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Family History and Cardiovascular Disease Risk in At-Risk Young Adults: A Pilot Intervention Study

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Abstract

Family History and Cardiovascular Disease Risk in At-Risk Young Adults: A Pilot Intervention Study

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Approximately 82 million Americans have one or more types of cardiovascular disease (CVD). In 2008, 811,940 deaths were caused by CVD, accounting for 32.8% of all deaths in the United States. There are two types of risk factors for CVD: non-modifiable and modifiable. Health-promoting behaviors aimed at the modifiable risk factors can prevent or reduce CVD. Through exercise, proper diet, and smoking cessation, an individual can decrease their risk for developing CVD. Family history is an independent risk factor for CVD and has the potential to become a screening tool to identify people at increased risk.

The purpose of this pilot feasibility study was to examine the short-term impact of a theoretically driven, educational intervention on perceived CVD risk and behavioral

intention to change health-related behavior to reduce CVD risk in asymptomatic young adults with a known family history of CVD. The intervention incorporated each young adult's family medical history; utilized a three-generation pedigree to illustrate participants' inherited risk; and delivered personalized CVD risk information based on family history and CVD biomarkers.

The intervention was evaluated within a single group, pre-test post-test design. Quantitative data were examined using non-parametric statistics and the qualitative data was examined using thematic content analysis. Genetic testing was performed on blood samples from the participants to look for genetic variants associated with an elevated risk for coronary heart disease. These results were examined using the Hardy-Weinberg Equilibrium principal and the relationship between the susceptibility alleles and lab results was examined.

The study was feasible and the intervention significantly increased study participants' perceived lifetime CVD risk, heart disease knowledge, and behavioral intention to engage in CVD risk-reducing behavior. There were no significant differences in the frequency of susceptibility alleles in the study sample compared to a general population. Future testing of the intervention is warranted within a larger sample involving a more diverse population with a greater number of CVD risk factors. Further exploration on the use of genetic testing to predict at-risk individuals is recommended.

TABLE OF CONTENTS

Page

List of Figures..... iv

List of Tables..... vi

Glossary……..... vii

Chapter 1. Introduction..... 1
Purpose……..... 2

Chapter 2. Review of the Literature…..... 4
CVD Risk and Family History of CVD..... 4
Relationship between Family History of CVD and Health-Related Behavior Change..... 5
Relationship between Family History of CVD and Perceived Risk..... 6
Relationship between Perceived Risk and Health-Related Behavior Change..... 8
Summary..... 9
Young Adults and CVD……..... 11
Summary……..... 12
Selected CVD Biomarkers of Arterial Vulnerability..... 13
Elevated LDL-C and Increased CHD Risk …..... 13
Low HDL-C and Increased CHD Risk……..... 15
Elevated Apo B and Increased CHD Risk…..... 15
Low Apo A-I and Increased CHD Risk……..... 16
LDL and HDL Versus Apo B and Apo A-I…..... 16
Summary…..... 17
Common SNPs Associated with Increased CHD Risk..... 17
Protection Motivation Theory..... 19

Chapter 3. Intervention and Study Design..... 22
Purpose…..... 22
Study Aims, Sub-Aims, and Hypotheses..... 22
Primary Aim 1…..... 23
Primary Aim 2…..... 23
Primary Aim 3…..... 24
Exploratory Aim 1..... 24
Study Design and Methods..... 25
Conceptual Framework…..... 25
Sample and Recruitment…..... 26
Study Procedures…..... 28
Instruments and Measures…..... 33
Estimated Odds for Developing CVD…..... 36
CVD Biomarkers – LDL-C, HDL-C, Apo B, and Apo A-I..... 38
Genotyping..... 38

TABLE OF CONTENTS (continued)

Data Analysis..... 40
Analysis of Feasibility Results (Primary Aim 1) 40
Analysis of Baseline Data (Primary Aim 2) 40
Analysis of the Impact of the Intervention (Primary Aim 3)..... 41
Analysis of Genotyping Results (Exploratory Aim)..... 42
Chapter 4. Results..... 44
Introduction..... 44
Feasibility Results (Primary Aim 1)..... 44
Recruitment..... 44
Study Design and Adherence..... 45
Participants' Willingness to Provide a Blood Sample..... 47
Analysis of the Open-Ended Questions..... 47
Summary of Feasibility Results (Primary Aim 1) 49
Baseline Data (Primary Aim 2)..... 49
Study Sample..... 49
Factors that Influenced Study Variables at Baseline..... 51
Baseline Perceived CVD Risk..... 55
Relationship between Heart Disease Knowledge and Perceived CVD Risk at Baseline..... 56
Relationship between Perceived CVD Risk and Intentions to Engage in CVD Risk Reducing Behaviors..... 56
Summary of Feasibility Results (Primary Aim 2) 59
Impact of Intervention (Primary Aim 3)..... 60
Perceived CVD Risk..... 60
Heart Disease Knowledge..... 65
Intention to Engage in a Health-Promoting Lifestyle..... 66
Qualitative Analysis of the Impact of the Intervention..... 69
Summary of the Impact of the Intervention (Primary Aim 3) 72
Genotyping Data (Exploratory Aim)..... 72
Genotyping Results..... 72
Hardy-Weinberg Equilibrium..... 73
Number of Susceptibility Alleles and LDL-C and Apo B Levels..... 74
Summary of Genotyping Results (Exploratory Aim) 74

Chapter 5. Discussion..... 76
Summary of Findings..... 76
Discussion and Implications..... 77
Feasibility - Recruitment and Study Design..... 77
Baseline Data..... 79
Impact of the Intervention..... 81
Exploratory Analysis of Genotyping Data……..... 82
Limitations……..... 82
Conclusions with Recommendations for Future Research..... 83

References…..... 85

Appendix A: Study Measures and Questionnaires..... 101

TABLE OF CONTENTS (continued)

Appendix B: University Washington of Consent Form…...…….. 121

Vita..... 128

LIST OF FIGURES

Figure Number		Page
Figure 2.1.	Protection Motivation Theory…….....	20
Figure 3.1.	Protection Motivation Theory and Relationship to Components of Intervention.....	26
Figure 3.2.	Study Activities.....	29
Figure 4.1.	Recruitment Flow Diagram.....	46
Figure 4.2.	Mean Education Level and BMI at Baseline.....	54
Figure 4.3.	Heart Disease Knowledge Score and Perceived Influence of Current Age on Lifetime CVD Risk at Baseline…….....	57
Figure 4.4.	Heart Disease Knowledge Score and Perceived Influence of Family History on Lifetime CVD Risk at Baseline.....	57
Figure 4.5.	Intention to Eat a Healthy Diet and Perceived Lifetime CVD Risk Based on Current Lifestyle at Baseline.....	58
Figure 4.6.	Intention to Eat a Healthy Diet and Mean Score on CHD Susceptibility Questionnaire at Baseline.....	59
Figure 4.7a.	Pre-post Intervention Changes in Perceived CVD Risk Based on all Factors by Participant.....	61
Figure 4.7b.	Pre-post Intervention Changes in Perceived CVD Risk Based on all Factors….....	61
Figure 4.8a.	Pre-post Intervention Changes in Mean CHD Susceptibility Scores by Participant.....	63
Figure 4.8b.	Pre-post Intervention Changes in Mean CHD Susceptibility Scores.....	63
Figure 4.9a.	Pre-post Intervention Changes in Perceived Lifetime CVD Risk Based on Family Members with CVD or Conditions Known to Increase CVD Risk by Participant.....	64
Figure 4.9b.	Pre-post Intervention Changes in Perceived Lifetime CVD Risk Based on Family Members with CVD or Conditions Known to Increase CVD Risk.....	65
Figure 4.10a.	Change in Heart Disease Knowledge Score by Participant.....	66
Figure 4.10b.	Change in Heart Disease Knowledge Score.....	66

LIST OF FIGURES (continued)

Figure 4.11a. Changes in Intention to Engage in a Health-Promoting Lifestyle by Participant……..... 67

Figure 4.11b. Changes in Intention to Engage in a Health-Promoting Lifestyle..... 68

Figure 4.12a. Change in Likelihood to Take Action to Reduce CVD Risk by Participant..... 69

Figure 4.12b. Change in Likelihood to Take Action to Reduce CVD Risk..... 70

Figure 4.13. Correlation between Number of Susceptibility Alleles and LDL-C Levels 75

Figure 4.14. Correlation between Number of Susceptibility Alleles and Apo B Levels 75

LIST OF TABLES

Table Number		Page
Table 2.1.	SNPs Tested for in the Study Sample	19
Table 3.1.	Open-Ended Questions Asked at the End of Session Two	32
Table 3.2.	Study Sub-aims, Measures, and PMT Concepts	33
Table 4.1.	Recruitment Channels	45
Table 4.2.	Who Did You Talk To About Your Family History?	47
Table 4.3.	Demographic Data on Study Participants	50
Table 4.4.	Differences by Age at Baseline	51
Table 4.5.	Differences by Race/Ethnicity at Baseline	53
Table 4.6.	Baseline Perceived CVD/CHD Risk	55
Table 4.7.	Rank of the Perceived Influence of Various Factors on Lifetime CVD Risk	56
Table 4.8.	Correlation between Heart Disease Knowledge and Perceive Risk at Baseline	56
Table 4.9.	Correlation between Heart Disease Knowledge and Perceived Influence of Various Factors on Lifetime CVD Risk at Baseline	58
Table 4.10.	Impact of the Intervention on Intention to Engage in a Health-Promoting Lifestyle – Baseline to Post-Intervention	67
Table 4.11.	Genotyping Results by Sample	72
Table 4.12.	HapMap Report for rs3846662 (dbSNP Build 126)	73
Table 4.13.	HapMap Report for rs693 (dbSNP Build 126)	73
Table 4.14.	HapMap Report for rs6511720 (dbSNP Build 126)	73
Table 4.15.	Genotyping Results for Non-Hispanic Caucasian Participants Only	74
Table 4.16.	Genotyping Results: Are the Observed Genotyping Frequencies Consistent with Hardy-Weinberg Equilibrium for Non-Hispanic Caucasian Participants Only?	74
Table 5.1.	Summary of Study Results by Primary Aims	76

GLOSSSARY

Apolipoprotein A-I (apo A-I): A protein component of lipoprotein complexes found in high-density lipoprotein (HDL) and chylomicrons; it is an activator of lecithin-cholesterol acyltransferase, which forms cholesteryl esters in HDL

Apolipoprotein B (apo B): A protein component of lipoprotein complexes found in chylomicrons, low-density lipoprotein (LDL), very low-density lipoprotein (VLDL), and intermediate-density lipoprotein (IDL)

Atherosclerosis: A common form of arteriosclerosis, characterized by deposits of plaques (atheromas) containing lipids, carbohydrates, blood and blood products, fibrous tissue, and calcium deposits. These plaques are found in the intima of large- and medium-sized arteries.

Atherogenic: Having the capacity to initiate, increase, or accelerate the process of atherogenesis, which is the formation of abnormal fatty or lipid masses in arterial walls

Biomarker: A detectable cellular or molecular indicator of exposure, health effects, or susceptibility, which can be used to measure the absorbed, metabolized, or biologically effective dose of a substance, the response to the substance including susceptibility and resistance, idiosyncratic reactions, and other factors or conditions

Body mass index (BMI): An anthropometric measure of body mass, defined as weight in kilograms divided by height in meters squared; a method of determining caloric nutritional status

Congestive heart failure (CHF): Inadequacy of the heart so that as a pump it fails to maintain the circulation of blood, with the result that congestion and edema develop in the tissues; also known as heart failure

Diastolic blood pressure (DBP): The intracardiac pressure during or resulting from diastolic relaxation of a cardiac chamber; the lowest arterial blood pressure reached during any given ventricular cycle

GLOSSARY (continued)

Coronary artery disease (CAD): Narrowing of the lumen of one or more of the coronary arteries, usually due to atherosclerosis; can cause congestive heart failure, angina pectoris, or myocardial infarction; also known as coronary heart disease (CHD)

Feasibility study: A small-scale test to determine the feasibility of a larger study (see pilot study)

First-degree relative: A first-degree relative is a family member who shares about 50 percent of their genes with a particular individual in a family; first-degree relatives include parents, offspring, and siblings

Hazard ratio: A measure of how often a particular event happens in one group compared to how often it happens in another group, over time

Heart disease: Heart disease is a broad term used to describe a range of diseases that affect your heart; the various diseases that fall under the umbrella of heart disease include diseases of your blood vessels, such as coronary artery disease (CAD); heart rhythm problems (arrhythmias); heart infections; and heart defects you're born with (congenital heart defects)

High-density lipoprotein cholesterol (HDL-C): Class of lipoproteins that promote transport of cholesterol from extrahepatic tissue to the liver for excretion in the bile; synthesized by the liver as particles lacking a lipid core, they accumulate a core of cholesterol esters during reverse cholesterol transport and transfer them to the liver directly or indirectly via other lipoprotein; serum HDL-C has been negatively correlated with premature coronary heart disease

Hypercholesterolemia: The presence of an abnormally large amount of cholesterol in the blood; hypercholesterolemia is a risk factor for coronary artery disease

Hyperlipidemia: Elevated levels of lipids in the blood plasma; high lipid levels can speed up atherosclerosis

GLOSSARY (continued)

Hypertension: Transitory or sustained elevation of systemic arterial blood pressure to a level likely to induce cardiovascular damage or other adverse consequences; hypertension has been arbitrarily defined as a systolic blood pressure above 140 mmHg or a diastolic blood pressure above 90 mmHg; consequences of uncontrolled hypertension include retinal vascular damage (Keith-Wagener-Barker changes), cerebrovascular disease and stroke, left ventricular hypertrophy and failure, myocardial infarction, dissecting aneurysm, and renovascular disease

Hypertriglyceridemia: Elevated triglyceride concentration in the blood; in epidemiologic and interventional studies, hypertriglyceridemia is a risk factor for coronary artery disease

Intermediate-density lipoprotein cholesterol: Intermediate density lipoproteins, or IDL, are a combination of cholesterol, triglycerides and protein that circulate through the body and transport cholesterol throughout the body; IDLs are a result from the degradation of very low-density lipoproteins (VLDLs); IDLs can be further degraded to low-density lipoprotein (LDLs); also know as nascent VLDL

Intron: A portion of a gene that does not code for amino acids

Ischemic stroke: An acute event that occurs when the blood supply to part of your brain is interrupted or severely reduced, depriving brain tissue of oxygen and food. Within minutes, brain cells begin to die; also known as stroke

Low-density lipoprotein cholesterol (LDL-C): A class of lipoproteins responsible for transport of cholesterol to extrahepatic tissues; formed in the circulation when very-low-density lipoproteins are degraded first to intermediate-density lipoproteins (IDL) and then to LDL by the gain and loss of specific apolipoproteins and the loss of most of their triglycerides; serum LDL-C has been positively correlated with premature coronary heart disease

Myocardial infraction (MI): An acute episode of heart disease marked by the death or damage of heart muscle due to insufficient blood supply to the heart muscle usually as a result of a coronary thrombosis or a coronary occlusion and that is characterized especially by chest pain; also known as heart attack

GLOSSARY (continued)

Odds ratio: The ratio of one odds to another odds, for example, the ratio of the odds of an event in one group to the odds of an event in another group

Pilot study: A small-scale version, or trial run, done in preparation for a major study

Polymerase chain reaction (PCR): A laboratory technique used to amplify DNA sequences. The method involves using short DNA sequences called primers to select the portion of the genome to be amplified. The temperature of the sample is repeatedly raised and lowered to help a DNA replication enzyme copy the target DNA sequence. The technique can produce a billion copies of the target sequence in just a few hours

Real-time polymerase chain reaction (RT-PCR): A form of polymerase chain reaction (PCR) in which data are collected in real-time as the reaction proceeds

Single nucleotide polymorphisms (SNPs): A type of polymorphism involving variation of a single base pair

Systolic blood pressure (SBP): The intracardiac pressure during or resulting from systolic contraction of a cardiac chamber; the highest arterial blood pressure reached during any given ventricular cycle

Very low-density lipoprotein cholesterol (VLDL-C): A lipoprotein subclass assembled in the liver from cholesterol and apolipoproteins. It is then converted in the bloodstream to low density lipoprotein (LDL). VLDL is prone to accelerate atherosclerosis, and is elevated in a number of diseases and metabolic states.

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CHAPTER 1.

INTRODUCTION

Approximately 82 million Americans have one or more types of cardiovascular disease (CVD), which includes hypertension, coronary heart disease (CHD), myocardial infraction, angina pectoris, heart failure, and stroke. Over 6 million have hypertension (defined as systolic blood pressure ≥ 140 mm Hg and/or diastolic blood pressure ≥ 90 mm Hg), 16 million have CHD, almost 6 million have heart failure, and over 7 million have had a stroke (Roger et al., 2012). In 2008, 811,940 deaths were caused by CVD, accounting for 32.8% of all deaths in the United States (Roger et al., 2012). There are two types of risk factors for CVD: non-modifiable and modifiable. The non-modifiable risk factors, or risk factors that cannot be changed, include genetic factors, ethnicity, sex, and age. The modifiable risk factors, or the risk factors that can be changed, include body weight, blood pressure, lipid and lipoprotein levels, and smoking status. Health-promoting behaviors aimed at the modifiable risk factors can prevent or reduce CVD. Through exercise, proper diet, and smoking cessation, an individual can decrease their risk for developing CVD (Delaney et al., 2007; Schaefer, 2002; Toborek, Lee, Garrido, Kaiser, & Hennig, 2002).

Family history is an independent risk factor for CVD and has the potential to become a screening tool to identify people at increased CVD risk (Valdez, Greenlund, Khoury, & Yoon, 2007). A pedigree "is genetic representation of a family tree that diagrams the inheritance of a trait or disease though several generations that shows the relationships between family members and indicates which individuals express or silently carry the trait in question" (Pedigree, n.d.). Pedigrees, especially pedigrees that include three or more generations, are a valuable tool that aid healthcare providers' ability to obtain details about an individual's family history, which can assist in diagnostic and screening decisions. Pedigrees can function as a visual tool that makes "invisible knowledge" visible (Bennett, 2000; Nukaga & Cambrosio, 1997).

However, the usefulness of a family history is only as good as the quality of the information. If the family history provided to the healthcare provider is not correct or accurate, then it is not helpful for the healthcare provider or the individual giving the information.

A few studies have shown that knowledge of a family history of CVD can play a role in behavior change, but no standardized way of gathering the family medical history or presenting that information to individuals has been examined. Many organizations, including the American Heart Association (AHA) and the Department of Health and Human Services, promote the public's use of their own pedigrees to raise awareness of their individual family history to aid in health behavior choices. However, the true value of pedigrees, especially in asymptomatic young adults, in influencing perceived disease risk, behavior change, and biological changes is unknown.

A recent National Institutes of Health (NIH) State-of-the-Science Conference Statement on family history and improving health generated a set of research recommendations for short-term and intermediate goals in three categories: 1) structure and characteristics of a family history, 2) the process of acquiring a family history, and 3) outcomes of family history acquisition, interpretation, and application (Berg et al., 2009). The current study is an early step toward helping to meet those large and lofty goals.

Purpose

The purpose of this feasibility and pilot study was to examine the short-term impact of a theoretically driven, educational intervention that incorporated family health history and pedigree information on perceived CVD risk and behavioral intention to reduce risk factors in asymptomatic young adults with a known family history of CVD. The impact of the intervention was evaluated within a single group pre-test post-test design using mixed methods, which included examining the quantitative data by non-parametric statistics and using thematic content analysis to examine the qualitative data.

Chapter 2 contains: a belief review of epidemiological research linking family history of CVD and increased CVD risk; an examination of studies exploring the relationship between family history of CVD, perceived CVD risk, and health-promoting behaviors; a review of selected CVD biomarkers of arterial vulnerability; a discussion about three common single nucleotide polymorphisms (SNPs) associated with increased CHD Risk; and an introduction to the Protection Motivation Theory. Chapter 3 contains the study methods, including its primary and exploratory aims, how the Protect Motivation Theory guided the intervention, the description of the intervention, and the study design. Chapter 4 contains results for each study aim. Finally, Chapter 5 includes a discussion of the results, implications, limitations of the study, and recommendations for future research.

CHAPTER 2.

REVIEW OF THE LITERATURE

Portions of this chapter and chapter 3 were published in *Biological Research for Nursing* (Imes & Austin, 2012).

CVD Risk and Family History of CVD

A family history of CVD is defined as a blood-related grandparent, parent, brother, sister, child, aunt, uncle, or cousin with a history of high blood pressure (hypertension), heart attack (coronary heart disease, myocardial infarction), heart failure (congestive heart failure), elevated cholesterol or triglyceride levels (hypercholesterolemia/hypertriglyceridemia/ hyperlipidemia), or stroke (ischemic stroke). Having one or more family members with a history of CVD increases an individual's risk for developing CVD (Lloyd-Jones et al., 2010). However, the knowledge of a family history can be a powerful tool and motivator to promote a healthy lifestyle.

There is substantial epidemiologic evidence for the familial aggregation of CVD. Researchers from the Framingham Study reported that having CVD in at least one parent doubled the 8-year risk of CVD among men and increased the risk among women by 70% (Ciruzzi et al., 1997; Lloyd-Jones et al., 2004). The excess risk was independent of other risk factors such as age, ratio of total/high-density lipoprotein cholesterol level, systolic blood pressure (SBP), antihypertensive therapy, diabetes, body mass index (BMI), and current smoking status (Lloyd-Jones et al., 2004). Additionally, retrospective studies have estimated the odds ratio (OR) of a lifetime cardiovascular event for an individual with a single first-degree relative with a history of a cardiovascular event to be 1.1-2.63 (Bertuzzi, Negri, Tavani, & La Vecchia, 2003; Ciruzzi et al., 1997; Friedlander et al., 2001; Leander, Hallqvist, Reuterwall, Ahlbom, & de Faire, 2001; Silberberg, Wlodarczyk, Fryer, Robertson, & Hensley, 1998). The OR increases to 2.66-4.1 when the first-degree relative had a premature cardiovascular event (Friedlander et al., 2002; Silberberg et al., 1998).

Family histories serve as a bridge from genetics to genomics in clinical practice because they reflect the presence of not only single-gene disorders, but also of shared genes that may be responsible for polygenic disorders, environments, and complex gene-environment interactions that may influence risk (Khoury, 2003). Yet, there is still a lot about family histories that we do not know. In a recent NIH State-of-the-Science Conference on family history and improving health, the panel "recognized that family history has an important role in the practice of medicine and may motivate positive lifestyle changes, enhance individual empowerment, and influence clinical intervention" (Berg et al., 2009). The panel also stated that it is currently unclear how family history information can be effectively gathered and that substantial additional research is needed for family history collection to become an evidenced-based tool (Berg et al., 2009).

Relationship between Family History of CVD and Health-Related Behavior Change

A review of the literature identified four studies that examined the relationship between family history and health-related behavior change when perceived risk is not assessed. Overall, study participants' awareness of family history had little or no effect on health-related behavior.

Results from the large study by Kip and colleagues revealed that health-related behavior did not change in young adults after a cardiovascular event in a family member or the death of a family member from a heart attack or stroke (Kip, McCreath, Roseman, Hulley, & Schreiner, 2002).

Kelley and colleagues (2004) compared the dietary intake of at-risk children (average age 10) to non-risk children based on their family history. There were no differences between the two groups on intake of macronutrients, fiber, cholesterol, or percentage of calories as fat. For each group, the percentage of calories as fat and saturated fat were higher than recommended (Kelley, Krummel, Gonzales, Neal, & Fitch, 2004).

McCusker and colleagues (2004) compared individuals with no reported family history of CVD (average risk) to individuals with one reported relative with a history of CVD (moderate risk) and individuals with two or more reported relatives with a history of CVD (high risk). After adjusting for age, there were no differences between the average risk group and the combined moderate/high risk group in their health-related behavior (McCusker et al., 2004). Specifically, there were no differences in cutting back on high-fat foods, increasing consumption of fruits and vegetables, increasing physical activity, or trying to stop smoking (among smokers only) (McCusker et al., 2004). However, the two groups did differ on serum cholesterol screening ($p<0.01$) and aspirin use ($p=0.02$) (McCusker et al., 2004).

A recent study by Andersson and colleagues (2009) examined the impact of a family history of CVD on health promoting behaviors in a sample of Swedish and Polish participants. Compared to individuals with no family history, there was no difference in smoking habits and exercise habits in individuals with a family history (Andersson, Sjoberg, Ohrvik, & Leppert, 2009).

None of the above studies directly measure perceived risk. The researchers assumed that having family members with CVD was the same as an individual perceiving himself or herself as being at increased risk for developing CVD. However, being aware of family members with CVD may not mean that you are aware of your increased risk for developing CVD in the future. Therefore, perceived risk based on family history is distinct from a simple awareness of family members with CVD.

Relationship between Family History of CVD and Perceived Risk

Multiple studies have documented that individuals who reported a family history of heart disease perceived their heart disease risk as higher than average or higher than individuals who did not report a family history (Acheson et al., 2010; Hunt, Davison, Emslie, & Ford, 2000; Montgomery, Erblich, DiLorenzo, & Bovbjerg, 2003; Ponder, Lee, Green, & Richards, 1996). In

two of these studies, individuals with an increased perceived risk for heart disease attributed their elevated risk to heredity or family history (Hunt et al., 2000; Ponder et al., 1996).

Ponder et al. (1996) found that 70% of individuals with an increase perceived risk attributed this increased risk to family history. Hunt and colleagues (2000) found that 76-78% (varied by cohort) of individuals with a family history of heart disease stated that family history had “quite [an] important effect” or “very important effect” on the etiology of heart disease. They also found that perceived family history of heart disease was significantly related to the number of relatives the participants reported as having heart disease ($p<0.0001$) (Ponder et al., 1996).

Despite results by Ponder’s and Hunt’s teams, half of the reviewed studies found that family history alone did not affect perceived risk. In the study by Hunt and colleagues (2000) a significant number of individuals with two first-degree relatives with heart disease (40% to 52% depending on the cohort) did not report a family history of heart disease. The percent of individuals who did not report a history of family heart disease when one first-degree relative was affected was even higher (56% to 83%, depending on the cohort) (Hunt et al., 2000). These individuals scored significantly lower on perceived heart disease risk compared to individuals “aware” of their family history ($p <0.001$), despite similar actual risk (Hunt et al., 2000).

In a study that examined perceived CHD risk in “healthy” offspring of women with premature CHD, about half (47%) of the offspring perceived their CHD risk as equal to or lower than others their age despite being at elevated risk (Allen & Blumenthal, 1998). The majority of the offspring (77%) had three or more major risk factors. Of those at high risk, only 54% perceived themselves at greater risk compared to others their age and gender (Allen & Blumenthal, 1998). An important finding from the study is that only 28% of the sample cited heredity as an important factor in the development of heart disease (Allen & Blumenthal, 1998).

The Family Healthware Impact Trial by Acheson and colleagues (2010) also illustrates the disconnection between family history and perceived risk. In that study, the majority of people

who were at increased risk for heart disease and stroke, based on first- and second-degree relatives with the disease, did not consider themselves at increased risk. For CHD, only 30% of individuals with one or more affected family member actually perceived their risk as being above or much above average risk (Acheson et al., 2010). The percentage of individuals at increased risk for stroke who perceived their risk to be above or much above the average risk was even lower at 21% (Acheson et al., 2010).

Findings from qualitative studies revealed that age, number and closeness of affected relatives (Hunt, Emslie, & Watt, 2001; Walter & Emery, 2005, 2006), symptoms of heart disease in family members (Brorsson et al., 1995; Walter & Emery, 2005, 2006), and fatal events, especially premature deaths (Brorsson et al., 1995; Walter & Emery, 2005, 2006), may influence perceived risk and if an individual is aware of their family history. However, in two of the qualitative studies, individuals did not always perceive themselves at increased risk based on their family history because they felt they were different in important ways from their affected relatives (Hunt et al., 2001; Walter & Emery, 2005, 2006).

Relationship between Perceived Risk and Health-Related Behavior Change

Based on a review of the literature, findings on the relationship between increased perceived CVD risk and positive health-related behavior change are inconsistent (Allen & Blumenthal, 1998; Hunt et al., 2000; Patel et al., 2007). As reported earlier, slightly less than 50% of the offspring in the study by Allen and Blumenthal (1998) reported that their risk for CHD was less or equal to others despite having a mother with premature CHD. This low perceived risk was reflected in the participants' health beliefs and behaviors. Almost one third (31%) of participants were smokers, 56% exercised less than three times a week, and 48% were overweight. In the past year of that study, only 26% of participants improved their diet and 15% increased their amount of exercise (Allen & Blumenthal, 1998). The authors concluded that, despite having multiple modifiable risk factors and a family history of CHD, participants did not

perceive themselves at risk for heart disease (Allen & Blumenthal, 1998). Due to the low perceived risk, participants did not engage in health-related behaviors that could lower their overall risk.

Hunt et al. (2000) examined the relationship between perceived risk and health promotion attitudes and beliefs. Researchers found that individuals with a reported family history were more likely to “agree” or “strongly agree” that not smoking and exercising were important for individuals with a family history of heart disease compared to those individuals with no reported family history ($p<0.001$ for smoking and $p<0.001$ for exercise) (Hunt et al., 2000). However, this relationship only occurred in the youngest cohort (around age 23), suggesting that younger individuals may have a greater awareness of the importance of smoking cessation and exercise in decreasing the risk for developing heart disease (Hunt et al., 2000). The study only examined health promotion attitudes and beliefs; actual behaviors were not measured.

The study by Patel et al. (2007) showed an increased perceived lifetime risk for myocardial infarction (MI) in men and women who reported a family history of MI, compared to those with no family history (in men, 75.0% versus 48.3%, $p=.004$; in women, 59.7% versus 47.4%, $p=.001$). This increased perceived risk resulted in different behaviors in men and women. Men with a family history of premature MI were less likely to be sedentary than men with no family history ($p=.001$) (Patel et al., 2007). However, women with a family history of premature MI were more likely to smoke than those with no family history ($p<.001$). This suggests that the women in the study had less awareness of the risk factors for CVD, resulting in the poor health-related behaviors (Patel et al., 2007).

Summary

There is suggestive evidence that a person’s awareness of their family history of CVD increases the person’s perceived risk for CVD. This increased perceived risk has some, albeit inconsistent, effect on a person’s health-related behavior and positive lifestyle change.

However, being able to list your family members with CVD is not the same as being aware of your family history, nor it is the same as being aware of an increased family risk or personal risk for CVD. Future studies need to use consistent notation and rigorously distinguish between these terms and their measurements.

Recently, the effect of prevention messages tailored to family history on health behaviors from the Family Healthware Impact Trial was published (Ruffin et al., 2011). The study found that individuals who received tailored messages based on their family history information were more likely to increase their fruit and vegetable consumption (OR=1.29; 95% confidence interval [CI]: 1.05-1.58) and increase physical activity (OR=1.47; 95% CI: 1.08-1.98) at six months after the intervention compared to individuals who received standardized messages about healthy lifestyle and screening (Ruffin et al., 2011). This is early suggestive evidence that the use of tailored messages, based on family history, has the potential to impact the health-related behaviors influencing CVD risk. In the intervention arm of that same study, approximately 60% of participants were at moderate or high risk for CHD and 48% were at moderate or high risk for stroke based on their family history (Ruffin et al., 2011). However, the authors of that study reported results in the aggregate for six diseases: CHD, stroke, diabetes, colorectal cancer, breast cancer, and ovarian cancer. It is still unknown if a homogenous sample of persons at risk for CVD based on their family history would demonstrate similar results.

The intervention (described in detail in Chapter 3), developed as part of the dissertation, builds on this study and the previous research by using family history information, along with three-generation pedigrees. The pedigree provides a graphic depiction of family inheritance and risk for CVD to move beyond a simple awareness of family members with CVD to an understanding of how that risk is inherited. The intervention includes tailored messages designed to increase both perceived CVD risk and health-promoting behaviors. The study measures lifetime perceived CVD risk, factors that may increase or decrease this risk, and

intention to engage in a health-promoting lifestyle to better understand the relationships between these variables.

Young Adults and CVD

The lack of a healthy lifestyle, as evidenced by increased obesity prevalence, is becoming more common in children and adolescents and these poor lifestyles choices have major effects later in life (Berenson et al., 1998; Ogden, Carroll, Kit, & Flegal, 2012; Patrick et al., 2004; Verbeeten, Elks, Daneman, & Ong, 2011). This is also true for young adults. According to the National Center for Health Statistics, only 29.1% of 18-44 year olds participate in “vigorous physical activity” three of more times per week. From the same source, 56.2% of 18-44 year olds are overweight or obese (Pleis & Lethbridge-Cejku, 2007).

Although CVD may manifest itself in middle age, it is a “pediatric problem.” The Bogalusa Heart Study, which included subjects between the ages of 2 to 39, found that both coronary and aortic fatty streaks and fibrous plagues increase with age. Among cardiovascular risk factors, BMI, SBP, diastolic blood pressure (DBP), and serum concentrations of cholesterol were strongly associated with the extent of lesions in the aorta and coronary arteries ($r=0.70$; $p<0.001$) (Berenson et al., 1998). These findings indicate that as the number of cardiovascular risk factors increases, so does the severity of asymptomatic coronary and aortic atherosclerosis in young people (Berenson et al., 1998). Results of the Pathobiological Determinants of Atherosclerosis (PDAY) study confirmed that advanced atherosclerosis, lesions vulnerable to rupture, is under way in 3-5% of males by the late teenage years (McGill, McMahan, & Gidding, 2008). The prevalence of these advance lesions increases to 7-23% in females and males between the ages of 30-34 (McGill et al., 2008). The PDAY study also showed that the risk factors measured early in life predict the severity of advanced lesions later in life (McGill et al., 2008).

Young adults are going through a transitional period in their lives. Moving into an

independent living situation creates the potential for unhealthy eating habits (Gores, 2008). The transition into college can cause significant and rapid weight gain (Gow, Trace, & Mazzeo, 2010). The lack of healthy food available on campus, snacking, late-night eating, alcohol-related eating, and eating because of stress or boredom have all been sited by students as factors that influence their weight and dietary habits (Nelson, Kocos, Lytle, & Perry, 2009). At the same time, approximately 30-50% of college students do not participate in adequate amounts of exercise and physical activity (Keating, Guan, Pinero, & Bridges, 2005). Factors related to decreased physical activity in college students include negative experiences when using campus recreation facilities, bad weather, and the lack of time, motivation, and social support (Nelson et al., 2009). Young adults claim they are too busy to participate in blood pressure or cholesterol screenings (Bost, 2005). There is a lack of understanding about their personal risk of developing CVD and they fear that screening may reveal a health problem (Bost, 2005; Deskins et al., 2006; Petrovici & Ritson, 2006). In addition to a lack of understanding about their risk, there is a lack of understanding about the long-term consequences of high blood pressure and elevated cholesterol (Deskins et al., 2006; Lynch, Liu, Kiefe, & Greenland, 2006).

Summary

The development of CVD is strongly correlated with the presence of obesity, hypertension, and elevated serum lipids, which are often present in children, adolescents, and young adults long before cardiovascular problems become symptomatic (Berenson et al., 1998). The degree of these elevated factors in earlier adulthood predict the severity of CVD in later adulthood (Berenson et al., 1998; McGill et al., 2008). These cardiovascular health indicators are influenced by an individual's lifestyle and the choices they make on a daily basis. Young adults with a family history of CVD, who are at higher risk for developing CVD later in life, should specifically be targeted by interventions that promote a healthy lifestyle (Daniels, Pratt, & Hayman, 2011). The intervention, discussed in detail in Chapter 3, was designed to increase

awareness of elevated CVD risk and intention to engage in a healthy lifestyle in young adults with a history of CVD.

Selected CVD Biomarkers of Arterial Vulnerability

This next section will review selected serological biomarkers of arterial vulnerability: LDL-C, apolipoprotein B (apo B), HDL-C, and apolipoprotein A-I (apo A-I). LDL-C and HDL-C were selected because they are methodology standardized, available and convenient, linked to CHD prospectively, part of the Framingham Heart Study Risk Score, and track with disease treatment (Vasan, 2006). Apo B and apo A-I were selected because they are the apolipoproteins found on the LDL and HDL molecules and recent studies suggest they may be a better predictor of CVD risk compared to the traditional markers (Benn, 2009; Andrikoula & McDowell, 2008; Chien et al., 2007; St-Pierre, Cantin, Dagenais, Despres, & Lamarche, 2006).

Elevated LDL-C and Increased CHD Risk

LDL are insoluble lipids containing a steroid-ring nucleus, a hydroxy group, and one double bond in the steroid nucleus (Grundy, 1990). They are the major cholesterol-carrying protein in plasma. LDLs have an apolipoprotein B molecule on its surface. Apo B serves as the ligand on the LDL surface that binds to LDL receptors, which are responsible for transporting LDL molecules into the liver where they are broken down (Grundy, 1990).

Excessive LDL, very-low density lipoprotein (VLDL), and VLDL remnants get infiltrated and entrapped into arterial walls, which is the first step in the process of atherosclerosis (Grundy, 1990; Insull, 2009). Once entrapped in the artery walls, the LDL, VLDL, and VLDL remnants are modified into proinflammatory particles, which initiate an innate inflammatory response. This response causes the endothelial cells to express cellular adhesion molecules and secrete chemokines from smooth muscles, which causes monocytes to enter the arterial wall. At the same time, the smooth muscle cells secrete collagen and elastic fibers into the extracellular matrix (Insull, 2009). Once in the arterial wall, monocytes are transformed into

macrophages producing oxidized foam cells (Hegele, 2009).

These foam cells continue to accumulate and the extracellular lipids combine into pools causing cell necrosis (Insull, 2009). Eventually, these lipid-rich cores grow until they occupy 30–50% of the arterial wall volume. Fibrous tissue is added above the lipid-rich core, just underneath the endothelium, to form a fibrous cap. Next, a thin-cap fibroatheroma develops and, possibly, ruptures. The fibrous cap becomes thin and weakened when enzymatic activity causes the fibrous tissue to dissolve (Insull, 2009). If it ruptures, the thrombogenic interior arterial wall is exposed, producing a potentially life-threatening occlusive clot (Hegele, 2009). However, many ruptures are clinically silent. They heal by forming fibrous tissue matrices of cells, collagen fibers, and extracellular space (Insull, 2009). These may rupture again causing a cycle of rupture-thrombosis-healing. Each of these steps results in calcium deposits. The increasing mass of the plaques can result in stenosis severe enough to cause lethal ischemia due to blood-flow restriction (Hegele, 2009).

Numerous observational epidemiological studies, including the Framingham Heart Study, found a relationship between elevated LDL-C levels and an increased incidence of CHD in both men and women (Stamler et al., 1999; Wilson et al., 1998). The relationship is similar for recurrent CVD events among individuals with established CHD (Pekkanen et al., 1990; Wong, Wilson, & Kannel, 1991).

Due to the extensive evidence of the association between elevated LDL-C levels and increased CHD risk, a normal LDL-C level is the goal to prevent or reduce the risk of CHD. According to the Adult Treatment Panel III guidelines (2002), LDL-C levels < 100 mg/dL throughout life are associated with a very low risk for CHD in populations and are considered optimal (Adult Treatment Panel III, 2002). LDL-C levels > 100mg/dL lead to the development of atherosclerosis, which may result in CHD (Adult Treatment Panel III, 2002).

Low HDL-C and Increased CHD Risk

Cholesterol can only be degraded and excreted by the liver (Grundy, 1990), and cholesterol must be transported to it in order to remove excess cholesterol from peripheral tissues. This process is known as reverse cholesterol transport. In one of the mechanisms of reverse cholesterol transport, apo A-I, which are found on HDL molecules, mediates the process through the adenosine triphosphate-cassette binding transporter (ABC) AI. Scavenger receptor B1 on hepatocytes allow the HDL particles to be taken into the liver where is converted into bile or removed from the body in stool (Grundy, 1990; Natarajan, Ray, & Cannon, 2010). Low HDL-C levels, less than 40 mg/dL, are associated with less removal of LDL from the arterial walls. This allows LDL in be infiltrated and entrapped in the arterial walls, which begins the process of atherosclerosis described above.

Elevated Apo B and Increased CHD Risk

Plasma level of apo B is a relatively new biomarker that may be a better measure of circulating LDL particle concentration and a better indicator of risk than LDL-C (Benn, 2009; Contois et al., 2009). Apo B is a component of all atherogenic or potentially atherogenic particles, including LDL, VLDL, nascent VLDL (also know as intermediate-density), and lipoprotein(a). Therefore, apo B provides a direct measure of the number of atherogenic lipoprotein particles in the circulation. Apo B levels can be reduced through exercise and dietary changes (Dreon, Fernstrom, Miller, & Krauss, 1994; Holme, Hostmark, & Anderson, 2007; Matthan et al., 2004).

The Copenhagen City Heart Study examined the prediction of ischemic heart disease and MI in a general population, both women and men, using apo B levels (Benn, Nordestgaard, Jensen, & Tybjaerg-Hansen, 2007). Women with high apo B levels, > 95 mg/dL, had a hazard ratio for ischemic heart disease of 1.8 (95% CI: 1.2–2.5) and for MI of 2.6 (95% CI: 1.4–4.7) versus women with low apo B levels, < 75 mg/dL. Men with high apo B levels, > 95 mg/dL, had

a hazard ratio for ischemic heart disease of 1.9 (95% CI: 1.5–2.6) and for MI of 2.4 (95% CI: 1.5–3.6) versus men with low apo B levels, < 76 mg/dL. Additionally, apo B was superior to LDL-C in the prediction of ischemic heart disease and MI in both genders ($p<0.001$ for prediction of ischemic heart disease and $p=0.004$ for prediction of MI in females; $p=0.01$ for ischemic heart disease and $p=0.03$ for MI in males). Several other studies have reported similar results with respect to the predictive ability of apo B for ischemic heart disease (Chien et al., 2007; Ridker, Rifai, Cook, Bradwin, & Buring, 2005; St-Pierre et al., 2006).

Normal apo B levels range from 55-150 mg/dL for men older than 18 years old and from 45-150 mg/dL for women older than 18 years old (Fischbach & Dunning III, 2008). Values above 110mg/dL indicate increased risk of CVD (Fischbach & Dunning III, 2008).

Low Apo A-I and Increased CHD Risk

Apo A-I is a component of HDL and, as previously mentioned, mediates the process of reserve cholesterol transport. Apo A-I levels measure the number of LDL-clearing apolipoproteins in circulation. Apo A-I is used with apo B to determine the ratio LDL-clearing particles to potential atherogenic particles in circulation.

Apo A-I levels range 90-155 mg/dL for men older than 18 years old and from 94-174 mg/dL for women older than 18 years old (Fischbach & Dunning III, 2008). Values less than 90 mg/dL indicate increased risk of CVD (Fischbach & Dunning III, 2008).

LDL and HDL Versus Apo B and Apo A-I

A recent study by the Emerging Risk Factors Collaboration that involved over 300,000 individuals, found that lipid assessment in vascular disease can be simplified by measuring either cholesterol levels or apolipoproteins (Di Angelantonio et al., 2009). In the study, the hazard ratios using non-high density lipoprotein cholesterol (non-HDL-C) and HDL-C were almost identical to the hazard ratios using apo B and apo A-I. Additionally, the study found that hazard ratios were similar for measures of non-HDL-C and directly measured LDL-C. The

authors suggest that discussion about whether is it better to measure cholesterol levels or apolipoproteins to assess vascular disease risk should be based on practical consideration such as cost and availability (Di Angelantonio et al., 2009). Another consideration is if one set of tests are more easily understood or comprehended by patients. A greater comprehension of the implications of a set of test could lead to behavior changes that reduce CHD risk.

Summary

Either LDL-C and HDL-C or apo B and apo A-I can be used to evaluate an individual's CVD risk. Both sets of tests measure the balance of particles known to cause atherosclerosis, LDL and apo B, and the particles known to remove LDL from the arterial wall, HDL and apo A-I, which prevents or slows atherosclerosis. LDL-C and HDL-C have been more extensively studied (Vasan, 2006) and the guidelines for reducing CHD risk utilized them (Adult Treatment Panel III, 2002). More providers are familiar with LDL-C and HDL-C compared to apo B and apo A-I (Contois et al., 2009). At the University of Washington Medical Center, the test for apolipoproteins (apo B and apo A-I) is twice the cost of a lipid panel (LDL-C and HDL-C) (Research Testing Services, personal communication, April 2011). However, the recent research suggests that apo B and apo A-I may be a better predictor of CVD risk (Chien et al., 2007; Ridker et al., 2005; St-Pierre et al., 2006).

As part of the intervention, a venous blood sample was drawn after 12-hours of fasting and levels of LDL-C, HDL-C, apo B, and apo A-I were analyzed. In Session Two, before the lab results were given to participants, a cartoon was used to explain the similarity and differences between the tests. Both sets of tests were used in the study to determine if participants had a preference or better understanding of one set of tests compared to the other. See Chapter 3 for more details.

Common SNPs Associated with Increased CHD Risk

Genetic factors often influence an individual's susceptibility to environmental risk factors

and contribute to elevated LDL-C levels. Perhaps the most studied type of genetic variants are SNPs, DNA sequence variations that occur when a single nucleotide (A, T, C, or G) in the genome sequence is altered (U.S. Department of Energy, 2008). Many SNPs have no apparent effect on cell function, but others can predispose people to disease by altering encoded proteins and gene expression (Hindorff et al., n.d.).

Discussed below are three SNPs in three different genes, Low-density Lipoprotein Receptor (*LDLR*), Apolipoprotein B *(APOB),* and 3-Hydroxy 3-Methylglutaryl Coenzyme A Reductase *(HMGCR),* that have been confirmed to be associated with increased CHD or MI in two or more candidate gene studies or genome wide association studies. The presence of each variant is associated with small, but statistically significant, increases (effect size) in CHD risk (Table 2.1).

The G allele of the intronic SNP rs6511720 in *LDLR* has been associated with hypercholesterolemia in Europeans/Caucasians (Kathiresan et al., 2009; Sabatti et al., 2009; Willer et al., 2008). The LDL receptor is essential in receptor mediated LDL uptake. The susceptibility allele is associated with higher rates of CAD (OR=1.29, 95% CI: 1.10–1.52) (Willer et al., 2008).

Variants in the *APOB* gene have been associated with high apo B levels. A synonymous SNP rs693 has been replicated in five GWASs, four involving Europeans/Caucasians and one involving a Japanese sample (Aulchenko et al., 2009; Kathiresan et al., 2008; Nakayama et al., 2009; Sabatti et al., 2009; Willer et al., 2008). The A allele is associated with increased LDL-C production rate and increased CAD risk (OR=1.07, 95% CI: 1.00-1.14) (Willer et al., 2008).

The association between the G allele at SNP rs3846662 in *HMGCR* and elevated LDL-C levels has been replicated in GWASs of European/Caucasians, Japanese, and Micronesians (Aulchenko et al., 2009; Burkhardt et al., 2008; Hiura et al., 2010; Kathiresan et al., 2008; Kathiresan et al., 2009; Sabatti et al., 2009). The intronic SNP results in the alternative splicing

for exon 13, alternating the rate limiting effect of the HMGCR enzyme in cholesterol synthesis (Hiura et al., 2010). The risk allele is associated with increased MI risk (OR=1.15, 1.04-1.28) after adjusting for age, sex, diabetes, hypertension, and smoking status (Hiura et al., 2010).

Table 2.1. SNPs Tested for in the Study Sample

Gene Name	Function	SNP (rs #)	Chromo-some location	Suscepti-bility Allele	Population Studied	MAF	OR
Low-density Lipoprotein Receptor (*LDLR*)	Essential for LDL uptake into liver cells	rs6511720	19p13.2	G	European/ Caucasians	0.90	For CAD: 1.29 (95% CI: 1.1-1.52)
Apolipoprotein B *(APOB)*	Serves as the ligand on the LDL surface that binds to LDLR	rs693	2p24.1	A	European/ Caucasians Japanese	0.49 0.06	For CAD: 1.07 (95% CI: 1.0-1.14) N/A
3-hydroxy 3-Methylglutaryl Coenzyme A Reductase *(HMGCR)*	Responsible for the rate-limiting effect in cholesterol synthesis	rs3846662	5q13.3	G	European/ Caucasians Japanese Micronesian	0.43 0.54 ~0.4	N/A For MI: 1.15 (95% CI: 1.04-1.28) N/A

SNP = single nucleotide polymorphism; rs # = reference sequence number; MAF = minor allele frequency from the HapMap database (refSNP 693, n.d.; refSNP 3846663, n.d.; refSNP 6511720, n.d.); OR = odds ratio

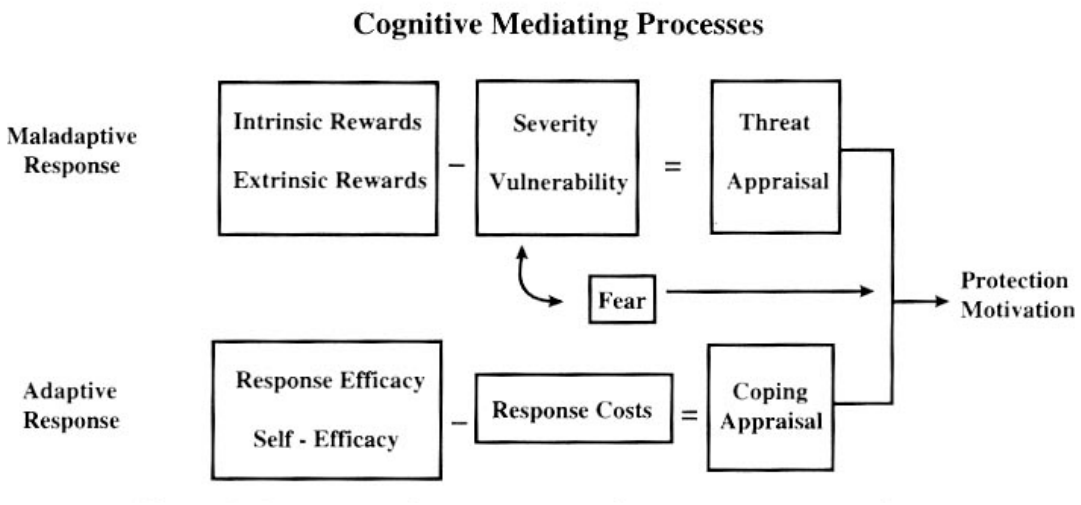
These SNPs were selected to be included in the study because the susceptibility allele is common (ranging from .43 to .90 is Non-Hispanic Caucasians) and commercially made primers for genotyping are readily available.

Protection Motivation Theory

Protection Motivation Theory was initially developed by Rogers in 1975 to provide conceptual clarity to the understanding of fear appeals (Prentice-Dunn & Rogers, 1986). It was later revised to focus on the cognitive process responsible for mediating attitudinal and behavior

change (Prentice-Dunn & Rogers, 1986). In PMT, environmental and intrapersonal sources of health threat initiate two cognitive processes, threat appraisal and coping appraisal (Figure 2.1).

Figure 2.1. Protection Motivation Theory



From: Floyd, Prentice-Dunn, & Rogers, 2000. Used with permission.

Threat appraisal involves the evaluation of maladaptive response (Fry & Prentice-Dunn, 2006). Maladaptive responses about CVD are to not quit smoking, not exercise, and not eating a healthy diet. The amount of threat experienced is a combination of severity and vulnerability minus the rewards. PMT defines severity as the degree of harm of an unhealthy behavior, vulnerability as the probability that you will personally experience harm, and rewards as the positive aspects of starting or continuing the unhealthy behavior (Floyd, Prentice-Dunn, & Rogers, 2000; Fry & Prentice-Dunn, 2006; Prentice-Dunn & Rogers, 1986).

The coping appraisal process involves a person's evaluation of their ability to address the threat. This is a combination of response efficacy and self-efficacy minus response costs. PMT defines response efficacy as the effectiveness of the recommended behavior in removing or preventing possible harm. Self-efficacy is the belief that one can successfully enact the recommended behavior. Response costs is defined as the costs associated with the

recommended behavior belief (Floyd et al., 2000; Fry & Prentice-Dunn, 2006; Prentice-Dunn & Rogers, 1986).

How the PMT was used to develop the intervention will be discussed in Chapter 3.

CHAPTER 3.

INTERVENTION AND STUDY DESIGN

Purpose

The purpose of this feasibility and pilot study was to examine the short-term impact of a theoretically driven, educational intervention on perceived CVD risk and behavioral intention to change health-related behavior to reduce CVD risk factors in asymptomatic young adults with a known family history of CVD. The impact of the intervention was evaluated within a single group, pre-test post-test design and the quantitative data was examined using non-parametric statistics and the qualitative data were examined using thematic content analysis. The intervention incorporated each young adult's family medical history; utilized a three-generation pedigree in order for participants to visualize the inherited risk within their family; and used the presentation of personalized CVD risk information based on family history and LDL-C, HDL-C, apo B, and apo A-I levels. Also, genetic testing was performed on blood samples from the participants to look for genetic variants associated with an elevated risk for CHD. These results were compared to allele frequencies in the HapMap database and the relationship between the susceptibility alleles and lab results were examined.

Study Aims, Sub-Aims, and Hypotheses

This study, named the My Family Medical History and Me Study, had three primary aims. The first primary aim was examining the feasibility of the intervention and the overall study design. Even though the intervention was built around a theoretical framework and was designed to address many of the weaknesses found in other studies, it was unknown if the intervention would be engaging and tolerated by the study participants. The second primary aim was to gain a better understanding of what young adults with a family history of CVD knew about CVD risk factors, what they perceived their lifetime CVD risk to be, their intentions to engage in a health promoting lifestyle, and to explore the relationships between these factors.

The third primary aim of the study was to evaluate the impact of the intervention on CVD knowledge, perceived risk, and intention to engage in a healthy lifestyle in order in reduce the risk factors for CVD.

Primary Aim 1

Examine the feasibility of recruitment; the overall study design and adherence; study participants' willingness to gathering family medical history; and their willingness to provide blood samples for biological testing and DNA genotyping. Assess which components of the intervention were useful to the study participants and the components that require improvement (analysis of the open-ending questions).

Hypothesis 1: The study with its current design is feasible. Young adults will actively gather medical history information from their family members and provide a blood sample for biological testing and DNA genotyping.

Primary Aim 2

Examine and describe baseline perceived CVD risk in asymptomatic young adults with a self-reported family history of CVD; the factors that influence perceived lifetime CVD risk in young adults; and the relationship between heart disease knowledge, perceived CVD risk, and behavioral intention to reduce CVD risk factors.

Sub-aim 2.1*:* Describe the baseline perceived lifetime CVD risk in asymptomatic young adults with a self-reported family history of CVD.

Hypothesis 2.1: Perceived lifetime CVD risk in asymptomatic young adults with a self-reported family history of CVD will be low (a score of 4 or less on the visual analogue scales).

Sub-aim 2.2: Describe factors that influence perceived CVD risk in young adults.

Hypothesis 2.2: Perceived CVD risk in young adults is influenced mainly by age and lifestyle.

Sub-aim 2.3: Describe the relationship between heart disease knowledge and perceived lifetime CVD risk.

Hypothesis 2.3: Increased heart disease knowledge will be associated with increased perceived CVD risk.

Sub-aim 2.4: Describe the relationship between perceived CVD risk and young adults' behavioral intentions to engage in CVD-risk reducing behaviors.

Hypothesis 2.4: An increased in perceived CVD risk will cause an increase in intention to quit smoking, intention to increase physical activity to meet the recommendations, and intention to eat a healthy diet.

Primary Aim 3

Compare heart disease knowledge, perceived CVD risk, and intention to engage in behavioral changes to reduce CVD risk factors at baseline and post-intervention.

Sub-aim 3.1: Examine, using both quantitative and qualitative data, the impact of young adults obtaining their family health history and the presentation of personalized CVD risk information on perceived CVD risk.

Hypothesis 3.1: Threat communications (discussions with family members about CVD, elevated risk based on family medical history and lab results, and the review of family medical history) will result in increased perceived lifetime CVD risk.

Sub-aim 3.2: Examine if heart disease knowledge and behavioral intention to engage in CVD risk reducing behaviors increases from baseline to post-intervention.

Hypothesis 3.2: CVD risk reducing health behaviors and heart disease knowledge will increase from baseline to post-intervention.

Exploratory Aim 1

Examine the presence of single nucleotide polymorphisms (SNPs) associated with an elevated risk of coronary heart disease in an at-risk, young adult population. Explore the relationship between susceptibility alleles and LDL-C and apo B levels.

Study Design and Methods

Conceptual Framework

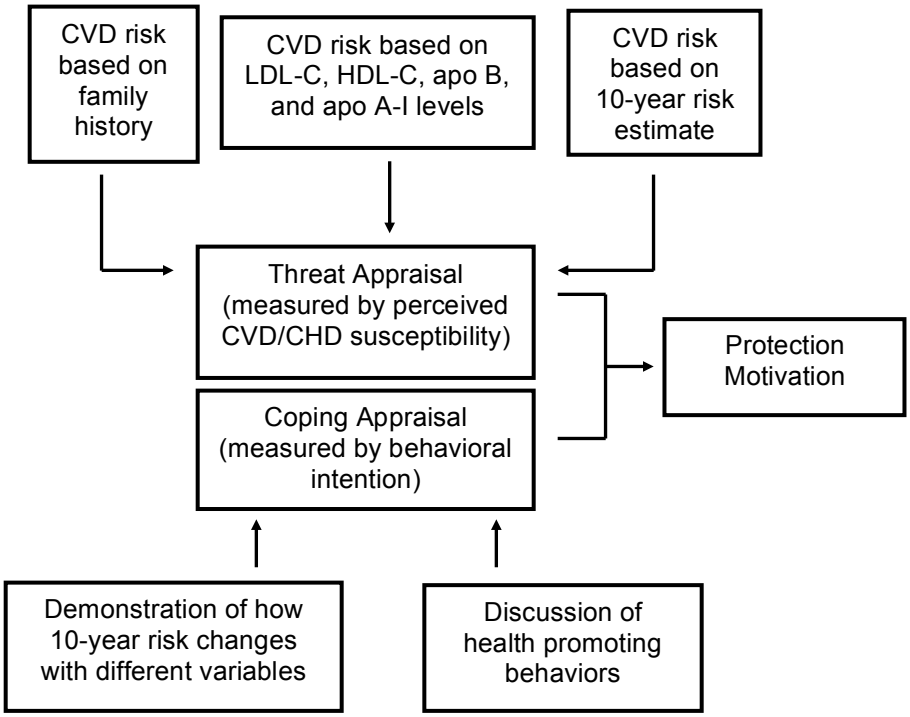
A two-session, educational intervention was designed based on a review of the previous research. The intervention was scripted and used a standardized protocol to provide tailored messages about lifetime CVD risk based on family medical history and CVD biomarkers and to provide brief counseling to promote a healthy lifestyle. The study measured perceived lifetime CVD risk and factors that may increase or decrease this risk and intention to engage in a health-promoting lifestyle. The content and structure of the intervention are derived from the Protection Motivation Theory (PMT), previously discussed in Chapter 2 (Figure 2.1).

This intervention focused on affecting both threat appraisal and coping appraisal. The intervention utilized multiple methods to increase threat appraisal by providing CVD risk information based on the participant's family history, the presentation of family history in a pedigree format in order for the participant to visualize the patterns of inheritance, current blood values of CVD risk indicators, and other factors including smoking status and blood pressure. The intervention also included information about how to decrease the individual's CVD risk through healthy lifestyle changes (Figure 3.1). This information, and the activities included in the intervention, were designed to increase the individual's understanding of the response efficacy of a healthy lifestyle and the person's self-efficacy to make those changes.

Sample and Recruitment

The target sample for the study was 12 to 20 participants. Although the focus of the study was on young adults with a family history of CVD, all individuals "interested in their

Figure 3.1. Protection Motivation Theory and Relationship to Components of Intervention



Abbreviations: CVD = cardiovascular disease; LDL-C = low-density lipoprotein cholesterol; HDL-C = high-density lipoprotein cholesterol; apo = apolipoprotein
Adapted from: Floyd, Prentice-Dunn, & Rogers, 2000; Fry & Prentice-Dunn, 2006.

family medical history" were initially recruited. This initially inclusive recruitment plan was done to help determine the number of young adults needed-to-be-screened to find those with a family history of CVD. After initial recruitment, all individuals were screened for a family history of CVD and the conditions know to increase CVD risk (see Inclusion/exclusion criteria). Those not eligible for the study were given the website for the Surgeon General's "My Family Health Portrait" (https://familyhistory.hhs.gov/). This website allows people to enter their family health history to share with family members or healthcare providers and the information can be saved and updated over time.

Every attempt was made to balance gender in the study sample. Attempts were also made to recruit a diverse sample that reflected the population of college students from universities in the urban region of a large city in the Pacific Northwest. Recruitment posters were

placed in both male and female dorms, common areas such as the undergraduate libraries and near dining establishments, and the hallways of lecture halls. Both males and females enrolled in the study were encouraged to talk to their friends about the study.

The main recruitment site was the University of Washington, Seattle Campus. After Institutional Review Board (IRB) review and approval, students were recruited through fliers placed throughout campus, a website that advertised research studies for healthy volunteers, and by word-of-mouth. The secondary recruitment site was Seattle University's Student Health Center. Recruitment brochures were placed in exam rooms for participants to review before their appointment with a provider. Additionally, providers were encouraged to give recruitment brochures to the patients that met the eligibility requirement. All recruitment was self-referral, meaning that it was up to the individual to contact the researcher to find out more information about the study. Participants received $20 after completing the first session and $30 after the second session to compensate for their time.

The study was approved by the University of Washington's Human Subjects Division (IRB application 40470). The IRB at Seattle University reviewed the study and determined that separate approval was not needed because all study procedures were reviewed and approved by the IRB at the University of Washington and the intervention occurred at the University of Washington.

Inclusion/exclusion criteria. To be eligible for the study, the individual had to be between the ages of 18 to 25; able to speak, read, and write English; have a family history of CVD or conditions known to increase CVD risk; and be able to attend the two intervention sessions at the study site campus. For the purpose of this study, a family history of CVD included myocardial infarction, angina, congestive heart failure, and stroke. The conditions that were used to reflect increased risk for developing CVD were hypertension, hypercholesterolemia, hypertriglyceridemia, or hyperlipidemia.

Exclusion criteria included being pregnant; having a history of congenital heart defects; a current diagnosis of hypertension, hypercholesterolemia, or diabetes; and the inability to gather the medical histories on their biological parents, grandparents, or siblings. Pregnancy was included in the exclusion criteria because the diet and exercise recommendations given in the intervention may not be consistent with the nutritional needs and exercise recommendations during pregnancy. Those with a diagnosis of hypertension, hypercholesterolemia, or diabetes were excluded from the study because they should already have an increased perceived lifetime CVD risk and be engaging in a health lifestyle to reduce this risk. Inclusion of these individuals would have increased the risk for a Type II error.

Study Procedures

The study protocol involved two sessions, each lasting approximately an hour to an hour and a half. In Session One, the focus was on collecting baseline data and the family medical history information from memory. After Session One, the participant was asked to contact their family members to check the accuracy of this information and make any corrections as needed. Session Two, which occurred approximately two weeks after Session One, focused on updating the family medical information based on anything the participant learned between the two sessions; providing the participant with information regarding their risk for developing CVD in their lifetime; interactive counseling on lifestyle changes to decrease the participant's CVD risk; and post-intervention data collection (Figure 3.3). Both sessions were digitally audio-recorded. The participants' responses to the open-ended questions at the end of Session Two were transcribed for data analysis purposes.

Session one. After informed consent was obtained (Appendix B), study participants were given an identification number. The identification number was the only personal link to the individual on all study forms, except the demographic information sheet, and lab specimens. Next, the participant's height, weight, and blood pressure were measured. If the study

Figure 3.3. Study Activities

Session One

- Consent
- Height, weight, and BP measurement
- 12-hour fasting blood sample
- Data collection
  - Demographic information
  - Heart Disease Knowledge Questionnaire
  - Visual Analogue Scales
  - CVD Susceptibility
  - Behavioral Intention Measures
- Family history collection
- Draw and review pedigree
- Review family history collection "assignment"

Session Two

- Discuss "baseline" family history versus "verified" family history
- Ask single-item questions about perceived risk and likelihood to take action
- Discuss updated family history information and pedigree
- Provide CVD risk based on family history
- Repeat single-item questions
- Review labs and provide CVD risk based on ATP-III Guidelines
- Provide 10-year CVD risk
- Discuss health promoting behaviors
  - Exercise
  - Healthy diet
- Repeat study measures
- Open-ended questions

participant agreed to provide a fasting blood sample, they were escorted to the University of Washington Medical Center's Blood Draw where a venous blood sample was obtained by a trained phlebotomist to determine their fasting LDL-C, HDL-C, apo B, and apo A-I levels. After the study participant was escorted back to the research study office, they completed a demographic information sheet, which included questions about alcohol and tobacco use and exercise. Study participants also completed the Heart Disease Knowledge Questionnaire, visual analog scales to measure perceived lifetime CVD risk, the CHD Susceptibility Questionnaire, and the measures of behavioral intention (See Appendix A for study measures/materials).

Next, the Family Medical History Form (Appendix A) was administered to obtain information about the individual's family members regarding their history of CVD and the conditions known to increase CVD risk. No identifying information, including name, initials, day of birth or death, and place of birth, were collected on the family members. As the information was collected, the study investigator entered the information into a computer-based questionnaire. A version of this form with the participant's ID number was then saved on a password protected computer file. Another version, without an ID number, was printed and

given to the participant. The printed version was reviewed for completeness and accuracy by the study participant while the study investigator entered the study participant's family medical history data into a computer program, Progeny, that created the pedigree. Once completed, the pedigree was also printed out and a copy was given to the study participant. The investigator then explained the importance of verifying the family history information and the participant was encouraged to talk to as many family members as possible to check the information. Session Two was scheduled at the completion of Session One.

Session two. The main focus of Session Two was to provide the participant with information about their CVD risk. The investigator used three sources to provide this information: lifetime CVD risk based on family history; current CVD risk based on LDL-C, HDL-C, apo B, and apo A-I levels; and 10-year CHD risk based on data from the Third Report of the Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults Guidelines, also known as the ATP-III Guidelines (Adult Treatment Panel III, 2002).

The second session began by having the participant discuss any differences between what he or she thought was his or her family history and what they found to be their actual family history, using information they obtained by interviewing their family members. This was followed by two verbally administered single-item questions about the study participant's perceived risk of developing CVD in their lifetime and their likelihood to take action to change their risk factors (Appendix A). Next, the three-generation pedigree was updated with any new information that participants had gathered. After the pedigree was updated, the participant was given a copy of the pedigree. The investigator used the pedigree to show the patterns of inheritance regarding CVD and explained their generalized CVD risk based on their family history ("low" if they had no family members with CVD, "moderate" if they had one family member with CVD, or "high" if they had more than one family member with CVD). This method of providing generalized risk information based on all family members was consist with the

methods used in studies by Acheson and colleagues (2010), McCusker and colleagues (2004), and Ruffin and colleagues (2011.) Next, they were told their personal odd ratios for developing CVD in the future or having a CVD event based on the number of first-degree relatives they had with CVD or premature CVD. See the “Estimated Odds for Developing CVD” section in this chapter for more information about the personal odd ratios provided in the intervention based on first-degree relatives. After this information was told to the participant, they were again asked the same two single-items questions about their perceived risk and likelihood to take action to change their risk factors. This measure was re-administered to assess if the review of their pedigree and explanation of their CVD risk based on family members had an immediate effect.

The second “method” used to communicate the individual’s CVD risk was the discussion of their lab values. The individual’s total cholesterol, LDL-C, HDL-C, apo B, and apo A-I levels were reviewed and discussed. For each of the lab values, the participant was told if they were within or outside of the recommended range based on their risk factors. The information provided to the participants was based on the ATP-III Guidelines and *A Manual of Laboratory and Diagnostic Tests (8th ed.)* (Adult Treatment Panel III, 2008; Fischbach & Dunning III, 2008).

Finally, the third “method” that was used to provide the participant with information about their CVD risk was the Risk Assessment Tool for Estimating 10-year Risk of Developing Hard CHD (Myocardial Infarction and Coronary Death) (Adult Treatment Panel III, n.d.). This tool, based on data from the Framingham study and the ATP-III report, determines a person’s 10-year risk for having or dying from a heart attack. It is based on the person’s age, sex, total cholesterol, HDL-C, smoking status, SBP, and if they are on medications for high BP. First, the participant was given his or her current risk. Then the data were altered (e.g., age increased, smoke status changed, total cholesterol changed) to show the participant how their risk changed with different variables. The investigator stressed to the participant that this estimate

did not include family history information and that if they had a family history of CVD, their 10-year risk was actually higher than that provided.

The other purpose of this intervention was to provide information on the lifestyle changes that have potential to lower the participant's risk for developing CVD. Study participants were given information on lifestyle changes, including increasing their physical activity and eating a healthy diet. Information on smoking cessation was available, but none of the study participants smoked. Many of the participants were already engaged in a healthy lifestyle. For those individuals, the information was a review. For participants not engaged in a healthy lifestyle, the information was aimed at helping them make better decisions and changes in their lives.

Additionally, study participants were given pamphlets from the American Heart Association (AHA). These pamphlets were selected because the information is accurate, written using everyday language, and avoids professional jargon. It is also widely available to all healthcare providers through the AHA website. The three pamphlets from the AHA that were used were: *Controlling Your Risk Factors: Our Guide to Reducing your Risk of Heart Attack and Stroke, Just Move: Our Guide to Physical Activity,* and *Making Healthy Food and Lifestyle Choices.*

Table 3.1. Open-Ended Questions Asked at the End of Session Two

- What, if anything, have you gained by collecting your family history?
- What, if anything, were you surprised to learn about your family's health?
- Based on the information you have provided and your family's pedigree, do you think you have a family history of CVD?
- What information that you received during your two sessions together, if any, was most influential on informing your personal knowledge of your family history of CVD?
- What information that you received, if any, was most influential on informing your personal risk for CVD in the future?
- Given what you have learned, what do you want to do to stay healthy and reduce your risk?
- What, if anything, would you like to learn from a health expert to be as healthy as possible, given your family's health history?

After the discussion of lifestyle changes, the participant was asked to complete the same set of measures of the study outcomes that had been administered at baseline. Finally, the participant was asked seven open-end questions (Table 3.1).

Instruments and Measures

A total of nine questionnaires and study measures were administered: a demographic information questionnaire; the Heart Disease Knowledge Questionnaire; a series of visual analogue scales; a CHD Susceptibility Questionnaire; three behavioral intention measures for smoking cessation, exercise, and eating a healthy diet; and two single-item questions about perceived CVD risk and likelihood to take action to change risk factors (Appendix A). Each of the study measures were selected to fit both the study aims and the concepts of PMT (Table 3.2).

Table 3.2. Study Sub-aims, Measures, and PMT Concepts

Study Sub-aims	Study Measure	PMT Concepts
Aim 2.1: Baseline perceived lifetime CVD risk	Visual analogue scales for CVD risk, CHD Susceptibility Questionnaire	Threat appraisal at baseline
Aim 2.2: Factors that influence perceived CVD risk in young adults	Visual analogue scales for CVD risk, Open-ended questions	Vulnerability for CVD
Aim 2.3: Relationship between heart disease knowledge and perceived CVD risk	Heart Disease Knowledge Questionnaire, visual analogue scales for CVD risk, CHD Susceptibility Questionnaire	Knowledge about CVD severity and vulnerability; Threat appraisal
Aim 2.4: Relationship between perceived CVD risk and behavioral intentions	Visual analogue scales for CVD risk, CHD Susceptibility Questionnaire, Smoking Cessation Intention, Intention to Exercise, Healthy Diet Intention, Single-item Questions, Open-ended Questions	Response efficacy and self-efficacy
Aim 3.1: Change in perceived CVD risk/CHD susceptibility	Visual analogue scales for CVD risk, CHD Susceptibility Questionnaire, Single-item Questions, Open-ended Questions	Threat appraisal
Aim 3.2: Change in CVD-risk reducing health behaviors and heart disease knowledge	Smoking Cessation Intention, Intention to Exercise, Healthy Diet Intention, Heart Disease Knowledge Questionnaire	Knowledge about CVD severity and vulnerability; Threat appraisal

The first questionnaire consisted of demographic information and questions about alcohol consumption, smoking status, and exercise habits. Alcohol use was measured using the AUDIT-C. This 3-item alcohol screen can identify individuals who are hazardous drinkers or have active alcohol use disorders (Bradley et al., 2003; Bradley et al., 1998; Bush, Kivlahan, McDonell, Fihn, & Bradley, 1998). The demographic questionnaire will be used in the first session only.

The second study measure was the Heart Disease Knowledge Questionnaire, which was a modified version of the Heart Disease Facts Questionnaire. The original Heart Disease Facts Questionnaire is a 25-item questionnaire that was developed to tests respondents' knowledge of major risk factors for the development of CHD; it is readable to an average 13-year old (Wagner, Lacey, Chyun, & Abbott, 2005). It has adequate internal consistency, with a Kuder–Richardson-20 formula of 0.77 (Wagner et al., 2005). The original questionnaire contained 10 items that tested knowledge regarding the increased risk for developing CHD in individuals with diabetes (Wagner, Lacey, Abbott, de Groot, & Chyun, 2006; Wagner et al., 2005). Because a current diagnosis of diabetes was part of the exclusion criteria, the questions related to diabetes were removed resulting in the 15-item modified version.

The third study instrument was a set of visual analog scales for perceived CVD risk. The instrument consisted of a 100-mm vertical line with half-inch perpendicular lines at each end with the words "High Risk" at the top and "No Risk" at the bottom. Every 10-mm there was an additional tick numbered 1 through 9 with the first tick mark on the bottom labeled as 1 with the number increasing the higher up the scale. The participant was asked to mark his or her risk for developing CVD in their lifetime base on their age, race/ethnicity, sex, current lifestyle, family history and overall CVD risk. A mark between numbers 1 and 4 was interpreted as low perceived risk. A mark on line number 5 was interpreted as uncertainty of risk. A mark between numbers 6 and 9 was interpreted as high perceived risk (Cline, Herman, Shaw, & Morton,

1992). In a recent study by Jones and colleagues, the scale had a five-week test-retest reliability of .79 (Jones, Weaver, & Friedmann, 2007). The participant was also asked to rank the order in which the five factors influences their lifetime CVD risk.

The fourth study measure was the CHD Susceptibility Questionnaire. The main dependent variable studied was perceived CVD risk. In order not to rely on only one measure, this second measure of perceived CHD risk was included. The CHD Susceptibility Questionnaire is a 5-item questionnaire that uses a 4-point Likert scale ranging from Strongly Disagree (1) to Strongly Agree (4). The CHD Susceptibility Questionnaire is the susceptibility subscale from the Health Beliefs Related to Cardiovascular Disease Scale, which is a 25-item questionnaire aimed at measuring the constructs of the Health Belief Model (Tovar, Rayens, Clark, & Nguyen, 2010). The entire 25-item scale is written at a sixth grade reading-level (Tovar et al., 2010). The susceptibility subscale has internal consistency reliability coefficient, Cronbach's alpha, of 0.91 (Tovar et al., 2010).

Behavioral intention to engage in exercise and healthy diet was measured by three questions about exercise and three questions about a healthy diet. The exercise intention measure was based on one used by de Bruijin and Rhodes (2010) and recommendations from Francis and colleagues (Francis et al., 2004). In their exercise study involving over 500 undergraduate students, the exercise intention measure had an internal consistency reliability coefficient, Cronbach's alpha, of 0.92 (de Bruijn & Rhodes, 2010). The three-question measure for eating a health diet is from Armitage and Conner (1999). In their study of 221 participants with a mean age of 23, the mean of the three items produced a composite scale with an internal consistency reliability coefficient, Cronbach's alpha, of .86 (Armitage & Conner, 1999).

The smoking cessation contemplation ladder was developed as a measure of readiness to consider smoking cessation (Biener & Abrams, 1991). Data collected from over 400 smokers at two sites indicate that the measure's scores were significantly associated with reported

intention to quit in the next six months (p<.001). The scores also predicted subsequent participation by the subject in a program designed to educate the individual on their smoking habit and its risks (p<.001) (Biener & Abrams, 1991). Due to that fact that no study participant smoked, this measure was not actually used in the study.

In order to determine if the discussion of family medical information regarding CVD and risk information based on family member with CVD, by itself, had an impact on perceived risk and intention towards taking action to reduce risk factors, two verbally administered single-item questions were developed. The first question assessed “risk for developing CVD in your lifetime” using a 7-point Likert Scale ranging from No Risk at All (1) to Very High Risk (7). The second question assessed “how likely are you to take action to change your risk factors” using a 7-point Likert Scale ranging from No Action (1) to All Possible Actions (7).

Estimated Odds for Developing CVD

In the intervention, participants were given their personal odds for developing CVD in the future or having a CVD event based on the number of first-degree relatives they have with CVD or premature CVD. This information was based on a review of the literature. Multiple retrospective and prospective studies have examined the odds of an individual developing CVD in their lifetime based on the CVD history of their parents and siblings (Austin et al., 2000; Bertuzzi et al., 2003; Ciruzzi et al., 1997; Friedlander et al., 2001; Friedlander et al., 2002; Jousilahti, Puska, Vartianinen, Pekkanen, & Tuomilehto, 1996; Leander et al., 2001; Lloyd-Jones et al., 2004; Murabito et al., 2005; Nilsson, Nilsson, & Berglund, 2004; Sesso et al., 2001; Silberberg et al., 1998). While each of these studies examined different measures of CVD, for example Bertuzzi and colleagues (2003) examined acute MI during lifetime while Leander and colleagues (2001) examined lifetime risk of CHD, it was possible to provide an individual with their CVD risk based the CVD history of their parents and siblings. Specific text in the study protocol follows.

In the intervention, when a study participant had one family member with CVD, they were told, “The research has shown that individuals with a single first-degree relative with a history of CVD are about twice as likely to develop CVD or have a future CVD event compared to someone without a family history of CVD.” Studies have estimated the odds ratio or relative risk for having a MI or CHD in their lifetime for the offspring of a parent who had a MI or CHD to be between 1.48-2.63 (Ciruzzi et al., 1997; Friedlander et al., 2001; Jousilahti et al., 1996; Silberberg et al. 1998). If that single first degree-relative had premature CVD, defined as before the age of 55 in males and 65 in females, they were told, “The research has shown that individuals with a single first-degree relative with a history of early or premature CVD are about three to four times more likely to develop CVD or have a future CVD event compared to someone without a family history of CVD.” Studies have estimated the odds ratio or relative risk for having a MI or CHD in their lifetime for the offspring a parent who had a premature MI or CHD to be between 2.66-4.6 (Friedlander et al., 2002; Jousilahti et al., 1996; Silberberg et al. 1998).

If the participant had two family members with CVD, they were told, “The research has shown that individuals with two first-degree relatives with a history of CVD are about two to four times more likely to develop CVD or have a future CVD event compared to someone without a family history of CVD.” This is based on studies by Ciruzzi et al., Sesso et al., and Silberberg et al., which estimated the odds ratio or relative risk for having a MI or CHD in their lifetime for the offspring of two parents who had a MI or CHD to be between 2.05-3.72. If both of the participant’s parents had premature CVD, they were told, “The research has shown that individuals with a two or more first-degree relatives with a history of early or premature CVD are about up to five times more likely to develop CVD or have a future CVD event compared to someone without a family history of CVD.” This was based on studies by Bertuzzi et al., Ciruzzi et al., and Silberberg et al., which estimated the odds ratio or relative risk for having a MI or

CHD in their lifetime for the offspring of two parents who had a premature MI or CHD to be between 3.72-5.3.

CVD Biomarkers – LDL-C, HDL-C, Apo B, and Apo A-I

Fasting lipid levels were analyzed in the University of Washington's Medical Center laboratory. The lipid panel included information on the total cholesterol level, triglyceride level, HDL-C, and LDL-C levels. The lab used spectrophotometric analysis to obtain the total cholesterol, triglyceride, and HDL-C levels. LDL-C levels are calculated (total cholesterol minus the HDL-C). Spectrophotometric analysis determines the quantity of substances by measuring their capacity to absorb light of various wavelengths (Editors of the American Heritage Dictionary, 2008). The concentration of substance can be determined by the spectrophotometer measurement and the calibration curve made using samples of know concentrations (Spectrophotometric analysis, n.d.).

Apo B and apo A-I were measured as part of the study. Analysis of the apolipoprotein levels was performed in The University of Washington's Medical Center Clinical Immunology laboratory using a Dade Behring BN100 Nephelometer. In an immunochemical reaction, the apolipoproteins in the human serum sample form immune complexes with specific antibodies. These complexes scatter a beam of light passed through the sample. The intensity of the scattered light is proportional to the concentration of the relevant apolipoprotein in the sample. The result is evaluated by comparison with a standard of known concentration (NHANES 2005-2006 Laboratory Procedure Manuel, 2008). Both the College of American Pathologists and the Clinical Laboratory Improvement Amendments (CLIA) accredit the University of Washington laboratory.

Genotyping

Genotyping for three SNPs in three genes were performed as part of this study. As previously mentioned, each susceptibility allele is associated with a small, but statistically

significant, increase (effect size) in CHD risk. The frequency of these susceptibility alleles in this at risk population was compared to a general population using the HapMap database. Also, the association between the number of susceptibility alleles and LDL-C and apo B levels were explored in the study population.

All DNA samples were genotyped for three common SNPs in three different genes associated with increased CAD or MI risk based on previous studies. The genotyping was performed by the investigator in the University of Washington School of Nursing's Molecular Biology lab. The intronic SNP rs6511720 in the Low-density Lipoprotein Receptor (*LDLR*), the synonymous SNP rs693 in Apolipoprotein B *(APOB),* and the intronic SNP rs3846662 in 3-Hydroxy 3-Methylglutaryl Coenzyme A Reductase *(HMGCR)* were genotyped (Table 2.1).

Genomic DNA from each participant's blood sample was isolated using the FlexiGene DNA kit from Qiagen (N=15). After the DNA was isolated, each sample was given a new, unique identification number, de-identified from the original sample. The amount of genomic DNA in each sample was quantified using a NanoDrop 1000 Spectophotometer. Two samples were excluded from the RT-PCR genotyping due to low DNA quantity, which may have been indicative of low DNA quality. Genotyping was preformed using real-time polymerase chain reaction (RT-PCR) and Sequence Detection System Software to determine if a specific SNP is present in a sample. This software used the fluorescence measurements made during the PCR process to plot fluorescence values based on the signals from each sample. The plotted fluorescence signals indicate which alleles are in each sample (Applied Biosystems, 2006). All reagents used during the RT-PCR were from Applied Biosystems by Life Technologies. The TaqMan™ SNP Genotyping protocol, available from Applied Biosystems, was used to prepare all samples and perform the RT-PCR reactions. All samples were run in triplicate to ensure correct results. Any conflicting results were excluded from the analysis. One sample was excluded from any additional analysis due to conflicting genotyping results. Final analysis was

conducted on DNA from 80% of the participants (n=12).

Data Analysis

Analysis of Feasibility Results (Primary Aim 1)

All data were analyzed using SPSS 17.0. Before data analysis was conducted, all data were examined to ensure that data entry was “clean.” Next, the completion rate for each measure was examined. No measure had more than one missing data point. The variables were then inspected for sampling distribution, and floor and ceiling effects. Overall, there was good variability in the data. A few potential outliers were found in the data. In the results chapter, all statistically significant findings with a potential outlier, e.g. a BMI of 30.9 when the next highest BMI was 24.2, were calculated with the outlier and without the outliner to determine if it remained statistically significant with the potential outlier removed.

Analysis of the feasibility results included: examining the number of persons who were “approached” but declined; drop out rates at all junctures of the study; the average length of time to complete the measures (subject burden); the average length of time for each session; and the completeness of all self-reported measures. Additionally, which family members study participants spoke to about their medical history were examined. Information from the open-end questions, which were transcribed and analyzed using thematic analysis, were examined to further evaluate the intervention and the areas that participants thought could be improved. The thematic analysis was conducted using the qualitative data analysis software Nvivo 7 (QSR International, 2006).

Analysis of Baseline Data (Primary Aim 2)

The baseline data from study participants were examined using descriptive statistics (mean and range). This included analysis of Heart Knowledge Scores, perceived CVD risk based on the visual analogue score for each of the five factors and the overall perceived CVD risk, how each factor was ranked regarding its perceived importance on influencing lifetime risk

for developing CVD, CHD susceptibility, and likelihood to engage in a health promoting lifestyle. The data were also were examined by sex, age, race/ethnic groups, and education level using the Mann-Whitney U Test and the Kruskal-Wallis H Test. Correlation coefficients between the study variables were examined using Spearman Rho.

The Mann-Whitney U Test is the non-parametric alternative to the t-test but does not have the restrictive assumptions and requirements associated with the t-test (Siegel, 1956). The Kruskal-Wallis H Test is the nonparametric test equivalent to the one-way ANOVA (Siegel, 1956). The test statistic used in the Kruskal-Wallis test is distributed as a chi-square with the degrees of freedom (df) = k-1 (Siegel, 1956). The Mann-Whitney U Test and the Kruskal-Wallis H Test both have the power-efficiency of approximately .95 of their parametric equivalents (Siegel, 1956). The Spearman Rho is the non-parametric alternative to the Pearson's correlation coefficient; it has .91 of the power-efficiency of the Pearson's correlation coefficient (Siegel, 1956).

In the results section, any finding that was statistically significant with an unadjusted p value of .05 was potentially suspect because of multiple comparisons that likely inflated the Type I error. As a caution, an adjusted p value using the Bonferroni correction was also calculated. This adjusted p value was .00096 and was applied to the analyses of the difference groups in Primary Aim 2. Findings from this adjusted analysis were reported when they were significant.

Analysis of the Impact of the Intervention (Primary Aim 3)

Both the quantitative and qualitative data were examined to analyze the impact of the intervention. The non-parametric Wilcoxon Signed Ranks Test was used to examine differences between pre- and post-test scores on the visual analogue scale for overall perceived lifetime CVD risk; CHD Susceptibility scores; and on intention to engage in a health promoting lifestyle to decrease the risk for developing CVD. The Wilcoxon Signed Ranks Test was also used to

determine the specific impact of reviewing participants' family medical history as a three-generation pedigree and providing lifetime CVD risk information based on all family members and on first-degree relatives. For these analyses, differences in scores on two single-item questions were examined.

The Wilcoxon Signed Rank Test utilizes information about both the direction and magnitude of differences between matched pairs of pre- and post-intervention scores (Siegel, 1956). This non-parametric test has a power-efficiency of .95 of the paired t-test, its parametric equivalence (Siegel, 1956).

Any finding that was statistically significant using an unadjusted p value of .05 was also re-analyzed using the Bonferroni correction. For the analysis of the impact of the intervention on perceived lifetime CVD risk, the adjusted p value was .016. For the analysis of the impact of the intervention on intention to engage in a healthy lifestyle, the adjusted p value was .0125. The impact of the intervention on heart disease knowledge did not require adjustment, so the p value for a statistically significant finding remained .05. Any finding that was significant at the adjusted p value was noted.

The qualitative analyses were conducted using thematic analysis of the open-ended interview questions. The analysis was conducted for each participant and then the themes were aggregated across participants and grouped by category.

Analysis of Genotyping Results (Exploratory Aim)

The genotype results were first examined using the Hardy-Weinberg equilibrium (HWE) principal. The Hardy-Weinberg equilibrium principle is used to predict genotype frequencies in a population (Hartl & Jones, 2009). HWE can be affected by multiple factors including: nonrandom mating, migration, small populations, selection, mutations, and genotyping errors (Gelehrter, Collins, & Ginsberg, 1998). In the study, the goodness of fit chi-square test was used to determine if the observed genotyping results departed from the expected results (Wittke-

Thompson, Pluzhnikov, & Cox, 2005). With a large enough sample, a statistically significant finding would indicate departure from HWE. This can inflate the chances of a false-positive association. Therefore, HWE is essential for a valid association study.

This analysis was conducted only on the genotyping results for the Non-Hispanic Caucasians due to potential confounding if the analysis was conducted using all samples.

Additional exploratory analysis was conducted to examine if there was a correlation between the number of susceptibility alleles per participant and their LDL-C and apo B levels. This analysis was done using the Spearman Rho correlation coefficient.

CHAPTER 4.

RESULTS

Introduction

The first section of Chapter 4 contains the results for Primary Aim 1, a description of the feasibility results. The second section includes the results for Primary Aim 2, including: a description of the study sample; a description of baseline measures of perceived CVD risk; factors affecting lifetime CVD risk at baseline and the relationship between heart-disease knowledge and perceived disease risk; and the relationship between perceived CVD risk and participants' intentions to engage in CVD risk reducing behaviors. The third section includes the results for Primary Aim 3. This section consists of a description of the impact of the intervention on perceived CVD risk, heart disease knowledge, and intention to engage in a health-promoting lifestyle. Finally, the last section includes the results of the Exploratory Aim. It includes the results of the genotyping, an examination of the Hardy-Weinberg Equation for each SNP, and tests for a correlation between the number of susceptibility alleles and LDL-C and apo B levels.

Feasibility Results (Primary Aim 1)

Recruitment

Over a seven-week period, the study was able to recruit the required number of participants needed to conduct the pilot and feasibility study. Nonetheless, slight changes to the recruitment strategy along with additional recruitment sites should increase the number of individuals screened and enrolled in a larger version of the intervention.

A total of 31 people requested more information about the study by either calling the research office or e-mailing the principal investigator. Four people could not be reached to provide more information about the study and to be screened for eligibility. After two e-mails were sent requesting their phone number or two unsuccessful attempts to reach them by phone

were made, the individual was dropped for the recruitment list. A fifth person requested more information about the study after recruitment was closed.

Twenty-six individuals were screened for eligibility. All screening occurred over the phone. Of the 26 people, eight people did not meet the inclusion criteria for the study. Specifically, five people (19.2% of all individuals screened) did not have a family history of CVD. Two people (7.7% of all individuals screened) were too old to participate. One individual (3.8% of all individuals screened) had already been diagnosed with hyperlipidemia. Therefore, a total of 18 young adults were accrued into the study (69.2% of all individuals screened). Of these 18 individuals, three (11.5% of all individuals screened; 16.7% of all eligible individuals) were lost before Session One. Of the 15 participants enrolled in the study, all completed both sessions (57.7% of all individuals screened; 83.3% of all eligible individuals). See Figure 4.1 for a diagram of the recruitment process.

Of the 26 individuals screened, 23 were asked how they found out about the study (See Table 4.1). Over half (n=13; 57%) of the individuals saw a flyer advertising the study on campus. Almost a third (n=7, 30%) found out about the study through the University of Washington's Studies Seeking Healthy Volunteers website. Three individuals (13%) were told about the study from a friend. None of the individuals were recruited from Seattle University.

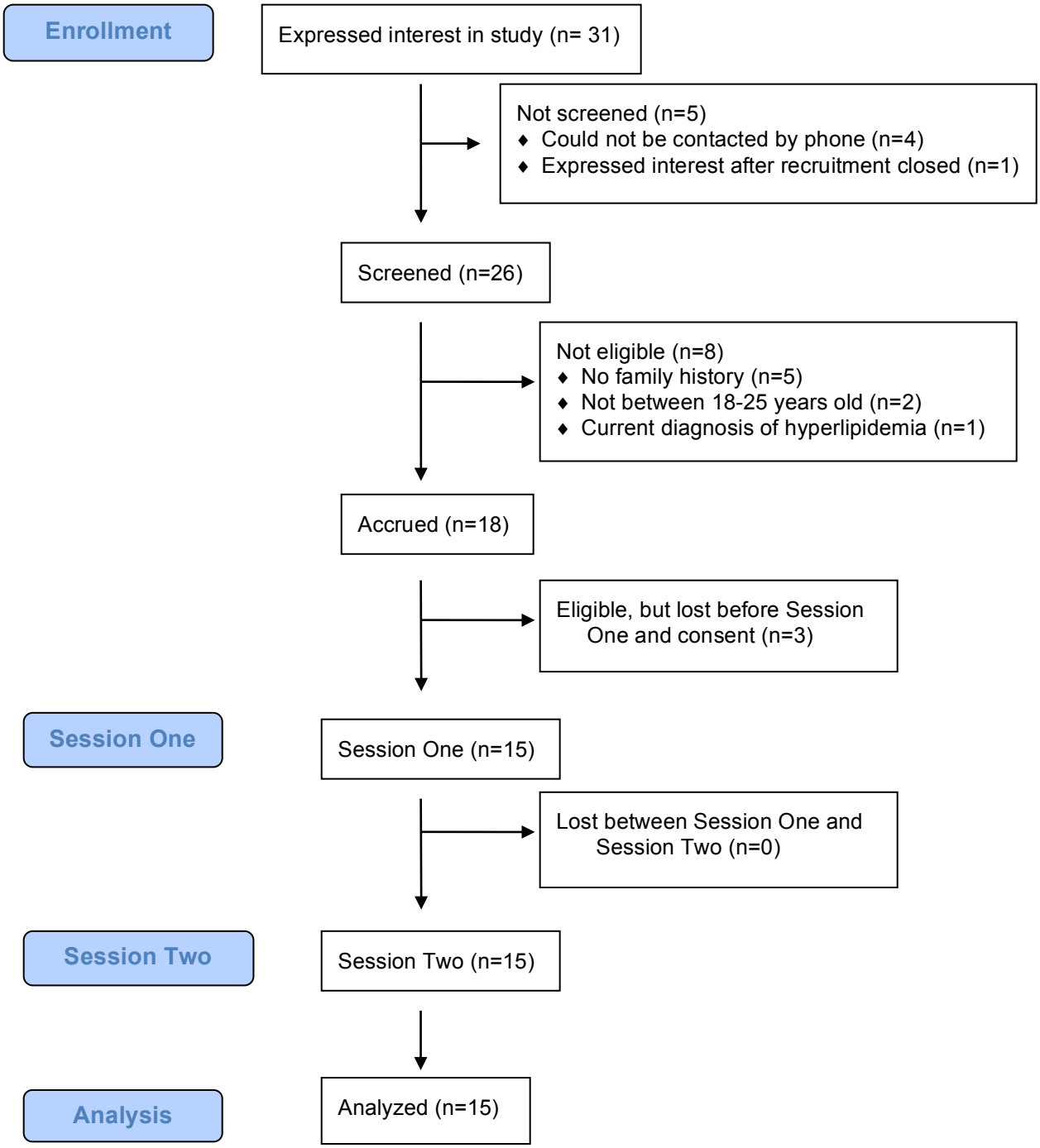
Table 4.1. Recruitment Channels (n=23)

Flyers placed throughout campus	n=13 (57%)
Studies seeking healthy volunteers website	n=7 (30%)
Word of mouth/friend referral	n=3 (13%)
Seattle University Student Health Center	n=0 (0%)

Study Design and Adherence

Fifteen young adults (mean age 20.8, [SD] 2.2 years; range 18-25 years) were enrolled in the study. There were no "drop-outs" between Session One and Session Two, meaning that all participants completed the full intervention. The average amount of time for Session One was 76 minutes (range 65-94 minutes) and 47 minutes (range 36-64 minutes) for Session Two.

Figure 4.1. Recruitment Flow Diagram



During Session One, participants spent an average of 6:32 minutes (range 5:50-7:28 minutes) completing the demographic and study questionnaires. There were only two pieces of missing data from all participants on these questionnaires (99.7% completion rate). During Session Two,

participants spent an average of 3:16 minutes (range 2:00-4:40 minutes) completing the study questionnaires. That does not include the time spent on answering the open-ended questions at the end of the session. On the Session Two questionnaires, only one piece of data was missing (99.8% completion rate).

All study participants talked with at least one family member about their family history between Sessions One and Two (Table 4.2). The majority spoke to only one or both parents who provided the study participant with information about their health and the health of the other family members listed in the pedigree (n=11, 78.6%). Only one participant (7.1%) spoke to all living members in their pedigree. With this individual, a family event occurred between Session One and Session Two, giving her an opportunity to talk to all of her family members.

Table 4.2. Who Did You Talk To About Your Family History? (n=14)

One parent only	n=4 (28.6%)
Both parents	n=7 (50%)
Both parents and one grandparent	n=2 (14.2%)
All living family members in three-generation pedigree	n=1 (7.1%)

Note: n=14 because one participant was not explicitly asked who he spoke to about his family's medical history

Participants' Willingness to Provide a Blood Sample

Study participants expressed no hesitation or concerns with providing blood samples for biological testing and genotyping. During the informed consent, participants could chose to be part of the study but refused to provide a blood sample for both biological testing and DNA genotyping or provide a blood sample for biological testing only. All participants agreed to provide a 12-hour fasting venous blood sample for both lipid and lipoprotein testing and DNA genotyping. This occurred despite their not receiving any information regarding the genotyping results.

Analysis of the Open-Ended Questions

Thematic analysis of the open-ended interview questions was conducted for each participant and then the themes were aggregated across the participants and grouped by

category. Using this method, two main themes regarding the feasibility of the study were constructed: information that the participants found valuable and areas where more information would have been useful.

The majority of participants (n=11; 73.3%) stated that discussing the family medical history with their family members either revealed previously unknown family members with CVD, the risk factors for developing CVD, or gave them greater awareness of their increased risk. During the open-ended questions, less than a third (n=4; 26.7%) of the participants reported they were surprised by what they learned when discussing the medical history of their family members.

In response to being asked, “What have you gained by collecting your family history?,” one study participant said:

> Knowing that I have a high risk for cardiovascular disease. I never thought about it. It never crossed my mind. But, looking back at it, when I was younger, almost my entire side of my mom’s family always told me they had high blood pressure. I never thought that I would get it or that I was at high risk. Especially for my Dad’s side. I never thought… you know… I didn’t know my aunt had heart failure. So… and I didn’t know my Dad had high cholesterol. So… I am at a high risk (ID #002).

Overall, participants reported that the intervention included useful information for them. They claimed that reviewing the pedigree and the lab values had the most influence on how participant’s understood their risk for developing CVD in the future. As another participant stated:

> [I now have] a better understanding of where I stand. I knew I was at risk, but now I really, really, actually know my risk factors. It is different then when your parents say, “Oh, you will probably have a risk.” When you actually see the numbers, look at the

pedigree and see there is a high risk, it is kind of an awake-up call. But it's nice to know, really. It is good information to have (ID # 006).

Despite identifying multiple aspects of the intervention that were helpful, participants suggested information they want added to the intervention. A few participants wanted to know how age, sex, and race/ethnicity influenced CVD risk. Others wanted more detailed information on how saturated fats contributed to cholesterol levels, what foods to avoid or eat to lower cholesterol, and what exercises are best to decrease CVD risk. Also, one participant wanted to know how dietary sodium influenced BP.

No participants cited a preference for one set of CVD biomarkers over the other (LDL-C and HDL-C versus apo B and apo A-I).

Summary of Feasibility Results (Primary Aim 1)

The recruitment strategy was effective in recruiting asymptomatic, young adults with a family history of CVD. There were no "drop-outs" between Session One and Session Two, indicating that the study was engaging and created an incentive for participants to complete the intervention. Participants' spoke to their family members about their medical history as instructed by the investigator. Overall, the methods used to communicate participants' increased lifetime CVD risk were effective. Participants offered suggestions on what information to add to the intervention for future versions.

Baseline Data (Primary Aim 2)

Study Sample

A total of fifteen individuals enrolled and completed the study (Table 4.3). The majority of the study sample were females (n=13, 86.7%), Caucasian (n=10, 66.7%), with some college education (n=11, 73.3%). The average age was 20.8 ([SD] 2.2 years; range 18-25 years). None of the study participant's smoked. Twelve (n=80%) had a normal weight, two (13.3%) were

underweight, and one was obese (6.7%) based on their BMI (BMI Calculator, n.d.). Nine (60%) of the participants exercised, on average, two times or less per week. Three participants (20%) reported exercising an average of five or more times per week.

Table 4.3. Demographic Data on Study Participants

Variable	Mean [SD]	Range
Age	20.8, 2.2 years	18-25 years
Gender, n (%)	13 females (86.7%) 2 males (13.3%)	
Ethnicity, n (%)	10 Caucasian, Non-Hispanic (66.7%) 2 Asian (13.3%) 2 Hispanic or Latino (13.3%) 1 Asian and Native Hawaiian or other Pacific Islander (6.7%)	
Education, n (%)	11 Some college (73.3%) 2 Completed college (13.3%) 2 Some graduate school (13.3%)	
BMI	21.9, 3.4	16-30.9
Smoking status, n (%)	15 Non-smokers (100%)	
Systolic BP	110.6, 11.9 mmHg	90-138 mmHg
Diastolic BP	82, 3.9 mmHg	70-82 mmHg
Total cholesterol	168.9, 35.4 mg/dL	109-245 mg/dL
LDL-C	93.5, 23.4 mg/dL	58-132 mg/dL
HDL-C	58.6, 13.7 mg/dL	39-86 mg/dL

Based on blood pressure and lipid levels, the sample was, overall, healthy. None of the participants had hypertension based on the single blood pressure measured at baseline, although one (6.7%) participant did have a SBP of 138 mmHg. The average LDL-C ("bad" cholesterol) level was 93.5 mg/dL ([SD] 23.4; range 58-132 mg/dL). The average HDL-C ("good" cholesterol) level was 58.6 mg/dL ([SD] 13.7, range 39-86 mg/dL). Based on the ATP-III Guidelines (2002), the goal LDL-C level is based on the number of risk factors. Risk factors for CHD include: cigarette smoking; hypertension or on antihypertensive medications; low HDL-C (<40 mg/dL); family history of CVD; and age (men older than 45 years; women older than 55 years) (Adult Treatment Panel III, 2002). For individuals with only one or no risk factors for CHD, the goal for LDL-C is <160 mg/dL. Only two individuals (13.3%) had an additional risk factor for

CHD, which was low HDL-C. Therefore, only two individuals were at increased risk and had a lower LDL-C goal of <130 mg/dL.

Factors that Influenced Study Variables at Baseline

There were no significant differences in the baseline data between females and males.

To determine if age had an influence on the baseline demographic data and heart disease knowledge, the sample of 15 was divided into two groups: ages 18-21 and ages 22-25. Statistically significant differences occurred for five independent variables when examined by age using an unadjusted p value of .05: BMI (p=.020); Heart Disease Knowledge Score (p=.009); total cholesterol (p=.008); LDL-C; (p=020); and apo B (p=.014) (Table 4.4). The younger group had a higher BMI and scored lower on the Heart Disease Knowledge Questionnaire compared to the older group. This difference in the BMI remained significant after the individual between 18-21 years with a BMI of 30.9 was removed as an outliner (U=6.0, Z=-2.205; p=.027).

The difference in Heart Disease Knowledge Score also remained significant when the individual between 18-21 years with the lowest score of 73% was removed (p=.011). The older group, however, had higher total cholesterol, LDL-C, and apo B levels. Also, the difference in total cholesterol, LDL-C, and apo B levels remained significant after a potential outlier was excluded from the analysis (U=3.5, Z=-2.336, p=.019 for total cholesterol; U=6.0, Z=-1.980, p=.048 for LDL-C; and U=5.0, Z=-2.131; p=.033 for apo B).

Table 4.4. Differences by Age at Baseline

Variable	Ages 18-21 (n=10)	Ages 22-25 (n=5)	Mann-Whitney U Test Statistic[a]
BMI	23.3 (2.91; 20.90-30.90)	19.18 (2.68; 22.90)	U=6.0, Z= -2.331 p=.020*
SBP	114.7 (10.39; 100-138)	102.4 (11.35; 90-120)	U=10.5, Z=-1.779 p=.075
DBP	74.8 (4.34; 70-82)	71.6 (1.67; 70-74)	U=14.5, Z=-1.324 p=.185
Total cholesterol	152.1 (26.53; 109-190)	202.6 (26.14; 175-245)	U=5.5, Z= -2.636 p=.008*

Table 4.4. Differences by Age at Baseline (continued)

LDL-C	82.6 (16.55; 58-108)	115.2 (20.41; 81-132)	U=6.0, Z= -2.327 p=.020*
Apo B	63.3 (11.94; 43-79)	91.8 (18.86; 63-105)	U=5.0, Z= -2.460 p=.014*
Heart Disease Knowledge Score	.906 (.781; .73-1)	1 (no range)	U=5, Z= -2.619 p=.009*
Perceived lifetime risk of CVD based on age	3.1 (1.79; 1-7)	3.8 (1.79; 1-5)	U=18, Z= -0.897 p=.369
Perceived lifetime risk of CVD based on race/ethnicity	3.33 (1.5; 1-6)	3.8 (0.9; 3-5)	U=16.5, Z= -0.838 p=..402
Perceived lifetime risk of CVD based on sex	3.9 (2.03; 1-8)	4.8 (1.3; 4-7)	U=18, Z= -0.908 p=.364
Perceived lifetime risk of CVD based on lifestyle	3.0 (1.41; 1-5)	2.8 (1.3; 2-5)	U=23.5, Z= -0.195 p=.846
Perceived lifetime risk of CVD based on family history	5.5 (2.55; 2-9)	5.6 (0.9; 5-7)	U=24, Z= -0.125 p=.90
Perceived lifetime risk of CVD based on all factors	4.3 (2.0; 2-7)	4.4 (1.52; 2-6)	U=24.5, Z= -0.063 p=.95

Notes: Values are mean ([SD]; with range); a = Two-tailed test
* Unadjusted p value < .05

There were statistically significant differences using an unadjusted p value of .05 between self-reported racial/ethnic groups (Asians, and Hispanic or Latino, Non-Hispanic Caucasians) at baseline in three variables: Heart Disease Knowledge Score (p=.022), perceived lifetime risk for CVD based on family history (p=.022), and influence of age on lifetime CVD risk (p=.032). For the analysis of the differences by racial/ethnic groups, the one study participant who self-identified her race/ethnicity as both Asian and Native Hawaiian or other Pacific Islander was classified as Asian.

At baseline, there was a statistically significance difference based on an unadjusted of p value of .05 in Heart Disease Knowledge Scores between the three racial/ethnic groups (Table 4.5). Hispanics or Latinos, on average, had the lowest scores and Non-Hispanic Caucasians had the highest scores.

Table 4.5. Differences by Race/Ethnicity at Baseline

Variable	Asians (n=3)[a]	Hispanic and Latinos (n=2)	Non-Hispanic Caucasians (n=10)	Chi-Square[b] and p-value
BMI	21.6 (0.66; 20.9-22.2)	23.9 (4.95; 23.9-30.9)	20.93 (2.71; 16-24.2)	4.17 .124
SBP	109.67 (8.74; 100-117)	119 (1.41; 118-120)	109.2 (13.63 (90-138)	2.644 .267
DBP	74.33 (4.16; 72-80)	75 (4.24; 72-78)	73 (4.03; 70-82)	1.961 .375
Total cholesterol	174.67 (16.62; 157-190	136 (1.41; 135-137)	173.8 (40.12; 109-245)	1.433 .488
LDL-C	99 (9; 90-108)	67.5 (3.54; 65-70)	97 (25.68; 58-132)	3.042 .219
Apo B	71 (9.85; 60-79)	55.5 (3.54; 53-58)	76.8 (22.2; 34-105)	2.383 .304
Heart Disease Knowledge Score	.91 (.035; .87-1)	.80 (.099; .73-.87)	.97 (.046; .87-1)	7.619 .022*
Perceived lifetime risk of CVD based on age	2 (1; 1-3)	2 (1.41; 1-3)	4 (1.7; 1-7)	4.755 .093
Perceived lifetime risk of CVD based on race/ethnicity	3.33 (0.58; 3-4)	1	3.8 (1.23; 2-6)	3.095 .213
Perceived lifetime risk of CVD based on sex	3.33 (2.08; 1-5)	2.5 (2.12; 1-4)	4.8 (1.55; 3-8)	2.486 .288
Perceived lifetime risk of CVD based on lifestyle	2.67 (2.08; 1-5)	2	3.2 (1.23; 2-5)	1.874 .392
Perceived lifetime risk of CVD based on family history	3.33 (1.528; 2-5)	3.5 (2.121; 2-5)	6.6 (1.43; 5-9)	7.589 .022*
Perceived influence of age on lifetime CVD risk	3.67 (.577; 3-4)	2.0 (1.414; 1-3)	4.5 (.972; 2-5)	6.871 .032*

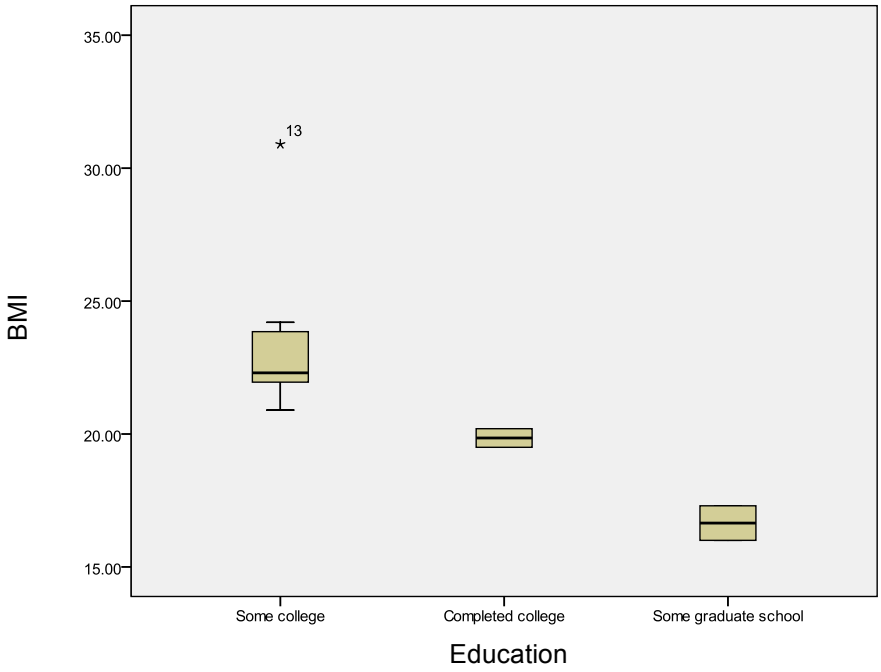
Data given as means ([SD] with range); a = Includes the study participant who self-identified her race/ethnicity as both Asian and Native Hawaiian or other Pacific Islander; b = 2 degrees of freedom; * Unadjusted p value < .05

There were statistically significant differences using an unadjusted p value of .05 at baseline between Asians, Hispanic or Latinos, and Non-Hispanic Caucasians on their perceived risk for developing CVD in their lifetime based on their family history (Table 4.5). Asians had the lowest perceived lifetime CVD risk based on family history, followed by Hispanic or Latinos. Non-Hispanic Caucasians scored the highest on perceived risk.

Asians and Non-Hispanic Caucasians comparably ranked the perceived influence of age on lifetime CVD risk (means of 3.33 and 3.5, respectively). However, Hispanic or Latinos gave the influence of age on lifetime CVD risk a significantly lower rank, based on an unadjusted p value of .05, meaning greater perceived influence (Table 4.5).

The role of education (some college, completed college, and some graduate school) on baseline demographic data and heart disease knowledge was also examined. Education significantly affected BMI only based on an unadjusted p value of .05 (Chi-square=8.480, df [degrees of freedom]=2; p=.014). BMI decreased as education increased (mean BMI of 23.26 [SD] 2.77 for some college; 19.85 [SD] .49 for completed college; and 16.65 [SD] .92 for some graduate school; See Figure 4.2). BMI remained statistically significant after the “some college” individual with a BMI of 30.9 was excluded from the analysis (Chi-square=8.265, df=2; p=.016). There were no statistical significant associations between education level and the other study variables.

Figure 4.2. Mean Education Level and BMI at Baseline



When adjusted for multiple comparisons using the Bonferroni correction, the p value for a statistically significant finding decreased to .00096. No results previously discussed were statistically significant using this adjusted p value.

Baseline Perceived CVD risk

Perceived lifetime risk for CVD was measured by a set of visual analogue scales and the CHD Susceptibility Questionnaire. The visual analogue scales asked participants to rate their lifetime risk for developing CVD based on their current age, race/ethnicity, sex, current lifestyle, family history, and all factors (age, race/ethnicity, sex, current lifestyle, and family history). At baseline, study participants, on average, rated their risk for developing CVD in their lifetime as low (mean of 4 or less) based on their current age, race/ethnicity, and current lifestyle (Table 4.6). Their perceived lifetime CVD risk based on their sex and all factors was between low and uncertain (mean of 4.2 and 4.33, respectively). Their perceived lifetime CVD risk based on their family history was between uncertain and slightly elevated (mean of 5.53). The mean baseline score on the CHD Susceptibility Questionnaire was 1.67 on a 4-point Likert scale ranging from Strongly Disagree (1) to Strongly Agree (4).

Table 4.6. Baseline Perceived CVD/CHD Risk (n=15)

Variable	Scale	Value [SD]	Range
CVD risk based on current age	0-10	3.33 (1.76)	1-7
CVD risk based race/ethnicity	0-10	3.5 (1.29)	1-6
CVD risk based on sex	0-10	4.2 (1.82)	1-8
CVD risk based lifestyle	0-10	2.93 (1.34)	1-5
CVD risk based on family history	0-10	5.53 (2.1)	2-9
CVD risk based on all factors	0-10	4.33 (1.8)	2-7
CHD Susceptibility Questionnaire	1-4	1.67 (0.22)	1.2-2.8

In order to determine what most influenced perceived CVD risk in young adults, participants were asked to “rank the factors … on how much they influence your lifetime cardiovascular disease risk the most (1 = most influence, 5 = least influence).” Participants, on

average, ranked family history as having the most influence, followed by lifestyle, sex, race/ethnicity, and current age (Table 4.7).

Table 4.7. Rank of the Perceived Influence of Various Factors on Lifetime CVD Risk

Variable	Mean Rank [SD]	Range
Family history	1.87 (1.06)	1-5
Current lifestyle	2.0 (1.26)	1-4
Sex	3.53 (1.36)	2-5
Race/ethnicity	3.6 (0.63)	3-5
Current age	4 (1.25)	1-5

Note: Lower rank means higher perceived influence on lifetime CVD risk

Relationship between Heart Disease Knowledge and Perceived CVD Risk at Baseline

There were no statistically significant correlations between Heart Disease Knowledge Scores and perceived lifetime CVD risk, for each of the five individual factors, the overall risk, or the mean CHD Susceptibility Questionnaire score (Table 4.8).

Table 4.8. Correlation between Heart Disease Knowledge and Perceive Risk at Baseline

	PRAge	PRSex	PRRace	PRLife	PRFH	PRAll	HDMMean
Heart Disease Knowledge	.290 p=.295	.339 p=.217	.060 p=.839	.181 p=.518	.332 p=.227	.223 p=.424	.220 p=.430

PRAge = perceived risk based on current age; PRSex = perceived risk based on sex; PRRace = perceived risk based on race/ethnicity; PRLife = perceived risk based on current lifestyle; PRFH = perceived risk based on family history; PRALL = perceived based on all five factors; HDMMean = mean score on CHD Susceptibility Questionnaire

There was a statistically significant correlation at baseline between Heart Disease Knowledge Score and the perceived influences of age and family history on lifetime CVD risk. As Heart Disease Knowledge Score increased, the perceived influence of current age on lifetime CVD risk decreased (r=.545, p=0.36; Figure 4.3). The opposite relationship existed between Heart Disease Knowledge Score and the perceived influence of family history on lifetime CVD risk: as Heart Knowledge Scores increased so did the perceived influence of family history on CVD risk (r=-.631, p=.012; Figure 4.4).

Relationship between Perceived CVD Risk and Intentions to Engage in CVD Risk Reducing Behaviors

At baseline, there was a statistically significant relationship between behavioral intention to eat a healthy diet and perceived lifetime risk for developing CVD based on current lifestyle. There was also a statistically significant relationship between intention to eat a healthy

Figure 4.3. Heart Disease Knowledge Score and Perceived Influence of Current Age on Lifetime CVD Risk at Baseline

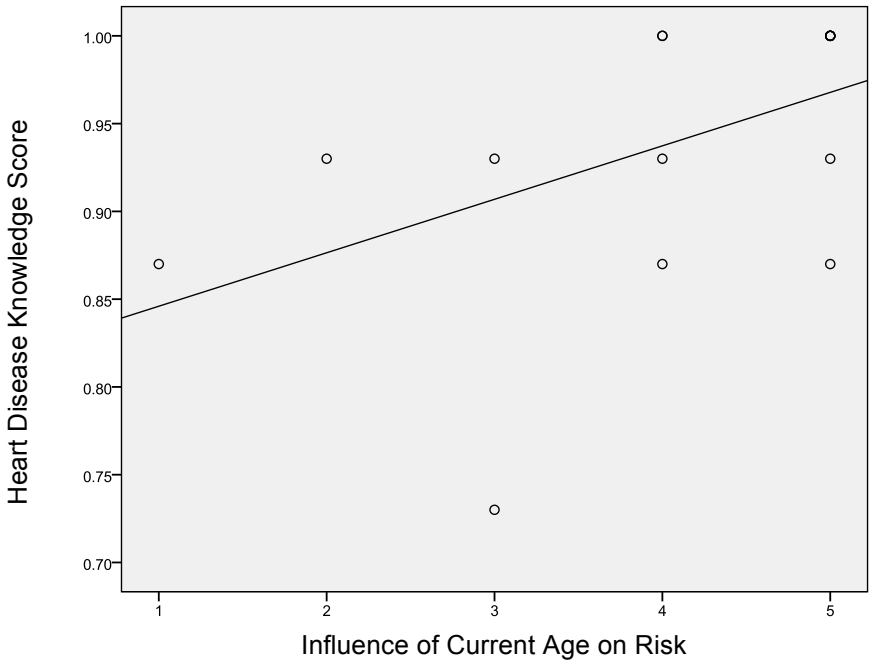
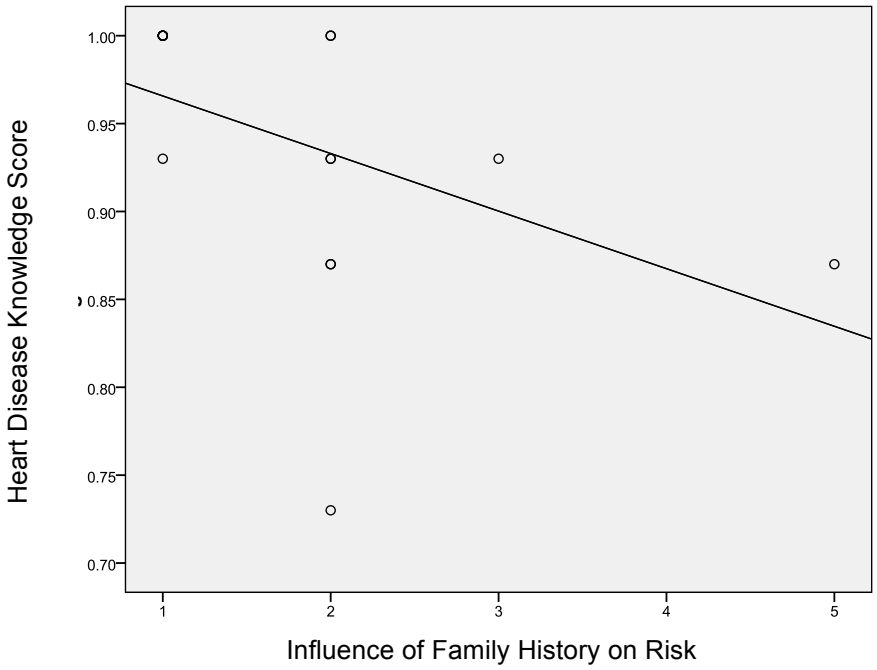


Figure 4.4. Heart Disease Knowledge Score and Perceived Influence of Family History on Lifetime CVD Risk at Baseline



diet and mean CHD Susceptibility Questionnaire scores (Table 4.9). Both measures decreased as intention to eat a healthy diet increased (Figures 4.5 and 4.6). There was no significant relationship between intention to eat a healthy diet and other measures of perceived lifetime CVD risk. There was also no significant relationship between intention to increase exercise and any measures of perceived lifetime CVD risk.

Table 4.9. Correlations between Perceived Risk and Intention to Engage in CVD Risk Reducing Behaviors at Baseline

	PRAge	PRSex	PRRace	PRLife	PRFH	PRAll	HDMMean
Intention to exercise sub-scale	.179 p=.523	-.262 p=.345	.022 p=.940	-.109 p=.698	.186 p=.507	-.016 p=.956	-.204 p=.498
Intention to eat a healthy diet sub-scale	-.084 p=.767	-.209 p=.454	.305 p=.290	-.534 p=.040*	-.149 p=.596	-.246 p=.376	-.540 p=.038*
Total score (physical activity and diet)	.043 p=.879	-.310 p=.261	.105 p=.721	-.412 p=.127	-.066 p=.816	-.181 p=.519	-.457 p=.087

PRAge = perceived risk based on current age; PRSex = perceived risk based on sex; PRRace = perceived risk based on race/ethnicity; PRLife = perceived risk based on current lifestyle; PRFH = perceived risk based on family history; PRALL = perceived based on all five factors; HDMMean = mean score on CHD Susceptibility Questionnaire
*p < .05

Figure 4.5. Intention to Eat a Healthy Diet and Perceived Lifetime CVD Risk Based on Current Lifestyle at Baseline

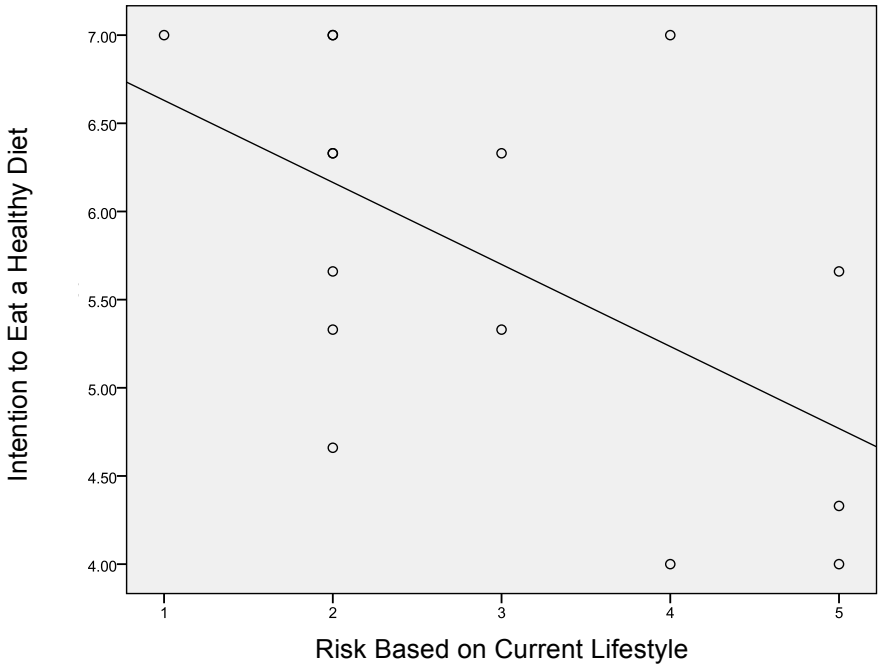
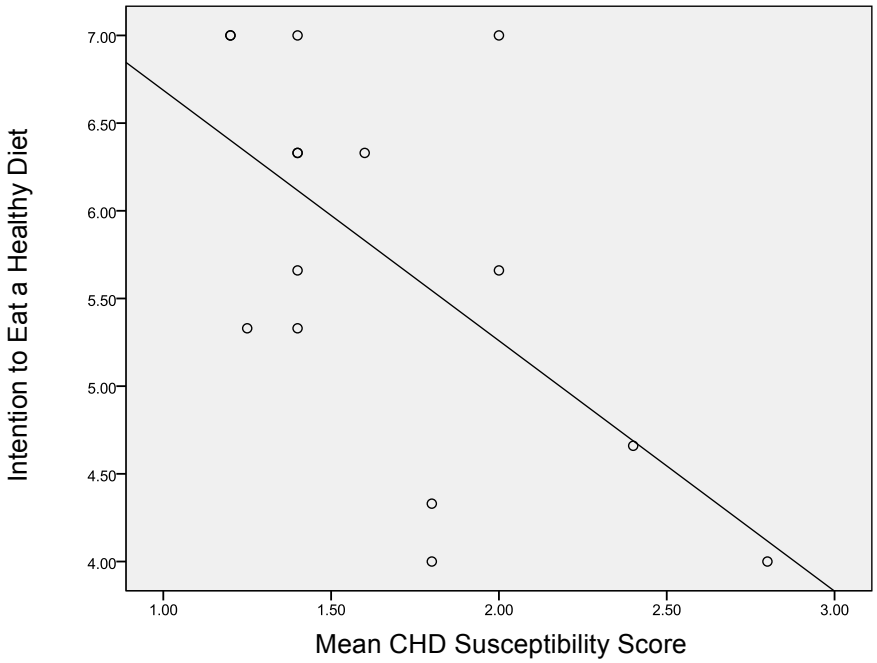


Figure 4.6. Intention to Eat a Healthy Diet and Mean Score on CHD Susceptibility Questionnaire at Baseline



Summary of Baseline Results (Primary Aim 2)

Gender had no influence on the baseline findings on measures of BMI, heart disease knowledge, lipid or lipoprotein levels, perceived lifetime CVD risk, factors that influence perceived lifetime CVD, and intention in engage in health-promoting lifestyle. Based on an unadjusted p value of .05, age influenced BMI, heart disease knowledge, total cholesterol, LDL-C levels, and apo B levels at baseline. Race/ethnicity influenced baseline heart disease knowledge, perceived lifetime risk for CVD based on family history, and influence of age on lifetime CVD risk. Education level influenced BMI.

At baseline, perceived lifetime CVD risk was low based on current age, race/ethnicity, and current lifestyle; between low and uncertain based on sex and all factors; and between uncertain and slightly elevated for perceived risk based on family history. Perceive CHD susceptibility was low. When ranking the perceived influence of certain factors on lifetime CVD risk, family history had the most influence, followed by lifestyle, sex, race/ethnicity, and current age.

There was no correlation between heart disease knowledge and overall lifetime perceived CVD risk at baseline. However, there were significant correlations between heart disease knowledge and the perceived influence of current age on lifetime CVD risk and between heart disease knowledge and perceived influence of family history on lifetime CVD risk. At baseline, perceived lifetime CVD risk based on current lifestyle and mean score on the CHD Susceptibility Questionnaire were influenced by intention to eat a healthy diet.

Impact of the Intervention (Primary Aim 3)

Perceived CVD Risk

Examining the changes in overall perceived lifetime CVD risk and CHD Susceptibility Scores from baseline to immediately post-intervention was used to evaluate the impact of the intervention on perceived risk. The impact of risk information based on the number of family members with CVD or the conditions known to increase risk was also evaluated.

Study results are graphically displayed in two difference figures. The first figure is a bar graph that depicts each study participant's scores at baseline and their post-intervention scores. The second figure depicts the same information along a 45-degree line. Any data point above the line reflects an increase from the study participant's baseline score compared to the post-intervention score. A data point on the line reflects no change from baseline to post-intervention. Any data point below the line reflects a decrease from baseline to post-intervention.

Perceived lifetime CVD risk based on visual analogue scale. From baseline to post-intervention, there was a statistically significant increase in perceived lifetime CVD risk based on all factors based on an unadjusted p value of .05 (T=-1.974, p=0.48). Eight participants (53.3%) scored higher post-intervention on perceived on overall lifetime CVD risk; four (26.6%) had no change in perceived risk, and three (20%) scored lower on perceived risk (Figures 4.7a and 4.7b).

Figure 4.7a. Pre-post Intervention Changes in Perceived CVD Risk Based on all Factors by Participant

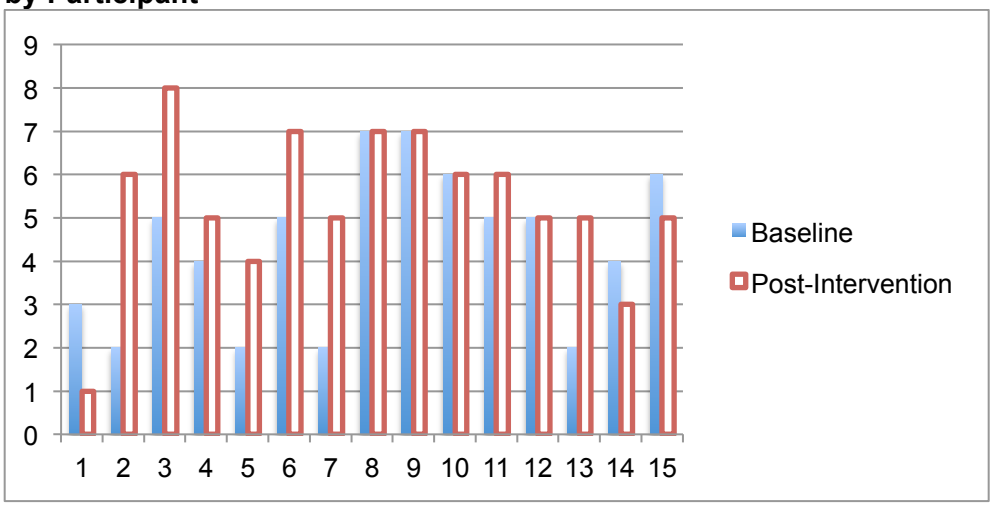
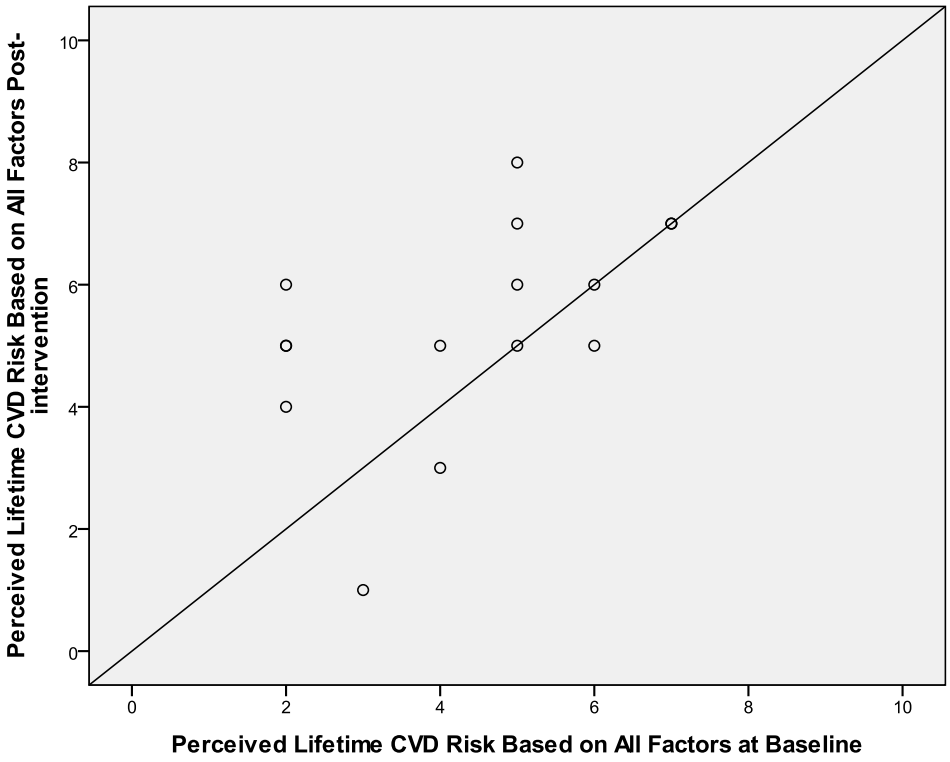


Figure 4.7b. Pre-post Intervention Changes in Perceived CVD Risk Based on all Factors



By examining the qualitative data, it was possible to speculate why perceived risk decreased in the three participants. Participant ID #001 had more than one family member with hypertension, but none of these individuals had obvious complications from the condition. Also, the intervention, as tested, contained very little information about hypertension, focusing more

on atherosclerosis and its complications (heart attack and stroke). By emphasizing atherosclerosis, it is possible that the low emphasis placed on hypertension likely contributed to that participant's decreased perceived lifetime CVD risk.

When providing his family medical history information from memory, Participant ID #014 reported multiple family members with CVD or the conditions that increase CVD risk. After reviewing the information with his parents, he found there were multiple family members with cancer, but only one family member with elevated cholesterol. This information likely led to a decrease in his perceived lifetime CVD risk.

Participant ID #015 was expecting her LDL-C level to be elevated. When she was informed that her LDL-C level met the current recommendations, she was relieved. She also felt that smoking and a high-stress lifestyle were major risk factors for CHD. Her normal LDL-C level, her relatively low stress lifestyle, and her not smoking, likely decreased her perceived disease risk at post-intervention compared to baseline.

Perceived CHD risk. The intervention did not result in a statistically significant increased in perceived CHD risk (T=-1.499, p=0.134). Seven participants (46.7%) increased their perceived mean CHD Susceptibility score from baseline to post-intervention; three participants (20%) showed no change; and five participants (33.3%) decreased their perceived CHD Susceptibility score (Figures 4.8a and 4.8b). Note that four of the five participants with a decrease in perceived CHD susceptibility had either an increase or had no change in their perceived lifetime CVD risk based on the visual analogue scale. The interview data did not identify the factors that may have negatively influenced perceived CHD susceptibility post-intervention.

Figure 4.8a. Pre-post Intervention Changes in Mean CHD Susceptibility Scores by Participant

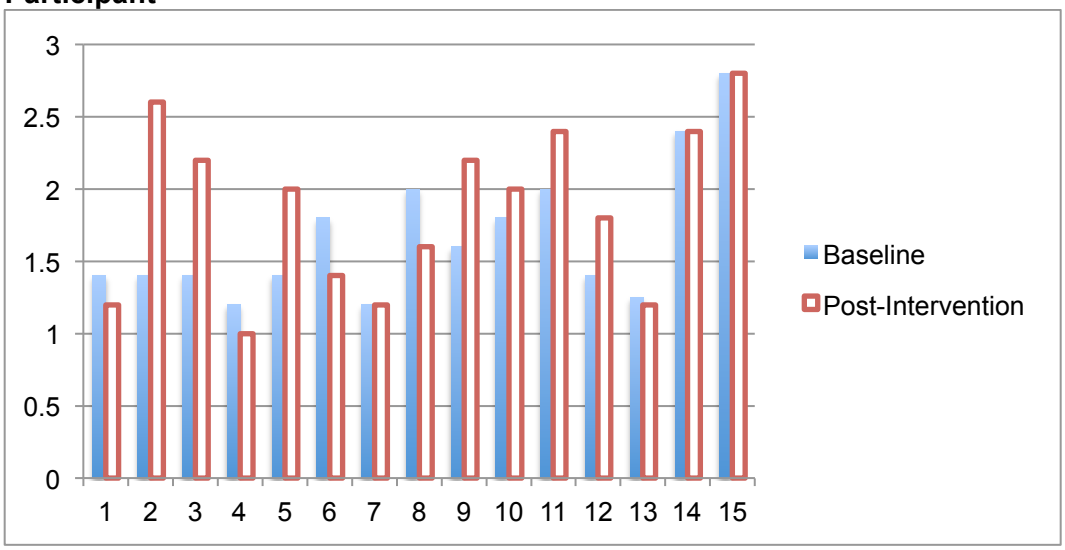
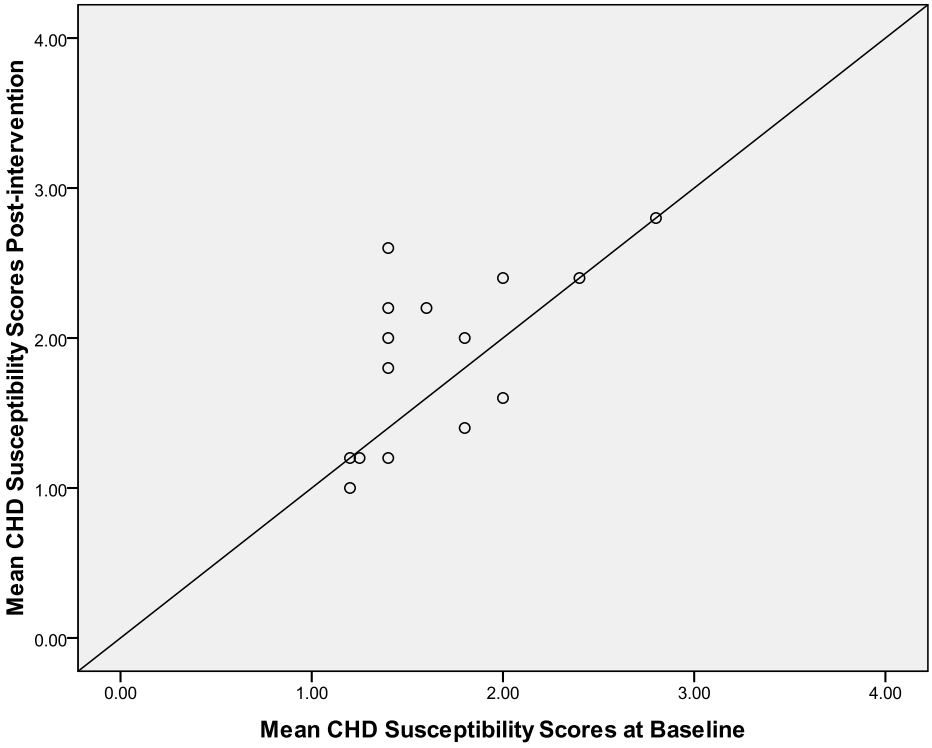


Figure 4.8b. Pre-post Intervention Changes in Mean CHD Susceptibility Scores



Perceived lifetime CVD risk after review of family history and risk information using information provided on CVD from family members. A single item question was used to assess participants' perceived risk for CVD, after the participant discussed their family history

with family members. Recall that this was done before they received an explanation of their risk from the investigator. The single item read, “Based on what you learned from your family, how at risk for developing CVD in your lifetime are you with ‘1’ being ‘no risk at all’ and ‘7’ being ‘very high risk’?” After the pedigree was updated, reviewed, and personalized risk information was given to the participant by the investigator, another single-item question was administered to see if the new and personalized pedigree-based risk information impacted the participant’s perceived disease risk.

Overall, there was a statistically significant increase in perceived CVD risk after the information was provided using both the unadjusted p value of .05 and the adjusted p value using the Bonferroni correction of .016 (T=-2.754, p=.006). Nine (60%) participants had an increase in perceived lifetime CVD risk after their risk based on family members only was explained. Six (40%) participants, showed no change in their perceived risk. No participants decreased their perceived risk based on this information (Figures 4.9a and 4.9b).

Figure 4.9a. Pre-post Intervention Changes in Perceived Lifetime CVD Risk Based on Family Members with CVD or Conditions Known to Increase CVD Risk by Participant

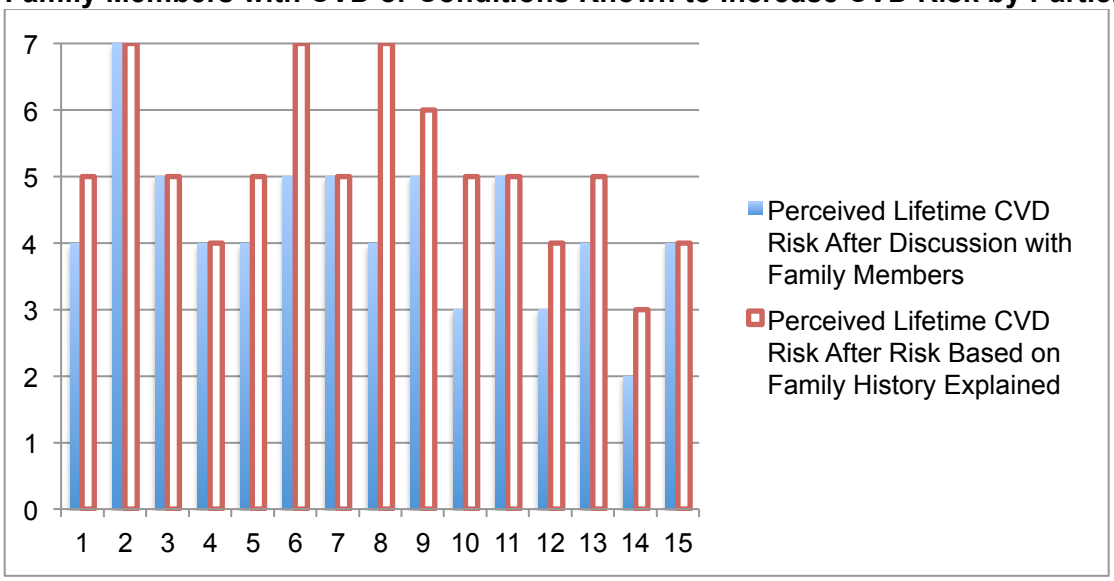
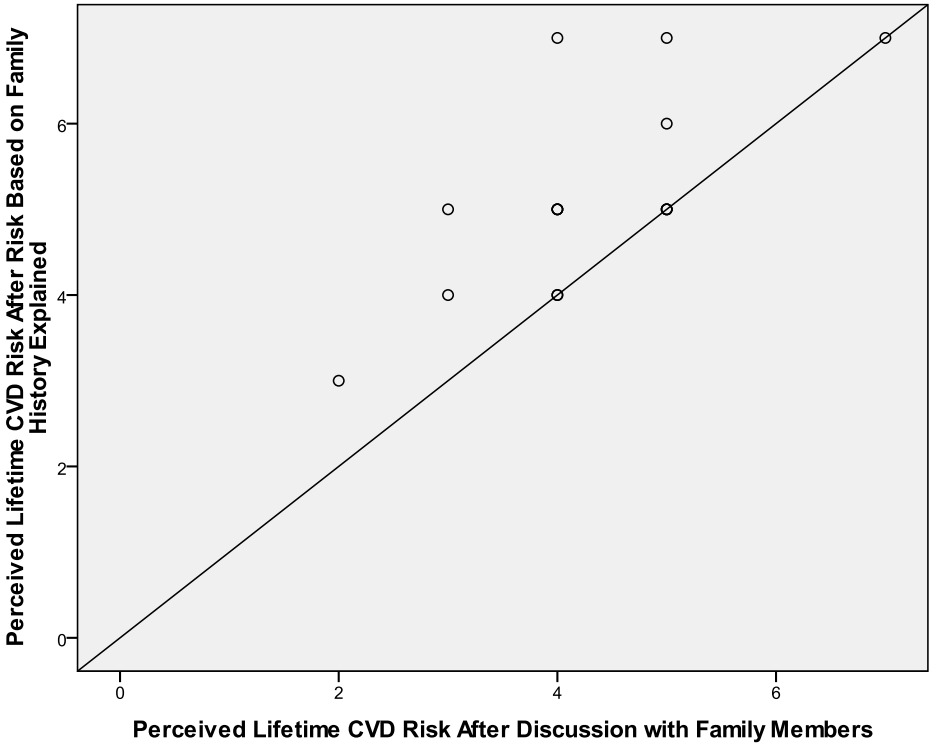


Figure 4.9b. Pre-post Intervention Changes in Perceived Lifetime CVD Risk Based on Family Members with CVD or Conditions Known to Increase CVD Risk



Heart Disease Knowledge

There was a statistically significant increase in heart disease knowledge from baseline to post-intervention, assessed by changes in Heart Disease Knowledge scores (T=-2.410, p=0.016). Almost half (n=7, 46.7%) of participants increased their score and the remaining eight (53.3%) scored the same. Ceiling effects were clearly operating: seven of eight participants had perfect scores at baseline and scored the same after the intervention (Figures 4.10a and 4.10b).

Figure 4.10a. Change in Heart Disease Knowledge Score by Participant

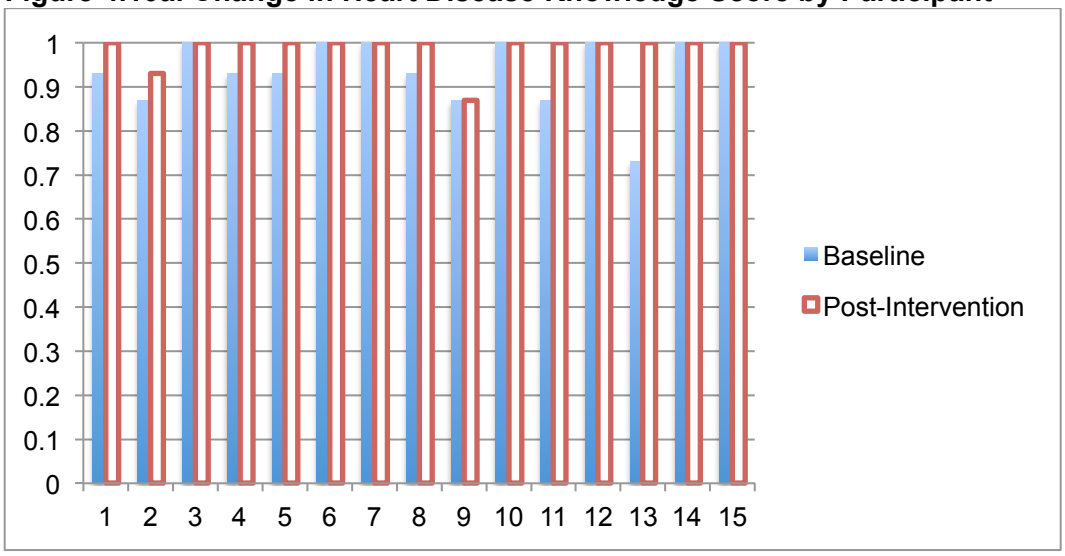
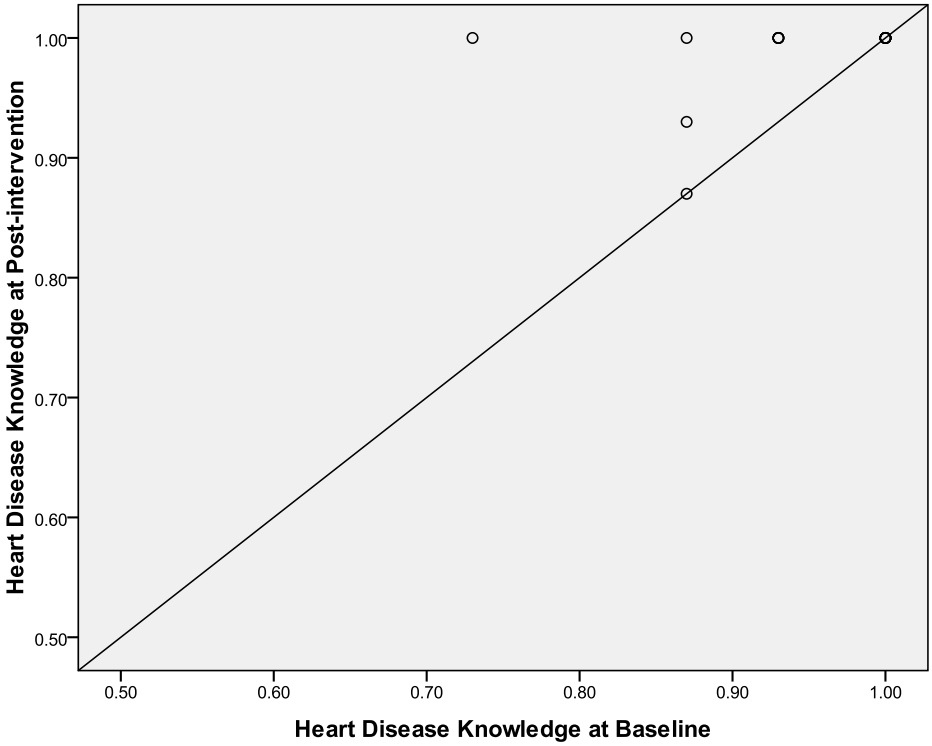


Figure 4.10b. Change in Heart Disease Knowledge Score



Intention to Engage in a Health-Promoting Lifestyle

There was a statistically significant increase in intention to engage in a health-promoting lifestyle comparing baseline to post-intervention using an unadjusted value of .05 (T=-2.121, p=0.034 for combined physical activity and diet score; T=-2.093, p=.036 for physical activity

subscale; and T=-1.849 for diet subscale) (Table 4.10). However, these results were not significant based on the adjusted p value of .0125.

Table 4.10. Impact of the Intervention on Intention to Engage in a Health-Promoting Lifestyle – Baseline to Post-Intervention

	Intention to Engage in a Health-Promoting Lifestyle	Intention to Exercise Subscale	Intention to Eat a Healthy Diet Subscale
T	-2.121	-2.093	-1.849
Significance (2-tailed)	0.034*	0.036*	0.064

* Unadjusted p value < .05

Nine (60%) participants intended to engage in a healthier lifestyle to reduce their lifetime CVD risk. Three participants (20%) had a slight decrease in their intention to engage in a health-promoting lifestyle after the intervention compared to baseline. Three participants had no intention to change their lifestyle. Two of these individuals had rated their intention to engage in a health-promoting lifestyle as high (6 out of 7 and 7 out of 7) at baseline (Figure 4.11a and 4.11b).

Figure 4.11a. Changes in Intention to Engage in a Health-Promoting Lifestyle by Participant

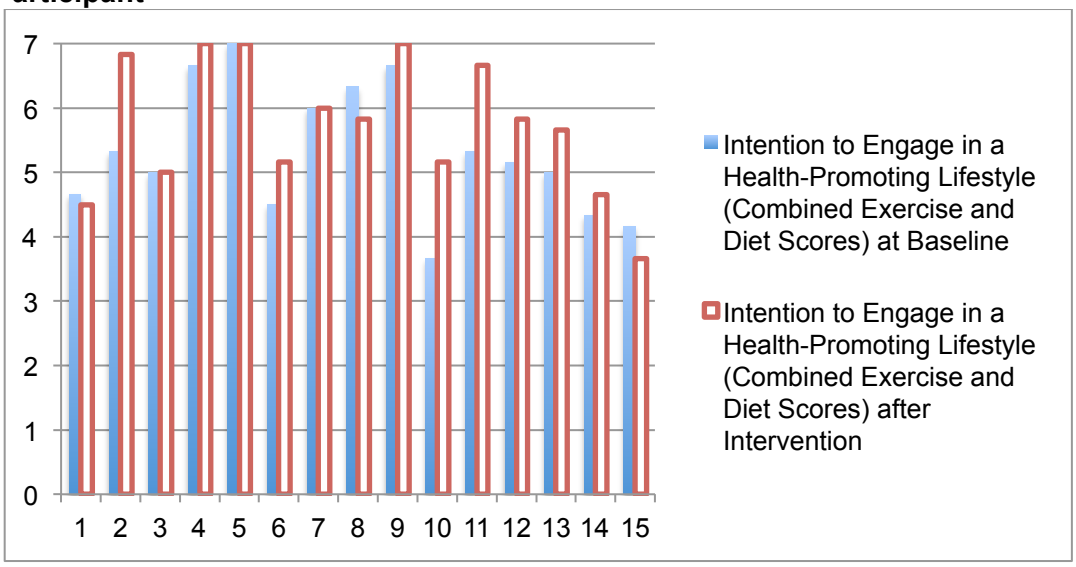
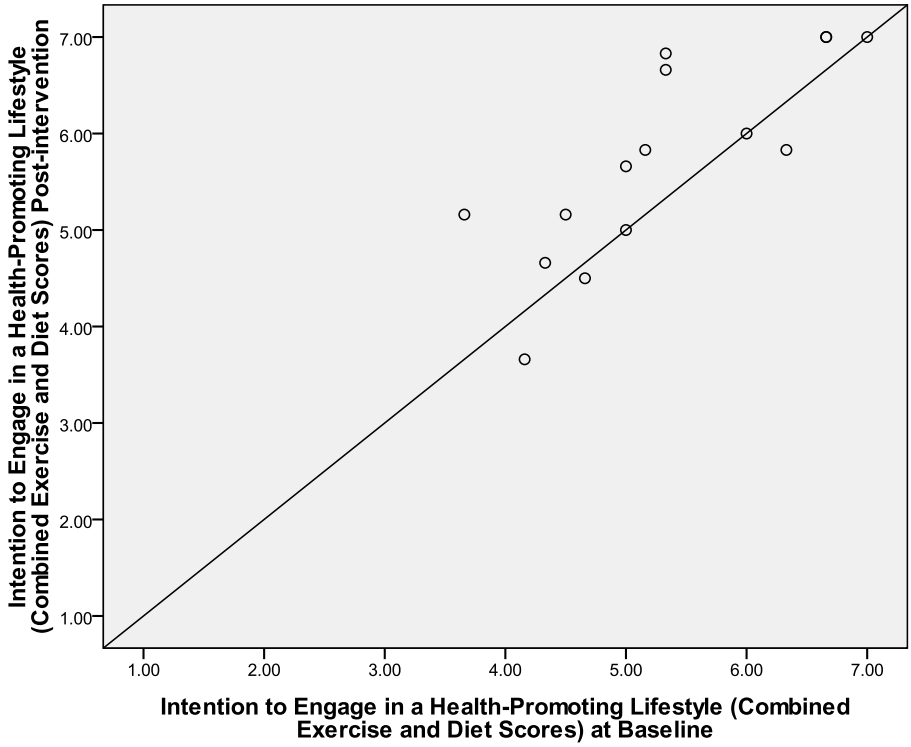


Figure 4.11b. Changes in Intention to Engage in a Health-Promoting Lifestyle

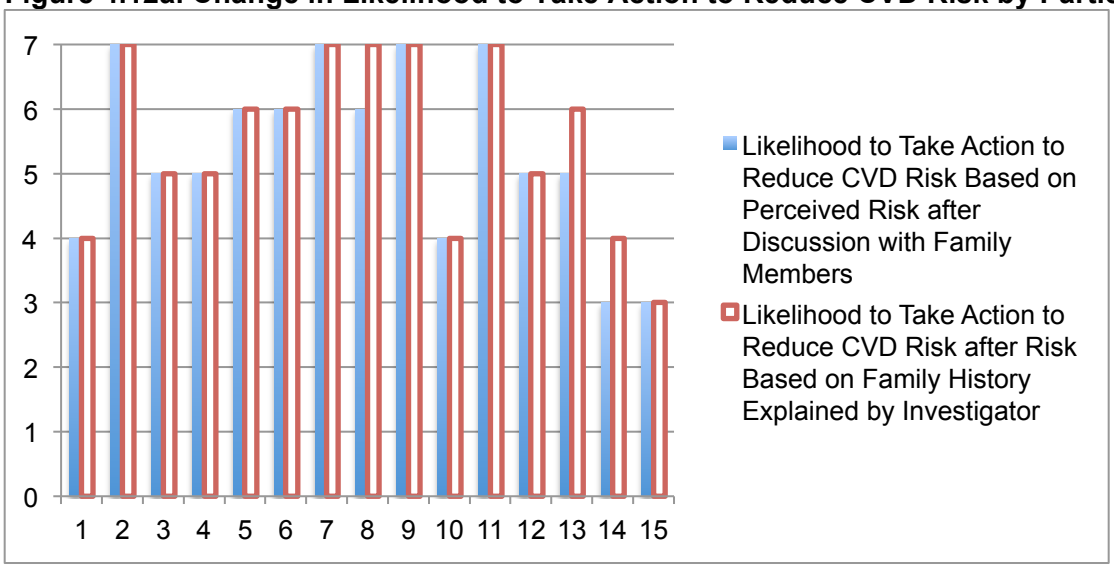


Both intention to exercise and intention to eat a healthy diet subscales were examined. For intention to exercise, nine (60%) participants' intended to increase their physical activity to meet the recommendations; two (13.3%) participants had less intention to exercise; and four participants (26.7%) had no change in their intention to exercise. For intention to eat a healthy diet, seven (46.7%) participants increased their intention to eat a healthy diet, three (20%) participant had less intention to eat a healthy diet, and five (33.3%) had no change in their intention to eat a healthy diet when comparing their baseline to after the intervention.

Likelihood to take action to reduce CVD risk after receiving explanation of risk based on family information. A single item question was used to assess participants' likelihood to take action based on their perceived risk after discussing their family history with family members, but before receiving an explanation by the investigator of their risk based on their family medical history. The single item indicator read, "Based on what you learned from your family and what you just told me, how likely are you to take action to change your risk factors with '1' being 'no

action' and '7' being 'all things possible'?", After the pedigree was updated, reviewed, and personalized risk information was given by the investigator, another single-item question was asked to see if this new information immediately affected participants' reported likelihood to take action to reduce their risk. Only three (20%) participants were more likely to take action after receiving an explanation of their risk based on family members (Figure 4.12a and 4.12b). This finding was not statistically significant (T=-1.732, p=0.083).

Figure 4.12a. Change in Likelihood to Take Action to Reduce CVD Risk by Participant

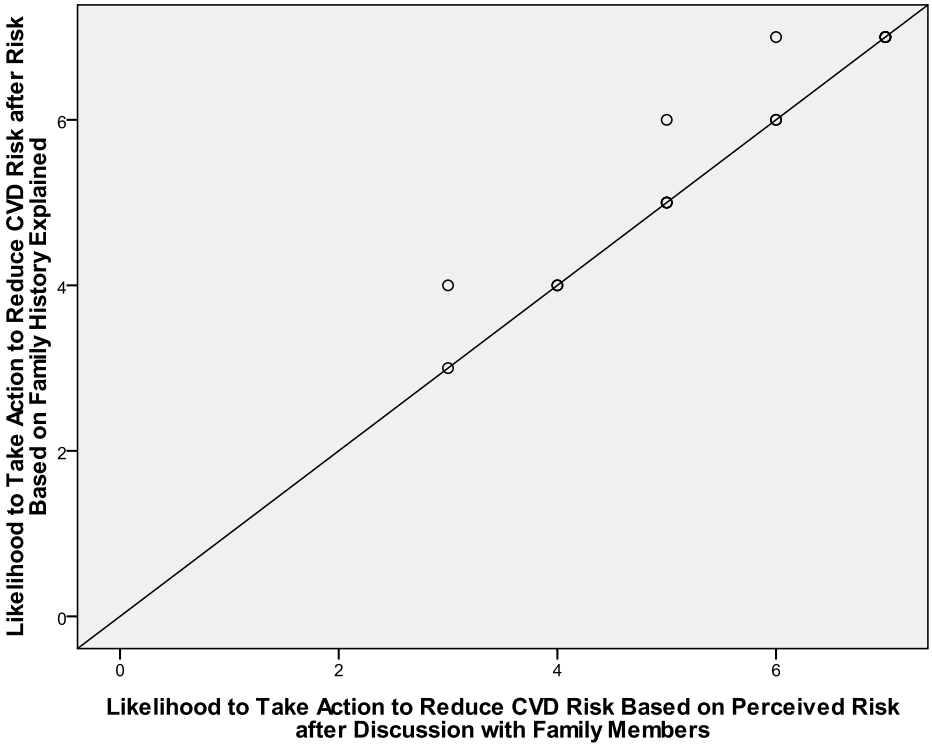


Qualitative Analysis of the Impact of the Intervention

Thematic content analysis was used to better understand how the intervention influenced participants' knowledge about their family history and their perceived lifetime CVD risk. Study results revealed that, overall, the intervention provided participants with information that changed what they knew about their family members and how they viewed their personal risk.

Impact on family history knowledge. Five participants (33%) claimed that their discussion of their family history with their family members had the most influence on their knowledge and understanding about their family history. One participant said: **"**We don't normally talk about this

Figure 4.12b. Change in Likelihood to Take Action to Reduce CVD Risk



[family medical history], so I was just learning about all this stuff about my family and the medical history and what not (ID #002)."

Almost half of the participants (n=6, 40%) claimed that generating the pedigree was what most influenced their knowledge and understanding of their family history. It showed them how the risk "trickles down" to the next generation. As one participant stated:

> I pretty much knew about all of it [my family medical history]. But like I said earlier, I didn't really add it all up. It is kind of hard to in your head. But, when you see it on that paper, it, it… that's really when I guess I learned. My entire family, almost every family member, to be honest, has a risk (ID # 006).

One participant (7%) said the review of the lab values revealed a risk factor, low HDL cholesterol, that was inherited within her family: "I did not know that having poor HDL cholesterol could affect you negatively and I did not know that that was in my family (ID #015)."

Three participants (20%) did not specify which component of the intervention had the most impact on informing their knowledge and understanding of their family history.

Impact on perceived lifetime CVD risk. Before the intervention, many participants were aware of family members with CVD or the conditions known to increase CVD risk, but they did not understand how that affected their personal risk. One participant (7%) said that the discussion of her family history with her family members, specifically her Mom, had the most impact on her understanding of her personal risk for developing CVD in her lifetime. She said, “Talking to my Mom about it, she is like, ‘You are definitely at high risk right now’ (ID #002).”

Another group of almost half of the study participants (n=6, 40%) reported that the three-generation pedigree and risk information based on the number of family members with CVD or the conditions known to increase CVD risk had the most impact on their perceived lifetime CVD risk. As one participant offered, “When you actually see the numbers, look at the pedigree and see there is a high risk, it is kind of a wake-up call (ID #006).” Another individual said, “Just knowing that it [CVD] is on both sides of my family. So, I am at greater risk … (ID # 011).”

Seven (47%) participants reported that the lab values had the greatest impact on their perceived CVD risk. One individual stated, “Well, definitely the cholesterol test was very informative. I had never had that tested before (ID #012).” As part of the intervention, the effects of LDL-C and HDL-C on atherosclerosis were explained. This was very useful for this participant, “What really helped was that cartoon. It helps you visualize what happens, what are the effects of having the bad cholesterol and how the good one helps (ID #013).”

One participant (7%) discussed the Risk Assessment Tool for Estimating 10-year Risk of Developing Hard CHD (Myocardial Infarction and Coronary Death) and its impact on her perceived risk. For her, it contributed to an overall lower perceived lifetime CVD risk. The goal of the intervention was to not only provide risk information, but to also provide information on how to decrease that risk. Comments from Participant ID #008 epitomized this distinction when

she said, “I learned that I am at high risk based on family history, but other factors play in. So, I can lower that risk (ID #008).” Additionally, all participants spoke of increasing their amount of physical activity or making dietary changes to lower their risk for developing CVD in the future.

Summary of the Impact of the Intervention (Primary Aim 3)

The intervention, as a whole, increased participant’s perception of their CVD risk based on all factors and increased participants’ intention to engage in a health-promoting lifestyle. Based on the qualitative data, different components of the intervention were most influential for different participants. Some participants claimed that discussing their family history information with a family member had the most impact. While others claimed that reviewing the pedigree or the lab values with the investigator had the most influence on them. A review of the participant’s family history information, in the form of a three-generation pedigree, and providing them with personalized risk information based on the number of family members with CVD or the conditions known to increase CVD risk, significantly increased their perceived lifetime CVD risk.

Genotyping Data (Exploratory Aim)

Genotyping Results

Table 4.11 includes the results on the samples included in the final genotyping analysis.

Table 4.11. Genotyping Results by Sample

Sample	*HMGCR* (rs3846662)	*APOB* (rs693)	*LDLR* (rs6511720)
4	GG	AA	GG
6	GA	GG	GG
27	AA	GG	GG
28	GA	GG	GG
33	AA	GA	GG
52	AA	GA	GT
54	GA	AA	GG
62	AA	GA	GG
79	GG	AA	GG
88	GA	AA	GG
92	GA	GA	GG

Hardy-Weinberg Equilibrium

Before examining the Hardy-Weinberg Equation (HWE) for each SNP, we must know the normal allele frequencies. Tables 14.14, 14.15, and 14.16 show the allele frequencies for five populations for each the three SNPs. This information was used to determine the expected allele frequency for the three SNPs.

Table 4.12. HapMap Report for rs3846662 (dbSNP Build 126)

Population	Reference Allele		Other Allele	
CEU	A	.575	G	.425
CHB	A	.460	G	.540
CHD	A	.440	G	.560
JPT	A	.460	G	.540
MEX	A	.612	G	.388

Notes: CEU = Utah residents with Northern and Western European ancestry from the CEPH collection; CHB = Han Chinese in Beijing, China; CHD = Chinese in Metropolitan Denver, Colorado; JPT = Japanese in Tokyo, Japan; MEX = Mexican ancestry in Los Angeles, California
From: refSNP rs3846663 (n.d.)

Table 4.13. HapMap Report for rs693 (dbSNP Build 126)

Population	Reference Allele		Other Allele	
CEU	G	.509	A	.491
CHB	G	.953	A	.047
CHD	G	.913	A	.087
JPT	G	.942	A	.058
MEX	G	.638	A	.362

Notes: CEU = Utah residents with Northern and Western European ancestry from the CEPH collection; CHB = Han Chinese in Beijing, China; CHD = Chinese in Metropolitan Denver, Colorado; JPT = Japanese in Tokyo, Japan; MEX = Mexican ancestry in Los Angeles, California
From: refSNP rs693 (n.d.)

Table 4.14. HapMap Report for rs6511720 (dbSNP Build 126)

Population	Reference Allele		Other Allele	
CEU	G	.894	T	.106
CHB	G	1	T	0
CHD	G	.991	T	.009
JPT	G	1	T	0
MEX	G	.914	T	.086

Notes: CEU = Utah residents with Northern and Western European ancestry from the CEPH collection; CHB = Han Chinese in Beijing, China; CHD = Chinese in Metropolitan Denver, Colorado; JPT = Japanese in Tokyo, Japan; MEX = Mexican ancestry in Los Angeles, California
From: refSNP rs6511720 (n.d.)

The HWE were only analyzed for the genotyping data for the Non-Hispanic Caucasian participants (Table 4.15) to avoid confounding due to population stratification. None of the

results were statistically significant, meaning that the genotype frequencies in this sample did not departure from the HWE (Table 4.16).

Table 4.15. Genotyping Result for Non-Hispanic Caucasian Participants Only

Sample	*HMGCR* (rs3846662)	*APOB* (rs693)	*LDLR* (rs6511720)
A	GA	GG	GG
B	AA	GA	GG
C	AA	GA	GT
D	GA	AA	GG
E	GG	AA	GG
F	GA	AA	GG
G	GA	GA	GG
H	GA	AA	GG

Table 4.16. Genotyping Results: Are the Observed Genotyping Frequencies Consistent with Hardy-Weinberg Equilibrium for Non-Hispanic Caucasian Participants Only?

SNP	Allele	Observed	Expected	Chi-Square[C] and p-value
rs3846662	AA	2	2.645	0.598; p=.7415
	AG	5	3.91	
	GG	1	1.445	
rs693	GG	1	2.073	3.028; p=.220
	GA	3	3.998	
	AA	4	1.929	
rs6511720	GG	7	6.394	0.323; p=.8508
	GT	1	1.516	
	TT	0	0.090	

c = with 2 degree of freedom

Number of Susceptibility Alleles and LDL-C and Apo B Levels

There were no correlations between the number of susceptibility alleles and LDL-C and apo B levels (r=-.189, p=.556 for LDL-C; r=0.059, p=.856 for apo B) based on the genotyping results from the 12 samples (Figures 4.13 and 4.14).

Summary of Genotyping Results (Exploratory Aim)

The exploratory analysis of the genotyping results showed no departure from the HWE in the SNPs from the Non-Hispanic Caucasian participants. There were no correlations between the number of susceptibility alleles a participant had based on genotyping and their LDL-C and apo B levels.

Figure 4.13. Correlation between Number of Susceptibility Alleles and LDL-C Levels

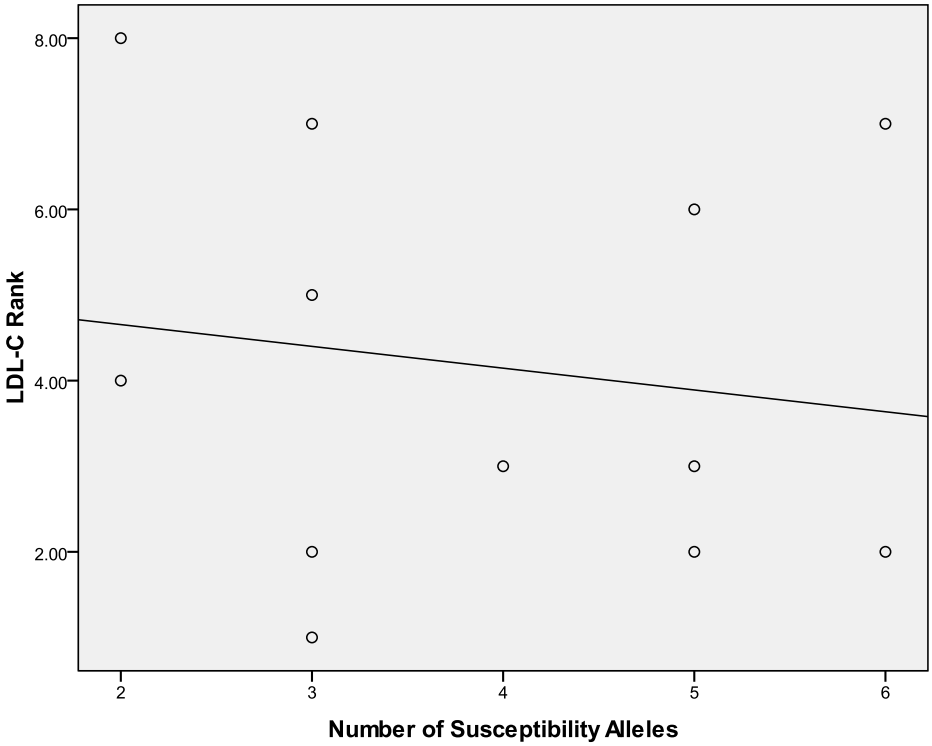
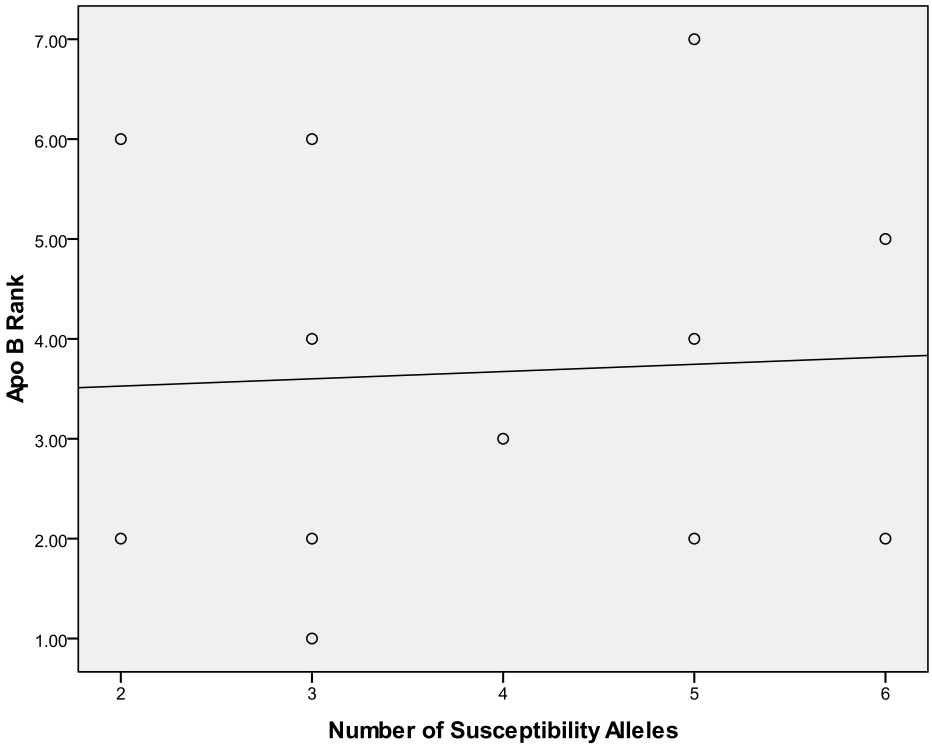


Table 4.14. Correlation between Number of Susceptibility Alleles and Apo B Levels



CHAPTER 5:

DISCUSSION

Summary of Findings

This study, called the My Family Medical History and Me Study, had three primary aims and one exploratory aim. Primary Aim 1 was to examine the feasibility of the study. Primary Aim 2 was to examine and describe the findings at baseline. Primary Aim 3 was to examine the impact of the intervention on perceived lifetime CVD risk, heart disease knowledge, and intention to engage in a health-promoting lifestyle to decrease this risk. The exploratory aim examined the results of genetic testing for three SNP associated with increased CHD risk, examined the allele frequencies using the Hardy-Weinberg equilibrium (HWE) principal, and examined if there were correlations between the number of susceptibility alleles per participant and their LDL-C and apo B levels.

Table 5.1. Summary of Study Results by Primary Aims

Study Aim	Result
Aim 1: Feasibility	• Study is feasibility • There were no “drop-outs” between Session One and Session Two • All participants agreed to provide a blood sample for lipid and lipoprotein levels and genotyping • All participants spoke to at least family member about family medical history • Participants, in general, felt the components of the intervention were useful
Aim 2: Baseline data	• Age influences BMI, heart disease knowledge, total cholesterol, LDL-C, and HDL-C levels • Race/ethnicity influences heart disease knowledge, perceived lifetime CVD risk based on family history, and perceived influence of current age of lifetime CVD risk • Education level influences BMI • Perceived lifetime CVD risk in young adults with a family history of CVD is low • Family history was ranked as the most important factor affecting perceived lifetime CVD followed by current lifestyle, sex, race/ethnicity, and current age • Heart disease knowledge correlates with perceived influence of current age and family history on lifetime CVD risk • Intention to eat a health diet correlates with perceived lifetime CVD risk based on current lifestyle and mean CHD Susceptibility Scores

Table 5.1. Summary of Study Results by Primary Aims (continued)

Aim 3: Impact of Intervention	• Perceived lifetime CVD risk based on all factors increased from baseline to post-intervention • Perceived lifetime CVD risk increased after discussion of risk based on family members • Heart disease knowledge increased from baseline to post-intervention • Intention to engage in a health-promoting lifestyle increased from baseline to post-intervention • Participants felt that the discussing family history with their family members, being explained their risk based on their family members, and being explained and given the results of their lab tests had the most influence on perceived lifetime CVD time and intention to engage in a health promoting lifestyle

Discussion and Implications

Overall, this brief, two-session intervention changed participants' short-term perceived lifetime CVD risk, heart disease knowledge, and their intention to engage in a healthy lifestyle to reduce their risk. The intervention, with further refinement and testing, has the potential to be incorporated into a clinical setting and could have an impact on reducing the CVD morbidity and mortality in an at-risk population.

Feasibility - Recruitment and Study Design

The recruitment strategy was effective in recruiting the desired study population over a seven-week period. All participants agreed to provide a blood sample after 12-hours of fasting for cholesterol and apolipoprotein levels and genetic testing.

Both study recruitment and the intervention should be modified in future studies. Less than half of the individuals who initially expressed interest in the study were included in the study. This occurred for two reasons. The study protocol limited contact attempts to potential participants to only two attempts before being dropped from the recruitment list. Expanding to four contact attempts may have increased recruitment success. Additionally, three participants met the inclusion criteria, but cancelled before the first session took place. Reasons for these

cancellations are unknown; the individuals could not be reached to reschedule their first session. Were these two sources of recruitment loss to occur in a future study, almost twice the number of individuals as the target study sample would need to be screened to achieve the target study sample.

In the current feasibility study, recruitment was passive. It utilized flyers, pamphlets, a website, and word-of-mouth to reach potential study participants. For a larger version of the study, more providers need to be involved, to either refer potential study participants to the investigator or to give individuals information about the study directly. Provider involvement in recruitment may result in participants with more risk factors (smoking, obesity, etc.) than what was seen in the current study.

Most of the components in the intervention worked well. However, providing participants with their estimated 10-year risk for having a heart attack did little to increase their perceived lifetime risk. It may have had the opposite effect, resulting in lower perceived lifetime CVD risk. Providing the 10-year risk information may have resulted in participants' receiving mix-messages. Despite being at high-risk for developing CVD in the future, they were at very low risk for having a cardiovascular event in the next ten-years. The purpose of the risk calculator was to show participants how their risk increases with age and negative lifestyles. This message may have been lost, resulting in a decreased in overall perceived lifetime CVD risk. The intervention still produced an increase in perceived lifetime CVD risk, but the effect may have been greater if the 10-year calculator component of the intervention was not included.

Analysis of the open-ended questions completed at the end of Session Two revealed that some participants wanted more information about the influence of age, sex, and race/ethnicity on their lifetime CVD risk. By examining the responses of participants whose perceived lifetime CVD risk decreased from baseline to post- intervention, to was determined that the intervention did not provide enough information about the causes and risks of

hypertension. These need to be added to the next version of the intervention to optimize its potential effect.

Baseline Data

Factors that influenced study variables at baseline. At baseline, a higher BMI was associated with both the younger group of study participants, those between 18 and 21 years old, and participants with less education. The higher BMI could be a result of the struggles new college students often face with weight gain (see Chapter 2). It is possible that older, more experienced students have learned to better balance the stresses of college life and manage their diet and exercise.

Lower heart disease knowledge was also associated with the younger group. However, there was no significant difference in heart disease knowledge based on education level. It is not known why this occurred.

The older group, between the ages of 22 and 25, had higher total cholesterol, LDL-C, and apo B levels. This is consistent with prior research about increased risk with older age (Adult Treatment Panel III, 2002), but to see a significant difference between two groups so close in age was surprising. It is important to note that even though there was a difference, both groups still met the recommended levels to reduce lifetime CVD risk.

Race/ethnicity appears to play a role in heart disease knowledge, perceived lifetime CVD risk based on family history, and perceived influence of age on lifetime CVD risk. Heart disease knowledge was lowest in Hispanics and Latinos and highest in Non-Hispanic Caucasians. Perceived lifetime risk for CVD based on family history was significantly lower in Asians and Hispanics and Latinos compared to Non-Hispanic Caucasians. Finally, Hispanics or Latinos attributed more influence to current age as a risk factor for lifetime CVD risk compared to Asians and Non-Hispanic Caucasians.

Awareness of CVD and its risks factors may be lower in Hispanics and Latinos and Asians, despite the fact that CVD, heart disease and stroke, is the leading cause of death in every race/ethnic group studied in the United States (Lloyd-Jones et al., 2010). This lower awareness may be the cause of the differences reported here. This suggests that greater effort is needed to educate minority groups about CVD and its risk factors.

Perceived lifetime CVD risk at baseline. Perceived lifetime CVD risk in asymptomatic, young adults with a family history of CVD was between low and uncertain for overall risk and risk based on current age, sex, race/ethnicity, and current lifestyle. However, lifetime CVD risk based on family history was between uncertain and slightly elevated.

This suggests that even though participants perceived their overall CVD risk as low, they are, at least slightly, aware that family history does play a role in CVD risk and that based on family history alone, their risk is higher. This finding also suggests that it is the combination of multiple risk factors that ultimately contributes to overall perceived risk. For young adults, the perceived slightly elevated risk associated with a family history is dampened by their perceived low risk based on their current lifestyle. Overall, these family history and current lifestyle factors were ranked as having the most perceived influence on lifetime CVD risk.

Relationship between heart disease knowledge and perceived risk. The baseline data showed a correlation between heart disease knowledge and perceived influence of current age on lifetime CVD risk and between heart disease knowledge and perceived influence of family history on lifetime CVD risk. As heart disease knowledge increased, current age was perceived as having less of an impact on lifetime CVD risk. However, as heart disease knowledge increased, so did the perceived influence of family history on lifetime CVD risk. Therefore, an intervention aimed at increasing heart disease knowledge and perceived risk based on family history, like the My Family Medical History and Me intervention, could have an impact on increasing overall perceived CVD risk.

Relationship between perceived risk and intention in engage in a healthy lifestyle. Intention to eat a healthy diet was negatively correlated with both perceived risk based on current lifestyle and mean CHD Susceptibility Questionnaire Scores. For both, higher intention to eat a healthy diet was associated with less perceived disease risk. While this may reflect participants' knowledge about CVD risk and how a healthy diet can reduce lifetime CVD risk, it may also reflect an over-confidence that lifestyle can completely mitigate the risks associated with the non-modifiable risk factors for CVD.

Impact of the Intervention

Perceived CVD/CHD risk. The intervention, as a whole, resulted in a significant increase in overall perceived lifetime CVD risk based on the analogue scale. However, there was not a significant increase in perceived CHD susceptibility. Seven (46.7%) participants had an increase in their mean CHD Susceptibility Scale, but five (33.3%) showed a slight decrease. This non-statistically significant finding may be the result of the small sample (N=15).

Providing participants with a pedigree and reviewing their risk information based on the number of family members with CVD or the conditions known to increase CVD risk, by itself, had a statistically significant impact on lifetime perceived CVD risk. Based on the qualitative analysis, this component of the intervention was one of the most influential on perceived lifetime CVD risk. Any modification to the intervention must retain this part of the intervention as intact as possible. Additionally, studies can be carried out to determine if an intervention focused on only risk information based family history of CVD, without the discussion of risk associated with the lab values, is effective in increasing overall perceived lifetime CVD risk.

Heart disease knowledge. Heart disease knowledge increased in participants from baseline to after the intervention. The intervention effectively transmitted information about CVD risk factors and the consequences of these risk factors. This increase in knowledge could be responsible, in part, for the increase in perceived CVD risk and intention to engage in health-promoting

behaviors by the study participants. Nonetheless, based on the qualitative data, the addition of information in future studies about the effects of age, sex, and race/ethnicity on CVD risk and the effects of hypertension have the potential to improve study outcomes.

Intention to engage in a health-promoting lifestyle. The intervention, as a whole, increased participants' intention to engage in health-promoting behaviors. This result suggests that the interactive counseling in Session Two was effective in providing information to participants about small changes they could make to decrease their overall lifetime CVD risk. In future studies, the measure of behavioral intention should be augmented and include a measure of actual behavior change, not just intention to change behavior.

Exploratory Analysis of Genotyping Data

There were no significant findings from the analysis of the genotyping data. This was expected due to the small sample size. Although not statically significant, the number of study participants homozygous for the A allele, the susceptibility allele, for SNP rs693 in *APOB* was higher than expected.

Limitations

The study had limitations. The study was a pilot and feasibility study; observed changes cannot be unconditionally attributed to the intervention. It is always plausible that other causes, such as sampling bias, social desirability bias, self-enhancement bias, and multiple comparisons affected study outcomes.

Sampling bias likely affected the study results (Polit & Beck, 2008). Recruitment came from a college population of young adults; results cannot be generalized to less well-educated young adults. The sample was biased because recruitment was limited to young adults in the Pacific Northwest, all of whom were enrolled in college, had a college degree, or were pursuing advanced degrees. At baseline, the participants were healthy, with only two participants having two or more CVD risk factors. It is always possible that the recruited sample included the

“walking well” or “worried well.” These are individuals who are asymptomatic but are still worried about their health. Such individuals may have already been motivated to change their health-related behavior, independent of the effects of the intervention. Future studies will need to include participants who are not so motivated. Therefore, study results are limited to study participants who were accrued into the study, not to young adults in the general population or young adults living in other parts of the country.

Social desirability, study participants providing responses they think the investigator wants, potentially threatened the validity of the results (Polit & Beck, 2008). Self-enhancement bias, the tendency to describe oneself in positive terms, may have inflated study participants’ report of their behavioral intention to engage in a healthy lifestyle (Krueger, 2010).

Type I error was likely a threat to the validity of some of the study findings. Such error inflation occurred because of the multiple comparisons that were made in the data analyses, especially related to Primary Aim 2. All study results were reported in the results section, including results that did not remain statistically significant after the Bonferroni correction. Such reporting is consistent with the exploratory nature of the study. When that correction factor was applied, only a small portion of the study findings remained statistically significant.

Additionally, the small number of Asians and Hispanics or Latinos participants likely attenuated results when examining the differences between the racial/ethnicity groups at baseline. The small sample sizes of these groups may have inflated the Type II error, resulting in falsely rejecting differences between racial/ethnic group and baseline measures that might have occurred. The small study sample may have been insufficient to detect differences, even if they occurred. Future studies need to recruit a larger study sample.

Conclusions with Recommendations for Future Research

The My Family Medical History and Me intervention is a feasible, well-accepted intervention that warrants additional testing in the future with a larger and more diverse sample.

The next version of the intervention should include additional measures of actual health-related behavior and additional content that includes more information about hypertension and its long-term risks. The study design should be modified to control for the plausible threats to internal validity. This could include adding a control group and utilizing research assistants to collect the baseline and outcome measures.

This pilot feasibility study was the first step in developing and testing an intervention aimed at decreasing the CVD risk factors in an at-risk population. When fully developed, the intervention has the potential for application in a clinical setting. A nurse, or other trained healthcare provider, along with at-home assignments to be completed with family members, can integrate family history information, current risk factors such as smoking and cholesterol levels, and brief counseling on health behaviors to change how an individual perceives their CVD risk and their ability to make changes to decrease their risk.

The use of an individual's family medical history and the utilization of pedigrees to show how CVD risk is inherited within their family were both influential in affecting perceived CVD risk as well as intention to engage in health-related behavior. This component of the intervention is low cost and low-tech. It can be performed outside of the clinic, in school and homes, at health fairs, and even in developing countries where CVD is increasing (Levenson, Skerrett, & Gaziano, 2002; Mendis, Puska, Norrving, 2011).

Future research is warranted with a more diverse study population. As mentioned, this study may have included the "walking well" or worried well." Future research should focus on study participants with more risk factors for CVD and with less motivation to change their lifestyle. This will be challenging, but needs to be done to further advance this potentially useful intervention and to maximize its impact. Further exploration and examination of the use of genotyping to predict at-risk individuals is also recommended.

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APPENDIX A:
STUDY MEASURES AND QUESTIONAIRES

ID Number _____

Demographic Data

Name:

Date of birth (MM/DD/YY):

Sex: Female / Male

Race/Ethnicity (Circle all that apply):

American Indian or Alaska Native

Asian

Black or African American

Native Hawaiian or Other Pacific Islander

Hispanic or Latino

Non-Hispanic Caucasian

Other (Please specify):

Education Level (Circle one):

Some high school education

Completed high school

Some college

Completed college

Some graduate school

Completed graduate school

Completed professional degree/PhD

How often do you have a drink containing alcohol (circle the answer that is correct for you)?

Never	Monthly or less	Two to four times a month	Two to three times per week	Four or more times a week

How many drinks containing alcohol do you have on a typical day when you are drinking (circle the answer that is correct for you)?

1 or 2	3 or 4	5 or 6	7 to 9	10 or more

How often do you have six or more drinks on one occasion (circle the answer that is correct for you)?

Never	Monthly or less	Two to four times a month	Two to three times per week	Four or more times a week

Have you smoked one or more cigarettes over the last 30 days? Yes / No

If yes, how many cigarettes do you smoke a week?

How many times a week, on average, do you participate in moderate to heavy physical activity lasting 30-minutes or longer?

Do you have diabetes? Yes / No

ID Number _____

Height/Weight and Blood Pressure Record Form

Height (feet and inches):

Weight (pounds):

BMI (calculated using http://www.nhlbisupport.com/bmi/bminojs.htm):

Blood pressure:

ID Number _____ Session # _____

What I Know About Heart Disease [Heart Disease Knowledge Questionnaire]

Please circle whether each statement below is True or False.

1) A person always knows when they have heart disease.	True or False
2) If you have a family history of heart disease, you are at risk for developing heart disease.	True or False
3) The older a person is, the greater their risk of having heart disease.	True or False
4) Smoking is a risk factor for heart disease.	True or False
5) A person who stops smoking will lower their risk of developing heart disease.	True or False
6) High blood pressure is a risk factor for developing heart disease.	True or False
7) Keeping blood pressure under control will reduce a person's risk for developing heart disease.	True or False
8) High cholesterol is a risk factor for developing heart disease.	True or False
9) Eating fatty foods does not affect blood cholesterol levels.	True or False
10) If your 'good' cholesterol (HDL) is high you are at risk for heart disease.	True or False
11) If your 'bad' cholesterol (LDL) is high you are at risk for heart disease.	True or False
12) Being overweight increases a person's risk for heart disease.	True or False
13) Regular physical activity will lower a person's chance of getting heart disease.	True or False
14) Only exercising at a gym or in an exercise class will lower a person's chance of developing heart disease.	True or False
15) Walking and gardening are considered exercise that will help lower a person's chance of developing heart disease.	True or False

ID Number _____ Session # _____

Heart Disease and Me [Visual Analogue Scale]

Mark your lifetime cardiovascular disease risk with an X on the line below **based on your current age**.

High Risk

9

8

7

6

5

4

3

2

1

No Risk

ID Number _____ Session # _____

Mark your lifetime cardiovascular disease risk with an X on the line below **based on your race/ethnicity**.

High Risk

9

8

7

6

5

4

3

2

1

No Risk

ID Number _____ Session # _____

Mark your lifetime cardiovascular disease risk with an X on the line below **based on your sex.**

High Risk

9

8

7

6

5

4

3

2

1

No Risk

ID Number _____ Session # _____

Mark your lifetime cardiovascular disease risk with an X on the line below **based your current lifestyle.**

High Risk

9

8

7

6

5

4

3

2

1

No Risk

ID Number _____ Session # _____

Mark your lifetime cardiovascular disease risk with an X on the line below **based on your family history.**

High Risk

9

8

7

6

5

4

3

2

1

No Risk

ID Number _____ Session # _____

Mark your lifetime cardiovascular disease risk with an X on the line below **based on all factors (current age, race/ethnicity, sex, current lifestyle, and family history).**

High Risk

9

8

7

6

5

4

3

2

1

No Risk

Please rank the factors below on how much they influence your lifetime cardiovascular disease risk the most (1 = most influence, 5 = least influence).

____ Current age

____ Race/Ethnicity

____ Sex

____ Current lifestyle

____ Family History

ID Number _____ Session # _____

Heart Disease and Me II [CHD Susceptibility Scale]

Indicate how strongly you agree with the following statements: (1) strongly disagree or (4) strongly agree

1. It is likely that I will suffer from a heart attack or stroke in the future.

Strongly Disagree 1 2 3 4 Strongly Agree

2. My chances of suffering from a heart attack/stroke in the next few years are great.

Strongly Disagree 1 2 3 4 Strongly Agree

3. I feel I will have a heart attack or stroke sometime during my life.

Strongly Disagree 1 2 3 4 Strongly Agree

4. Having a heart attack or stroke is currently a possibility for me.

Strongly Disagree 1 2 3 4 Strongly Agree

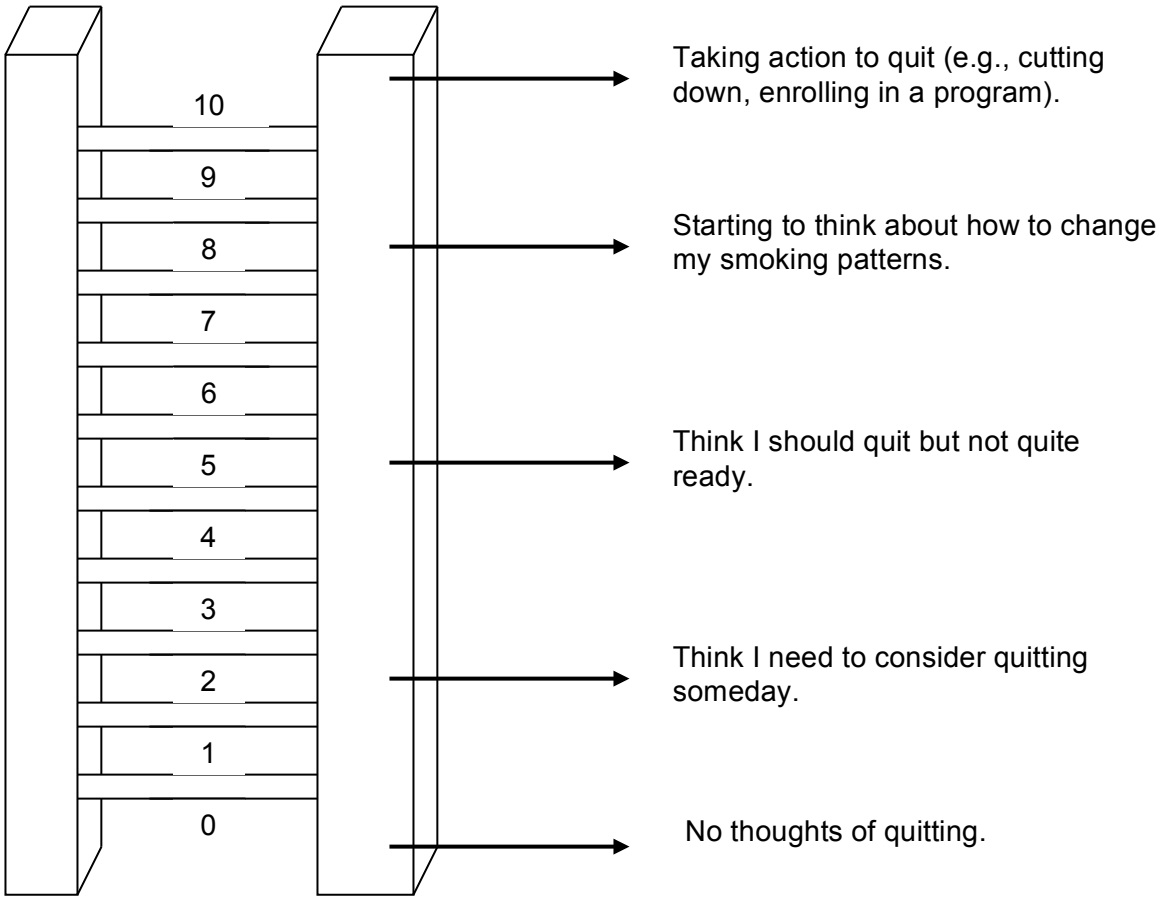
5. I am concerned about the likelihood of having a heart attack/stroke in the near future.

Strongly Disagree 1 2 3 4 Strongly Agree

ID Number _____ Session # _____

Are you thinking about quitting smoking?

Each rung on this ladder represents where various smokers are in their thinking about quitting. Circle the number that indicates where you are now.



ID Number _____ Session # _____

Exercise and Diet

Please answer the following questions:

1. I expect to engage in 150 minutes of moderate or 90 minutes of vigorous exercise a week for the next six weeks.

Strongly disagree 1 2 3 4 5 6 7 Strongly agree

2. I want to engage in 150 minutes of moderate or 90 minutes of vigorous exercise a week for the next six weeks.

Strongly disagree 1 2 3 4 5 6 7 Strongly agree

3. I intend to engage in 150 minutes of moderate or 90 minutes of vigorous exercise a week for the next six weeks.

Strongly disagree 1 2 3 4 5 6 7 Strongly agree

4. I expect to eat a healthy diet over the next six weeks.

Strongly disagree 1 2 3 4 5 6 7 Strongly agree

5. I want to eat a healthy diet over the next six weeks.

Strongly disagree 1 2 3 4 5 6 7 Strongly agree

6. I intend to eat a healthy diet over the next six weeks.

Strongly disagree 1 2 3 4 5 6 7 Strongly agree

ID Number _____

Single-item Questions about Perceived CVD Risk and Likelihood to Take Action to Reduce Risk

Note: These two single-item questions will be asked in session two. The questions will be administered verbally and will be recorded on this sheet by the individual conducting the second session. The questions will initially be asked after the participant has discussed the differences in their "baseline", or from memory, family history and their "verified" family history. The second time the questions will be asked is after the finalized pedigree has been discussed and risk information given to the participant based on the number of their family members with CVD.

After differences in "baseline" family history and "verified" family history are discussed:

Based on what you learned from your family, how at risk for developing CVD in your lifetime are you with "1" being "no risk at all" and "7" being "very high risk"?

No risk at all 1 2 3 4 5 6 7 Very high risk

Based on what you learned from your family and what you just told me, how likely are you to take action to change your risk factors with "1" being "no action" and "7" being "all things possible"?

No action 1 2 3 4 5 6 7 All possible actions

After risk information based on family members with CVD:

Based on what I just told you about your risk based on your family members with CVD, how at risk for developing CVD in your lifetime are you with "1" being "no risk at all" and "7" being "very high risk"?

No risk at all 1 2 3 4 5 6 7 Very high risk

How likely are you to take action to change your risk factors with "1" being "no action" and "7" being "all things possible"?

No action 1 2 3 4 5 6 7 All possible actions

ID Number _____

Family Medical History Form

Note: Initially, this form will be completed by the investigator while talking to the study participant. A copy, without the ID number, will be given to the participant to use while verifying the information with his or her family members.

You
What is your birthday?
Do you have any health or medical problems?
If yes, when were you diagnosed with this condition/illness?

Mother – Who did you talk to about this information?

When was your mother born (year of birth)?
Is your mother still living?
If she is still living, does she have any health or medical problems and what year were they diagnosed?

If she is no longer living, do you know what year she died?
Do you know the cause of her death?
When was the condition/illness diagnosed?
Did she have other health or medical problems and what year were they diagnosed?

Did any of this information change after talking to your family members?

Father – Who did you talk to about this information?

When was your father born (year of birth)?
Is your father still living?
If he is still living, does he have any health or medical problems and what year were they diagnosed?

If he is no longer living, do you know what year he died?
Do you know the cause of his death?
When was the condition/illness diagnosed?
Did he have other health or medical problems and what year were they diagnosed?

Did any of this information change after talking to your family members?

Maternal grandmother – Who did you talk to about this information?

When was your mother's mother born (year of birth)?
Is she still living?
If she is still living, does she have any health or medical problems and what year were they diagnosed?

If she is no longer living, do you know what year she died?
Do you know the cause of her death?
When was the condition/illness diagnosed?
Did she have other health or medical problems and what year were they diagnosed?

Did any of this information change after talking to your family members?

Maternal grandfather – Who did you talk to about this information?

When was your mother's father born (year of birth)?
Is he still living?
If he is still living, does he have any health or medical problems and what year were they diagnosed?

If he is no longer living, do you know what year he died?
Do you know the cause of his death?
When was the condition/illness diagnosed?
Did he have other health or medical problems and what year were they diagnosed?

Did any of this information change after talking to your family members?

Paternal grandmother – Who did you talk to about this information?

When was your father's mother born (year of birth)?
Is she still living?
If she is still living, does she have any health or medical problems and what year were they diagnosed?

If she is no longer living, do you know what year she died?
Do you know the cause of her death?
When was the condition/illness diagnosed?
Did she have other health or medical problems and what year were they diagnosed?

Did any of this information change after talking to your family members?

Paternal grandfather – Who did you talk to about this information?

When was your father's father born (year of birth)?
Is he still living?
If he is still living, does he have any health or medical problems and what year were they diagnosed?

If he is no longer living, do you know what year he died?
Do you know the cause of his death?
When was the condition/illness diagnosed?

Did he have other health or medical problems and what year were they diagnosed?

Did any of this information change after talking to your family members?

Sibling #1 – Who did you talk to about this information?

Is your oldest sibling male or female?
When was he or she born (year of birth)?
Does he or she have any health or medical problems and what year were they diagnosed?

If he or she is no longer living, how old was he or she when he or she died?
Do you know the cause of his or her death?
When was the condition/illness diagnosed?

Did he or she have other health or medical problems and what year were they diagnosed?

Is he or she adopted?

Did any of this information change after talking to your family members?

Sibling #2 – Who did you talk to about this information?

Is your next oldest sibling male or female?
When was he or she born (year of birth)?
Does he or she have any health or medical problems and what year were they diagnosed?

If he or she is no longer living, how old was he or she when he or she died?
Do you know the cause of his or her death?
When was the condition/illness diagnosed?

Did he or she have other health or medical problems and what year were they diagnosed?

Is he or she adopted?

Did any of this information change after talking to your family members?
Sibling #3 – Who did you talk to about this information?
Is your next oldest sibling male or female?
When was he or she born (year of birth)?
Does he or she have any health or medical problems and what year were they diagnosed?

If he or she is no longer living, how old was he or she when he or she died?
Do you know the cause of his or her death?
When was the condition/illness diagnosed?

Did he or she have other health or medical problems and what year were they diagnosed?

Is he or she adopted?

Did any of this information change after talking to your family members?

Repeat until all siblings are discussed.

Aunts and Uncles

Mother's Sibling #1 – Who did you talk to about this information?
Is your mother's oldest sibling male or female?
When was he or she born (year of birth)?
Does he or she have any health or medical problems and what year were they diagnosed?

If he or she is no longer living, how old was he or she when he or she died?
Do you know the cause of his or her death?
When was the condition/illness diagnosed?
Did he or she have other health or medical problems and what year were they diagnosed?

Is he or she adopted?

Did any of this information change after talking to your family members?

Mother's Sibling #2 – Who did you talk to about this information?
Is your mother's next oldest sibling male or female?
When was he or she born (year of birth)?
Does he or she have any health or medical problems and what year were they diagnosed?

If he or she is no longer living, how old was he or she when he or she died?
Do you know the cause of his or her death?
When was the condition/illness diagnosed?

Did he or she have other health or medical problems and what year were they diagnosed?

Is he or she adopted?

Did any of this information change after talking to your family members?

Mother's Sibling #3 – Who did you talk to about this information?
Is your mother's next oldest sibling male or female?
When was he or she born (year of birth)?
Does he or she have any health or medical problems and what year were they diagnosed?

If he or she is no longer living, how old was he or she when he or she died?
Do you know the cause of his or her death?
When was the condition/illness diagnosed?

Did he or she have other health or medical problems and what year were they diagnosed?

Is he or she adopted?

Did any of this information change after talking to your family members?

Repeat until all of your mother's siblings have been discussed.

Father's Sibling #1 – Who did you talk to about this information?
Is your father's oldest sibling male or female?
When was he or she born (year of birth)?
Does he or she have any health or medical problems and what year were they diagnosed?

If he or she is no longer living, how old was he or she when he or she died?
Do you know the cause of his or her death?
When was the condition/illness diagnosed?
Did he or she have other health or medical problems and what year were they diagnosed?

Is he or she adopted?

Did any of this information change after talking to your family members?

Father's Sibling #2 – Who did you talk to about this information?

Is your father's next oldest sibling male or female?
When was he or she born (year of birth)?
Does he or she have any health or medical problems and what year were they diagnosed?

If he or she is no longer living, how old was he or she when he or she died?
Do you know the cause of his or her death?
When was the condition/illness diagnosed?

Did he or she have other health or medical problems and what year were they diagnosed?

Is he or she adopted?

Did any of this information change after talking to your family members?

Father's Sibling #3 – Who did you talk to about this information?
Is your father's next oldest sibling male or female?
When was he or she born (year of birth)?
Does he or she have any health or medical problems and what year were they diagnosed?

If he or she is no longer living, how old was he or she when he or she died?
Do you know the cause of his or her death?
When was the condition/illness diagnosed?

Did he or she have other health or medical problems and what year were they diagnosed?

Is he or she adopted?

Did any of this information change after talking to your family members?

Repeat until all of your father's siblings have been discussed.

APPENDIX B:
CONSENT FORM

UNIVERSITY OF WASHINGTON
CONSENT FORM
My Family Medical History and Me Study

Researchers:

Investigator

Christopher C. Imes, BSN, RN Doctoral Candidate

Faculty Advisors

Frances M. Lewis, PhD, FAAN Professor, School of Nursing

Researcher's statement

We are asking you to be in a research study. The purpose of this consent form is to give you the information you will need to help you decide whether to be in the study or not. Please read this consent form carefully. You may ask me questions about the purpose of the research, what you will be asked to do, the possible risks and benefits of participating in this study, your rights as a volunteer, and anything else about the research or this consent form that is not clear. When I have answered all your questions, you can decide if you want to be in the study or not. This process is called "informed consent." I will give you a copy of this form for your records.

PURPOSE OF THE STUDY

The purpose of the study is to examine your family's history of cardiovascular disease, the influence of your family history on your risk for developing cardiovascular disease your lifetime, and things you can personally do to promote your health and decrease the risk for developing CVD in the future.

The study will also compare family medical history information given from memory to family medical history information after interviewing your family members.

The study includes personal and sensitive questions. Here are examples of the most personal and sensitive questions:

1) On one of the questionnaires, it asks "how often you drink alcohol, how much you drink on a typical day when you are drinking, and how often you have six or more drinks in one occasion."
2) On the same questionnaire, it asks if "you have smoked one or more cigarettes over the last 30 days and how many cigarettes you smoked in a week?"
3) There will also be questions about cardiovascular disease related illnesses and conditions in your family members and about "when and how your family members died."

Another purpose of this study is to look at three genes: (1) *LDLR*, (2) *APOB*, and (3) *HMGCR*. These genes are involved in cholesterol metabolism in your body. Naturally occurring variations in these genes can affect how easily or how quickly cholesterol is removed from your bloodstream which directly influences your cholesterol level. Studies have shown that variations in these genes can place an individual at slightly higher risk for developing coronary heart disease later in life.

STUDY PROCEDURES

This study will involve two sessions, each lasting between 1.5 to 2 hours. In the first session, I will measure your height and weight and blood pressure. After these measures, you will be escorted to a room at the University Medical Center to the Research Testing Services. A trained laboratory staff member will draw two tablespoons, or about 30 ml, of blood from a vein in your arm. In the event that we are unable to draw the blood on the first attempt, we will ask you if we can try again. Only two attempts to draw your blood will be made. This blood sample will be used to check your cholesterol, apolipoprotein A-I, and apolipoprotein B levels, and are important in helping me offer you ways to have a healthy lifestyle. The results from this blood analysis will be shared with you in the second session.

The blood sample will also be used to obtain your genetic material (DNA) to measure only: (1) *LDLR*, (2) *APOB*, and (3) *HMGCR*. No personal information will be “linked” to the DNA sample and all the samples will be analyzed at the end of the study. Therefore, there is no way for anyone to know which DNA sample was yours. For the same reason, there will be no way to determine which specific results belong to you. Additionally, only results from labs certified in the diagnosis of diseases can be given to individuals. Your results will be used for research purpose only. For all these reasons, you will not receive the results of the genetic testing.

The results of the genetic tests do not have implications on your clinical care. The current recommendations for lifestyle modification or the initiation of cholesterol reducing medications are based on current risk factors, which include a family history of cardiovascular disease but not the results of genetic tests, and current cholesterol level. Knowledge of the results of the genetic tests would not change any decision made regarding your clinical care. Your DNA will only be used for the three tests mentioned and will be destroyed at the end of the study.

After your blood sample is taken, I will escort you back to the study office, where you will be asked to complete some brief questionnaires. Your name will not be on any of the questionnaires., only a study ID number. Items on the questionnaires will ask you background information like your age, sex, and race/ethnic group, alcohol and tobacco use, and information about your exercise habits. The questionnaires will also ask you questions about your knowledge about heart disease, your own perceived risk for heart disease, and your intentions to quit smoking (if applicable), exercise, and eat a healthy diet. You may refuse to answer any question on the questionnaire. The questionnaire will take about 10 to 15 minutes to complete.

After completing the questionnaires, I will ask you if any of your family member members have had cardiovascular disease or conditions known to increase their risk for developing cardiovascular disease. For this study, cardiovascular disease will include a heart attack (myocardial infarction), chest pain (angina), heart failure (congestive heart failure), and a blood clot in the brain (stroke). Other questions that I will ask about your family members include year of birth, year or age when the disease or condition was diagnosed, and year or age when the family member died and cause of death (if applicable). Please do not give me full names, actual dates, or additional personal information about your family members. I will record this information on a form and I will use that form to draw a family pedigree, also known as a family tree. You will get a copy of these materials, including the pedigree.

Between the first and second sessions, I will ask you to contact as many of your family members as possible to verify the information you gave to me about your family's cardiovascular disease history. This includes your parents, grandparents, siblings, and aunts and uncles. You can use the form that I used to collect the information from you as a guide for what questions to ask. In that way, you can obtain any missing information and confirm what you said to me. The goal is to talk to as many family members as possible, but it OK if you cannot talk to all of your family members or if they do not want to share their information. No identifiable information about your family members will be collected and the data for the pedigree will be stored using a new "code name" not connected to your study ID number. If they have any questions or concerns, your family members can contact the principal investigator at XXX-XXX-XXXX.

The second session will take place approximately two weeks after the first session. During the second session, your family medical history will be updated based on any additional information you gathered from them and I will use that information to update your family's pedigree.

Based on the updated information on your family members, you will be given a "generalized" risk for developing cardiovascular disease or the conditions that increase the risk for cardiovascular disease in your lifetime. You will also be given your probability of developing cardiovascular disease or having a cardiovascular event in your lifetime compared to someone without a family history of cardiovascular disease based on the number of your first-degree relatives with cardiovascular disease. You will receive a copy of the updated pedigree.

Next, we will discuss results from your blood test. I will teach you about cholesterol, apolipoprotein A-I, and apolipoprotein B and how they influence your heart health. I will review your results from your blood tests and offer you brief counseling on how to maintain or enhance your healthy lifestyle for minimizing your risk of developing cardiovascular disease. You will be given a copy of your lab values.

Finally, I will compute your 10-year risk of having or dying from a heart attack. This will be based on your age, sex, cholesterol level, smoking status, blood pressure, and if you are on blood pressure lowering medications. I will help you learn ways you can increase or decrease your risk of having a heart attack based on lifestyle choices that are under your personal control.

After your risk information has been provided, you will have the opportunity to receive some brief counseling on how to engage in a healthier lifestyle, which can reduce your risk of developing cardiovascular disease. This will include information about smoking cessation (if applicable), exercising, and eating a healthy diet. Each topic will be discussed for about 5-10 minutes and will be interactive. You will receive pamphlets with additional information on each topic.

At the end of the second session, you will be asked to complete the same questionnaires you completed at the beginning of the first session. Again, you may refuse to answer any question or item. Also, you will be asked some open-ended questions about the activities done during the sessions and if you found them helpful.

Both sessions will be digitally recorded. The recording will be used by the researchers only and will not be used in any presentations. When quoted, your identity will not be disclosed.

All data from the study will be entered and stored on a password-protected desktop computer. The data will be entered under your ID number only. The document linking your identity and your ID number will be stored in a separate location and will be viewed only by the researchers. The desktop computer uses the Windows operating system and is secured by a continually updated integrated firewall, antivirus software, and the Faronics Corporation's DeepFreeze program, which prevents computers from corruption, intrusion or viral infection by locking the hard drive upon startup. The computer is kept in a locked research office. All data is backed-up on the secure School of Nursing Server.

RISKS, STRESS, OR DISCOMFORT

You may have brief discomfort and pain during the blood draw and bruising after it. If the blood cannot be drawn after the second attempt, no additional attempts will be made. If you have problems after you leave you can call the research staff at the phone number listed at the top of the consent form.

You may experience some emotional stress while having your height and weight measure, during the blood draw procedure, completing the questionnaires, or while answering the questions about your family members. You may experience distress while being told your risk for developing cardiovascular disease in your lifetime. After you are told your risk, you will be given tips and strategies on lifestyle changes you can make to reduce your risk.

There is a possible risk of loss of confidentiality. Your privacy will be strictly protected but we cannot absolutely guarantee there will be no breach of confidentiality. There is the risk that coded data could be released to the public, insurers, employers, or law enforcement agencies. There is also the risk that breach of computer security could release your information.

During the intervention, your blood pressure will be measured and lab tests will be done. It is possible that this will reveal pre-existing, but previously unknown, conditions such as high blood pressure (hypertension) or high cholesterol levels (hypercholesterolemia). This information will not go into your medical record and it will be up to you to inform your primary care provider of the results. Nonetheless, if there is a breath in confidentiality and the blood pressure and labs results can be linked to you and they reveal a “pre-existing condition,” then your insurability may be negatively affected.

The loss of confidentiality of genetic material could affect your insurability. For instance, information about your DNA might result in discrimination that would make it difficult for you to obtain certain health insurance coverage in the future. In this study, all identifying information will be removed from the sample and the results of the genetic tests will not be connected to your other data. Also, your DNA sample will be destroyed at the end of the study.

Genetic information about you will often apply (in one degree or another) to family members.

It is possible that genetic information might come to be associated with your racial or ethnic group.

ALTERNATIVES TO TAKING PART IN THIS STUDY

It is possible that your primary care provider would be able to provide you similar information about your risk for developing CVD based on your family medical history information and lab results. He or she could also provide you with information on ways to engage in a healthy lifestyle that reduced your CVD risk.

BENEFITS OF THE STUDY

There are no direct benefits to you for your participation in this study beyond insight your family history regarding CVD, a copy of your family’s pedigree based on the information you provided, a copy of your lab results, and information and pamphlets about things you can do to engage in or maintain a healthy lifestyle.

However, the study may advance our knowledge on ways family medical history information and pedigrees can be used to help young adults better understand their CVD risk. The results of the genetic tests may contribute to developing tests that identify individual at risk for CVD at a younger age when behavioral intervention can decrease the severity of the disease.

OTHER INFORMATION

Your identity will remain confidential. Access to your study information will be limited to the research team. However, there is one exception. The government or university staff sometimes reviews studies such as this one to make sure they are being done safely and legally. If a review of this study takes place, your records may be examined. The reviewers will protect your privacy. The study records will not be used to put you at legal harm.

We will label your samples and the information about you with a number, not your name. We will keep your name, address, telephone number, and other information that might identify you separate from your sample. Data will not be revealed to family members, insurance companies, employers, or other individuals or organizations. The blood sample used to extract your DNA will be labeled with a different number. This number will not be linked to your personal information. In this way the DNA information could never be traced back to a particular individual. For the same reason, you will not receive the results of the genetic testing.

The information that links your name to the data will be destroyed by January 1st, 2013 or six months after the study is completed (which ever one occurs first).

You may refuse to participate or may withdraw from the study at any time without penalty or loss of benefits to which they are otherwise entitled. However, depending on when you withdraw from the study, it may not be possible to destroy your blood sample before the genetic testing is performed. Please call XXX-XXX-XXXX if you would like your blood sample destroyed. All blood and DNA will be destroyed by January 1st, 2013 or six months after the study is completed (which ever one occurs first).

Please feel free to ask any questions before consenting to participate in this study.

COMPENSATION FOR INJURY

If you think you have an injury or illness related to this study, contact the investigator, Christopher Imes at XXX-XXX-XXXX, right away. He will refer you for treatment if necessary.

No money has been set aside to pay for things like lost wages, lost time, or pain. However, you do not waive any rights by signing this consent form.

The UW will pay up to $10,000 to reimburse for treatment of injury or illness resulting from the study.

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Printed name of study staff obtaining consent Signature Date

Participant's statement

This study has been explained to me. I volunteer to take part in this research. I have had a chance to ask questions. If I have questions later about the research, I can ask one of the researchers listed above. If I have questions about my rights as a research subject, I can call the Human Subjects Division at XXX-XXX-XXXX.. I will receive a copy of this consent form.

Please check and initial whichever one applies:

☐ I agree to participate in the study as described in this consent form and agree to have the sessions digitally recorded.

☐ I agree to participate in the study as described in this consent form, but I refuse to have the sessions digitally recorded.

☐ I agree to participate in the study, but will not provide a blood sample. I agree to have the session digitally recorded.

☐ I agree to participate in the study, but will not provide a blood sample. I refuse to have the session digitally recorded.

☐ I agree to participate in the study and will provide a blood sample for the lab testing only. I will not provide a blood sample for genetic testing. I agree to have the session digitally recorded.

☐ I agree to participate in the study and will provide a blood sample for the lab testing only. I will not provide a blood sample for genetic testing. I refuse to have the session digitally recorded.

_____

Printed name of participant Signature of participant Date

Copies to: Researcher
Participant

VITA

Christopher C. Imes was born in Willoughby, Ohio, which is near Cleveland, Ohio. He has lived in San Antonio, Texas, El Paso, Texas, Kailua, Hawaii, Tacoma, Washington, and Seattle, Washington. His heart will always belong to Cleveland. He received his Bachelor of Science in Nursing from Case Western Reserve University in May 2000. In June 2012, he earned a Doctor of Philosophy at the University of Washington in Nursing Science.