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The Perceived Utility of Personalized Genomic Medicine in Individuals with a Family History of Heart Disease: A Pilot Study

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The Perceived Utility of Personalized Genomic Medicine in Individuals with a Family History of Heart Disease: A Pilot Study

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Abstract

According to the World Health Organization (2005), cardiovascular disease (CVD) is the number one cause of death in most countries. Assessing a patient's risk for heart disease may include incorporating factors such as their gender, age, weight, tobacco history, cholesterol, blood pressure, family history, and more recently, genetics. Genome-wide association studies (GWAS) have made it possible to identify risk loci for many of the common, complex disorders, including coronary artery disease (CAD). As the medical genetics community undergoes a shift from a genetics focus to a genomics oriented focus, genomic medicine is becoming more accessible. Research has begun to examine how individuals perceive and utilize genomic information; however, little has been done to explore preliminary feelings towards personalized genomic medicine in those with a family history of heart disease alone.

This study explores the perceived utility of genomic testing in individuals with a family history of heart disease and begins to define a role for genetic counselors within the genomic medicine context. Individuals 18 years of age or older with at least one first-degree or two second-degree relatives with heart disease were invited to participate. An online questionnaire was distributed to patients at a local cardiology clinic, students at a local university, and through Facebook.

A total of 29 participants met eligibility criteria and completed 80% or more of the questionnaire. Frequencies, means, and standard deviations were calculated. Our results indicate that our study population had low genetic literacy. After viewing a

genetic information video, most participants perceived genomic information to be useful in understanding their risk of developing heart disease. Most participants also believed that a genetic counselor would be helpful in explaining not only genomic test results, but also one's risk for developing heart disease and medical management options. Lastly, respondents typically indicated they were more likely to exercise regularly than engage in diet modifications, take prescription medications, or regularly follow-up with a specialist if their risk for heart disease was increased because of genetics.

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Chapter 1. Background

1.1 Overview of Cardiovascular Disease

According to the World Health Organization (2005), cardiovascular disease (CVD) is the number one cause of death in most countries. It is a disease affecting the heart and blood vessels. Many of the complications of cardiovascular disease are associated with atherosclerosis (American Heart Association, 2016). Atherosclerosis, also called coronary heart disease (CHD) or coronary artery disease (CAD), affects the arteries that bring oxygenated blood to the heart (National Heart, Lung, and Blood Institute, 2015). It occurs when plaque accumulates along the arterial walls (American Heart Association, 2016). This plaque can continue to accumulate over time, and eventually it will either harden or burst. Plaque that hardens will narrow the arteries, restricting blood flow, and plaque that bursts can result in the formation of a blood clot that restricts blood flow (National Heart, Lung, and Blood Institute, 2015).

When blood flow to the heart becomes restricted, it can cause chest pain or myocardial infarction. Eventually, CHD can result in heart failure or arrhythmias due to a weakened heart muscle. Recommendations for preventing and treating CHD include making lifestyle modifications to address obesity, taking statins, which lower cholesterol, and possibly undergoing necessary surgical procedures (National Heart, Lung, and Blood Institute, 2015; American Heart Association, 2013).

Assessing a patient's risk for CVD may include incorporating factors such as their gender, age, weight, use of tobacco products, cholesterol, blood pressure, and family history (Anderson, Odell, Wilson, & Kannel, 1991; Backer et al., 2003; Conroy et al., 2003; Murabito et al., 2005; Nasir et al., 2004). In addition, it is possible to incorporate certain genetic variants into a patient's risk assessment for CVD. One single gene condition associated with early-onset CVD is familial hypercholesterolemia (FH). This condition results in poor metabolism of low-density lipoprotein (LDL), which is a type of cholesterol found in the body. The frequency of this condition in Western countries is believed to be around 1 in 400 to 1 in 500 (Austin, Hutter, Zimmern, & Humphries, 2004). Management of this condition for adults requires decreasing the risk factors associated with coronary artery disease (CAD). This includes engaging in exercise regularly, eating a healthy diet and managing one's weight, quitting smoking, treating high blood pressure, taking statins potentially in addition to other medications to decrease lipid levels, taking a low-dose aspirin for those at high risk, and possibly referring to a lipid specialist. Children with FH are recommended to engage in the same healthy lifestyle activities as adults and see a lipid specialist. Children with this condition may begin statin therapy starting at about eight years of age. When left untreated, affected men have a 50% chance of experiencing a coronary event, either fatal or non-fatal, by 50 years of age. For untreated woman, this risk is 30% by 60 years of age (Youngblood & Knowles, 2016).

In addition, genome-wide association studies (GWAS) are being used to identify risk loci for many of the common, complex disorders including coronary artery disease (Jostins & Barrett, 2011). The variants, or SNPs, found in GWAS confer a modest effect

(Bodmer & Bonilla, 2008; Ding, Bailey, & Kullo, 2011). However, in one study, researchers determined that including genetic information at 11 SNPs into the Framingham Risk Score resulted in a significant reclassification of the approximate 10-year risk for CHD (Ding, Bailey, & Kullo, 2011). More recently, the Myocardial Infarction Genes, or MI-GENES, clinical trial utilized genotype information from 28 SNPs associated with increased susceptibility for CHD to investigate whether genetic risk for CHD affects health outcomes. In this trial, researchers utilized 28 SNPs to create genetic risk scores (GRS). After incorporating the GRS into the total CHD risk, risk approximations in the high GRS group rose by at least 10% (Kullo et al., 2016).

Further evidence for the genetic basis of CAD is that this condition clusters within families. This familial clustering suggests that genetics contribute to the development of this condition. Twin studies have been used to estimate the heritability of this disease. According to these large studies, the heritability of CAD is estimated to be about 50% to 60%. Similarly, the heritability of myocardial infarction is estimated to be about 50% to 60% (Dai, Wiernek, Evans, & Runge, 2016). Given what has been uncovered about the etiology of heart disease, it is undeniable that a genetic basis for this condition exists.

1.2 Personalized Genomic Medicine

Within the field of medical genetics, there is an ongoing shift from a narrower genetics focus to a broader genomics focus (Collins and Guttmacher, 2001). Genomic medicine is defined as "the diagnosis, optimized management, and treatment of disease – as well as screening, counseling, and disease gene identification – in the context of information provided by an individual patient's personal genome." (Boone, Wiszniewski, & Lupski, 2011). The Human Genome Project and the International Haplotype Map

have made it possible to perform GWAS studies (Morton, 2008). As such, genomic medicine is becoming more accessible. Some healthcare providers will incorporate a patient's genomic information to help guide disease management. In the past, direct-to-consumer genetic testing companies have included analyzing complex diseases in their tests (Marshall, 2011; Kaufman et al., 2012). Personalized medicine can be used to provide a risk assessment for complex diseases and help guide decision-making regarding which therapy to pursue (Mills, Barry, & Haga, 2014). The aim of personalized medicine is to incorporate an individual's genomic data (as well as other relevant variables) into their clinical evaluation to more effectively guide that individual's medical management (Abul-Husn, Owusu Obeng, Sanderson, Gottesman, Scott, 2014).

While there is a potential for genomic medicine to give patients information they can preemptively act upon to improve their health, how genomic test results are received and utilized by patients continues to be investigated. It has been found that when compared to a control group without a genetic predisposition for cardiovascular disease, individuals with a single-gene genetic predisposition (FH) believe medication to be more effective, but they do not differ with the control group in terms of the perceived effectiveness of living a healthy life or engaging in preventive behavior (Claassen et al., 2012). In terms of providing genomic information to individuals, it has been shown that although participants generally understand genomic risk information, they more frequently remember results indicating an increased risk or those they are particularly interested in (Gordon et al., 2012). Most undergoing genomic testing say that a desire to improve their health was the primary reason they pursued genomic testing (Gollust et al.,

2012; Su et al., 2011), but it has been shown that not all change their lifestyle or discuss their results with their physician (Gordon et al., 2011).

However, the MI-GENES clinical trial found a somewhat different result. When providing participants with a 10-year probability of developing CHD using either a conventional risk score (CRS) or a conventional risk score and genetic risk score (GRS), those that received genetic risk information had lower LDL-C levels at 6 months than those who received just the CRS. The difference between the groups in terms of LDL-C levels was due to initiation of statin therapy. Although presentation of genetic risk information resulted in initiation of statin therapy, after a discussion with a physician, there were no differences in dietary fat intake, exercise, or level of anxiety between the two groups. This indicates that those at genetic risk may be willing to engage in medical interventions to reduce their risk of developing CHD, but making lifestyle modifications may be more difficult for them (Kullo et al., 2016).

Genomic risk information not only affects a patient's behavior and medical management; it also has psychological effects. Families and individuals affected with cardiogenetic conditions report a mix of psychological stressors (i.e., guilt about passing on the condition, isolation, and anxiety) and positive results (i.e., resolution and a positive attitude). For families and individuals receiving genetic testing or personalized genomic medicine, it may be helpful to provide psychological counseling You'rto address these stressors that may arise (Hidayatallah et al., 2014).

1.3 Genetic Counseling within the Personalized Genomic Medicine Context

In the past, direct-to-consumer (DTC) genetic tests provided consumers with a risk assessment of certain complex diseases based on the consumer's genomic

information. Members of the public frequently misinterpreted genomic DTC results even though they considered these results to be straightforward. In addition, the public thought these results would be more beneficial in guiding their medical management than genetic counselors did. This indicates that patients receiving genomic test results may need assistance to interpret the meaning and utility of these results correctly (Leighton, Valverde, & Bernhardt, 2011).

When genetic counselors provide genomic risk information, it is typically associated with positive results. In one study, participants receiving genomic risk information for Type 2 Diabetes Mellitus reported greater trust in the results if a genetic counselor provided them (Mills, Barry, & Haga, 2014). In addition, the MI-GENES clinical trial assessed how presentation of CHD genetic risk information by a genetic counselor affected perceived personal control and genetic counseling satisfaction as a secondary study. In this study, all participants received their CHD risk from a genetic counselor. In comparison to those receiving a conventional risk score only, those who received a genetic risk score in addition to a conventional risk score reported greater perceived personal control and genetic counseling satisfaction. This result indicates that patients want to be receiving CHD genetic risk information and report greater genetic counseling satisfaction when they do receive this information (Robinson et al., 2015).

The genetic counseling approach of facilitating open communication while integrating disease information with psychosocial counseling leads to greater empowerment and self-efficacy for patients. These effects may lead to behavior change (Inglis et al., 2015). Therefore, genetic counselors may be useful in the process of

relaying information regarding common complex diseases in such a way that would result in positive lifestyle changes (Austin, 2015).

In one prospective study, researchers aimed to develop feedback strategies for genomic test results for genetic counselors and other healthcare professionals. They asked 60 women diagnosed with breast cancer at a young age (40 or younger) in semi-structured interviews what information they would like to receive when genomic test results are disclosed. They found that those who participated were most interested in the possible health impact associated with a variant. They were interested in the health-related implications of variants for both themselves and their family members. Participants also wanted to know the quantitative risk associated with a variant and the variant's prevalence in the population. Regarding variants increasing risk for preventable/treatable disorders, interviewees were most interested in education on decreasing their risk, preventing the condition, or treating the condition (Seo et al., 2016). Although this study examined this topic in individuals diagnosed with breast cancer at a young age, the majority opinion regarding variants associated with preventable or treatable disorders can be applied to CHD.

1.4 Genetic Counselors as Genomic Counselors

> Genetic counseling is the process of helping people understand and adapt to the medical, psychological and familial implications of genetic contributions to disease. This process integrates:
>
> - Interpretation of family and medical histories to assess the chance of disease occurrence or recurrence
> - Education about inheritance, testing, management, prevention,

resources and research.

- Counseling to promote informed choices and adaptation to the risk or condition. (National Society of Genetic Counselors, N.D.)

Genetic counselors are trained in the scientific principles of genetics, communication, risk evaluation, and incorporating a patient-focused approach into their practice (O'Daniel, 2010). They have been described as useful in recording family histories, discussing inheritance and clinical features of a condition, and addressing psychosocial concerns related to heritable conditions. They also discuss genetic testing including the different types of results, limitations, and benefits as well as risks of testing (Hershberger, Cowan, Morales, & Siegfried, 2009). Therefore, genetic counselors are the ideal professionals to not only explain the inheritance of complex diseases, such as heart disease, but also to consent for genomic testing and discuss the potential implications of undergoing this type of expansive testing.

As such, genetic counselors are excellent candidates to play a pivotal role in integrating genomic disease risks into the healthcare field. Within the genomic medicine context, genetic counselors are an appropriate choice for facilitating testing, interpreting results, speaking with patients about their risk assessment, addressing the limitations of genomic testing, and providing information to the public (O'Daniel, 2010).

The National Society of Genetic Counselors (NSGC) also sees the value of the genetic counselor's role in the genomic era. They have created a Personalized Medicine Special Interest Group (SIG) (Mills & Haga, 2014). This special interest group is now called the Precision Medicine SIG (NSGC, 2017). In addition, the 35th Annual Education Conference was titled "A Landmark in Genomics: Our Value in Healthcare." In the 2012

NSGC Professional Status Survey, 1.2% of genetic counselors included in the survey indicated that they have a specialty in genomic medicine or personal genomics/genomic profiling (NSGC, 2012, as cited in Mills & Haga, 2014). An updated value could not be found for 2016.

This new era of genomic testing will demonstrate a shift from reactive testing with the purpose of determining a diagnosis for mostly single-gene disorders to proactive large-scale testing to prevent complex diseases. Genomic counseling will deviate from the traditional model of genetic counseling in: "1) the number and/or type of diseases for which testing is available and discussed, 2) purpose of testing, 3) intervention and clinical utility and 4) access to testing" (Mills & Haga, 2014). The type of patient for which genetic testing is ordered may also differ. In typical genetic counseling, those undergoing genetic testing either have a genetic condition or are at risk for having inherited a genetic condition. This may also be the case for those pursuing large-scale genome testing; however, patients with no health complications or family history may have this testing too (Patel *et al.*, 2013).

Genomic counselors will also be filling expanded roles. One of the key areas in which role expansion is predicted is in health promotion whose aim is to reduce the chance of developing a disease. In addition to helping individuals comprehend the genetic and environmental basis of risk, counselors may also discuss prevention information, screening, and further suggestions to inspire engagement in preventive behavior (Mills & Haga, 2014). Motivational counseling, which is more directive, will likely be useful in helping patients follow behavior modifications and comply to

treatment recommendations, in addition to bettering health outcomes (Hettema, Steele, & Miller 2005, as cited in Mills & Haga, 2014).

Studies have begun publishing recommendations for "genomic counseling." Following a case where a genetic counselor and medical geneticist provided genomic counseling for a patient after direct to consumer (DTC) genetic testing, two authors suggested practice recommendations for this area of genetic counseling. The recommendations included studying the genomic test results before the session takes place and focusing on results of significance. They also suggest using resources, such as primary literature and other sources online (i.e., dbSNP), to further study genetic variants. The creation of visual aids to provide education on complex genomic concepts was encouraged. Lastly, the educational component is stressed for these types of sessions. The authors suggested that "education should be a major component of genomic counseling sessions, including the provision of additional resources for the patient to use after the session" (Sturm & Manickam, 2012).

Recognizing the suitability of the genetic counseling profession in providing genomic counseling, studies are starting to be published addressing how to train both students and working professionals to enter this new era of medicine (Hooker, Ormond, Sweet & Biesecker, 2014). In addition, many program directors recognize the need to incorporate genomic medicine topics into genetic counseling program curricula. Most program directors believe it is important to incorporate the topic of genomics into genetic counseling training courses. In addition, during interviews, program directors used adjectives like "critical" and "vital" when addressing the importance of training students for genomic counseling (Profato, Gordon, Dixon, & Kwan, 2014). Within these

programs, students should gain observation and experience to be exposed to the nuances of genomic counseling (Mills & Haga, 2014).

1.5 Value of Study

Currently, the medical genetics community is shifting from a genetics focus to a genomics orientation (Collins and Guttmacher, 2001). Investigations on how patients receive and utilize genomic results have begun (Gordon et al., 2012; Kullo et al., 2016). Scientists have also begun to investigate the benefits of using a genetic counselor to explain genetic risk information for complex diseases (Mills, Barry, & Haga, 2014); however, there are still some gaps in the literature. First, there is little research on presenting a genomic risk assessment to patients at high risk for cardiovascular disease. Until the MI-GENES Clinical Trial was published last year, patient response to knowledge of the complex genetics of cardiovascular disease went largely uninvestigated in the literature (Kullo et al., 2016). Whereas there has been literature exploring personal utility after receiving genome test results and literature exploring how health messages about genetic risk for common conditions affect perception of susceptibility in the public, little has been done to explore preliminary feelings towards personalized genomic medicine in individuals with a family history of heart disease (Lewis et al., 2015; Smerecnik et al., 2009). Therefore, exploring whether those with a family history of heart disease find genomic information beneficial and of use would further add to our knowledge of the public perception of personalized genomic medicine.

This study explores the perceptions of individuals with a family history of cardiovascular diseases in regard to genetic risk factors associated with heart conditions, such as coronary heart disease. This study has four goals: (1) to assess individuals'

understanding of the genetic basis of heart disease, (2) to determine whether these individuals think personalized genomic medicine would be helpful in assessing their risk of developing heart disease, (3) to identify the genetic counselor's role in providing genomic risk information, and (4) to determine whether these individuals intend to make lifestyle modifications having learned about the genetic basis of heart disease. This exploratory research provides insight into the perceived utility of genomic testing for individuals with a family history of a complex disease. In addition, it begins to define a role for genetic counselors within a genomic medicine context.

Chapter 2. The Perceived Utility of Personalized Genomic Medicine in Individuals with a Family History of Heart Disease: A Pilot Study

2.1 Abstract

According to the World Health Organization (2005), cardiovascular disease (CVD) is the number one cause of death in most countries. Assessing a patient's risk for heart disease may include incorporating factors such as their gender, age, weight, tobacco history, cholesterol, blood pressure, family history, and more recently, genetics. Genome-wide association studies (GWAS) have made it possible to identify risk loci for many of the common, complex disorders, including coronary artery disease (CAD). As the medical genetics community undergoes a shift from a genetics focus to a genomics oriented focus, genomic medicine is becoming more accessible. Research has begun to examine how individuals perceive and utilize genomic information; however, little has been done to explore preliminary feelings towards personalized genomic medicine in those with a family history of heart disease alone.

This study explores the perceived utility of genomic testing in individuals with a family history of heart disease and begins to define a role for genetic counselors within the genomic medicine context. Individuals 18 years of age or older with at least one first-degree or two second-degree relatives with heart disease were invited to participate. An online questionnaire was distributed to patients at a local cardiology clinic, students at a local university, and through Facebook.

A total of 29 participants met eligibility criteria and completed 80% or more of the questionnaire. Frequencies, means, and standard deviations were calculated. Our results indicate that our study population had low genetic literacy. After viewing a genetic information video, most participants perceived genomic information to be useful in understanding their risk of developing heart disease. Most participants also believed that a genetic counselor would be helpful in explaining not only genomic test results, but also one's risk for developing heart disease and medical management options. Lastly, respondents typically indicated they were more likely to exercise regularly than engage in diet modifications, take prescription medications, or regularly follow-up with a specialist if their risk for heart disease were increased because of genetics.

2.2 Introduction

According to the World Health Organization (2005), cardiovascular disease (CVD) is the number one cause of death in most countries. It is a disease affecting the heart and blood vessels. Many of the complications of CVD are associated with atherosclerosis (American Heart Association, 2016). Atherosclerosis, also called coronary heart disease (CHD) or coronary artery disease, affects the arteries that bring oxygenated blood to the heart (National Heart, Lung, and Blood Institute, 2015). It occurs when plaque accumulates along the arterial walls (American Heart Association, 2016). This plaque can continue to accumulate over time, and eventually it will either harden or burst. Plaque that hardens will narrow the arteries, restricting blood flow, and plaque that bursts can result in the formation of a blood clot that restricts blood flow (National Heart, Lung, and Blood Institute, 2015).

Assessing a patient's risk for CVD may include incorporating factors such as their gender, age, weight, use of tobacco products, cholesterol, blood pressure, and family history (Anderson, Odell, Wilson, & Kannel, 1991; Backer et al., 2003; Conroy et al., 2003; Murabito et al., 2005; Nasir et al., 2004). In addition, it is possible to incorporate certain genetic variants into a patient's risk assessment for CVD. One single gene condition associated with early-onset CVD is familial hypercholesterolemia (FH). This condition results in poor metabolism of low-density lipoprotein (LDL), which is a type of cholesterol found in the body (Austin, Hutter, Zimmern, & Humphries, 2004). When left untreated, affected men have a 50% chance of experiencing a coronary event, either fatal or non-fatal, by 50 years of age. For untreated woman, this risk is 30% by 60 years of age (Youngbloom & Knowles, 2016).

Additionally, GWAS studies have identified SNPs that confer a modest effect contributing to common complex disorders (Jostins & Barrett, 2011; Bodmer & Bonilla, 2008). SNPs stands for single nucleotide polymorphisms (Kullo et al., 2016). A recent clinical trial that aims to assess whether genetic susceptibility for CHD affects health outcomes, the MI-GENES Clinical Trial, utilized 28 SNPs to create genetic risk scores (GRS). In this trial, after incorporating the GRS into the total CHD risk, risk approximations in the high GRS group rose by at least 10% (Kullo et al., 2016). Both the condition FH and this clinical trial provide evidence for a genetic basis to heart disease.

Given this, within the field of medical genetics, there is an ongoing shift from a narrower genetics focus to a broader genomics focus (Collins and Guttmacher, 2001). The aim of personalized medicine is to incorporate an individual's genomic data (as well as other relevant variables) into their clinical evaluation to more effectively guide that

individual's medical management (Abul-Husn, Owusu Obeng, Sanderson, Gottesman, Scott, 2014). Personalized medicine can be used to provide a risk assessment for complex diseases and help guide decision-making regarding which therapy to pursue (Mills, Barry, & Haga, 2014).

Most undergoing genomic testing say that a desire to improve their health was the primary reason they pursued genomic testing (Gollust et al., 2012; Su et al., 2011), but it has been shown that not all change their lifestyle or discuss their results with their physician (Gordon et al., 2011). However, the MI-GENES clinical trial found a somewhat different result. When providing participants with a 10-year probability of developing CHD using either a conventional risk score (CRS) or a conventional risk score and genetic risk score (GRS), those that received genetic risk information had lower LDL-C levels at 6 months than those who received just the CRS. The difference between the groups in terms of LDL-C levels was due to initiation of statin therapy. Although presentation of genetic risk information resulted in initiation of statin therapy, after a discussion with a physician, there were no differences in dietary fat intake, exercise, or level of anxiety between the two groups. This indicates that those at genetic risk may be willing to engage in medical interventions to reduce their risk of developing CHD, but making lifestyle modifications may be more difficult for them (Kullo et al., 2016).

When genetic counselors are the professionals providing genomic risk information, it is typically associated with positive results. In one study, participants receiving genomic risk information for Type 2 Diabetes Mellitus reported greater trust in the results if a genetic counselor provided them (Mills, Barry, & Haga, 2014). In addition, the MI-GENES clinical trial assessed how presentation of CHD genetic risk

information by a genetic counselor affected perceived personal control and genetic counseling satisfaction as a secondary study. In comparison to those receiving a conventional risk score only, those who received a genetic risk score in addition to a conventional risk score reported greater perceived personal control and genetic counseling satisfaction. This result indicates that patients want to be receiving CHD genetic risk information and report greater genetic counseling satisfaction when they do receive this information (Robinson et al., 2015). As such, genetic counselors are excellent candidates to play a pivotal role in integrating genomic disease risks into the healthcare field (O'Daniel, 2010).

Recognizing the suitability of the genetic counseling profession in providing genomic counseling, studies are starting to be published addressing how to train both students and working professionals to enter this new era of medicine (Hooker, Ormond, Sweet & Biesecker, 2014). Similarly, most program directors believe it is important to incorporate the topic of genomics into genetic counseling training courses (Profato, Gordon, Dixon, & Kwan, 2014). Within these programs, students should gain observation and experience to be exposed to the nuances of genomic counseling (Mills & Haga, 2014).

This present study is exploratory research that will provide insight into the perceived utility of genomic testing for individuals with a family history of a complex disease. In addition, it will begin to define a role for genetic counselors within a genomic medicine context. Existing literature explores how complex genetic risk information is received and utilized by those having undergone genomic testing, but none of these studies investigate the pre-test perceived utility of this technology in individuals with a

family history of heart disease alone (Gordon et al., 2012; Gollust et al., 2012; Kullo et al., 2016). Addressing this question in the current study will broaden our understanding of whether individuals at risk for complex diseases anticipate genomic medicine to be useful. Moreover, although literature has begun to address the benefits of integrating the process of genetic counseling into providing genetic risk assessment for complex diseases, this study aims to directly address whether individuals prefer receiving these results from a genetic counselor (Mills, Barry, & Haga, 2014).

Current research has also indicated that presentation of genomic risk information does not lead to lifestyle modifications in a majority of participants (Gordon et al., 2011). In the MI-GENES clinical trial, although the researchers found that the initiation of statin therapy resulted in lower LDL-C levels in the group presented with a GRS, they also found that there were no differences in dietary fat intake or exercise between those presented with a GRS and those not presented with a GRS (Kullo et al., 2016). Through assessing participants' intention to change behavior following education of the genetic risks associated with heart disease, we can generate a pre-genetic test measure of whether participants are willing to change behavior. In addition, it will allow us to address the question of how high a genetic risk would need to be to prompt the participants to engage in health-related behavioral changes.

2.3 Materials and Methods

2.3.1 Study Population

This study surveyed individuals age 18 or older with a family history of heart disease. Participants were required to have at least one first-degree relative or two second-degree relatives with heart disease to participate in the survey developed on

SurveyMonkey.com. Participants were excluded if they did not have at least one first-degree or two second-degree relatives with heart disease. Eligibility was ascertained by a series of questions at the start of the study. If participants did not meet eligibility criteria, they were routed out of the survey using branch logic developed by SurveyMonkey. Individuals with a family history and current heart disease were not excluded from the study. Participants were offered the chance to take part in a drawing for one of five, $5 Amazon gift cards. All answers to questions were completely anonymous. Participants were redirected to a separate survey to provide their email addresses if they were interested in the opportunity to take part in the gift card drawing.

2.3.2 Survey Distribution

Information to take part in the study was provided to a local cardiology clinic, Palmetto Heart, and to a local American Heart Association chapter. The clinic and association were provided with a flyer and letter to participants (Appendix A and B) via email. Students at a small liberal arts university in the Southeastern United States were also invited to take part in the study. In addition, the survey was posted on both the American Heart Association Facebook page as well as the principle investigator's personal Facebook. It was posted on the principle investigator's Facebook wall and shared by Facebook friends.

2.3.3 Instrumentation

An online questionnaire (Appendix C) was developed on SurveyMonkey.com. The questionnaire was composed of primarily quantitative questions as well as a few qualitative questions. One qualitative question was used to assess the participant's intent of sharing personalized heart disease genetic risk information with their family members.

Another was asked to determine which healthcare providers participants thought would be most helpful in explaining genomic test results and medical management. Question and answer formats found in this questionnaire included multiple choice, comment box, and Likert scale. A full set of the questions asked in the questionnaire can be found in Appendix C. A participant consent agreement (Appendix D) was found on the first page of the questionnaire. By pressing the "Next" button at the bottom of the page, participants indicated their consent to participate in the study. The questionnaire was designed with four goals in mind:

1). To assess participants' baseline understanding of the genetic risk factors associated with heart disease

2). To assess the perceived utility of genomic information for participants

3). To determine the genetic counselor's role in providing genomic risk information

4). To assess whether participants would intend to alter their lifestyle having learned that genetics increased their risk for developing heart disease

After a series of questions determining eligibility, participants' baseline understanding of the genetic risks associated with heart disease was assessed. Following this portion of the questionnaire, a link to a short educational video about the genetic risks associated with heart disease was provided. The script to this video can be found in Appendix E. Questions assessed the perceived utility of the information presented in the video. Participants were asked to indicate if they would share genetic risk information with family and doctors. A comment box was used so that participants could identify those family members with whom they would share this information.

Participants were then presented with a description of the genetic counseling profession, cited from the National Society of Genetic Counselors. After this, questions were asked to determine whether participants thought genetic counseling would be helpful in understanding the genetic risk, genomic test results, and medical management of heart disease. The participants were also asked to indicate other healthcare professions that may be helpful in explaining genomic test results and their implications using a comment box. Lastly, a Likert scale was utilized to assess participants' intention to undergo lifestyle modifications if they learned genetics alone increased their risk of developing heart disease by 10%. As part of this section of the questionnaire, comment boxes were used to determine the percent genetic risk at which participants would be willing to alter their lifestyle.

The categorical order of questions was as follows: gauging background knowledge of genetics, assessing the usefulness of the genomic risk information presented in the genetic education video, determining the role of the genetic counselor and other healthcare providers in discussing genomic risk information and management, assessing intention to change lifestyle, and demographics. Demographic information included the participant's age, preferred gender, highest education level completed, and current heart disease status (i.e., affected vs. unaffected). All information presented in the questionnaire was used from references cited in the Background section.

2.3.4 Data Analysis

Both quantitative and qualitative questions from the questionnaire were analyzed using descriptive statistics. Statistical Package for the Social Sciences 23.0 (SPSS) and Excel 2016 were utilized to analyze quantitative data. Two sets of Likert scale questions

can be found in this questionnaire. The first set was used to determine participants' baseline understanding of the genetics of heart disease. For this question, answers were chosen from a drop-down menu with all numbers between 0-10. A value of 0 indicated 0%, and a value of 10 indicated 100%. The second Likert scale was utilized to assess participants' intention to undergo lifestyle modifications if they learned genetics alone increased their risk of developing heart disease by 10%. For this question, answers were coded between 1 to 5, with a value of 1 indicating that the intention to change was very likely, and a value of 5 indicating that the intention to change was unlikely.

Frequencies were calculated for all questions. Mean and standard deviations were calculated when appropriate to address one of the four goals of this study. Chi-square tests were used to determine relationships between questions; however, most results from these tests were statistically insignificant. Pearson correlation tests did not show statistically significant results. All Chi-square and Pearson Correlation tests were analyzed and discussed using Laerd Statistics. Means and standard deviations were reported as suggested in the APA Publication Manual.

The principal investigator coded qualitative data into themes. These themes were reviewed by all committee members. Themes regarding which relatives participants would share personal genomic information with and which providers would be helpful in explaining this information were elucidated.

2.4 Results

2.4.1 Participant Demographics

Fifty people began the questionnaire; however, only 29 of these participants met eligibility criteria and completed 80% of the survey or more (58.0%). Of these 29

participants, 20.7% had relatives with heart disease on their mother's side, 37.9% had relatives with heart disease on their father's side, and 41.4% had heart disease on both sides of their family.

Most participants were female (65.5%). Participants were between 18-66 years of age (M = 28.276, SD = 13.849). The majority of participants were unaffected with heart disease (96.6%). All demographic information collected for these participants can be found in Table 2.1.

2.4.2 Background Genetic Knowledge

Both a Likert scale and multiple choice questions were used to assess participants' baseline knowledge of genetics. These questions had a particular emphasis on a participant's knowledge in relation to heart disease. The first two questions used a Likert scale. This scale was presented as a drop-down menu containing all numbers between 0-10. In this scale, 0 equated to 0% and 10 equated to 100%. When asked what participants thought the risk of heart attack was based on genetic factors, 34.5% indicated a correct value of 5 or 6. The average value indicated was 6.655 (SD = 2.525). When asked what the risk of atherosclerosis is based on genetic factors, 34.5% of participants indicated a correct value of 5 or 6 (M = 6.552, SD = 2.213). Participants were also asked to assess whether those with a family history of a single gene condition related to coronary artery disease, called FH, are at higher, the same, or lower risk for developing heart disease than those with a family history of heart attacks. Approximately 72% of all participants accurately indicated that those with a family history of FH are at a higher risk for heart disease than those with a family history of heart attacks.

The last three questions of this section assessed participants understanding of the genetic relatedness between various relatives. A minority of participants accurately answered that having a sister with heart disease or a mother with heart disease would put them at equal risk for developing the condition (27.6%). A total of 55.2% of participants correctly answered that having a mother with heart disease would put them at greater risk for developing the condition than having a grandmother with the condition. Similarly, 55.2% of participants accurately answered that having an aunt with heart disease would put them at greater risk for the condition than having a cousin with heart disease.

None of the 29 participants answered all six background genetic knowledge questions correctly. The average number of questions answered correctly was 2.793 (*SD* = 1.236). A graphical representation of the frequencies of the number of correct answers can be found in Figure 2.1.

2.4.3 Perceived Utility of Personalized Genomic Medicine

After watching a short genetic education video, participants were asked to specify the usefulness of genomic information and the individuals with whom they would share this information with. A total of 51.7% of participants strongly agreed that genetic/genomic information would be useful for understanding their risk of developing heart disease. In addition, 44.8% of participants agreed that genetic/genomic information would be useful in understanding their risk for this condition. Only one stated a neutral stance on this question (3.4%). No participants indicated that they disagreed or strongly disagreed with the usefulness of this information.

Most participants indicated they would share this information with their doctor (96.6%). Only one participant indicated they would not share this information with their

physician (3.4%). Most participants also indicated they would share this information with family members (96.6%). Again, only one participant indicated they would not (3.4%).

When asked which family members participants would share this information with, a couple of themes were identified. Answers that could not be easily coded into immediate and extended family members were excluded from analysis. For instance, participants who indicated they would share this information with "all" family members were not included. Most participants would share this information with immediate family members. A total of 79.3% participants specifically indicated they would share this information with at least one of the following: a parent, a sibling, or children. A majority of participants indicated they would share this information with their mother and/or father. One participant noted:

> [I] would share this information [with] my parents who do not already have great knowledge about this subject. I would also share this information with other family members that [may be] at high risk for heart problems in their later life, and I along with them will discuss actions that we can take now [being young] that will lower our chances or prevent our chances of heart problems in our later life.

Most participants also indicated they would inform their siblings of this information.

Only seven participants indicated they would share this information with extended family members. Some participants explicitly listed extended family members as with whom they would share this with. These answers included grandmother, grandparent(s),

aunts/uncles, and cousins. A few others listed they would share this information with extended/non-immediate family members.

2.4.4. Genetic Counselors in the Genomic Context

After being provided with a description of the genetic counseling profession, cited from the National Society of Genetic Counselors, participants were asked to indicate which healthcare professionals would be helpful in understanding the risk for developing heart disease, genomic test results, and medical management. When asked whether a genetic counselor would be helpful to discuss a participants' risk for heart disease, 82.8% of participants indicated a genetic counselor would be helpful. A total of four participants indicated they were unsure about this (13.8%), and one participant indicated a genetic counselor would not be helpful in understanding this information (3.4%). Additionally, 86.2% of participants indicated genetic counselors would be helpful in explaining genomic/genetic test results. Only two participants indicated genetic counselors would not be helpful in explaining these results (6.9%), and two participants indicated they were unsure (6.9%). Participants were also asked to indicate whether genetic counselors would be helpful in discussing management options related to heart disease. Approximately 72% participants indicated that genetic counselors would be helpful in discussing this topic. Only one participant indicated they would not (3.4%), and 24.1% participants indicated they were unsure.

Participants were then asked to indicate other healthcare providers that would be helpful in explaining genomic test results and discussing medical management. The frequency of those that said a cardiologist or other specialist would be helpful in this regard was 96.6%. A majority of participants also indicated that a geneticist would be

helpful in explaining this information (72.4%). Fewer participants indicated a nutritionist would be helpful in this regard (44.8%), and only 20.7% of participants indicated that a nurse would be helpful in explaining this information. Participants were also asked to indicate other providers that would be helpful in explaining genomic test results and management. One participant indicated a primary care provider (3.4%), and one participant indicated someone from the sports medicine, physical therapy field would be helpful (3.4%). This information is summarized on Table 2.2.

2.4.5 Intention to Alter Lifestyle

Participants were asked the likelihood they would engage in the following lifestyle modifications having learned that genetics alone increased their risk of developing heart disease by 10%: change diet, exercise regularly, take prescription medications, and regularly follow-up with a specialist. Most participants indicated their intention to change diet was between probable to neutral ($M = 2.069$, $SD = 1.25160$). A chi-square test for association was conducted between gender and likelihood of changing diet. There was a statistically significant association between gender and likelihood of changing diet, $\chi^2(8) = 18.958$, $p = .015$, with females being more likely to change diet than males. Participants were more likely to engage in exercise regularly ($M = 1.7931$, $SD = 1.048$). The average value for participants' intention to take prescription medications was 2.069 ($SD = 1.132$). The mean for participants' intention to regularly follow-up with a specialist was 2.036 ($SD = 1.261$). Frequencies for these Likert scale questions can be found in Table 2.3.

The next set of questions asked how high participants' genetic risk would have to be for them to undergo lifestyle modifications. The mean percent value for how high

genetic risk would have to be to warrant changes to diet was 41.041 (*SD* = 21.698). A total of five participants gave non-numerical answers to this question; therefore, their answers were not included in the quantitative analysis. The average percent value for how high genetic risk would have to be for participants' to be willing to regularly exercise was 33.909 (*SD* = 24.102). A total of seven answers were excluded from quantitative analysis due to non-numerical or unclear answers.

The mean percent value for the genetic risk at which participants indicate they would be willing to take prescription medications was 47.917 (*SD* = 26.137). This quantitative analysis excluded five non-numerical answers. Lastly, the average genetic risk percent value at which participants would be willing to regularly follow-up with a specialist was 44.250 (*SD* = 23.988). A total of five participants gave non-numerical answers for this question and were therefore excluded from quantitative analysis. A summary of these findings can be found in Table 2.4.

2.5 Discussion

This study explored the perceived utility of personalized genomic medicine in those with a family history of heart disease. This study had four goals in mind. The first goal was to assess participants' baseline understanding of general genetics and genetic risk factors associated with heart disease. The second was to assess whether participants perceive utility in genomic information. Third, this study sought to determine the genetic counselor's role in providing genomic risk information. Lastly, this study attempted to understand whether participants would intend to alter their lifestyle having learned that genetics increased their risk of developing heart disease.

Overall, participants tended to overestimate the risk genetic factors confer for different heart conditions. According to previous research, the heritability of coronary artery disease and myocardial infarction was estimated to be between 50% and 60% (Dai, Wiernek, Evans, and Runge, 2016). However, in this study, the average value participants indicated for the risk of a heart attack based on genetic factors was 66.55%. Similarly, the mean value participants indicated for the risk of atherosclerosis based on genetic factors was 65.52%. Although participants tended to overestimate the genetic risk factors for multifactorial heart conditions, according to our research, most participants understood that a family history of a Mendelian condition, FH, confers a greater risk for heart disease than a family history of heart attacks.

The genetic relatedness between various relatives seemed to be a confusing point for many participants. Most were able to correctly assess that a mother is more genetically related than a grandmother and that an aunt is more genetically related than a cousin. However, only 27.6% of participants were able to accurately determine that a sister and mother are equally genetically related.

Out of all six questions asked in the section assessing background genetic knowledge, none of the participants were able to answer all six questions correctly. In fact, the average number of questions answered correctly was 2.793. This is less than 50% of the questions asked. These results indicate that the baseline genetic literacy of this surveyed population was rather low.

Following the viewing of an educational video about the genetic risk associated with heart disease, 96.5% of participants either agreed or strongly agreed that genetic/genomic information would be helpful in understanding their risk. Previous

research has found similar results. In a study of patients with inflammatory bowel disease (IBD), researchers found that participants perceive usefulness in genetic testing for understanding the causes of IBD and risk to other family members (Hooker et al., 2014). Our results, although in a population chosen based on family history as opposed to personal disease history, largely found genetic information to be helpful in understanding personal risk in the context of a family history of heart disease.

Most participants in the present study indicated they would share these results with their doctor. Previous research has shown that most undergoing genomic testing say that a desire to improve their health was the primary reason they pursued this testing (Gollust et al., 2012; Su et al., 2011), but it has been shown that not all discuss results with their physician (Gordon et al., 2011). In a study by Gordon et al. (2011), 25 out 60 of their participants shared risk results for multifactorial diseases, which included genomic risk information, with their physician. Another 14 participants indicated they had not seen their physician since they had received their results, but that they intended to share them. Although 96.6% of participants in our study indicate they intend to share results with their physician should they undergo genomic testing, whether or not they would follow through with this claim cannot be confirmed. Further research on this topic is warranted.

The majority of participants responded favorably to discussing heart disease risk and management with a genetic counselor. Greater than 80% of participants indicated that a genetic counselor would be helpful in discussing their risk for heart disease and explaining genetic/genomic test results. In addition, 72.4% of participants indicated that genetic counselors would be helpful in discussing heart disease management options.

This result is unsurprising as previous studies have shown that including a genetic counselor in the process of reporting genomic test results is associated with positive outcomes. One study found that when participants receive genomic risk information for Type 2 Diabetes Mellitus from a genetic counselor, they report greater trust in the results (Mills, Barry, & Haga, 2014). Although our work is prospective in nature, it supports the claim that genetic counselors should be involved in the genomic medicine context. Most participants also indicated that a cardiologist/other specialist and geneticist would be helpful in explaining genomic test results and discussing medical management. This result was expected as these two specialties are directly involved in the treatment of heart disease and the interpretation of genetic results.

When presented with a hypothetical scenario where genetics alone increased the participant's risk for developing heart disease by 10%, respondents typically reported that their intention of changing diet, taking prescription medications, and following up with a specialist was between probable to neutral. The average likelihood of exercising regularly was between very likely to probable. As 65.5% of participants were between 18-24 years of age and 51.7% had completed some college, it is possible that some of these participants were student athletes or involved in intramural sports at the time of this study. If this were the case, the finding that participants were more likely to regularly exercising than make other lifestyle alterations is unsurprising. It is important to note that the intention to positively alter one's lifestyle is not equitable to actually participating in actions that promote one's health. Therefore, based on previous research, it would be reasonable to hypothesize that presentation of personalized genomic

information may not lead to lifestyle modifications, but may lead to engagement in medical interventions, such as taking prescription medications (Kullo et al., 2016).

We also found that women are more likely to indicate an intention to alter diet than men are. This result coincides with other literature. One study found that women are more likely to adhere to healthy eating recommendations than men. In addition, dieting is more common in women than men (Wardle et al., 2004).

When participants were asked how high their genetic risk would have to be to make lifestyle modifications, we observed results that aligned with what we expected based on their previous responses to questions determining the likelihood of engaging in health-related behaviors. The percent genetic risk required for participants to be willing to change diet, take prescription medications, and regularly follow-up with a specialist on average fell between 40% to 50%. Participants typically reported the lowest percent genetic risk required for them to be willing to exercise regularly. As respondents indicated they were more likely to exercise regularly than to engage in any other health-promoting behavior, this result was expected. There was a lot of spread between this data, indicating there was little agreement between participants in terms of the value of genetic risk that would result in behavioral changes. As perception of risk is a subjective experience influenced by an assortment of factors (Veach, LeRoy, & Bartels, 2003), a large variety of answers was expected.

In summation, this study found participants largely had low genetic literacy. After viewing a genetic information video, a majority of participants perceived genomic information to be useful in understanding their risk of developing heart disease. In addition, they believed a genetic counselor would be helpful in explaining not only

genomic test results, but also one's risk for developing heart disease and medical management options. Lastly, participants were typically most likely to indicate an intention to exercise regularly if their risk for heart disease were increased because of genetics. They were less likely to engage in diet modifications, take prescription medications, or regularly follow-up with a specialist. This exploratory analysis provides preliminary insight into how individuals with a family history of a complex disease perceive genomic information. It also begins to assess from which healthcare providers patients would like to receive this information from and how they will utilize this information.

This study had some limitations. First, the results were based on the thoughts and opinions of 29 participants. The study population was largely composed of young adults, and all participants had at least some college education background. Therefore, these results are not representative of larger, more diverse populations with differing ages and education levels. In addition, although patients were invited to participate at a local cardiology clinic and American Heart Association chapter, only one respondent was affected with heart disease. These results may be different in a research project focusing on the opinions of those affected with this condition. Lastly, it is possible that the sample is primarily composed of highly motivated individuals, resulting in sampling bias (Barratt, H. & Kirwan, M. 2009). If this occurred in the present study, the results would not be representative of all individuals with a family history of heart disease.

Given these results, there are a number of directions future research can take. As this study is a pilot study, assessing the perceived utility of genomic medicine in a larger sample population would help researchers and clinicians better understand the general

population's thoughts and opinions on this newer field of medicine. In addition, in our study, we saw that nearly all participants would share genetic risk information with their doctor; however previous research has shown that not all patients disclose this information with their healthcare provider (Gordon et al., 2011). It would be interesting to explore what factors influence a patient's decision to share their genetic risk information with their physician.

A particularly informative future direction would be to do a qualitative analysis of participants' reasons for rating the likelihood to engage in health-related behaviors differently. In our study, we observed that participants were most likely to exercise regularly. It would be interesting to understand why changing diet, taking prescription medications, and regularly following-up with a specialist were not rated as likely.

2.6 Conclusions

The focus of this study was to assess the perceived utility of personalized genomic medicine in individuals with a family history of heart disease. We surveyed individuals 18 years or older with at least one first-degree or two second-degree relatives with heart disease. This exploratory research had four goals: to assess individuals' baseline understanding of basic genetic knowledge and the genetic basis of heart disease, to determine whether these individuals think personalized genomic medicine would be helpful in assessing their risk for developing heart disease, to identify the genetic counselor's role in providing genomic risk information, and to determine whether participants would intend to alter their lifestyle having learned that genetics increased their risk of developing heart disease.

We found that participants tended to overestimate the risk of both a heart attack and atherosclerosis based on genetic factors. In addition, we found that on average, respondents answered 2.793 of the six background genetic knowledge questions correctly. This indicated that the baseline genetic literacy of this surveyed population was rather low. All but one participant strongly agreed or agreed that genetic/genomic information would be useful in understanding their risk of developing heart disease. This result further adds to our knowledge of public perception of personalized genomic medicine.

When asked about the genetic counselor's role in discussing heart disease risk and management, a majority of participants indicated genetic counselors would be helpful in discussing their risk of developing heart disease, genetic/genomic test results, and medical management options related to heart disease. This result illustrates that there is a role for genetic counselors within a genomic medicine context and begins to define that role.

Lastly, on average, participants indicated they were more likely to exercise regularly than engage in other health promoting behaviors if they were told that genetics alone increased their risk of developing heart disease by 10%. Participants tended to rate the likelihood of altering diet, taking prescription medications, and regularly following-up with a specialist between probable to neutral. In addition, women were more likely to indicate they would alter their diet than men. These results may help clinicians prioritize which lifestyle modifications they will discuss with patients at risk for heart disease.

This study provides preliminary insight into how individuals with a family history of a complex disease perceive and utilize genomic information and what the genetic

counselor's role will be within the genomic medicine context. Our results support the expansion of genomic medicine from the perspective of a sample population at risk for a multifactorial condition. In addition, they illustrate the importance of the genetic counselor within this field. Participants overwhelmingly supported the assistance of a genetic counselor in explaining risk for developing heart disease, explaining genomic test results, and discussing management options. Genetic counselors will be pivotal in interpreting, communicating, and contextualizing genomic information. As a cardiologist/other specialist and geneticist were also considered by a majority of participants to be helpful in this capacity, we stress the importance of a multidisciplinary approach to genomic medicine. Our results also support the genetic counselor's role in discussing disease management options. As participants indicated they were most likely to exercise regularly, a medical management discussion should emphasize the importance of other lifestyle modifications, such as healthy eating, prescription medications, and following up with specialists. A multidisciplinary team, that includes a genetic counselor, will be beneficial in ensuring the patient receives and understands the information they need to manage their health. An in-depth discussion about complex disease management does not typically include a genetic counselor currently; therefore, the genetic counselor scope of practice may expand within the genomic medicine context.

Table 2.1 Participant Demographics

Participants	N=29	(%)
Preferred Gender		
Male	9	(31.0)
Female	19	(65.5)
Prefer not to answer	1	(3.4)
Highest Education Completed		
Some college	15	(51.7)
2-year college	3	(10.3)
4-year college	7	(24.1)
Graduate school	4	(13.8)
Age		
18 – 24	19	(65.5)
25 – 31	4	(13.8)
32 – 38	1	(3.4)
39 – 45	0	(0.0)
46 – 51	1	(3.4)
52 – 58	2	(6.9)
>59 years	2	(6.9)
Heart Disease Status		
Affected	1	(3.4)
Unaffected	28	(96.6)

Table 2.2 Helpful Healthcare Providers for Discussing Test Results and Management

Healthcare Providers	Participants (N=29)	(%)
Cardiologist, or other specialist	28	(96.6)
Geneticist	21	(72.4)
Nutritionist	13	(44.8)
Nurse	6	(20.7)
Primary care physician	1	(3.4)
Sports medicine, physical therapy	1	(3.4)

Table 2.3 Intention to Undergo Lifestyle Modifications

	Very Likely (%)	Probable (%)	Neutral (%)	Possible (%)	Unlikely (%)
Change Diet	44.8	27.6	6.9	17.2	3.4
Exercise Regularly	51.7	27.6	13.8	3.4	3.4
Take Prescription Medications	41.4	24.1	24.1	6.9	3.4
Follow-up with a Specialist	48.3	17.2	13.8	13.8	3.4

Table 2.4 Genetic Risk Value Associated with Intention to Change Lifestyle

	Mean (%)	Standard Deviation (%)
Change Diet	41.042	21.698
Exercise Regularly	33.909	24.102
Take Prescription Medications	47.917	26.137
Follow-up with a Specialist	44.250	23.988

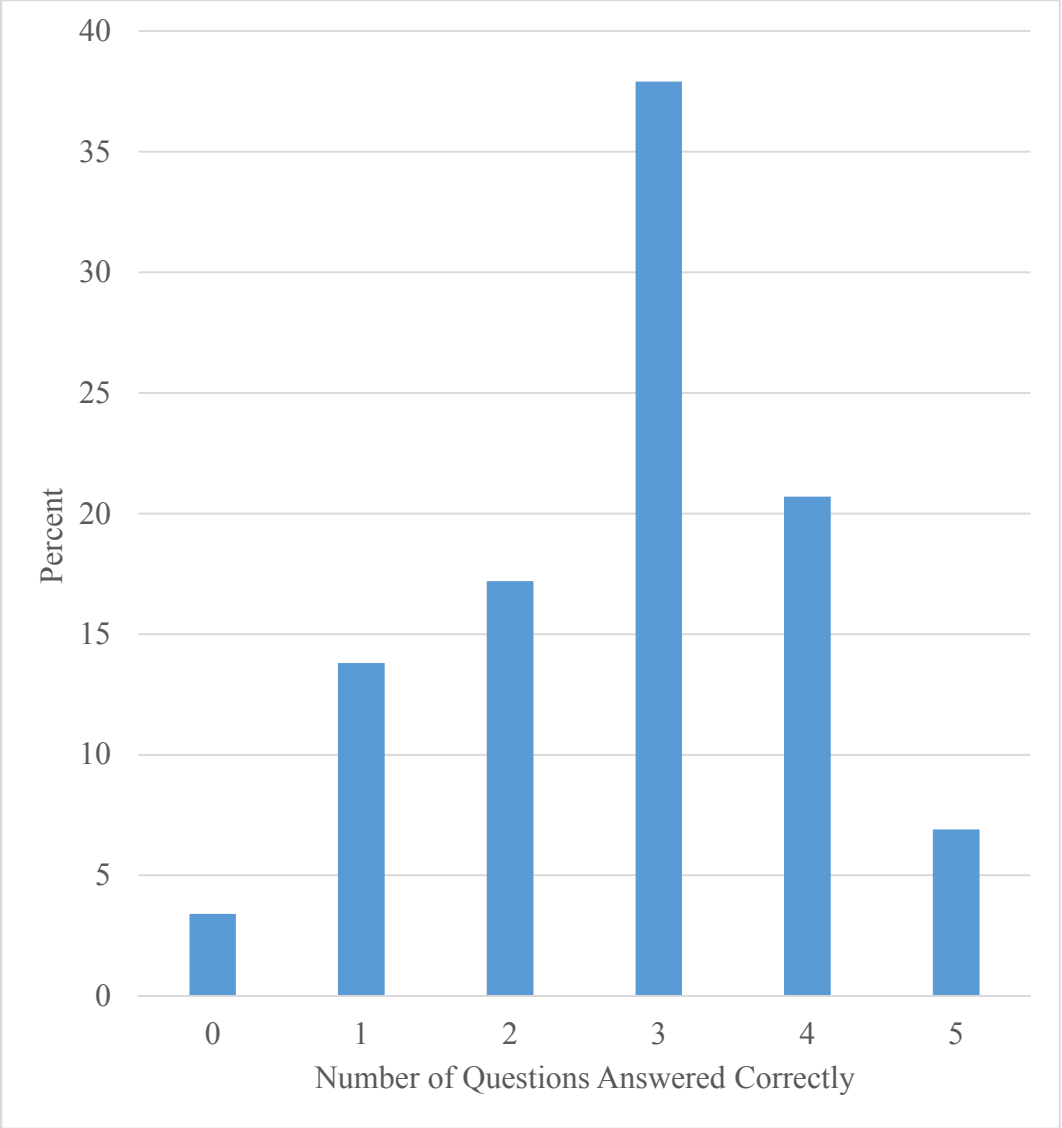

Figure 2.1 Background Genetic Knowledge

Chapter 3. Conclusions

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We found that participants tended to overestimate the risk of both a heart attack and atherosclerosis based on genetic factors. In addition, we found that on average, respondents answered 2.793 of the six background genetic knowledge questions correctly. This indicated that the baseline genetic literacy of this surveyed population was rather low. All but one participant strongly agreed or agreed that genetic/genomic information would be useful in understanding their risk of developing heart disease. This result further adds to our knowledge of public perception of personalized genomic medicine.

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discussing their risk of developing heart disease, genetic/genomic test results, and medical management options related to heart disease. This result illustrates that there is a role for genetic counselors within a genomic medicine context and begins to define that role.

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This study provides preliminary insight into how individuals with a family history of a complex disease perceive and utilize genomic information and what the genetic counselor's role will be within the genomic medicine context. Our results support the expansion of genomic medicine from the perspective of a sample population at risk for a multifactorial condition. In addition, they illustrate the importance of the genetic counselor within this field. Participants overwhelmingly supported the assistance of a genetic counselor in explaining risk for developing heart disease, explaining genomic test results, and discussing management options. Genetic counselors will be pivotal in interpreting, communicating, and contextualizing genomic information. As a cardiologist/other specialist and geneticist were also considered by a majority of participants to be helpful in this capacity, we stress the importance of a multidisciplinary approach to genomic medicine. Our results also support the genetic counselor's role in

discussing disease management options. As participants indicated they were most likely to exercise regularly, a medical management discussion should emphasize the importance of other lifestyle modifications, such as healthy eating, prescription medications, and following up with specialists. A multidisciplinary team, that includes a genetic counselor, will be beneficial in ensuring the patient receives and understands the information they need to manage their health. An in-depth discussion about complex disease management does not typically include a genetic counselor currently; therefore, the genetic counselor scope of practice may expand within the genomic medicine context.

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Appendix A. Flyer

INDIVIDUALS WITH A FAMILY HISTORY OF HEART DISEASE

PARTICIPANTS NEEDED

You are invited to participate in a graduate research study. We are interested in learning your opinions regarding the usefulness of genetic test results in understanding risk for heart disease.

If you would like to share your thoughts, please visit the following link:
https://www.surveymonkey.com/r/GVXVCBR
For more information please contact:
Dana Mittag, BS
607-280-9858
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Appendix B. Letter to Participants

Dear Potential Participant:

You are invited to participate in a graduate research study focusing on the genetic risks associated with heart disease. I am a graduate student in the genetic counseling program at the University of South Carolina School of Medicine. My research investigates the perceived usefulness of genetic test results in individuals with a family history of heart disease. In order to participate, you must have one first-degree relative with heart disease, such as a parent, sibling, or child, or two second-degree relatives with heart disease, such as aunts, uncles, or grandparents. In addition, you must be 18 years of age or older. The research involves completing an online questionnaire and watching a short video.

The questionnaire will attempt to understand your baseline genetic knowledge, whether you would find genomic testing to be useful in understanding your risk of developing heart disease and which healthcare providers you would prefer receiving this information from, and whether knowledge of the genetic risks associated with heart disease would result in any lifestyle modifications. If you do not wish to answer a certain question, please skip that question and continue with the rest of your questionnaire.

All responses gathered from the questionnaires will be kept anonymous and confidential. We only ask for your email in order to enter that email address into a drawing to be chosen to receive a $5 Amazon gift card. It is not necessary that you provide this information. The results of this study might be published or presented at academic meetings; however, participants will not be identified. If you are chosen for the drawing, your prize will be sent to you at a later date, after having collected all data. Your contact information will not be used for any other purposes beyond to send you the drawing prize if you have won.

Your participation in this research is voluntary. By completing this questionnaire, you are consenting that you have read and understand this information. At any time, you may withdraw from the study by not completing the questionnaire.

Thank you for your time and consideration to participate in this questionnaire. Your responses may help members of the medical community better understand how those with a family history of heart disease perceive the area of personalized genomic medicine and the topic of genomic test results. If you have any questions regarding this research, you may contact myself or my faculty adviser, Crystal Hill-Chapman, using the contact information below. If you have any questions about your rights as a research participant, you may contact the Office of Research Compliance at the University of South Carolina at (803)-777-7095.

Sincerely,

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Appendix C. Questionnaire

Family History

* 1. Please indicate which of your immediate relatives were diagnosed with a heart disease. Click all that apply.

- [ ] Parent
- [ ] Sibling
- [ ] Child
- [ ] None of the above

Family History

* 2. Please indicate which of your close relatives were diagnosed with heart disease. Click all that apply.

- [ ] 2 or more grandparents
- [ ] 2 or more aunts or uncles
- [ ] 2 or more nieces or nephews
- [ ] None of the above

Family History

* 3. Please indicate which of your close relatives were diagnosed with heart disease. Click all that apply.

- [ ] 1 grandparent and 1 aunt or uncle
- [ ] 1 grandparent and 1 niece or nephew
- [ ] 1 aunt or uncle and 1 niece or nephew
- [ ] None of the above

Family History

4. From which side of the family do you have relatives with heart disease?

- ◯ Mother's
- ◯ Father's
- ◯ Both

Background Genetic Knowledge

Please use the following scale to answer the first two questions. For your reference, 0 on the scale indicates a 0% genetic risk, 5 indicates a 50% genetic risk, and 10 indicates an 100% genetic risk.

0---1---2---3---4---5---6---7---8---9---10

5. When blood flow to the heart is blocked, a heart attack can occur. What do you think the risk of a heart attack is based on genetic factors?

6. Atherosclerosis, often called coronary artery disease, occurs when plaque builds up in the arteries. This can block blood flow, causing a heart attack or stroke. What do you think the risk of atherosclerosis is based on genetic factors?

7. Familial hypercholesterolemia (FH) is a condition caused by a change in a gene. In those with FH, cholesterol is not metabolized well. This will lead to plaque build-up in arteries. Is someone with a family history of FH at higher, the same, or lower risk for heart disease than someone with a family history of heart attacks?

- ◯ Higher
- ◯ The same
- ◯ Lower

8. For which situation are you at greater risk for developing heart disease:

- ◯ Sister has heart disease OR
- ◯ Mother has heart disease
- ◯ I am at the same risk for both situations

9. For which situation are you at greater risk for developing heart disease:

- ◯ Grandmother has heart disease OR
- ◯ Mother has heart disease
- ◯ I am at the same risk for both situations

10. For which situation are you at greater risk for developing heart disease:

- ◯ Cousin has heart disease OR
- ◯ Aunt has heart disease
- ◯ I am at the same risk for both situations

Please watch the following video for a brief explanation of the genetics of heart disease:

Genetic Education Video

Usefulness of the Information Presented in the Video

11. Indicate how much you agree with the following: genetic/genomic information would be useful for understanding my risk of developing heart disease.

- ◯ Strongly agree
- ◯ Agree
- ◯ Neutral
- ◯ Disagree
- ◯ Strongly disagree

12. If you had access to your genetic risk information for heart disease, would you share this information with your doctor?

- ◯ Yes
- ◯ No
- ◯ Unsure

13. If you had access to your genetic risk information for heart disease, would you share this information with your family?

- ◯ Yes
- ◯ No
- ◯ Unsure

14. With which family members would you share this information?

Genetic Counseling

Please read the following description of the genetic counseling profession:

"Genetic counseling is the process of helping people understand and adapt to the medical, psychological and familial implications of genetic contributions to disease. This process integrates:

- *Interpretation of family and medical histories to assess the chance of disease occurrence or recurrence.*
- *Education about inheritance, testing, management, prevention, resources and research.*
- *Counseling to promote informed choices and adaptation to the risk or condition."*

- National Society of Genetic Counselors

15. Would a genetic counselor be helpful to talk with about your risk for developing heart disease?

- ◯ Yes
- ◯ No
- ◯ Unsure

16. Would a genetic counselor be helpful in explaining genomic/genetic test results?

- ◯ Yes
- ◯ No
- ◯ Unsure

17. Would a genetic counselor be helpful in discussing medical management options, such as medications and living a healthy lifestyle?

- ◯ Yes
- ◯ No
- ◯ Unsure

18. Please indicate any other doctors or healthcare providers you think would be helpful in explaining genomic test results and medical management. Click all that apply.

- [ ] Cardiologist, or other specialist
- [ ] Geneticist
- [ ] Nutritionist
- [ ] Nurse
- [ ] Other (please specify)

Lifestyle Changes

19. Having learned that genetics alone increased your risk for developing heart disease by 10%, how likely would you be to consider doing the following:

	Very Likely	Probable	Neutral	Possible	Unlikely
Change diet	◯	◯	◯	◯	◯
Exercise regularly	◯	◯	◯	◯	◯
Take prescription medications	◯	◯	◯	◯	◯
Regularly follow-up with a specialist	◯	◯	◯	◯	◯

20. How high would your genetic risk have to be for you to be willing to change your diet? Please indicate a percent value.

21. How high would your genetic risk have to be for you to be willing to regularly exercise? Please indicate a percent value.

22. How high would your genetic risk have to be for you to be willing to take prescription medications? Please indicate a percent value.

23. How high would your genetic risk have to be for you to be willing to regularly follow-up with a specialist? Please indicate a percent value.

Demographics

24. Please indicate your age:

25. Please indicate your preferred gender:

- ◯ Male
- ◯ Female
- ◯ Prefer not to answer

26. Please indicate the highest education level completed.

- ◯ Some high school
- ◯ High school/GED
- ◯ Some college
- ◯ 2-year college
- ◯ 4-year college
- ◯ Graduate degree

* 27. Are you currently diagnosed with a heart disease?

- ◯ Yes
- ◯ No

Appendix D. Participant Consent Agreement

We would like to invite individuals with a family history of heart disease to participate in a study about the perceived usefulness of genetic information in regards to heart disease. In order to participate, you must have one first-degree relative with heart disease, such as a parent, sibling, or child, or two second-degree relatives with heart disease, such as aunts, uncles, or grandparents. Your participation would be greatly appreciated, as your opinions will increase our understanding of the usefulness of genetic information in individuals with a family history of heart disease. We believe the results of this study will aid members of the medical community in understanding how those with a family history of heart disease perceive the area of personalized genomic medicine.

Your participation in the study is voluntary, and you can withdraw at any time. Participation in the study involves completing an online questionnaire and watching a short video. The questionnaire is anonymous, meaning that we will not collect any personal information that could identify you or connect you to your responses. However, if you are interested in being entered into a drawing for one of five, $5 Amazon gift cards, you can include your email address at the end of the questionnaire. Your contact information will not be used for any other purposes beyond sending you the drawing prize if you have won. This questionnaire should take approximately 15 minutes to complete. Questions in the questionnaire will attempt to understand your baseline genetic knowledge, whether you would find genomic testing to be useful in understanding your risk of developing heart disease and which healthcare providers you would prefer receiving this information from, and whether knowledge of the genetic risks associated with heart disease would result in any lifestyle modifications.

Dana Mittag, a genetic counseling student at the University of South Carolina Medical School for a Master's Thesis project, is conducting this study. Crystal Hill-Chapman, the thesis director and an associate professor, is the faculty thesis advisor for this study. If you have any questions about this study, please contact us.

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For questions about your rights as a participant, you may contact the Office of Research Compliance at the University of South Carolina at 803-777-7095.

By clicking the "Next" button below, you are indicating your consent to participate in this study. Thank you for sharing your insight.

Appendix E. Script for Genetic Education Video

Heart disease, also known as cardiovascular disease, is a disorder affecting the heart and blood vessels. As you may already know, many of the complications associated with heart disease are due to a process called atherosclerosis, also called coronary artery disease. Atherosclerosis occurs when a substance called plaque begins to accumulate along the walls of the arteries. This will narrow the arteries, which will restrict blood flow through these important vessels. Plaque will continue to build up over time, and eventually a blood clot can form, substantially or completely blocking blood flow. When a blood clot blocks blood flow to a portion of the heart, a heart attack occurs. If blood flow is restricted completely as a result of a blood clot, part of the heart will start to die [1][5].

It is known that coronary artery disease clusters in families. This means that when we see patients with this type of heart disease, there are often other members of that same family that are or were affected with the disease as well. Because we see this clustering in families, it suggests that genetics plays a large role in causing this disease. In fact, it is estimated that the genetic influence of both coronary artery disease and myocardial infarction, also known as a heart attack, is between 50-60%. Another way to look at this is genetic factors account for 50-60% of the risk for coronary artery disease and heart attacks, with 40-50% of the risk being accounted for by other factors, such as high blood pressure, diabetes, high cholesterol, lack of exercise, and obesity to name a few [3].

Genomic tests can identify very small changes in DNA that are relatively common in the general population. These changes are called single nucleotide polymorphisms, or SNPs. It is estimated that certain well-known SNPs increase the risk for coronary heart disease, also called coronary artery disease, by at least 10% [4].

One single gene condition associated with early-onset heart disease is familial hypercholesterolemia (FH). We inherit two copies of our genes, one from mom and one from dad. Some diseases are caused by changes in genes. Familial hypercholesterolemia is a condition caused by changes in a gene that results in poor metabolism of a type of cholesterol found in the body. When left untreated, it is approximated that those with a change in just one copy of a gene associated with FH have a 20-fold increased chance for CHD. Those affected with familial hypercholesterolemia have a 50% chance of passing on the condition to their children [2][6].

So as you can see, estimating the genetic risk for heart disease is complicated. In some conditions, like familial hypercholesterolemia, there is a defined genetic risk for heart disease. The inheritance of the condition is well defined as those with the condition having a 50% chance of passing that same condition down to their children. Other genetic factors have a less well-defined risk associated with them, such as the well-known SNPs, which are the small, common genetic changes, that can increase risk of coronary heart disease by at least 10%. As we do more genomic testing and learn more

about the genetics associated with heart disease, we will likely provide a better personalized assessment of an individual's risk for heart disease.

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