on a CVD risk factor profile. The results showed that individuals who are not overweight but lead a more sedentary lifestyle (do not meet ACSM recommended weekly exercise times and spend 7.7 or more hours per day sitting) are at as much risk for CVD as obese individuals (21).

Obesity

Obesity may be measured in several different ways. The most used measures within CVD risk factor studies are body fat percent, BMI, and waist circumference. Body fat percent is

often measured through skinfold calipers (8), bio-electrical impedance (18), and dual energy x-ray absorptiometry (DXA) (10), while BMI is a calculation based on height and weight (9, 10, 17, 18, 22), and waist circumference is simply a measure in inches or centimeters of the waist of an individual (23). When examining obesity as measured by both BMI and body fat percent, Christou et al. (2005) found that both higher body fat percent and BMI are associated with all other metabolic risk factors and are associated with higher mortality rates from CVD. The relationship the authors (10) found was a better predictor of CVD risk factors than aerobic fitness, which is considered to have a protective effect against CVD. Additionally, BMI was found to be associated with hemodynamic risk factors (10). From these results, BMI status should be considered when examining CVD and constructing CVD risk profiles.

Hypertension

Clinically high BP is known as hypertension and has been defined as a systolic BP of at least 140 and a diastolic BP of at least 90 (3). Increased BP is shown to increase prevalence of CVD (24). One study, when examining participants in the NHANES data set, found that a BP of 140/90 is significantly more likely to predict CVD than a lower BP (24).

Cholesterol/HDL

Cholesterol is associated with CVD in two main ways. Firstly, high total cholesterol levels are a CVD risk factor (3). When examining participants from the Framingham study, it was found that in individuals under 50, a low total cholesterol level is associated with a lower risk of mortality from CVD (25). Secondly, a type of cholesterol known as HDL has been shown to have a protective effect against risk of CVD (26). HDL levels are strongly inversely associated with CVD mortality at all ages, sexes, and risk levels, although slightly more protective within women than within men (26).

Blood Glucose and Diabetes

Blood glucose levels and diabetes are also an ACSM risk factor for CVD (3). According to the CDC (27), fasted blood glucose levels of 100-125 mg/dL indicate that the individual is pre-diabetic, while levels of 126 mg/dL and above indicate that the individual is diabetic. The ACSM considers fasted blood glucose levels of 100 mg/dL or more, indicating both individuals with pre-diabetes and individuals with diabetes, as a CVD risk factor (3). When comparing dysglycemia in both individuals with pre-diabetes and those with diabeties, it was found that both have a relationship to the development of CVD (28). However, this relationship may be impacted by several other metabolic disorders observed within individuals with hyperglycemia hyperglycemic (28).

Special Consideration: Metabolic Syndrome

Metabolic syndrome, a metabolic disorder caused by obesity (29) that consists of the simultaneous metabolic disturbances of insulin resistance, obesity, atherogenic dyslipidemia, and hypertension (30), shares many risk factors with CVD (29). The four defining aspects of metabolic syndrome (insulin resistance, obesity, atherogenic dyslipidemia, and hypertension) are all either direct CVD risk factors (obesity, dyslipidemia, and hypertension) or related to CVD risk factors (insulin resistance is the cause of the risk factor blood glucose/diabetes (31)). Therefore, in this paper, metabolic syndrome was discussed as a cluster of CVD risk factors in relation to muscular strength, although it was not specifically analyzed separate from the individual CVD risk factors that comprise it.

Muscular Strength

Muscular strength within this population (i.e., ≥ 50 years) may be lower than that of younger populations, as muscular strength has been shown to decrease with age (15), even

shown within the NHANES data set (32). Despite this, muscular strength has been suggested to have a protective effect against certain CVD risk factors (4). It is important to examine to what extent this protective effect may occur. Some studies have measured 1-repetition maximum bench press, leg press, or back squat to define muscular strength and evaluate how they relate to CVD risk factors (11, 12) ; however, the present study examines leg isokinetic strength as represented by peak force of the quadriceps knee extensor at a single speed (60 degrees/second). Isokinetic strength, which involves making a contraction while moving at a constant speed, may be more useful to measure in this population than other types of strength (33). This is partially because it is known to be related to functional performance (33), which is especially important as people age. Additionally, increases in isokinetic strength have been shown to improve fall risk in older individuals, which can greatly reduce their risk of injury as adults age (34). Other measures, such as isometric handgrip strength, have been shown to be strongly associated with isokinetic strength, but lower body isokinetic strength is known to be more functional in this population (35). Lee et al. (2015) (36) found that an intervention designed to increase isokinetic muscular strength in women aged 65-75 years not only increased isokinetic muscular strength but also lowered CVD risk factors such as BMI and percent body fat significantly as compared to individuals who had gone through only an aerobic training intervention. This suggests that isokinetic muscular strength may correlate to specific CVD risk factors. It is known that muscular strength has an inverse relationship with all-cause mortality in the United States (5-7), for which CVD is the largest contributor nationwide (1), especially in adults over 50 (2). However, several studies also show an inverse relationship between muscular strength and specific risk factors (11-13). For instance, a study by Jackson et al. in 2010 found an inverse relationship between muscular strength and the CVD risk factor of obesity. Using body fat

percentage measures for obesity and a one-repetition max for both bench press and leg press for muscular strength, the researchers (12) found as much as a 70% lower risk of excessive body fat and excessive abdominal fat at the highest levels of muscular strength. Additionally, muscular strength has been shown to be inversely associated with metabolic syndrome (11). A 44% lower risk of metabolic syndrome in healthy-weight individuals and 39% in obese individuals was shown at the highest levels of strength measured, even independent of age and body size (11). Muscular strength is even inversely associated with hypertension (13). Over a 19-year longitudinal study with 4,147 participants, researchers found a significant inverse relationship between risk of hypertension and muscular strength; however, this relationship was only found in prehypertensive participants (13).

From these studies, there appears to be a strong case for muscular strength having some protective effect against certain CVD risk factors; however, not all studies have found the same results. One study by Vaara et al. (2014) found no relationship between CVD risk factors and muscular strength. This study (14) examined plasma glucose, HDL cholesterol levels, triglyceride levels, and BP as CVD risk factors, and compared these to both muscular strength and muscular endurance. Contrary to some of the previous studies (11-13), the researchers (14) found that maximal muscle strength was not independently associated with the cluster of CVD risk factors. However, they found that muscular endurance and CRF were both associated with the risk factors independent of each other (14). Other studies have found inverse relationships between CRF and CVD risk factors (8, 9, 37-44), suggesting that this relationship is a well-established phenomenon. Because of the contradiction in the literature regarding associations between CVD risk factors and muscular strength, more research needs to be done to ascertain the

true relationship. Additionally, differences in muscular strength between males and females (45) indicate a need to analyze males and females separately.

National Health and Nutrition Examination Survey

Accordingly, the NHANES data set provides a uniquely useful sample for a measurement of older Americans. NHANES includes age and demographic information in the survey, as well as diabetes status, medical and health status, sedentary lifestyle status, BMI, waist circumference, smoking and tobacco use, BP, blood glucose, and cholesterol information (27). This information can be practically applied; for example, Yusuf et al. (1998) (17) used variables from the NHANES data set to create and test CVD risk profiles. According to the NHANES physicians' examinations procedures manual, the procedures for these factors are:

(1) self-report for diabetes, smoking habits, and age; and

(2) a physician examination for BP and cholesterol; height and weight calculations for BMI; waist measurements for waist circumference (27).

Several studies have previously used these variables or a subset thereof to successfully create risk factor profiles (17, 22, 46). NHANES also examines muscular strength, in the form of knee extensor strength. This is done through the use of a dynamometer to measure PF of the quadriceps at the speed 60 deg/s (47). Several studies have successfully used the muscular strength variable from the NHANES data set as well (48, 49). NHANES also provides a large representative sample size nationwide of this population, according to Centers for Disease Control and Prevention (2019), making it the ideal data set to study the relationship between muscular strength and CVD risk factors in older Americans (50 and older).

Conclusion

There are numerous CVD risk factors, many of which have been studied and clustered together into CVD risk profiles (10, 16, 17). CVD is also the number one cause of death in Americans, especially those over the age of 55 (1, 2). This population also experiences lower muscular strength, as muscular strength has been shown to decrease with age (32, 50). Despite this, muscular strength has been suggested to have a protective effect against CVD risk factors (4), demonstrating an inverse relationship with risk factors such as obesity (12), metabolic syndrome (11), and hypertension (13). While these inverse relationships suggest a potential protective effect of muscular strength on CVD risk factors, not all research concurs, with at least one study (14) finding no correlation between maximal muscular strength and CVD risk factors and instead proposing muscular endurance as protective. Several studies have also found inverse relationships between CVD risk factors and CRF instead (8, 9, 14). In light of the relatively contradictory nature of the literature, more research ascertaining the true relationship between muscular strength and CVD risk factors is warranted.

CHAPTER III

METHODOLOGY

Sample

NHANES, the National Health and Nutrition Examination Survey, uses a stratified, multi-stage, probability cluster design to generate a representative sample of the non-institutionalized American population. The survey includes both an examination in a mobile examination center (MEC) and a household interview. For the present study, data were drawn from the 1999-2000 and 2001-2002 NHANES cycles. Participants within these two cycles were screened for all variables involved, while some participants were excluded due to missing variables on CVD risk factors. All surveyed males over the age of 50 that met inclusion criteria were included in the examination, while only females aged 55 and older were included to account for differences in age as a risk factor by gender as specified by the ACSM. After all exclusion criteria, there were 10,858 participants available for full analysis, out of 25,316 total individuals screened by the NHANES from 1999-2002.

Demographic, Anthropometric, and Health History Information

Relevant variables in these categories include age, gender, race/ethnicity, family poverty income ratio (PIR) (a ratio of total family income over the federal poverty level), BMI, and CVD history (any previous incidence of congestive heart failure, coronary heart disease, heart attack, or stroke). Demographics and health history are taken as a self-report in the interview section of NHANES, and race/ethnicity was categorized as non-Hispanic white, non-Hispanic black, Mexican American, other Hispanic, and other non-Hispanic. PIR is a ratio of family income to poverty threshold and is calculated by dividing family income by the poverty guidelines, specific

to family size, depending on the year and state. BMI was calculated from height and weight measured during the MEC component.

Muscular Strength

Only individuals 50 years old and older were eligible for the muscular strength test. Individuals with incidence of myocardial infarction within the past 6 weeks, chest or abdominal surgery in the past three weeks, severe back pain, knee or knee replacement surgery, or a history of brain aneurysm or stroke were excluded from this test by the NHANES protocol. The testing protocol consisted of a measurement of peak torque (Newton/meters) of the quadriceps' knee extensor strength at one speed, 60 degrees/second. Although peak torque was measured, peak force (PF) (N) was recorded by NHANES. Measurements were taken using a Kin Com MP dynamometer manufactured by Chattanooga Group, Inc., Chattanooga, TN. Six strength measurements were recorded: three warm-up trials which accounted for familiarization, and three test trials. The trial that recorded PF was used for further analyses. Measurements were taken during the MEC portion of NHANES.

CVD Risk Factors

The presence of CVD risk factors in the participants was determined through self-report in the interview, or through measurements in the examination or laboratory sessions, of NHANES. Nine risk factors are included in this analysis: age, family history, smoking status, sedentary lifestyle, overweight/obesity status, BP, cholesterol, blood glucose/diabetes, and HDL levels. We determined risk factor profile by assigning each respondent a score from 0 to 8 depending on the number of risk factors present. Those who have HDL levels greater than or equal to 60 mg/dL qualified for a negative risk factor, receiving a minus one on their risk factor profile.

Age

Age is self-reported during the household interview. For the purposes of this analysis, all female participants below the age of 55 were not included in the sample, with all female participants above the age of 55 included. For this reason, all participants did not need to be coded for the age risk factor and age was used as the only continuous variable.

Family History

Family history includes whether a blood relative (father, mother, mother's father, mother's mother, father's father, father's mother, brother, sister, or other) has had hypertension, stroke, or a heart attack or angina in the past. This is measured through the interview section of NHANES as a self-report and is originally measured as two separate variables (see Appendix 1), which were coded as one dichotomous variable.

Smoking Status

Smoking status was determined by a serum cotinine cutoff value, which was measured through a blood draw in the laboratory section of NHANES. Smoking status is coded as "yes" or "no" in response to whether the individual had a value of greater than or equal to 3.0 ng/mL (51). Serum cotinine was chosen over a smoking questionnaire included in NHANES because of cotinine's ability to predict exposure to multiple forms of tobacco, including environmental smoke (52). The cutoff point of 3.0 ng/mL was chosen as to where participants would be considered a "yes" regarding smoking status. This decision is based off of a previous analysis of the NHANES population from 1999-2004 determining the 3.0 ng/mL cutoff point, rather than the previously standard 14-15 ng/mL, was more accurate in determining actual smokers vs non-smokers and did not overestimate the amount of non-smokers in a population (51).

Sedentary Lifestyle

ACSM defines sedentary lifestyle as less than three days of 30 minutes of moderate activity per week (3). Sedentary lifestyle status is taken in the interview section of NHANES; however, it does not define activity congruently with ACSM. In the 1999-2000 and 2001-2002 NHANES cycles, this section is a self-report of the average level of physical activity each day coded 1-4: (1) sit during the day and not walk about very much; (2) stand or walk about a lot during the day but does not carry or lift things very often; (3) lifts light load or have to climb stairs or hills often; (4) does heavy work or carries heavy loads. This variable was split into a dichotomous variable (1 = sedentary; 2, 3, or 4 = not sedentary; Appendix 1).

Overweight/Obesity Status

Overweight/obesity status is determined during the examination portion of NHANES, through a measurement of waist circumference (WC) in the MEC. WC cutoff values of >40 in (101.6 cm) in males and >35 in (88.9 cm) in females were used to classify obesity. BMI (kg/m^2) values were taken through measurements of weight (kg) and standing height (m) but were reported only as descriptive information, as waist circumference has been shown to be a better predictor of visceral fat than BMI (53) and is used by the ACSM as a screening tool for the obesity risk factor (3).

Hypertension

BP is measured during the examination section of NHANES in the MEC. A mercury sphygmomanometer is used to take 3-4 BP measurements, and separate averages of systolic and diastolic BPs were taken for the analysis. Hypertension is defined as a BP of (1) greater than 140 mmHg systolic or (2) greater than 90 mmHg diastolic, or (3) a self-report of a prescription of antihypertensive medications. These three factors (Appendix 1) were used to created one dichotomous variable, coded "yes" if the participant had at least one of the three, and "no" if the

participant did not have any of the three. Participants missing up to two variables of either the systolic measurement, diastolic measurement, or a self-report of hypertensive medication were coded based off of the remaining variable(s).

Cholesterol

To determine total cholesterol levels, blood is taken during the laboratory section of NHANES, where it is processed, stored, and shipped to the Johns Hopkins University Lipoprotein Analytical Laboratory to be analyzed. A heparin-manganese (Mn) precipitation method is used to determine HDL cholesterol levels. Low-density lipoprotein (LDL) cholesterol is measured via a calculation of total cholesterol, HDL cholesterol, and triglycerides [LDL-cholesterol] = [total cholesterol] – [HDL-cholesterol] – [triglycerides/5]. An (1) HDL of less than 40 mg/dL, (2) LDL of greater than 130 mg/dL, or (3) self-report of taking cholesterol medication is used to determine dyslipidemia and/or qualification as a CVD risk factor. Three separate variables (Appendix 1) were used to created one dichotomous variable. Participants missing up to two variables of either LDL measurement, HDL measurement, or a self-report of cholesterol medication were coded based off of the remaining variable(s). Elevated HDL, defined as HDL cholesterol >60 mg/dL (3), is included as a separate variable that lowers the overall CVD risk profile (coded opposite: "no" meaning presence of elevated HDL >60 mg/dL).

Blood Glucose/Diabetes

Diabetes is measured as a self-report of a diagnosis from a healthcare professional during the interview section of NHANES. Additionally, fasting plasma glucose is measured on randomly selected participants who had fasted between 8 and 24 hours. Blood sugar is considered diabetic if fasting blood glucose levels are above 125 mg/dL. This cutoff point was used to be in congruence with the American Diabetes Association's guidelines for diagnosing

diabetes (54). This study did not distinguish between type 1 and type 2 diabetes. Two separate variables (Appendix 1) were used to created one dichotomous variable, coded as "yes" if the subject either (1) reported a diagnosis of diabetes in the past or (2) measured fasting blood glucose levels above 125 mg/dL, and coded as "no" if the subject met neither of these conditions. Participants missing either the diabetes self-report or the blood sugar measure were coded based off of the remaining variable.

Statistical Analyses

Data files were downloaded from the NHANES website and processed using SAS (v 9.4; SAS Institute Inc, Cary, North Carolina). The 1999-2000 and 2001-2002 files were merged, and sampling weights (examination population-weights) were recalculated to account for four years of combined data.

The mean ± standard deviation (SD) (i.e., age) and the prevalence (i.e., gender, race/ethnicity, PIR categories, BMI categories, CVD history) of demographic factors were calculated where appropriate. To assess the CVD risk factors associated with strength levels, a multivariable model was conducted for males and females, separately. The ordinal logistic regression model estimated the odds of PF status (i.e., quintiles; Q1 lowest, Q5 highest). The ordering of categories within the outcome variable assessed the odds of having lower PF (i.e., Q1 vs. Q2-5; Q 1-2 vs. Q 3-5; Q1-3 vs. Q4-5; Q1-4 vs. Q 5). Predictor variables in the model included: age (in years), family history (yes vs. no), smoking status (yes vs. no), sedentary lifestyle (yes vs. no), obesity status (yes vs. no), high BP (yes vs. no), high cholesterol (yes vs. no), low HDL cholesterol (yes vs. no), high blood sugar/diabetes (yes vs. no). Adjusted odds ratios (OR) with 95% confidence intervals (CI) were calculated, with those not including 1.00 being deemed statistically significant. Mean (standard error) of PF and normalized PF (by body

mass) were reported for each risk factor profile number (0-8). Two separate one-way analyses of variance (ANOVA) using the weighted data were performed to evaluate differences in PF between three risk factor groups (low: 0-2 risk factors, moderate: 3-5 risk factors, high: 6 risk factors) for males and females, respectively. Scheffe post-hoc tests were used to obtain adjusted *P*-values. A family-wise alpha level was set *a priori* at 0.05 for all analyses. Data were analyzed using SAS software (v 9.4).

CHAPTER IV

RESULTS

Demographics

Of the 13,341 participants meeting age requirements, 10,858 met all inclusion criteria

(6,080 male and 4,778 female). Characteristics and demographics are reported in **Table 2**. Of all

participants, 12.7% had reported previous incidence of CVD (14.8% of males and 9.9% of

females). The mean age of the participants was 66.4 years (64.9 males and 68.3 females), and

the majority of individuals sampled were either overweight (42.7% total, 48.1% male and 35.9%

female) or obese (29.9% total, 26.8% male and 33.8% female).

Table 2: Descriptive Characteristics of 10,858 Participants by Gender

Characteristic	Category	All	Male	Female
Sample size		10858	6080	4778
Age (years)		66.4 (9.4)	64.9 (9.8)	68.3 (8.5)
Race/ethnicity (%)				
	Mexican American	19.1%	18.5%	19.8%
	Other Hispanic	3.9%	3.5%	4.5%
	Non-Hispanic white	59.4%	61.3%	57.1%
	Non-Hispanic black	15.2%	14.7%	15.8%
	Other race/ethnicity	2.4%	2.1%	2.8%
Poverty income ratio (%)				
	< 1.5	28.3%	25.3%	32.2%
	1.5 to < 3.5	34.7%	32.7%	37.2%
	≥ 3.5	37.0%	42.0%	30.6%
BMI mean (kg/m²)				
		28.1 (5.2)	27.9 (4.5)	28.4 (5.9)
BMI (%)	< 18.5	1.2%	1.0%	1.4%
	< 25[†]	27.4%	25.1%	30.3%
	25 to < 30	42.7%	48.1%	35.9%
	≥ 30[†]	29.9%	26.8%	33.8%
	≥ 35	9.9%	7.0%	13.5%
CVD History				
	Previous Incidence of CVD	12.7%	14.8%	9.1%
	No Previous Incidence of CVD	87.3%	85.2%	90.9%

[†] Indicates that category is not mutually exclusive – i.e., values can range through both categories.

Strength Quintiles and Odds Ratios

Table 3 presents the associations between quintiles (Q) of muscular strength and each

CVD risk factor, stratified by gender. The muscular strength quintiles, measured by PF, range

from (Q1 mean) 192.6 - (Q5 mean) 541.5 N for males and (Q1 mean) 191.9 – (Q5 mean) 490.4

N for females. Adjusted (accounting for all CVD risk factors) odds ratios (ORs) for each CVD

risk factor were calculated in Table 4. Controlling for all covariates, the odds of having lower

PF (i.e., Q1 v Q2-5; Q 1-2 v Q 3-5; Q1-3 v Q4-5; Q1-4 v Q 5) were increased in males who: had

elevated serum cotinine levels (OR = 1.72; 95% CI: 1.31-2.26), had diabetes (OR = 1.41; 95%

CI: 1.07-1.86), and were not obese as measured by waist circumference (OR = 0.54; 95% CI:

0.40-0.72). Furthermore, the odds of having a lower PF were increased in females who: had

elevated serum cotinine levels (OR = 1.39; 95% CI: 1.04-1.86) and were not obese by a measure

of waist circumference (OR = 0.58; 95% CI: 0.41-0.82). Additionally, the odds of having lower

PF increased with age in males (OR = 1.13; 95% CI: 1.11-1.15) and females (OR = 1.12; 95%

CI: 1.10-1.15). ORs were close to null and nonsignificant for all other CVD risk factors. When

we further controlled our models for CVD history, the results were similar. When examining the

CVD risk factors that make up metabolic syndrome (i.e., blood glucose/diabetes status, obesity,

dyslipidemia, and hypertension), obesity in males and females and diabetes status in males were

significant in the regression model, similar to our original models.

CVD Risk Factor Profiles

Table 5 presents a CVD risk factor profile, showcasing the number of individuals

presenting with 0, 1, 2, 3, 4, 5, 6, 7, or 8 risk factors and their mean PF, stratified by gender.

Few of the individuals surveyed had either 0 risk factors (0.7% of males and 2.7% of females) or

8 risk factors (0.1% of males and 0.2% of females), with the plurality of individuals showcasing

four risk factors (27.5% of males and 25.4% of females). For both males and females,

individuals presenting 0 risk factors had lower mean PF than individuals presenting 8 risk

factors. When normalizing PF to body mass (PF/body mass, N/Kg), the opposite is seen, with

individuals presenting 0 risk factors having greater normalized PF than individuals presenting 8

risk factors. **Figure 1** depicts mean PF, body mass, and normalized PF in relation to CVD risk

factor profiles. As CVD risk factor profiles increased, mean PF increased among both males and

females. It was also shown that as CVD risk factor profiles increased, body mass also increased

for both males and females. However, when PF was normalized to body mass, the opposite was

seen, with normalized PF decreasing as CVD risk factor profiles increased across both males and

females. In **Figure 2**, the risk factor profiles were grouped and classified as low risk (0-2 risk

factors), moderate risk (3-5 risk factors), and high risk (6-8 risk factors), to account for few

participants with either 0 or 8 risk factors. **Figure 2** showcases the distribution of normalized PF

across low-risk (0-2), moderate-risk (3-5), and high-risk (6-8) groups. There was a main effect

for group for both males and females ($P<0.001$). Scheffe post-hoc tests revealed that among both

males and females, the moderate-risk group had significantly lower normalized PF than the low-

risk group ($P<0.001$), and the high-risk group had significantly lower normalized PF than the

moderate ($P=0.02$), and low risk group ($P<0.001$). Females showed a difference of 0.4 N/Kg

(95% CI 0.35-0.49) between means of the low-risk group and the moderate-risk group, and a

difference of 0.4 N/Kg (95% CI: 0.29-0.50) between means of the moderate-risk group and the

high-risk group. Males showed a difference of 0.6 N/Kg (95% CI: 0.55-0.72) between means of

the low-risk group and the moderate-risk group, and a difference of 0.2 N/Kg (95% CI: 0.06-

0.27) between means of the moderate-risk group and the high-risk group.

Table 3: Weighted Prevalence of CVD Risk Factors Across Strength Quintiles in Males and Females

Risk factors	Male						Female					
	All	Q1 Lowest	Q2	Q3	Q4	Q5 Highest	All	Q1 Lowest	Q2	Q3	Q4	Q5 Highest
Hypertension												
No	32.3%	26.8%	22.1%	35.4%	31.0%	39.9%	23.4%	21.3%	21.8%	24.1%	26.6%	22.8%
Yes	67.7%	73.2%	77.9%	64.6%	69.0%	60.1%	76.6%	78.7%	78.2%	75.9%	73.4%	77.2%
Cotinine												
No	72.0%	70.4%	73.4%	72.9%	71.5%	71.7%	84.7%	85.3%	79.1%	89.1%	83.9%	85.7%
Yes	28.0%	29.6%	26.6%	27.1%	28.5%	28.3%	15.3%	14.7%	20.9%	10.9%	16.1%	14.3%
Sedentary												
No	75.9%	72.9%	76.0%	82.7%	77.8%	71.1%	76.9%	73.6%	72.8%	81.7%	79.6%	76.5%
Yes	24.1%	27.1%	24.0%	17.3%	22.2%	28.9%	23.1%	26.4%	27.2%	18.3%	20.4%	23.5%
Waist Circumference												
No	49.4%	52.8%	64.0%	53.5%	41.7%	42.0%	33.1%	38.0%	39.6%	41.5%	24.4%	24.0%
Yes	50.6%	47.2%	36.0%	46.5%	58.3%	58.0%	66.9%	62.0%	60.4%	58.5%	75.6%	76.0%
Family History												
No	78.4%	82.3%	79.8%	85.1%	75.4%	73.5%	70.0%	72.5%	71.8%	75.0%	64.6%	66.8%
Yes	21.6%	17.7%	20.2%	14.9%	24.6%	26.5%	30.0%	27.5%	28.2%	25.0%	35.4%	33.2%
Diabetes												
No	64.3%	60.3%	54.4%	64.8%	66.8%	69.7%	70.0%	69.9%	72.7%	69.7%	68.8%	69.2%
Yes	35.8%	39.7%	45.6%	35.2%	33.2%	30.3%	30.0%	30.1%	27.3%	30.3%	31.2%	30.8%
Poor Cholesterol												
No	38.2%	38.2%	40.1%	43.6%	35.3%	35.5%	53.3%	59.7%	55.8%	49.7%	51.4%	50.7%
Yes	61.8%	61.8%	59.9%	56.4%	64.7%	64.5%	46.7%	40.3%	44.2%	50.3%	48.6%	49.3%
Poor HDL												
No	12.3%	17.0%	14.5%	9.9%	11.1%	11.4%	43.4%	46.5%	46.4%	51.4%	37.5%	36.5%
Yes	87.7%	83.0%	85.5%	90.1%	88.9%	88.6%	56.6%	53.5%	53.6%	48.6%	62.5%	63.5%

Table 4: Adjusted Odds Ratios (ORs) for Males and Females

Risk Factors	OR (95% CI)	
	Males	**Females**
Age	1.13 (1.11, 1.15)*	1.12 (1.10, 1.15)*
Hypertension	1.29 (0.95, 1.73)	0.80 (0.56, 1.15)
Cotinine	1.72 (1.31, 2.26)*	1.39 (1.04, 1.86)*
Sedentary Lifestyle	1.20 (0.87, 1.66)	1.27 (0.92, 1.75)
Waist Circumference	0.54 (0.40, 0.72)*	0.58 (0.41, 0.82)*
Family History	0.78 (0.49, 1.22)	1.35 (0.98, 1.87)
Diabetes Status	1.41 (1.07, 1.86)*	1.06 (0.78, 1.45)
Cholesterol Status	0.80 (0.61, 1.07)	0.84 (0.66, 1.05)
HDL Status	0.93 (0.60, 1.44)	0.79 (0.58, 1.06)

Odds ratios (ORs) assessed the odds of having a lower level of PF (i.e., the odds of being in Q1 v Q2-5; Q 1-2 v Q 3-5; Q1-3 v Q4-5; Q1-4 v Q 5) when controlling for all other covariates.
* Statistical significance (i.e., 95% CI does not include 1.00).

Table 5: Weighted Mean PF and Normalized PF Across CVD Risk Factor Profiles in Males and Females

Males

CVD Risk Factor Profile	N	Percent	Mean PF (SE)	Normalized PF (SE)
0 Risk Factors	45	0.7	453.0 (15.0)	6.4 (0.2)
1 Risk Factor	337	5.5	446.2 (6.4)	5.9 (0.1)
2 Risk Factors	840	13.8	458.1 (4.2)	5.8 (0.0)
3 Risk Factors	1335	22.0	440.9 (3.0)	5.4 (0.0)
4 Risk Factors	1674	27.5	454.3 (3.0)	5.2 (0.0)
5 Risk Factors	1064	17.5	429.6 (3.7)	4.7 (0.0)
6 Risk Factors	615	10.1	481.0 (4.5)	5.1 (0.1)
7 Risk Factors	165	2.7	475.7 (11.4)	4.7 (0.1)
8 Risk Factors	5	0.1	502.0 (0.0)	4.6 (0.0)

Females

CVD Risk Factor Profile	N	Percent	Mean PF (SE)	Normalized PF (SE)
0 Risk Factors	128	2.7	272.0 (6.5)	4.5 (0.1)
1 Risk Factor	349	7.3	255.1 (3.5)	4.4 (0.1)
2 Risk Factors	695	14.5	274.3 (2.7)	4.3 (0.0)
3 Risk Factors	1116	23.4	271.5 (2.1)	3.9 (0.0)
4 Risk Factors	1215	25.4	285.1 (2.2)	3.8 (0.0)
5 Risk Factors	845	17.7	278.0 (3.1)	3.5 (0.0)
6 Risk Factors	315	6.6	285.3 (3.5)	3.6 (0.1)
7 Risk Factors	105	2.2	291.3 (7.2)	3.5 (0.1)
8 Risk Factors	10	0.2	315.5 (0.3)	4.4 (0.2)

Mean PF is the raw score mean of PF for all individuals with a specific risk factor profile. Normalized PF is the mean of the PF/body mass (N/Kg) of each individual with a specific risk factor profile. SE = standard error.
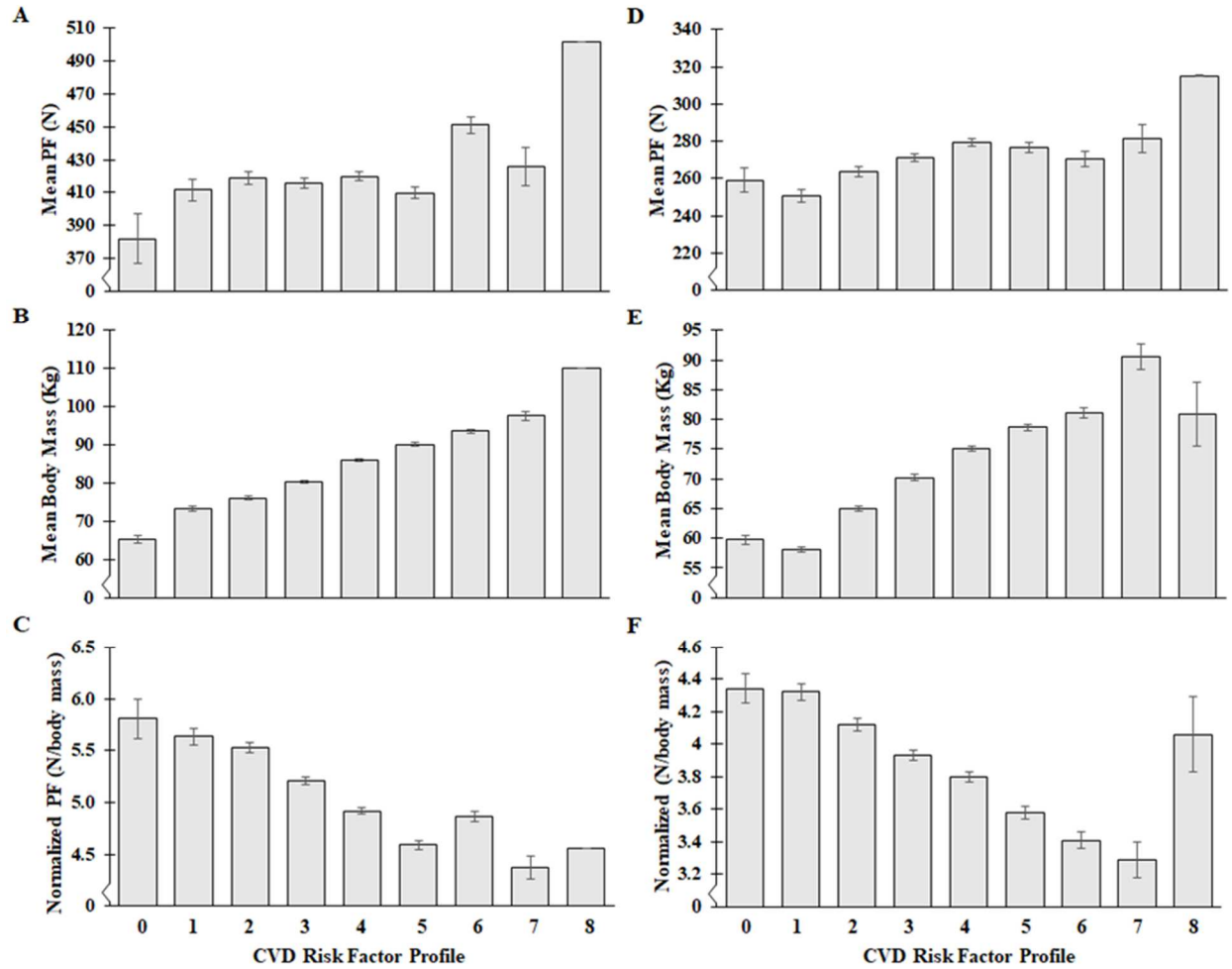
Figure 1 CVD risk factor profiles (presenting 0-8 CVD risk factors) for males (A-C) and females (D-F). For males, risk factor profiles are in relation to (A) mean PF (N), (B) mean body mass (Kg), and (C) normalized PF (N/Kg). For females, risk factor profiles are in relation to (D) mean PF (N), (E) mean body mass (Kg), and (F) normalized PF (N/Kg). Standard error is represented with error bars on each graph.
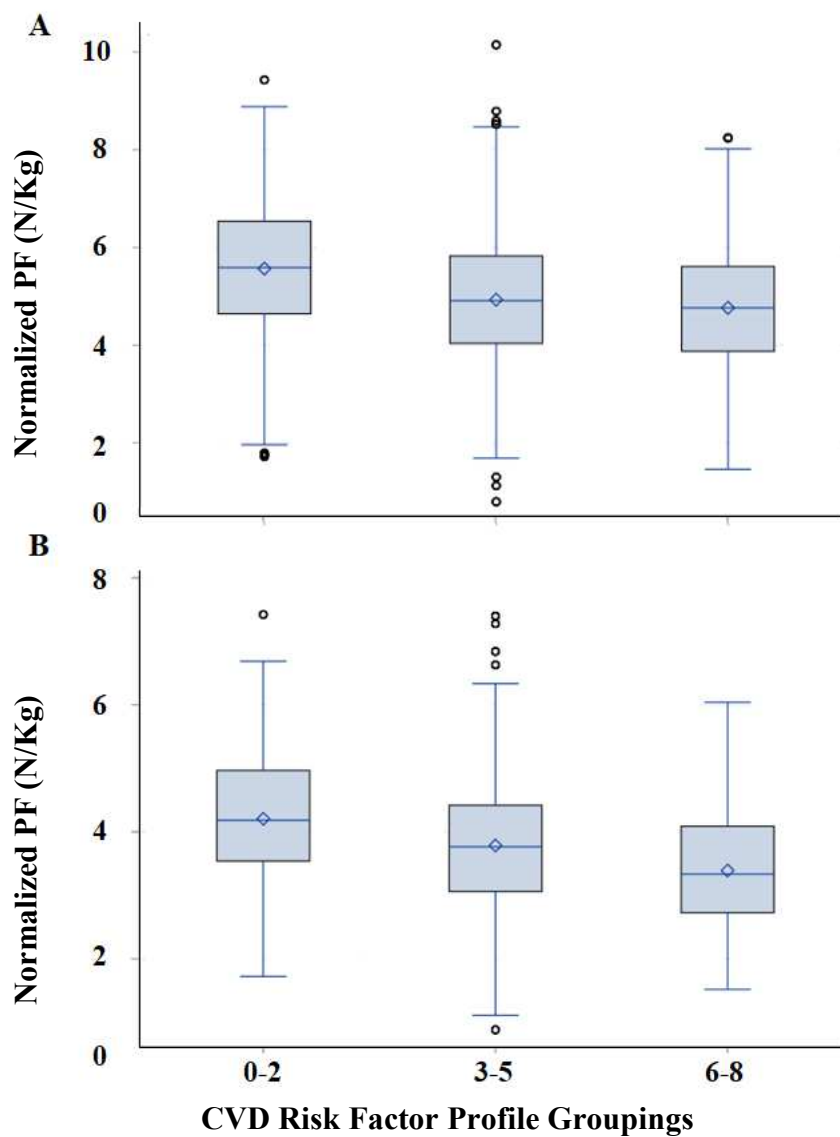
Figure 2 CVD risk factor profiles grouped as low risk (0-2), moderate risk (3-5), and high risk (6-8) in relation to normalized PF (N/Kg) in males (A) and females (B). The plots depict normalized PF (N/Kg) values compared to CVD risk factor profile groupings with medians, upper and lower quartiles, and minimum and maximum ranges. Outliers were identified as ○.

CHAPTER V

DISCUSSION

The present study assessed the impact of CVD risk factors and profiles on isokinetic leg extensor absolute and normalized maximal strength. Our findings provide further support that the association between specific CVD risk factors (11-13, 55, 56) or CVD risk factor profiles (4, 57) and normalized muscular strength (normalized to either body mass or BMI) is inverse but extend upon the current literature by demonstrating this inverse association using CVD risk factor profiles that include all nine ACSM CVD risk factors, in a nationwide sample of American males age 50 and older and females age 55 and older. These findings also indicate that there is a positive association when only raw PF is considered, reinforcing ideas that normalized muscular strength may be a better measure than raw muscular strength when measuring obese populations (4, 56).

CVD and Exercise

Exercise has long been known to help with the prevention and management of CVD risk (58-61). This is likely due to the fact that physical exercise (of any type) is associated with improving mortality risk from aging (62, 63) and family history of CVD (64), smoking (65), sedentary lifestyle (66, 67), obesity (68, 69), hypertension (70-73), high cholesterol (55, 71, 74, 75), diabetes (69, 76, 77), and HDL cholesterol (78), as well as decreased mortality from CVD itself (61). The modality of exercise most associated with improvements in maximal muscular strength is resistance training (58).

Resistance training is a form of exercise where the muscles are put under stress by working against or holding a resistance (force or weight) that is applied (58). Although resistance training was not analyzed in this study, it is known to increase maximal muscular

strength in older individuals (58) and can effectively treat both sarcopenia (79, 80) and dynapenia (80). Because of resistance training's ability to increase maximal muscular strength within this population (58), findings from this study suggest that resistance training interventions may be able to assist in the treatment or management of CVD. Specific resistance training recommendations for this population can be found in the ACSM's position stand on "Exercise and Physical Activity for Older Adults" (58). Resistance training has also been shown to improve several ACSM CVD risk factors, such as waist circumference (81) and obesity (71), total and LDL cholesterol (75, 82), hypertension (70, 72), and diabetes (83) and glycemic control (77), although there is conflicting evidence regarding resistance training's effects of blood cholesterol (14, 76, 84). It is important to note that while resistance training can increase maximal muscular strength, increasing normalized muscular strength may require dietary interventions focused on reducing adiposity and lowering or maintaining total body mass (85).

CVD Risk Factor Profiles and Characterization on Isokinetic Peak Force

Previous research has shown that measures of muscular strength are inversely associated with CVD risk factors such as hypertension (4), obesity (12), and metabolic syndrome (11), and that normalized muscular strength may also demonstrate an inverse relationship with the development of type 2 diabetes mellitus (56). However, our study is unique in that we used all nine ACSM risk factors to build/create NHANES participant CVD risk factor profiles, which is the first study to have done so in relation to measures of raw and normalized muscular strength. Additionally, this study used isokinetic leg muscular strength, which measures force generated by the leg extensors against a resistance at a constant speed (60 degrees per second) (86). This was chosen because it is an effective measure of knee extension strength (86), which is associated with gait speed (87) and functionality in older adults (33). Because muscular strength

on its own is related to factors such as body mass, BMI, and waist circumference, it was decided to analyze normalized PF as well as raw PF (4, 56). **Figure 1** demonstrates the difference between raw and normalized PF, and how body mass has masked the relationship between PF and CVD risk factor profiles (i.e., mean PF for males and females slightly increase as CVD risk factor profiles increase). When mean body mass for males and females is plotted against CVD risk factor profiles, we can see that CVD risk factor profiles also increase steadily with mean body mass similar to PF. Accounting for body mass, normalized PF for males and females shows an inverse relationship with CVD risk factor profiles. It has been suggested that strength may have a protective effect on CVD risk factors (4, 11, 88-91). In conjunction, our findings may suggest that, within the U.S. population, higher leg extensor muscular strength (normalized to body mass) may have a protective effect against CVD risk factors.

Every additional risk factor added to the CVD risk factor profile was associated with a decreased normalized PF (**Table 4**), except in two cases. First, when increasing from 7 to 8 CVD risk factors, there was an increase in normalized PF for both males and females. Second, when going from 5 to 6 CVD risk factors, normalized PF increased for only males. The former is likely due to the small number of participants with 8 risk factors (N=5 males; N=10 females); however, the latter may be due to other factors. To correct for the small number of participants with either very many or very few CVD risk factors, we grouped CVD risk factor profiles into low (0-2 CVD risk factors), moderate (3-5 CVD risk factors), and high (6-8 CVD risk factors) categories and plotted normalized muscular strength across them (**Figure 2**). For both males and females, there were significant differences in normalized muscular strength based on CVD risk factor characterization, with higher risk factor characterization having lower normalized PF. This

provides further support for the significant inverse association seen between normalized muscular strength and CVD risk factor profiles.

Adjusted Individual CVD Risk Factors (Accounting for Other Risk Factors)

The most prevalent risk factors in the present study sample were hypertension, overweight/obesity (by waist circumference), high total blood cholesterol, and low HDL cholesterol. The majority of participants had between two and five risk factors (N=8,784), with only 1.6% (N=173) presenting zero risk factors (excluding age) and 0.1% (N=15) presenting every risk factor. This is consistent with literature examining the prevalence of CVD risk factors in this time frame (1999-2002), as hypertension has been found to affect between 40% and 80% of U.S. individuals aged 50 years and older (92), while roughly 70% of individuals aged 60 years and older in the U.S. were found to be either overweight or obese from 1999-2004 (93). In addition, over 40% of adults age 20 and older in the U.S. have high blood cholesterol levels (94).

Hypertension, sedentary lifestyle, family history of CVD, high total cholesterol, and low HDL cholesterol levels were not observed to be significantly associated with muscular strength in either males or females, while diabetes status was not shown to be significantly associated with muscular strength among females. Age, smoking status (by serum cotinine level), and waist circumference were all shown to be significantly associated with muscular strength in both males and females, when accounting for all other risk factors. However, diabetes status was shown to be significantly associated with muscular strength in males, but not females.

Non-Significant CVD Risk Factors

Hypertension

Hypertension has been shown in previous research to be inversely associated with muscular strength (13); however, Maslow et al. (13) found that this inverse association

disappears after accounting for CRF. Contrary to this, Bakker et al. (55) found in 2017 that resistance exercise, independent of CRF, is associated with a lower risk of developing metabolic syndrome, which is characterized by glucose intolerance, insulin resistance, obesity, dyslipidemia, and hypertension (55). Although previous authors have suggested that muscular strength may be associated with hypertension regardless of CRF (4, 95), this was not observed within this population.

Sedentary Lifestyle

It has been observed that although lower body muscular strength has some association with sedentary lifestyles, other correlates such as gender, age, and BMI have much stronger associations with physical activity levels (96); this may in part explain why sedentary lifestyle as a CVD risk factor was not observed in this study to be independently associated with levels of muscular strength.

Family History

A family history of CVD was also not observed to be significantly associated with muscular strength in this study; this may in part be due to limitations with the specific years of NHANES used. The ACSM defines a family history of CVD as a risk factor for CVD disease only when that family member had a heart attack, bypass surgery, or sudden death before the age of 55 (3). However, during the 1999-2002 NHANES data set, there was no way to determine at what age a family member had had a heart attack, bypass surgery, or sudden death, and so the defining criteria for this study were simply whether a blood relative had had a heart attack or stroke, hypertension, or angina.

Total Cholesterol and HDL

In regard to blood cholesterol, one study by Vaara et al. (14) found no associations between muscular strength independent of CRF and LDL cholesterol. Similarly, this study found no associations between either HDL or total cholesterol and muscular strength. However, resistance training, which is known to increase maximal muscular strength within this population (58), has been shown to increase blood HDL cholesterol in subjects with diabetes (76) and to decrease LDL cholesterol when performed at high volumes (97). Other research has shown that resistance training, even after increasing muscular strength, does not decrease LDL cholesterol (76, 84).

Significant CVD Risk Factors

Age

Sarcopenia, the age-related loss of skeletal muscle mass and strength (98), and dynapenia, the age-related loss of muscular strength without muscular disease or atrophy (15), both lead to lower muscular strength among older individuals. Results from this paper show the odds of having lower PF increases in both males (OR = 1.13; 95% CI: 1.11-1.15) and females (OR = 1.13; 95% CI: 1.11-1.15) as they age, further confirming the veracity of these concepts. The differences observed in normalized PF for the low, moderate, and high CVD risk factor characterizations may indicate that this population of older individuals who are at a higher risk of low muscular strength may especially benefit from resistance training interventions designed to increase PF (99) as well as nutritional interventions designed to reduce adiposity (85).

Smoking

It has been observed that exposure to tobacco smoke is associated with decreased muscular strength (100-103). It has been suggested by Petersen et al. (104) that this is due to an impairment of muscle protein synthesis and the increased expression of genes regularly regarded

as atrophy-related (such as MAFbx/atrogin-1) that accompanies exposure to tobacco smoke. It has also been suggested that smoking may be related to increased muscular fatigue (105), as cigarette smoke may cause both a reduced oxygen carrying capacity of the blood and impaired oxygen delivery (106). Increased muscular fatigue can cause decreased maximal force output (107). This would likely explain the inverse association observed within this paper regarding muscular strength and serum cotinine, a measure of exposure to tobacco smoke.

Obesity

Obesity has also been shown to be positively associated with muscular strength (108, 109), as was seen in the present study. However, this is likely due to increased overall mass, so many studies instead use normalized muscular strength to account for the high associations between BMI and muscular strength (12, 110).

Blood Glucose and Diabetes

It has also been shown that normalized muscular strength has an inverse relationship with type 2 diabetes mellitus (56) and that increasing muscular strength is associated with decreasing risk for type 2 diabetes mellitus in men (111, 112). One potential explanation our results differ based on gender may be due to sex hormone (i.e., testosterone and estrogen) differences between men and women. For instance, low testosterone levels in men are associated with lower muscular strength (113). Low testosterone levels in men are also associated with increased risk of diabetes (114) and is common in men with type 2 diabetes (115-117). Therefore, testosterone levels in men may effect both their levels of muscular strength and their diabetes status (118, 119). Additionally, it has been proposed that estrogen is protective against CVD to some degree (120, 121), which is thought to be why women in general develop CVD 10 to 15 years later than men (122). While it is not currently known whether estrogen has a protective effect against diabetes

mellitus specifically, it has been shown that lower levels of circulating estradiol is related to diagnosis of diabetes (123). Thus, differences in sex hormones may influence blood glucose/diabetes status, which was significantly associated with muscular strength in males and not in females. Unfortunately, sex hormone values for the 1999-2000 and 2001-2002 NHANES data sets were not available.

ACSM Exercise Guidelines

The ACSM currently has recommendations for exercise training for older individuals within their position stand, "Exercise and Physical Activity for Older Adults" (58). In this position stand, the ACSM recommends that older adults engage in resistance training, as it can substantially increase their maximal muscular strength (58). To safely and effectively accomplish this, the ACSM along with the American Heart Association came up with guidelines to recommend resistance training for older individuals (58). It is recommended that resistance training be done at least twice weekly at moderate to vigorous intensities, with modalities including progressive weight training programs, weight bearing calisthenics programs, stair climbing, and other strengthening movements. It is recommended that 8-10 exercises per session, for 8-12 repetitions per exercise, be done when resistance training for this population (58).

Limitations and Future Research

There are several limitations in the present study. First, the NHANES 1999-2002 cycle did not include any way to ascertain the age of family members when they were diagnosed with CVD or had their first cardiac event. The ACSM defines a family history of CVD as a risk factor for CVD disease only when that family member had a heart attack, bypass surgery, or sudden death before the age of 55 (3). However, with the 1999-2002 NHANES data set, there

was no way to determine at what age a family member had had a heart attack, bypass surgery, or sudden death, and so the defining criteria for this study were simply whether a blood relative had had a heart attack or stroke, hypertension, or angina. Additionally, ACSM defines sedentary lifestyle as less than three days of 30 minutes of moderate activity per week (3). Sedentary lifestyle status is taken in the interview section of NHANES; however, it does not define activity congruently with ACSM. In the 1999-2000 and 2001-2002 NHANES cycles, this section is a self-report of the average level of physical activity each day coded 1-4: (1) sit during the day and not walk about very much; (2) stand or walk about a lot during the day but does not carry or lift things very often; (3) lifts light load or have to climb stairs or hills often; (4) does heavy work or carries heavy loads.

Self-report survey results were used in this study for five of the nine ACSM CVD risk factors (family history, sedentary lifestyle, hypertension, diabetes, and cholesterol status); two of these CVD risk factor variables were created solely with questionnaire data (sedentary lifestyle and family history), while the other three combined questionnaire data with laboratory results to create dichotomous variables (hypertension, diabetes status, and cholesterol status). This was done to make sure individuals that exhibited the conditions (diabetes, hypertension, and dyslipidemia) but were treating them with medication would still be included in the analyses.

It is not known whether the inverse association between normalized muscular strength and CVD risk factor profiles is present when accounting for CRF. Unfortunately, the NHANES did not include measures of CRF within the 1999-2002 data set for individuals 50 and older, and thus we did not include CRF in our analyses. It is known that CRF has an inverse relationship with CVD (8, 9), even when other risk factors such as smoking or high cholesterol are present (37). It is possible that those with high normalized PF may also have high CRF, making CRF a

confounding factor. Ruiz et al. (110), when examining the association between muscular strength and risk of death from CVD, found inconclusive results when adjusting for CRF. However, Bakker et al. (55) found that muscle strengthening resistance exercise, independent of aerobic exercise, is associated with a lower risk of developing metabolic syndrome. Future research will have to be done regarding the link between normalized muscular strength and CVD risk factor profiles independent of CRF.

Additionally, this study was cross-sectional and observational, and therefore cannot ascertain causation of any associations or trends seen. Clinical trials assessing the impact of increased muscular strength on CVD risk factor profiles in this population would be necessary before any sort of cause or protective effect could be deduced from the findings of this study.

Conclusions

While keeping in mind the limitations of cross-sectional, observational research, it was seen here that normalized muscular strength, but not raw muscular strength, has an inverse relationship with CVD risk factor profiles. This has been suggested to indicate a protective effect of muscular strength against CVD (4), especially in an older population that has higher prevalence of CVD as well as lower rates of muscular strength (15, 80, 96, 98, 124-132). Further research reproducing these findings independent of CRF levels in participants will be necessary before such an effect can be concluded. Additionally, men with diabetes were shown to have significantly increased odds of low PF, but this was not observed for women. It is possible this is due differences in sex hormone levels, but more research must be done to establish this link. These findings may highlight a key role of normalized muscular strength in the prevention of CVD. Additionally, the present study is unique both that (1) all nine ACSM CVD risk factors were included for analysis, and (2) the sample included is a representative sample of the entire

population of older individuals in the U.S. Interventions intent on increasing normalized

muscular strength in this population must address both increasing raw muscular strength with

exercise (resistance training) and decreasing body mass and/or excess adiposity with nutritional

strategies. Interventions such as these may be beneficial in lowering CVD risk factor profiles in

this population.

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Appendices

Appendix A: NHANES Variable Names and Coding

MEASUREMENT	VARIABLE	DEFINITION	CODING COMMENTS	
MUSCULAR STRENGTH	MSDPF	PF, Newtons	Continuous	
AGE (AND DEMOS)	RIAGENDR	Gender	0=male; 1=female	
	RIDAGEYR	Age	Continuous - report mean ± SD	
	RIDRETH1	Race	1 = Mexican American 2 = Other Hispanic 3 = Non-Hispanic White 4 = Non-Hispanic Black 5 = Non-Hispanic Race/Multiracial	
	INDFMPIR	Family PIR	Low: 0 = else; 1 = less than 1.5 Mid: 0 = else; 1 = between 1.5 and 3.4 High: 0 = else; 1 = 3.5 and above	
FAMILY HISTORY	MCQ250F	Blood relatives w/hypertension/stroke	Turned into dichotomous variable: 0 = no family history of hypertension/stroke/angina;	
	MCQ250G	Blood relatives have angina	1 = yes family history (either yes to MCQ250F or MCQ250G)	
SMOKING	LBXCOT	Serum cotinine (ng/mL)	0 = Below 3.0 ng/mL; 1 = 3.0 ng/mL and above	
SEDENTARY LIFESTYLE	PAQ180	Average level of physical activity each day, 1-4	0 = A score of 2, 3, or 4 on the questionnaire 1 = A score of 1 on the questionnaire	
OBESITY	BMXWAIST	Waist Circumference (cm)	0 = Below 102 cm in males and 89 cm in females 1 = 102 cm and above in males and 89 cm and above in females	
HYPERTENSION	BPQ040A	Prescribed hypertension medicine	0 = no medication 1= yes medication	Turned into dichotomous variable:
	BPXSAR	Average systolic blood pressure of 3-4 measures	0 = below 130 mmHg 1 =130 mmHg and above	0 = no hypertension; 1 = yes hypertension (either yes to BPQ040A or
	BPXDAR	Average diastolic blood pressure of 3-4 measures	0 = below 80 mmHg 1 = 80 mmHg and above	BPXSAR or BPXDAR)
DIABETES/BLOOD GLUCOSE	DIQ010	Doctor told you have diabetes	0 = no medication 1= yes medication	Turned into dichotomous variable:
	LBXGLU	Glucose, plasma (mg/dL)	0 = below 100 mg/dL 1= 100 mg/dL and above	0 = no diabetes; 1 = yes diabetes (either yes to DIQ010 or LBXGLU)
CHOLESTEROL/LOW HDL	LBDLDL	LDL-cholesterol (mg/dL)	0 = below 130 mg/dL 1= 130 mg/dL and above	Turned into dichotomous variable:
	LBDHDL	HDL-cholesterol (mg/dL)	0 = 40 mg/dL and above 1 = below 40 mg/dL	0 = no poor cholesterol; 1 = yes poor cholesterol (either yes to LBDLDL or LBDHDL or BPQ100D)
	BPQ100D	Taking Cholesterol Medication	0 = no medication 1= yes medication	

ELEVATED HDL	LBDHDL	HDL-cholesterol (mg/dL)	0 = above 60 mg/dL 1 = 60 mg/dL and below	
CARDIOVASCULAR DISEASE	MCQ160B	Ever told had congestive heart failure	0 = no 1= yes	Turned into dichotomous variable: 0 = no CVD history; 1 = yes CVD history (either yes to MCQ160B or MCQ160C or MCQ160E or MCQ160F)
	MCQ160C	Ever told you had coronary heart disease	0 = no 1= yes	
	MCQ160E	Ever told you had heart attack	0 = no 1= yes	
	MCQ160F	Ever told you had a stroke	0 = no 1= yes	

VITA

Joel Harden

914 Summerfield Crescent, Springfield, VA 23322 · (808)499-9717 · jhard042@odu.edu

EDUCATION
Master of Science, Exercise Science   Projected Graduation: December 2021
Old Dominion University
Bachelor of Science, Major in Kinesiology, Minor in Psychology   May 2020
Jacksonville University

EXPERIENCE
Research Assistant, Old Dominion University, Cardiometabolic Research Laboratory,
Department of Human Movement Science (HMS); September 2021 – Present

Research Assistant, Old Dominion University, Neuromechanics Research Laboratory,
Department of Human Movement Science (HMS); September 2020 – May 2021

Head Coach, Old Dominion University Rowing Club, Norfolk, VA; June 2021 – Present

Intern Research Assistant, Jacksonville University (JU), Running Biomechanics Laboratory,
Brooks Rehabilitation College of Healthcare Sciences (BRCHS); August 2017 – May 2020

Sport and Performance Psychology Intern, Jacksonville University (JU), Dr. Derek Mann,
Brooks Rehabilitation College of Healthcare Sciences (BRCHS); May 2019 – August 2019

Assistant Coach, Resilient Rowing LLC, Fairfax, VA; May 2018 – August 2018

PUBLICATIONS
REFEREED JOURNAL ARTICLES
Carr JC, Gerstner GR, Voskuil CC, **Harden JE**, Dunnick D, Badillo KM, Pagan JI, Harmon KK,
Girts RM, Beausejour JP, Stock MS. The Influence of Sonographer Experience on Skeletal
Muscle Image Acquisition and Analysis. *Journal of Functional Morphology and Kinesiology*.
2021; 6(4):91. https://doi.org/10.3390/jfmk6040091

MEMBERSHIP IN PROFESSIONAL SOCIETIES
National Strength and Conditioning Association (NSCA); 2021 – Present
American College of Sports Medicine (ACSM); 2021 – Present

PROFESSIONAL CERTIFICATIONS
Certified Strength and Conditioning Specialist. (CSCS). National Strength and Conditioning
Association Certification Commission. August 31, 2021.