Psychosocial Concerns of Patients with Dilated Cardiomyopathy

THESIS

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Abstract

Purpose
Recent advances have expanded our knowledge of the genetic etiology of dilated cardiomyopathy (DCM). With these advances, recommendations for cardiovascular screening and genetic testing of patients and families with DCM have been published, including involvement of genetic counselors in the healthcare team caring for these individuals. However, little research is available describing the psychosocial concerns experienced by DCM patients and their families. This study thus sought to identify recurring psychosocial concerns of DCM patients and their families, as well as identify correlations between demographic and health history information with the expression of these concerns.

Methods
Qualitative analysis, using components of grounded theory and constant comparison, was performed examining follow-up correspondence data recorded from DCM Research Project participants. Thematic categories were created, refined, and validated by a second independent reviewer. After thematic analysis was completed, selected participants representing key thematic findings were contacted for follow-up telephone interviews to provide deeper insight into the concerns expressed. Statistical correlations were
performed using phi coefficients and point biserial analyses comparing the emergent themes with demographic information as well as clinical data available for participants.

Results

From 1638 eligible participants, 430 data points were coded from the correspondence of 239 individuals from 158 kindreds. A total of 152 (63.4%) were female and 87 (36.6%) were male. Most participants (89.5%) were non-Hispanic Caucasian. Eight thematic categories were identified: Concern for children/relatives (n=115, 26.7%); Emotional adjustment (n=61, 14.2%); Communication (n=56, 13.0%); Research (n=51, 11.9%); Insurance (n=51, 11.9%); Genetics (n=37, 8.6%); Physician issues (n=34, 8.6%); Disease/Medications/Treatment (n=25, 5.8%).

From 19 participants selected for follow-up interviews, 5 were re-consented and their follow-up interviews confirmed their personal psychosocial experiences and revealed deeper insight into the concerns they expressed during their participation in the DCM Research Project.

Correlational analyses demonstrated statistically significant (p<0.05) associations between some demographic and health history data with identified themes. For example, women shared more concerns across all themes when compared to men. In particular, men shared significantly less concerns regarding insurance (p=0.035), as well as emotional issues (p=0.0329). Expression of concerns also differed by age, with older age participants sharing less concerns for children (p=0.0195), but shared more issues regarding research participation (p=0.0396). Correlational analyses also showed statistically significant associations between identified themes and other factors such as
ethnicity, genetic testing results, method brought to medical attention, and history of invasive procedures.

Conclusion

This is the first formal analysis, to our knowledge, of psychosocial concerns of individuals with DCM. The most frequent concern among this patient cohort is concern for children and relatives (26.7%), along with other concerns impacting emotional status, genetic education, and issues with their medical care. The expression of these concerns may be impacted by differences in demographic data as well as personal health history. While these results must be confirmed in a larger controlled cohort, these data can better inform genetic counseling sessions for individuals with DCM and their families, highlighting the importance of patient education, emotional support, and guidance when seeking medical care.
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Chapter 1: Background

Cardiomyopathy is a generic term meaning disease of the heart muscle.

Cardiomyopathies are characterized morphologically into dilated cardiomyopathy (DCM), hypertrophic cardiomyopathy (HCM), or restrictive cardiomyopathy (RCM), with each characterized by enlargement and reduced force of contraction, thickening and preserved force of contraction, or increased rigidity, respectively of the left ventricular myocardium (Hanson & Hershberger, 2001). In dilated cardiomyopathy (DCM), the focus of this work, the contractile force of the myocardium weakens over time and loses the ability to pump sufficient quantities of blood to the body (Hanson & Hershberger, 2001). Symptoms of dilated cardiomyopathy include dyspnea (shortness of breath), peripheral edema (swelling), thromboembolism, arrhythmia (irregular heart rate), and sudden cardiac death.

Dilated Cardiomyopathy

DCM is the most common form of cardiomyopathy with an estimated prevalence of approximately 1/200 to 1/500, and the leading cause of heart failure in the United States (Hershberger, Hedges, & Morales, 2013; Morales & Hershberger, 2015). It is also the most common indication for heart transplantation in both the adult and pediatric populations (Morales & Hershberger, 2015). The diagnosis of DCM is based on left ventricular enlargement (LVE) or dilation, often with relative thinning of the ventricular
wall, and decreased force of contraction (systolic dysfunction). When examined by echocardiography, LVE is deemed present when the diastolic left ventricular diameter increases over the 95th percentile of population-based height and gender-based approach (Vasan, Larson, Levy, Evans, & Benjamin, 1997). Left ventricular systolic dysfunction is deemed when the ejection fraction (the fraction of blood volume ejected with each cardiac cycle, a usual measure of LV ability to pump blood) is less than 50% (Morales & Hershberger, 2013). Other structural findings that may be present in DCM include right ventricular enlargement, fatty infiltration of the myocardium, as well as left ventricular non-compaction. It should be noted that these additional structural finding are not unique to DCM and should be differentiated from other forms of cardiomyopathy (Morales & Hershberger, 2013).

Causes of DCM

There are a variety of etiologies that can underlie a diagnosis of DCM, when the DCM term is used to describe the morphology and physiology of the left ventricle. Ischemic DCM, the most common type of DCM (50-60%), is caused by loss of myocardium due to coronary artery disease (CAD) and/or myocardial infarction. Non-ischemic DCM (40-50%) can be due to a variety of causes including exposure to cardiotoxic drugs including chemotherapy exposure, endocrine disease, congenital heart defects, heart valve dysfunction, and a variety of infections including bacterial, viral, parasitic and fungal (Morales & Hershberger, 2013). DCM can also be a manifestation of an existing syndrome. Syndromic causes include a variety of muscular dystrophies (Duchene muscular dystrophy, limb girdle muscular dystrophy, etc.) as well as mitochondrial
disorders (Kearns-Sayre syndrome) that affect the structure and/or function of skeletal and cardiac muscles (Morales & Hershberger, 2013).

Cases of non-ischemic DCM in which all usual clinically identifiable causes have been reasonably excluded are termed idiopathic dilated cardiomyopathy (IDC) (Morales & Hershberger, 2013). For this reason IDC is considered a diagnosis of exclusion based on the underlying cause or lack-there-of (Hanson & Hershberger, 2001). The term IDC was implemented prior to the knowledge that a subset of DCM can be due to genetic mutations. As such, the IDC group of DCM patients, those without a clear etiology, became the starting point for family studies to identify a possible genetic cause of DCM. Before 1985, it was suggested that only 1-2% of patients with IDC had other family members also identified with disease (Hanson & Hershberger, 2001). This knowledge led to the genesis of the term familial dilated cardiomyopathy (FDC), which distinguishes this subset of patients with IDC and a family history of disease. Further family history studies conducted from the mid-1980s to the 1990s suggested a higher rate of FDC upwards of 2-10% (Burkett & Hershberger, 2005; Hanson & Hershberger, 2001). More recent data that combines clinical evaluation, using echocardiography, of first-degree relatives of patients with IDC has again increased the predicted prevalence of FDC from 20-48% (Hanson & Hershberger, 2001; Hershberger et al., 2013). In the clinical setting, individuals with IDC who are found to have two or more close relatives with a diagnosis of IDC can be them termed as having FDC, while those individuals with no discernable family history retain the IDC, or simplex, classification (Morales & Hershberger, 2013)
Genetics of DCM

During the 1990s and beyond, advancements in the technology and utilization of molecular testing methods, has allowed for the identification of genetic causes in many cases of FDC. Studies examining large kindreds with FDC have led to the discovery of genetic variants in over 40 genes that can account for approximately 40-50% of FDC (Hershberger, Cowan, Morales, & Siegfried, 2009; Hershberger et al., 2013; Lakdawala et al., 2012), and of note, it is estimated that approximately 50% of children affected with DCM before age 18 appear to have a genetic cause (Hershberger et al., 2009). Implicated genes code for a variety of proteins and are involved in biochemical pathways within the cardiomyocytes, including transcription factors, ion channels, nuclear envelope proteins, sarcomere elements, proteins associated with the dystrophin cytoskeleton complex, as well as mitochondrial proteins (Hershberger et al., 2009). In contrast, other forms of cardiomyopathy do not exhibit the extreme genetic heterogeneity of DCM. Genetic links to HCM began to emerge over 25 years ago (L. Y. Teo, Moran, & Tang, 2015). HCM has been commonly associated with defects in proteins of the sarcomere. If genetic cause can be identified in HCM, 80% can be attributed to variants in one of two genes (MYBPC3 and MYH7), and including three additional genes (TNNT2, TNNT2, and TPM1) accounts for more than 95% (Hershberger et al., 2013). Arrhythmogenic right ventricular cardiomyopathy/dysplasia (ARVC/D), a cardiomyopathy that affects mainly the right ventricle, is primarily a disease of desmosomal proteins. 50% of ARVC has been associated with a genetic etiology with five desmosomal genes implicated (DSC2, DSG2, DSP, JUP, and PKP2) as well as two non-desmosomal genes (RYR2 and...
Although several genes and disease mechanisms have been implicated in FDC, myocardial injury is the common end stage result of variants (Morales & Hershberger, 2013). Some of genes in which variants have been identified including TTN (25%), LMNA (6%), MYH6 (4%), MYH7 (4%), MYPN (3-4%), as well as SCN5A (2-3%) (Morales & Hershberger, 2013). The frequency of identified variants in the remaining DCM-associated genes is estimated at 1% or less (Hershberger et al., 2013). Types of variants span from missense, frameshift, nonsense, and splice-site variants to both small insertions/deletions and large gene deletions. Due to the extreme genetic heterogeneity of DCM, a variety of inheritance patterns can be seen in FDC families. Most FDC is inherited in an autosomal dominant pattern, but autosomal recessive, X-linked, and mitochondrial inheritance modes have been reported in FDC kindreds (Kushner et al., 2006). Adding to the complexity of DCM genetics, variants may exhibit reduced penetrance and variable expression even within a single kindred. Some studies estimate penetrance of DCM-related variants to be approximately 10% at <20 years, 34% between 20 to 30 years, 60% between 30 to 40 years, and up to 90% by age 40 (Hershberger et al., 2013), though this does not hold true for all DCM-associated genes. Variants in the LMNA gene have been estimated as high as 100% in subject’s ≥30 years old (Hanson & Hershberger, 2001). Variants in LMNA, as well as DES, have also been associated with a symptom onset at younger ages and increased risk for sudden cardiac death when compared to individual with variants in other DCM-associated genes (Saga et al., 2009). Members of the same FDC kindred have also demonstrated varying symptom onset and severity from mild to severe across
generations. The disease may present with subtle symptoms while others experience severe symptoms that may lead to heart failure, arrhythmias, and even sudden death (Hanson & Hershberger, 2001). Complexity of DCM genetics is also compounded by the fact that many genetic variants discovered in kindreds are unique to that family with little to no data available to help confirm the pathogenicity of such variants. In a study of genetic testing of 29 genes in 235 patients with DCM, 197 different variants were discovered, of which 88% were previously unreported variants (Hershberger et al., 2013; Norton et al., 2012). Also, some kindreds may exhibit more than one disease-associated variant co-segregating in the family, many of which are novel findings (Morales & Hershberger, 2013). This creates difficulty in defining the relevance of these variants for these particular families. Adding to the genetic complexity, it has also been hypothesized that genetic disease may underlie some proportion of DCM identified in simplex/nonfamilial cases, due to reduced penetrance variations that do not manifest overtly in some families (Kushner et al., 2006).

**DCM Disease Course**

DCM is a progressive disorder and is commonly asymptomatic until later stages of the disease. It has been estimated that the prevalence of asymptomatic DCM may be $\geq 1$ in 250 individuals with DCM (Hershberger et al., 2013). The pre-symptomatic period of DCM may persist for months to years, and may be discovered incidentally during cardiovascular screening for routine health or sports physical, prenatal examination, or pre-operative screening (Hanson & Hershberger, 2001). Onset of symptoms typically occurs between the ages of 30 and 60 in most cases, but symptoms of DCM have been
observed at a spectrum of ages from infancy and childhood to the elderly (Morales & Hershberger, 2015). A subset of DCM have also been observed during and/or soon after pregnancy termed either peripartum cardiomyopathy (PPCM) or pregnancy-associated cardiomyopathy (PACM) depending on the onset of symptoms (Morales & Hershberger, 2013). Regardless of the cause, the onset of symptomatic heart failure has been associated with a 50% five-year mortality rate (Hanson & Hershberger, 2001).

Presenting symptoms of DCM can vary between individuals. Many present with common symptoms of heart failure which include dyspnea on exertion (DOE), edema (especially in the lower extremities), orthopnea and/or paroxysmal nocturnal dyspnea, generalized fatigue, or thromboembolism. Due to the risk of arrhythmia in DCM, some individuals may present with symptoms of irregular heart rate including palpitations, syncope (sudden loss of consciousness) or pre-syncope (dizziness), or even sudden cardiac death (Hanson & Hershberger, 2001).

DCM Management

Current management for DCM includes pharmacologic therapy with angiotensin-converting enzyme (ACE) inhibitors and/or beta-blockers (Hanson & Hershberger, 2001; Morales & Hershberger, 2013). ACE inhibitors are neurohormonal antagonists of the renin angiotensin aldosterone axis that in DCM that has progressed to heart failure can mitigate symptoms, improve heart function and improve survival. ACE inhibitors also slow disease progression in asymptomatic patients with DCM (Hanson & Hershberger, 2001). Beta-blockers are neurohormonal antagonists of the adrenergic nervous system that improve heart failure symptoms, prevent lethal arrhythmias, and improve survival
and quality of life. An intracardiac defibrillator (ICD) is indicated for those individuals with a history of or risk for lethal arrhythmias (Morales & Hershberger, 2013). In individuals with severe progressive and refractory heart failure, consideration of heart transplantation may be necessitated (Lakdawala et al., 2012). With the availability of effective treatments, identifying those individuals at risk for DCM, in particular those with a genetic predisposition, becomes an important goal. Early identification, especially during the asymptomatic phase of DCM, allows for the implementation of serial cardiovascular screening as well as medical intervention to delay or prevent symptomatic disease, and thereby reduce the mortality and morbidity that accompanies most cases of DCM (Morales & Hershberger, 2015).

**DCM Guidelines**

In 2009, in response to the developing knowledge and complexity surrounding the genetic etiology of some forms of DCM and other cardiomyopathies, the Heart Failure Society of America (HFSA) developed practice guidelines for the genetic evaluation of cardiomyopathies. Recommendations are described below (Hershberger et al., 2009):

- A careful family history of three or more generation.
- Clinical cardiomyopathy screening in asymptomatic first-degree relatives. (For DCM, screening consists of history and physical exam, electrocardiogram, echocardiogram, and measurement of creatine kinase levels)
- Clinical screening for cardiomyopathy should be considered at the following times and intervals or at any time that signs or symptoms appear (for DCM):
• Interval if genetic testing is negative in the proband and/or if clinical family screening is negative: Every 3-5 years beginning in childhood

• Screening interval if a variant is present in the at-risk family member: Yearly in childhood; every 1-3 years in adults

• Referral to a medical center that has expertise in genetic evaluation with family-based management should be considered.

• Genetic testing should be considered for the most clearly affected individual in the family to facilitate family screening and management.

• Genetic and family counseling is recommended for all patients and families with cardiomyopathy.

• Medical therapy based on cardiac phenotype is recommended as outlined in general guidelines.

• Device therapies for arrhythmia and conduction system disease based on cardiac phenotype are recommended as outlined in general guidelines.

• In patients with cardiomyopathy and significant arrhythmia or known risk of arrhythmia an ICD may be considered before the left ventricular ejection fraction falls below 35%.

In 2011, the Heart Rhythm Society (HRS) and the European Heart Rhythm Association (EHRA) partnered with each other to release a consensus statement on the state of genetic testing for channelopathies and cardiomyopathies, including DCM. The expert consensus recommendations are described below (Ackerman et al., 2011):
• Comprehensive or targeted (LMNA and SCN5A) genetic testing is recommended for patients with DCM and significant cardiac conduction disease and/or a family history of premature unexpected death.

• Genetic testing can be useful for patients with familial DCM to confirm the diagnosis, to recognize those who are at high risk of arrhythmia and syndromic features, to facilitate cascade screening within the family, and to help with family planning.

• Variant-specific genetic testing is recommended for family members and appropriate relatives following the identification of a DCM-causative variant in the index case.

**Complexity of DCM Genetics**

Although these guidelines provide a much-needed framework to approach screening and genetic testing in DCM patients, they do not fully address the continued evolution of knowledge surrounding the genetic complexity of DCM and the ever-changing landscape of genetic testing options and results. As an example, the above-mentioned guidelines were released prior to the report that TTN variants may lead to DCM (Morales & Hershberger, 2013). Rapid innovations in genetic testing technology have lead to the availability of large gene panels for various laboratories, including panels that include over 50 genes associated with several forms of cardiomyopathy, and some also contain mitochondrial genes that may be more relevant in pediatric or multisystem involvement cases. As knowledge continues to expand, panels ordered on patients, even in recent
years, may quickly become outdated as new genes are discovered and testing panels are updated (Morales & Hershberger, 2013).

Studies examining the genetic testing outcomes in subsets of DCM patients reveal the need for continued research and evaluation in the complex arena of genetic knowledge and testing. In 2008, the DCM Research Project (formerly the Familial DCM Project) performed DNA sequencing on over 300 IDC/FDC patients, examining 6 genes associated with DCM. Testing revealed that 36 subjects (11.5%) carried 31 unique variants not observed in unaffected controls. 10.2% of these variants were considered possibly or likely disease causing. Study members concluded that variants in the genes examined are only a very small portion of the genetic alterations that may lead to DCM (Hershberger et al., 2008). Another study by Lakdawala, et al., published in 2012, performed DNA sequencing on 264 unrelated adult and pediatric DCM patients testing up to 10 genes. This study concluded that patients’ presenting phenotype is not a good predictor of identifying a disease-causing mutation in the genes examined, but they did reveal that patients with a younger age of presentation that had a family history of disease were more likely to harbor a gene mutation than patients presenting over age 40 with no family history. They explain that genotyping of broader populations and more rigorous standard variant classification measures are needed to improve the sensitivity and clinical utility of current genetic testing methods (Lakdawala et al., 2012).

**Genetic Care of DCM Patients**

The complex and ever-evolving landscape of the genetics of DCM warrants a skilled team of clinicians and medical professionals to help guide patients and their families.
through the process of diagnosis, genetic testing, screening, and education on the disease. The guidelines presented by the Heart Failure Society of American and the HRS/EHRA specifically recommend that patients with DCM seek care at medical centers with expertise in cardiovascular genetics to direct proper initiation of testing, interpretation of complex results, and implementation of cascade screening and genetic testing of other at risk family members if necessary (Somers et al., 2014). A retrospective study of the uptake of cardiac screening and genetic testing of family members with a relative with a diagnosis of HCM (n=46) or DCM (n=11) revealed that out of 302 relatives where cardiac screening was recommended only 57% completed screening, and out of 213 relatives where predictive genetic testing was recommended only 39% completed the testing (Miller, Wang, & Ware, 2013). It was suggested that the lower uptake of genetic testing compared to screening may be due to factors such as the perception of high cost of testing, fear of discrimination based on genetic results, and perceived lack of access to genetic professionals (Miller et al., 2013). Studies comparing practices in both a general hospital (GH) compared to a university medical center (UMC) with specialty in treating patients with DCM demonstrating that 21% of DCM patients were told their disease may be genetic at a UMC compared to only 6% at a GH. Also, 25% of UMC DCM patients were specifically referred to clinical genetics while only 6% of DCM patients at a GH received the same type of referral (Ruiter et al., 2010). These findings highlight both the need for further education of cardiologists and physicians caring for these patients as well as the importance of an integrated approach for the care and management of patients with
cardiomyopathy and their families. This team should include both cardiologists and
genetic counselors to help patients navigate the complexities of a diagnosis of DCM.
Genetic counselors are specially trained to help people understand and adapt to the
medical, psychological and familial implications of genetic contributions to disease
(National Society of Genetic Counselors' Definition Task Force et al., 2006). Genetic
counselors interpret medical and family history to assess the likely look of a genetic
etiology of a condition and educate patients on the inheritance, management, prevention,
and available resources. They help patients navigate the complexity of genetic testing
options and possible outcomes and help them to make informed decisions regarding
testing and aid in the interpretation and explanation of complex genetic testing results. A
policy statement released by the American Heart Association regarding genetics and
cardiovascular disease states that patient access to centers with expertise in
cardiovascular genetics that include genetic counseling should be considered as a major
component to the comprehensive care for those patients with genetic cardiovascular
disorders and can optimize the benefits of clinical genetic testing (Ashley et al., 2012;
Somers et al., 2014). For DCM patients, genetic counselors perform pedigree
construction and analysis to determine risk of an inherited etiology, determine
appropriate genetic testing options and available laboratories, review implications of the
often complex results that may be returned including the incomplete penetrance and
variable expression, review of existing literature and data regarding identified variants, as
well as encourage and facilitate communication of results to at risk relatives and provide
accurate recommendations for screening and testing that may be warranted.
In addition to educating patients on the nature of inherited disorders and genetic testing, genetic counselors also are trained to help patients and their families cope and adapt to the unique emotional and psychosocial concerns that may arise after the diagnosis of a hereditary disease. The discovery of a genetic etiology to a disorder can elicit various questions, concerns, and emotional responses for affected individuals and their family members. In order to effectively provide psychosocial support and guidance, it is helpful for a genetic counselor to have prior knowledge of the major concerns or emotional reactions that they may encounter during interactions with patients and family members. Unfortunately, in the case of DCM, little data has been published delineating the major psychosocial issues encountered by this unique population. This may be due, in part, to the relatively low numbers of genetic counselors practicing in the cardiovascular subspecialty. In 2012, the National Society of Genetic Counselors (NSGC) reported the results of their Professional Status Survey (PSS). Only 24 genetic counselors (1.9%) identified cardiology as their primary specialty area (Somers et al., 2014). In 2014, a study performed at the University of Cincinnati, surveyed 188 genetic counselors. 40% identified themselves as cardiovascular genetic counselors (CVGCs), but it was postulated that this high number could be due to an ascertainment bias with overrepresentation of cardiovascular genetic counselors, as these professional may have been more apt to participate in the survey. Even with this high reported number, 31% of total respondents reported they had not seen a cardiac genetic patient in the previous 12 months, indicating that cardiac patients may not be the majority of some genetic counselors patient populations. A large majority of both groups (CVGCs 95%, non-
CVGCs 78%) reported a need for cardiovascular genetic counseling services in their cities (Somers et al., 2014). A study examining the uptake of genetic testing for individuals at risk for HCM reported that a major cue to action to pursue genetic testing was a consultation with a genetics professional. Only one-third of over 300 participants consulted with a genetics professional, including genetic counselors, but 86% of those that had these consultations chose to proceed with testing, suggesting that information provided by a genetics professional can positively impact a patient’s decision to pursue genetic testing (Khouzam, Kwan, Baxter, & Bernstein, 2015).

DCM Patient Psychosocial Issues

Existing literature, specifically focused on patients with DCM, mostly centers on the psychiatric co-morbidities experienced by this group and their relation to disease phenotype as well as quality-of-life measurements. Steptoe et al. reported that patients with DCM particularly suffer from high levels of anxiety (52%) and restrictions in social functioning when compared to other cardiac patients, and experienced similar levels of depression (22%) as those with coronary artery disease. They also indicated that phenotypic features such as impaired myocardial function and heart failure increased the likelihood of poor quality of life experienced by these patients (Steptoe, Mohabir, Mahon, & McKenna, 2000). Similarly, Rasoul et al. reported an increase in clinical depression among DCM patients. They also reported that 1/10 patients with DCM suffer from a psychiatric co-morbidity, with substance abuse being the most common (Rasoul et al., 2015). Teo et al. also reported similar findings and reported that it is undeniable that there is increasing prevalence (R. Teo et al., 2014) of psychiatric co-morbidity in
cardiomyopathy patients, including DCM, with alcohol abuse, depression, and anxiety disorders predominating (R. Teo et al., 2014). These studies did not focus on or account for the genetic basis of DCM.

Psychosocial Issues in Patients with Other Genetic Disorders

With the lack of current knowledge regarding the specific psychosocial issues facing patients with DCM, we can look to reported findings on issues faced by individuals with other forms of genetic disorders to identify potential issues surrounding genetic testing and diagnoses that DCM patients may also experience.

Issues identified in other forms of cardiomyopathy and genetic cardiovascular disorders have also been reported. For HCM, Long QT (LQT), and ARVC patients, clinically relevant levels of distress in the form of anxiety and depression are well reported, with female gender, lack of understanding of carriership, and stronger belief of consequences associated with increased levels of distress (Aatre & Day, 2011; Christiaans et al., 2009; Cox, O'Donoghue, McKenna, & Steptoe, 1997; Ingles, Lind, Phongsavan, & Semsarian, 2008; James et al., 2012). A study examining the quality of life and psychosocial distress in HCM variant carriers attributed impaired mental and physical quality of life to high perceived risk of being a carrier, experienced symptoms, and physical co-morbidities (Christiaans et al., 2009).

In a general report on adaptation to the diagnosis of a genetic disorder, that difficulty in adjusting to a genetic diagnosis included increased amounts of stress and somewhat lower self-esteem. These issues seemed to worsen with increased chronicity, lethality, and severity of the condition (Biesecker & Erby, 2008). Several studies exist examining the
psychosocial issues faced by individuals diagnosed with an inherited predisposition to cancer, such as hereditary breast and ovarian cancer (HBOC) and hereditary non-polyposis colorectal cancer (HNPCC). Similar to the DCM studies, patients with inherited risk for cancer syndromes experience increased levels of anxiety and depression (Bleiker, Esplen, Meiser, Petersen, & Patenaude, 2013; Esplen et al., 2001; Meiser, 2005; Montazeri, 2008). Combined studies demonstrate that anywhere from 6-30% of HNPCC patients have clinically relevant levels of distress, including anxiety and depression (Bleiker et al., 2013) Indicators for increased risk of distress for patients with both HBOC and HNPCC include female gender, increased perceived cancer risk, experiencing a cancer-related death in the family, and having young children (Bleiker et al., 2013; Meiser, 2005) Feelings of guilt, both for passing increased risk to future generations as well as guilt for being the first to bring a familial condition to light are also reported (Esplen et al., 2001; Meiser, 2005).

Genetic Testing Concerns

Studies exploring patient experiences and issues surrounding the genetic testing process have been target toward both hereditary cancer and genetic cardiovascular disorders. Some common themes can be identified in all of these groups regardless of diagnosis. Concerns regarding health insurance, cost and the possibility of discrimination based on testing results is a frequently discussed issue and barrier to acceptance of genetic testing (Klitzman, 2010). In a study of the concerns the BRCA1/2 testing population, it was reported that 52% of the patients eligible for testing declined due to the concerns of cost, confidentiality, and discrimination (Christiaans et al., 2009; Klitzman, 2010). A study of
genetic decision making in patients with HNPCC reported that the most frequently stated reasons for declining genetic testing included concerns about health insurance (41%), cost of testing and counseling (32%), potentially adverse emotional impacts (30%), low anticipated benefit (30%), and time commitment (24%) (Bleiker et al., 2013). A study of psychological issues of genetic testing in cardiovascular disorders explains that not only does fear of insurance discrimination play a role in the decision to undergo testing but the lack of insurance coverage and financial resources can also prevent individuals from pursuing testing (Aatre & Day, 2011). In 2008, The Genetic Information Nondiscrimination Act (GINA) was signed into law protecting individuals from loss or denial or insurance or an increase in insurance rates based on the results of genetic testing (Clifton, VanBeuge, Mladenka, & Wosnik, 2010). Even with this federal law in place, concerns have still been reported, as patients fear that discrimination may not be fully eliminated through this legislation alone and continue to have an impact on treatment and testing decisions for inherited disorders (Klitzman, 2010).

In contrast to concerns that may prevent individuals from pursuing genetic testing, a strong motivation for those at risk for a genetic disorder is the ability to inform children and other relatives of the potential risk for an inherited disease (Aatre & Day, 2011; Esplen et al., 2001; Etchegary, Pullman, Simmonds, Young, & Hodgkinson, 2015; Hallowell et al., 2003; Meiser, 2005). Genetic testing allows these families the ability to identify individuals at risk for a particular disorder and implement risk reducing treatments, procedures, or lifestyle changes that may reduce the risk of developing disease in the future. For most adult-onset genetic disorders, such as HBOC and
HNPCC, practice standards indicate individuals not undergo predictive testing prior to adulthood, as recommendations for screening and prevention are not indicated until over the age of 18. In contrast, many genetic cardiovascular disorders can often have symptoms presenting in childhood and even infancy. For this reason, genetic testing is often performed on minors to allow early screening and treatment for at-risk children. Discovering that a child carries a disease-causing variant, can lead to issues for parents and caretakers, especially in cardiovascular conditions were there may be a risk of sudden cardiac death. A recent study assessing genetic testing decisions in ARVC, participants related a strong need to rule out risk for the disease more for children than themselves (Etchegary et al., 2015). A study of psychological issues in genetic testing for HCM and LQT reported that 64% of parents chose to undergo genetic testing due to the desire to define risk to their children (Aatre & Day, 2011). Another study exploring the motivations of individuals at risk for LQT syndrome as well as other inherited channelopathy disorders reported that a desire to pursue genetic testing was also impacted by a family history of sudden cardiac death in the family and a need to bring meaning to the death of a family member, especially a child (Erskine et al., 2014). Even with the desire to obtain this knowledge, when positive results in children are returned, studies indicate that parents experience increased levels of distress, especially anxiety (Aatre & Day, 2011; Hendriks et al., 2005). A study of parents whose children underwent predictive testing for LQT reported up to 50% of parents of carrier children showed high levels of clinically relevant distress (Aatre & Day, 2011; Hendriks et al., 2005). Predictors of increased distress in these parents include familiarity with disease, lower
education levels, family history of SCD, and dissatisfaction with provided information (Aatre & Day, 2011; Bratt, Ostman-Smith, Axelsson, & Berntsson, 2013; Hendriks et al., 2005). Positive genetic testing results can also lead to feelings of guilt in parents (Esplen et al., 2001; Hidayatallah et al., 2014). Feelings of guilt may surface as knowledge that they have passed a genetic variant to their children conflicts with strong parental feelings of duty to protect their children from harm and distress. Even with these negative emotional responses to genetic testing results.

Family Communication Issues

When an individual is found to carry a disease causing genetic variant that may have implications for both immediate and extended family members, the issue of communication of this information arises. Many individuals who receive positive genetic testing results feel an inherent duty to warn those family members that may be at risk of carrying the same gene variant (Aatre & Day, 2011; Batte et al., 2015). Even though many individuals may wish to share this information with other relatives, several barriers to communication have been reported that may impede this process. Studies of individuals with both inherited cancer syndromes and genetic cardiovascular disorders describe similar communication barriers including geographical distance, social/personal dynamics with relatives, concern that relatives will not understand, difficultly relaying complex genetic information, and desiring to protect others from worry and distress (Batte et al., 2015; Bleiker et al., 2013; Ormondroyd, Oates, Parker, Blair, & Watkins, 2014; van Oostrom et al., 2007). Communication within families can be complex and varied, and while there are several motivators and barriers to communication, one
common theme predominates. This is the discovery that genetic information dissemination is a gendered activity, with women taking on the primary role of communication (d'Agincourt-Canning, 2001). Women are considered the “kin-keepers” in many families and are more likely than men to communicate information to relatives, especially extended family, even when a genetic risk is discovered in a spouse’s kinship (Batte et al., 2015; Bleiker et al., 2013; d'Agincourt-Canning, 2001). This may place more of the burden and stress associated with communication of genetic susceptibility hereditary disorder on females in a family. Another issue surrounding communication within a family may be that those family members tasked with the dissemination and discussion of genetic results are not trained to communicate the complexities of genetics and testing procedures. They may not be equipped to navigate the psychosocial and emotional issues that could arise during discussion with other family members. This may be especially true when parents are tasked to discuss the implications of disease and genetic testing to children. Studies reveal that parents struggle when sharing genetic information with children and adolescents in regards when to have this difficult conversation and how much information to reveal about a disorder (Hidayatallah et al., 2014).

**Current Study Hypothesis and Goals**

Since many of these issues and concerns are shared among individuals diagnosed with various genetic disorders including HBOC, HNPCC, HCM, LQT, and other cardiovascular disorders (See reference summary Table 1) it can be hypothesized that patients with DCM may also experience some of these same issues (distress, anxiety,
insurance concerns, concerns for children/relatives, and communication barriers).
Currently there is little to no research available discussing the specific psychosocial issues of patients with DCM. The aim of the current study is to gain a deeper understanding of the major, recurring concerns of patients with DCM/FDC and their family members, and attempt to discern how these concerns may correlate with other informative data such as gender, ethnicity, age, genetic status, and history of invasive cardiac procedures or sudden cardiac death. To accomplish this, documented correspondence, notes, and telephone call logs that were recorded and maintained as part of the DCM Research Project, was qualitatively examined and coded for any themes regarding psychosocial issues or concerns that emerged.
The goal of the project is to discover the genes associated with DCM and to incorporate these discoveries into the practice of cardiovascular medicine, and as of 2015, the DCM Research project has enrolled more than 700 families and sequenced the exomes of over 400 participants.
After 2001, the project began to evolve and expanded to accept participants with non-familial DCM as well. The project was moved to the University of Miami in 2007, and then to The Ohio State University in 2012. The project has recruited various types of professionals including genetic counselors, nurses, laboratory geneticists and technicians, as well as biostatisticians. Focus of the project has included the development of the DCM Consortium with research involving cardiovascular screening, genetic testing with return of results to patients, and trial of communication among relatives regarding genetic risk.
As of 2015, the DCM Research project has enrolled more than 700 families and sequenced the exomes of over 400 participants.

As part of the DCM Project protocol, research staff documented correspondence and telephone encounters related to the process of consenting, enrolling, and following up with participants. The data pertains to information routinely documented during informed consent and interactions between subjects and staff in the setting of follow up or assistance provided to participating subjects as they express concerns and seek information from study staff. Investigators for the current study reviewed these notes and correspondence for 1638 participants to attempt to identify any reoccurring themes pertaining to psychosocial concerns, issues, or questions expressed by DCM patients and their families. This large database of information provided a unique opportunity to explore the issues faced by patients and families with DCM, a topic for which very little research currently exists.

Previously published data for other patient disease groups often utilized questionnaires, surveys, and/or interviews to obtain information regarding issues for their participants. For this study, the information from DCM patients was not obtained from direct questions or targeted investigations to elicit concerns, but obtained organically through conversations between DCM patients and genetic counselors and other research staff members for the purpose of consenting and information sharing. This allowed for the identification of issues that were unsolicited by study team members or other medical professional, but presented by the patients and family members themselves through
natural interaction with research staff, mimicking how these concerns may be presented
during a medical or counseling appointment for DCM patients.

The DCM Research Project database contains demographic and health-related data for all
participants. This allowed for the correlation of this information with expressed concerns
to identify any trends that may emerge, adding further depth to themes discovered in the
research.

We hypothesized that we would likely identify psychosocial concerns in participants of
the DCM Research Project that have been identified in other genetic disorders, including
issues regarding personal distress, insurance and discrimination, concern for children and
relatives, as well as barriers to communication. For example, similar to other recent
studies of patients at risk for genetic cardiovascular disorders, individuals may not
necessarily make decisions regarding screening or genetic testing to satisfy their own
autonomy, but rather to make medical and testing decisions in the context of their
family’s needs, with young at-risk children taking priority over their own concerns (Aatre
& Day, 2011; Etchegary et al., 2015; Hendriks et al., 2005). This is an important issue,
as a finding of this nature in DCM would support a counseling agenda that more
specifically addresses the needs of patients with DCM as well as other cardiovascular
disorders. We hypothesize that challenges in communicating genetic risk to family
members reported in other genetic disorders including complex family dynamics and
issues discussing complex genetic information is also an issue for DCM families and may
require intervention of a genetic counselor, especially considering the allelic
heterogeneity, reduced penetrance, and variable expressivity of DCM-associated
mutations (Batte et al., 2015; Bleiker et al., 2013; Ormondroyd et al., 2014; van Oostrom et al., 2007). We also postulated that we might uncover issues not previously reported, particularly for individuals with a diagnosis of DCM, including concerns unique to research participants. In comparing emergent themes with demographic and cardiovascular health data, we predicted that we may identify a subset of DCM patients with particular or increased concerns, especially those with a history of invasive cardiac procedure, such as ICD, pacemaker, or cardiac ablation, or even sudden cardiac death, as well as those with a disease-related genetic variant. For example, it may be possible that a family history of heart transplant or sudden cardiac death leads to a greater interest and engagement in cardiovascular screening and genetic counseling. Also, even with the publication of genetic evaluation guidelines and consensus statements supporting cardiovascular screening, testing, and counseling for patients with DCM, patients and their families are still underserved due to the limited number of cardiovascular genetic providers as well as a lack of incentives among cardiologists to incorporate cardiovascular genetics in their practice. The purpose of reporting this data is to provide a deeper insight into the psychosocial issues present in the DCM patient population. This will allow medical professionals, including genetic counselors, to better anticipate concerns of patients and families in a clinic setting and allow for better education, support, and comprehensive care of families affected by DCM.

In summary, the aims of this study are as follows:
- Identify the primary and recurring psychosocial concerns of DCM patients and their family members through systematic qualitative review of correspondence as participants of the DCM Research Project.
- Correlate these findings with demographic data from the DCM Research Project database including age, gender, ethnicity, family diagnosis status, health-related information, and genetic testing results.

This study seeks to answer the question: Are the concerns of this cohort of DCM patients and their family members unique or similar to those documented in patients with other genetic disorders, and do differences in demographic and medical background information correlate to the level of expression of the identified concerns?
<table>
<thead>
<tr>
<th>Disorder</th>
<th>Issue</th>
<th>Cause</th>
<th>Method</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>DCM</td>
<td>Anxiety</td>
<td>Adjustment to disease</td>
<td>QOL Measures</td>
<td>(Steptoe, Mohabir, Mahon, &amp; McKenna, 2000)</td>
</tr>
<tr>
<td>DCM</td>
<td>Depression</td>
<td>Question disease is causative or correlational</td>
<td>Database review for psychiatric co-morbidities</td>
<td>(Rasoul et al., 2015)</td>
</tr>
<tr>
<td>DCM</td>
<td>Depression</td>
<td>Question disease is causative or correlational</td>
<td>Database review for psychiatric co-morbidities</td>
<td>(Teo et al., 2014)</td>
</tr>
<tr>
<td>HCM</td>
<td>Depression</td>
<td>Question disease is causative or correlational</td>
<td>Database review for psychiatric co-morbidities</td>
<td>(Christiaans et al., 2009)</td>
</tr>
<tr>
<td>HCM</td>
<td>Depression</td>
<td>Symptom pattern and adjustment to diagnosis</td>
<td>Questionnaire</td>
<td>(Cox, O'Donoghue, McKenna, &amp; Steptoe, 1997)</td>
</tr>
<tr>
<td>HCM</td>
<td>Depression</td>
<td>Inadequate care and disease discussion</td>
<td>Questionnaire</td>
<td>(Ingles, Lind, Phongsavan, &amp; Semsarian, 2008)</td>
</tr>
<tr>
<td>HCM (children)</td>
<td>Anxiety</td>
<td>Adjustment to disease</td>
<td>Questionnaire</td>
<td>(Spanaki et al., 2015)</td>
</tr>
<tr>
<td>ARVC</td>
<td>Anxiety</td>
<td>IDC implantation</td>
<td>Questionnaire</td>
<td>(James et al., 2012)</td>
</tr>
<tr>
<td>ARVC</td>
<td>Concern for children</td>
<td>Genetic testing</td>
<td>Interview</td>
<td>(Etchegary, Pullman, Simmonds, Young, &amp; Hodgkinson, 2015)</td>
</tr>
</tbody>
</table>

Table 1. Summary of Issues Reported in the Literature
Table 1 continued

<table>
<thead>
<tr>
<th>Disorder</th>
<th>Issue</th>
<th>Cause</th>
<th>Method</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>HBOC HNPCC</td>
<td>Anxiety Distress Concern for family</td>
<td>Genetic testing</td>
<td>Literature review</td>
<td>(Meiser, 2005)</td>
</tr>
<tr>
<td>HNPCC</td>
<td>Depression Guilt Concern for children Screening questions</td>
<td>Genetic testing</td>
<td>Survey</td>
<td>(Esplén et al., 2001)</td>
</tr>
<tr>
<td>HNPCC</td>
<td>Anxiety Depression Insurance concerns Cost of testing Family communication</td>
<td>Adjustment to disease Genetic testing</td>
<td>Literature review</td>
<td>(Bleiker, Esplén, Meiser, Petersen, &amp; Patenaude, 2013)</td>
</tr>
<tr>
<td>HBOC HNPCC</td>
<td>Coping Distress Family communication</td>
<td>Adjustment to disease Genetic testing</td>
<td>Questionnaire</td>
<td>(van Oostrom et al., 2007)</td>
</tr>
<tr>
<td>HCM LQT</td>
<td>Anxiety Worry Distress Concern for children Insurance concerns</td>
<td>Diagnosis, genetic status, disease symptoms</td>
<td>Literature review</td>
<td>(Aatre &amp; Day, 2011)</td>
</tr>
<tr>
<td>HCM FH LQT</td>
<td>Concern for children</td>
<td>Burden of care-giving Own mental status</td>
<td>Questionnaire</td>
<td>(Smets et al., 2008)</td>
</tr>
<tr>
<td>LQT</td>
<td>Parental distress Concern for children</td>
<td>Positive gene testing in child</td>
<td>Questionnaire</td>
<td>(Hendriks et al., 2005)</td>
</tr>
<tr>
<td>LQT ShortQT Brugada CPVT</td>
<td>Parental distress Anxiety Guilt Family communication (children)</td>
<td>Genetic testing</td>
<td>Interviews Focus groups</td>
<td>(Hidayatallah et al., 2014)</td>
</tr>
</tbody>
</table>
Table 1 continued

<table>
<thead>
<tr>
<th>Disorder</th>
<th>Issue</th>
<th>Cause</th>
<th>Method</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Family communication</td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>HCM LQT</td>
<td>Concern for Children</td>
<td>Sudden cardiac death experienced in family</td>
<td>Interview Focus group</td>
<td>(Erskine et al., 2014)</td>
</tr>
<tr>
<td></td>
<td>Explanation of child’s death</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HBOC</td>
<td>Family communication</td>
<td>Duty to warn Bearing bad news</td>
<td>Interview</td>
<td>(Ormondroyd, Oates, Parker, Blair, &amp; Watkins, 2014)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Uncertainty how to disclose</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HBOC</td>
<td>Family communication</td>
<td>Gender</td>
<td>Literature review</td>
<td>(d'Agincourt-Canning, 2001)</td>
</tr>
<tr>
<td>HBOC</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HCM</td>
<td>Family communication</td>
<td>Emotional closeness</td>
<td>Questionnaire</td>
<td>(Batte et al., 2015)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Geography</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>Dynamics</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>Gender</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HBOC</td>
<td>Insurance discrimination</td>
<td>Positive genetic testing results</td>
<td>Survey</td>
<td>(Peterson, Milliron, Lewis, Goold, &amp; Merajver, 2002)</td>
</tr>
<tr>
<td>Genetic disease</td>
<td>Insurance discrimination</td>
<td>Positive genetic testing results</td>
<td>Interview</td>
<td>(Klitzman, 2010)</td>
</tr>
<tr>
<td>(general)</td>
<td></td>
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</tr>
</tbody>
</table>

Legend: DCM (dilated cardiomyopathy), HCM (hypertrophic cardiomyopathy), ARVC (arrhythmogenic right ventricular cardiomyopathy), HBOC (hereditary breast and ovarian cancer), HNPCC (hereditary non-polyposis colorectal cancer), FH (familial hypercholesterolemia), LQT (long QT), CPVT (catecholaminergic polymorphic ventricular tachycardia), QOL (quality of life)
Chapter 2: Methods

Participants

Participants eligible for the current study were those enrolled in the DCM Research Project. The goal of the DCM Research Project, established in 1993 at Oregon Health & Science University (OHSU), is to identify the genetic basis of DCM. Initially, the project focused on familial cases and eventually evolved to enroll cases with a negative family history. The study moved to the University of Miami (UM) in 2007 and to The Ohio State University (OSU) in 2012. Institutional Review Boards (IRBs) at OHSU, UM, and OSU have approved the study.

Individuals whose data was analyzed for the current study include those enrolled in the DCM Research Project who have been classified as FDC, probable FDC, possible FDC, and IDC as defined in Kushner et al., 2006. FDC was defined as confirmed IDC in index patient, IDC diagnosis confirmed by medical records, in another family member. Probable FDC consists of confirmed IDC in index patient, at least 1 first- or second-degree relative with a clear or compelling history of IDC unable to be confirmed by medical records. Possible FDC was defined as confirmed IDC in index patient, family history account in at least one first- or second-degree relative or one or more of the following unable to be confirmed by medical records: heart transplant or history of heart failure with cause attributed to DCM without evidence of other etiology including
ischemic disease; systolic dysfunction with normal left ventricular end-diastolic dimension; documented conduction system disease, or presence of a pacemaker, ICD, or history of sudden cardiac death without evidence of ischemic etiology. Finally, IDC were those with little or no evidence of a close relative with IDC.

During the consent process, individuals are informed that insights from their participation in the DCM Research Project will lead to novel strategies for the detection, screening, prevention, and treatment of DCM and heart failure. As part of the consent process, these individuals voluntarily elected to have their blood drawn and research genetic testing performed with notification of results availability. They were also given the choice to allow the use of all collected data and samples for future studies. All subjects were given the option to contact the investigators of the DCM Research Project at any time to express their desire to withdraw from the study. Participants that expressed this desire were not used in the current study.

Study data was stored in the study database (Progeny Software, LLC). This database contains pedigrees for participant families as well as demographic data (for example, age at time of consent, sex, and ethnicity) and cardiovascular data (diagnosis, genetic testing results, history of invasive procedures such as ICD or pacemaker implantation, cardiac ablation), and sudden death for all participants. This information has been validated by medical record review for all participants.

IRB Approval

As is standard practice for the study protocol, research staff has also documented in the study database correspondence and telephone encounters related to the process of
consenting, enrolling, and following up with research subjects. The data pertains to information routinely documented during informed consent or interactions between subjects and staff in the setting of follow up or assistance provided to participating subjects as they seek information from study staff. All notes and correspondence were recorded as part of the DCM Research Project protocol and was not elicited or documented for the intent of the current study.

The IRB review board at OSU approved the protocol for the current study (2014H0425, Psychosocial and Genetic Concerns of Patients with Dilated Cardiomyopathy), which also required a concurrent amendment to the DCM Research Project protocol (2012H0185, Dilated Cardiomyopathy Research Project). The amendment to the DCM protocol presented the aims and proposed methods of the study, including how participant identifiable information would be coded by a member on the DCM Research Project prior to use in the new protocol created for this study. For the new protocol, the database and correspondence stored within was described and a waiver of consent was requested, stating that these individuals had consented to the larger DCM Research Project protocol. The waiver explained that during that consent process, individuals were informed that the insights from their participation would lead to novel strategies for the detection, screening, prevention, and treatment of patients with DCM. It was explained that although these participants did not explicitly consent to the current study, the goals of the study support the overall goals of the DCM Research Project in which they had consented to participate and have their data used indefinitely. In the waiver it was also stated that only their existing data would be reviewed and only information relevant to
the goals of the study would be extracted. In subsequent amendments to both the DCM Research Project and the current protocol, it was proposed that selected participants would be chosen for follow-up interviews and they would be re-consented for this purpose.

Data Collection

Prior to review by the primary investigator (ASM), to comply with the approved protocol, patient information was coded, using study ID numbers in place of identifiers, by a member of the DCM Research Project (CM) and transferred from the DCM database into a separate document. The coding removed names of participants and family member names, but study ID numbers allowed to identify individuals as belonging to a particular kindred. This document contained all consent language and correspondence with participants as well as their recorded demographic and cardiovascular data.

Correspondence data for an entire kindred contained in the Progeny database was sorted by reporting participant so that each participant row in the document represented only data reported by that individual (CM, ASM). Any other non-correspondence (such as record of newsletter mailing dates, undeliverable notices from the postal service) and possible identifying data (telephone numbers, email addresses, and mailing addresses) were removed as part of the coding process. The data fields that were exported from Progeny included the following:

- Demographic data
  - Study ID number – identifies individual
  - Pedigree number – identifies kindred
- Gender
- Ethnicity
- Racial category
- Age at first consent – documents age when first consented to DCM Research Project
- First consent date – documents the date when the patient first consented to the study, in case the patient has been re-consented.
- Computed age died – based on date of birth and date of death.

- Consent and Correspondence data
  - Referral method – how the individual was referred (website, healthcare provider, etc.).
  - Consent language – Language that the participant chose to be consented in (choices: English or Spanish).
  - Informed consent DNA for other research – documents if sample can be used for other research.
  - Consent process documentation – notes from study staff documenting the conversation during which the participant was consented.
  - Individual correspondence – other correspondence unrelated to the consent process pertaining to an individual in a pedigree.
  - Correspondence – prior to 2011, pedigree level correspondence field documenting all types of correspondence with any family member, and after 2011, used to document correspondence pertaining to the entire
pedigree or copied email correspondence between participants and study staff.

- **Diagnosis data**
  - Data reviewed clinical status – based on medical records review, documents research clinical diagnosis, for example, if patient is confirmed to be affected with idiopathic DCM. The choices are:
    - **Reported Affected** - Individuals reported to have idiopathic dilated cardiomyopathy, but not confirmed by medical records.
    - **Affected** - Individuals confirmed by medical records/data or by PI’s judgment to have idiopathic dilated cardiomyopathy. Normally Vasan criteria >95th percentile LVIDd, ejection fraction < 50%, no other identifiable cause, or some other set of LV size + ECG/echo/history.
    - **Unaffected** - Individuals confirmed by medical records/data or by PI’s judgment not to have IDC. Normally < 95th percentile LVIDd and ejection fraction < 50%. It is possible that some normal variants are tolerated in this category, but not much.
    - **Unknown** - Subjects have some CV abnormality; not normal, but do not meet criteria for affected.
    - **Indeterminate** - No data (no echo) or data not evaluable, or confounding factors, most commonly other CV disease. Used prior to 2011.
    - **Indeterminate, no data** - Used after 2011 to distinguish individuals
who are indeterminate due to no data or data not evaluable from those with indeterminate status due to a confounding diagnosis. Examples of confounding diagnoses include: ischemic heart disease, valvular disease, hypertension, congenital heart disease, cardiotoxic drug exposure, alcoholism, severe obesity, or sleep apnea, among others.

- **Indeterminate, confounder** - Used after 2011 to distinguish individuals who are indeterminate due to a confounding diagnosis from individuals who are indeterminate due to no data or data not evaluable.

- **Possibly Affected** - Individuals who are not formally reported as having DCM/IDC but whose family history information is suspicious for DCM/IDC.

- **Spouse – n/a** - Used for spouses in whom screening data is not indicated.

  - **Family status** - diagnosis status of kindred (FDC, IDC, probable FDC, possible FDC)

  - **Diagnosis age** – age when the participant was diagnosed with IDC or another clinical status per the above-mentioned “Data Reviewed Clinical Status” field.

  - **Diagnosis 1** – presenting diagnosis from medical records

  - **Diagnosis 2** - presenting diagnosis from medical records

- **Circumstances leading to diagnosis**
- Screening – individuals diagnosed after cardiovascular screening due to family history.
- Asymptomatic – individuals diagnosed serendipitously (for example, after unrelated surgery clearance).
- Symptomatic presentation
  - Heart failure (signs of heart failure)
    - Shortness of breath
    - Fatigue
    - Dyspnea on exertion
    - Edema
    - Weight gain
    - Paroxysmal nocturnal dyspnea
    - Orthopnea
  - Arrhythmia (signs of arrhythmia)
    - Palpitations
    - Presyncope
    - Thrombosis
    - Syncope
  - Unknown – diagnosis circumstances unknown
- Invasive cardiovascular procedures (confirmed by medical records)
  - Ablation
  - Cardioversion
• Bypass
• Transplant
• ICD (implantable cardioverter device)
• Pacemaker
• Bi-pacemaker
• Sudden cardiac death

• Genetic testing information
  • Gene mutation status – documents if there is a research result available.
  • Research genetic testing results – including positive for genetic variant, negative for genetic variant, or unknown (No research testing performed or recorded).
  • Molecular testing – name of genes for which testing was performed
  • Molecular testing – date family notified of research result availability

All fields listed above were imported from Progeny into the study document for completeness (198 fields), but not all categories were used for review or correlational analysis for the current study due to lack of available or informative data.

The exported document containing correspondence and the above-mentioned data fields was uploaded to NVivo (QRS, Version 10.0) qualitative research software for subsequent thematic coding and analysis (ASM). Consent language and correspondence were marked as qualitative data to allow for coding of themes, while demographic and clinical data was marked as qualifying data upon import into the NVivo software.
In order to gain further insight and clarity into themes that emerged during coding, some participants, for whom concerns were coded, were selected for follow-up interviews. The primary investigator selected participants on the basis of depth of concern presented, thematic category, and availability for re-contact (ASM). Selected individuals were contacted by telephone by members of the DCM Research Project to discuss purpose and scope of interview and to identify those willing to participate (JR, AM). The interested participants were consented and agreed to be contacted by DCM Research Project staff for a structured, recorded interview over the phone (JR).

Interviews consisted of questions probing for more in-depth explanation of concerns presented in past correspondence, current status or resolution of concerns, and allowed them to present new issues if present. The primary investigator provided interviewers with a guide of questions and a summary of the issue(s) to be explored (See Appendix A for interview script). Interviews were transcribed and names were coded and replaced with study ID numbers by members of the DCM Research Project and then provided to the primary investigator to be uploaded into the NVivo software (JR, AW). The primary investigator reviewed the transcripts to identify illustrative statements pertaining to existing thematic categories, and sorted selected quotes into corresponding thematic category in NVivo (ASM).

Data Analysis

Elements from Grounded Theory were used in the qualitative analysis of participant correspondence. Grounded Theory involves the use of both inductive and deductive reasoning to help identify and understand themes and patterns that may exist in a dataset
Analysis involved both looking for five themes that were hypothesized to exist that have been identified in previous research and published literature of genetic disorders (emotional distress, communication, concern for relatives/children, insurance concerns, research concerns, the latter included due to the particular population of participants being investigated) as well as identifying other novel themes that emerged during data review. This process employed constant comparative method, as the primary investigator reviewed participant correspondence using both selective coding to identify those themes predicted from previous reports as well as open coding to identify novel themes that emerged. Data was electronically coded into thematic categories using NVivo (ASM).

After the completion of initial thematic coding, data within major themes that had been identified (including five hypothesized themes as well as novel themes identified) were reviewed again to assess relevance of data under each identified theme and remove duplicate entries (ASM). A review was also performed to ensure coded data was explicitly expressed by the participants themselves and not simply a statement of information provided by study staff (ASM). For example, if the correspondence entry consisted of study staff stating, “inheritance was discussed,” the entry was not used for analysis. On the other hand, if the correspondence entry stated, “participant inquired about the inheritance,” the entry was used for analysis. This was done to ensure the likelihood that the analyzed data represents concerns volunteered by the participants.

Once major themes were established, data recorded under each thematic category was reviewed again and thematic subcategories were created under the umbrella of each
major theme that had been identified (including five hypothesized themes as well as novel themes identified). Subcategories were further delineated into two different classifications; either an issue expressed about the participant himself or herself or an issue described by a participant for another family member (ASM).

After completion of coding by the principal investigator, another member of the DCM Research Project independently reviewed and coded the original data in the same manner to identify both hypothesized themes as well as novel themes determined independently of the principal investigator (AW). This individual was provided with data from participants for whom information was thematically coded by the primary investigator in the same structure used for the main analysis. The second coder was only provided with the five hypothesized themes initially used by the primary investigator (emotional distress, communication, concern for relatives/children, insurance concerns, and research concerns). The coder was not provided information regarding the novel thematic categories or subcategories that had been identified by the primary investigator. Upon completion, the primary investigator and the second coder compared findings and examined similarities and differences in coded datasets for predicted categories and novel themes (ASM, AW). Initial co-review included examination of differing thematic categories until agreement was reached on the nomenclature of the major themes. Secondary discussion included review and comparison of subcategories and individually coded data between both coders. Any differences were reviewed in depth and discussed in subsequent meetings until at least 85% consensus was reached on accepted classification of thematic data between both coded datasets.
After final thematic categories were established, statistical analysis was performed to compare thematic findings with existing demographic and health-related data. Statistics were generated comparing major themes with data such as gender, ethnicity, family status (IDC/FDC), invasive procedures, and genetic testing results to identify any correlation between thematic and qualifying data. Correlations between thematic results and binary categories (gender, ethnicity, research genetic testing results, family status, invasive procedures, symptomatic data, family informed of result availability) were examined using phi coefficients (also known as mean square contingency coefficient), where positive values indicate increasing agreement between variable and negative values indicate decreasing agreement between variables. In this form of analysis a value of +1 indicates perfect agreement, -1 indicates perfect disagreement, and 0 indicates no relationship. For comparison of participant age to thematic categories, point-biserial correlation was performed, in which results that with a positive coefficient indicate positive association while negative coefficients indicate negative association between compared variables. Again, in this form of analysis a value of +1 indicates perfect agreement, -1 indicates perfect disagreement, and 0 indicates no relationship. For all comparison results, p-values were calculated to identify those associations that were statistically significant (p<0.05). Descriptive statistics were calculated for demographic information and thematic categories including direct counts and percentages to allow for presentation of this data.
Chapter 3: Results

Participants

A total of 1936 consented research participants were identified in the DCM Research Project database. Of these, 298 were excluded based on the fact that although the study had been open since 1994, the informed consent document did not include the study of genetic information until February 10, 1998. The excluded individuals had not been re-consented after February 10, 1998, and thus their data was not used. Removal of these individuals from further analysis resulted in 1638 participants spanning 494 families. These individuals were consented as part of the DCM Research Project between February 11, 1998 and September 2014.

Selected participants ranged in age from 1-90 years old (mean=40.5 years) at time of consent. There were near equal representation of genders, with 842 females (51.4%) and 796 males (48.6%). Participant reported race includes White/Caucasian (n=1411, 86.1%), Black (n=133, 8.1%), Asian (n=7, 0.4%), Native American (n=6, 0.4%), Other (n=15, 0.9%), Unknown race (n=22, 1.3%). Hispanic ethnicity was also recorded (n=44, 2.7%). The majority had a family status of FDC (n=1237, 75.5%, includes FDC and probable FDC), and most had unknown genetic testing results (n=1114, 68.0%). Detailed demographic data for this group is summarized in Table 2. Of the 1638 participants eligible for the current study, 932 (56.9%) had correspondence data recorded in the
Progeny database. The other 706 (43.1%) participants did not have any correspondence information recorded in the database and therefore no data existed to be analyzed. After reviewing the available data for the 932 participants with recorded correspondence, 693 participants were excluded on the basis that there was no explicit expression of concern or issue in the available correspondence, and thus thematic data was coded for 239 (14.6%) total participants. These participants (n=239) were from 158 families and ranged in age from 13-83 years old (mean=47.7 years) at time of first consent. There were more females represented than males, with 152 females (63.4%) and 87 males (36.6%). Participant reported race for this group include a majority of White/Caucasian participants (n=214, 89.5%), followed by Black (n=12, 5.0%), Other (n=3, 1.3%), Unknown race (n=2, 0.8%). Individuals of Hispanic ethnicity included 8 subjects (3.3%). The majority had a family status of FDC (n=174, 72.8% includes FDC and IDC probable FDC), similar to the larger cohort of 1638 participants. In this group, about half had unknown genetic testing results (n=132, 55.2%), although this group had more than twice the number of participants with positive genetic testing results (n=84, 35.1%) when compared to the larger cohort. Data for the thematic code cohort also includes the number of individuals who were informed of availability of their genetic variant research results. While genetic testing results data exists for the larger cohort, a total of those who were informed of their testing results was only obtained for the thematic cohort for purposes of correlational examination. Detailed demographic data for this group is summarized in Table 3.
In the cohort of participants with data suitable for coding (n=239), 167 (69.9%) had cardiovascular procedures or events recorded, with the largest number (n=63, 26.4%) having an implantable cardioverter defibrillator (ICD). For those that presented with symptoms, the largest amount presented with shortness of breath (n=16, 6.7%), fatigue (n=15, 6.3%), or dyspnea on exertion (n=14, 5.9%). Detailed information on cardiovascular data for this cohort is summarized in Table 4.

Interviews

Based on depth of concern presented, thematic category, and availability for re-contact, 19 of the 239 participants with coded data were selected for a follow-up interview after qualitative analysis. Of those 19 participants, 5 (26.3%) consented to be contacted by telephone and have their discussions recorded and transcribed. Quotes used in this manuscript were selected from the transcripts of these participant interviews. All potential interviewees were contacted in the fall of 2015, and those who chose to participate where consented soon after. The average length of time between expression of concern during study participation and follow-up interview for the current study was 5.2 years. The majority of those that did not consent for interviews failed to respond to initial contact. A detailed summary of time points for individuals contacted for interviews, including explanations for non-consent is described in Table 5. Demographic data for interviewed participants is summarized in Table 6.

Qualitative Thematic Analysis
Upon completion of the qualitative analysis of participant correspondence, 430 data entries of expressed concerns or issues from 239 participants were coded into 8 different main thematic categories:

- Concern for children and relatives (26.7%)
- Emotional adjustment (14.2%)
- Communication (13.0%)
- Research (11.9%)
- Insurance (11.9%)
- Genetics (8.6%)
- Physician issues (7.9%)
- Disease, medications, and treatment (5.8%)

Each category was organized into subthemes based on specific topics that emerged from the data. See Table 7 for hierarchy of major themes and subthemes.

**Concern for Children and Relatives**

The most prevalent theme that emerged from the qualitative analysis of participants’ correspondence was centered on the concern for other members of the family, especially children. 26.7% of participants expressed concerns related to this theme. Three subthemes emerged under this thematic category including children as motivation (n=25), pregnancy and future children (n=13), and screening and genetic testing (n=77).

**Children as Motivation**

With the knowledge that DCM can be hereditary, many participants expressed that their main motivation for participating in research was to help inform other relatives, in
particular their children and grandchildren. One participant, (48-year-old Caucasian female with some manifestations of cardiovascular disease not meeting criteria for DCM status but a family history of FDC) described that she was nervous about participation in the study and being screened for DCM, but wanted to proceed for the sake of her sons and other family members. Others (n=14) were hoping to identify a cause for DCM in their family to help ensure the health of their children and future generations. Those individuals that described a strong family history of members affected with DCM or a history of invasive cardiac procedures or sudden death in the family expressed a strong motivation to participate in research. One individual, (60-year-old Caucasian female affected with FDC and history of ablation and cardioversion) described a strong family history with a currently affected grandson and brother, as well as a father, uncle, and grandmother that all died from complications of DCM. She cited this as her motivation for participation and to pursue genetic testing to inform future generations. In a follow up interview, one participant (46-year-old Caucasian male affected with FDC with a history of ICD and positive for a genetic variant) described how the motivation for some family members to pursue genetic testing was affected by the death of a young individual from complications of DCM:

“The first time it happened [death of a family member affected with DCM] everybody showed interest [in genetic testing] but nobody wanted to get tested, but when we lost [family member] at 28 then people got really interested. I knew I had it [DCM], I had been diagnosed. Got them all interested, and I think almost everyone’s been tested.”

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Another participant (54-year-old Caucasian female affected with FDC with a history of ICD, biventricular pacemaker, sudden cardiac death, and a genetic variant) described how her sister died in her early twenties from sudden cardiac death, and how she had also suffered from sudden cardiac death and was resuscitated in her twenties. She now has children in their late teens and early twenties and expressed her concern for their health and desire to pursue genetic testing to determine if they had a genetic risk for DCM. A participant with a personal history of a heart transplant and who had lost two brothers to complications of DCM explained how emotional she was after the loss of her brothers and wanted her entire family to participate in the study to try and prevent disease from happening in her family. One participant that was contacted for a follow-up interview, a 45-year-old Caucasian mother affected with DCM and had tested positive for a DCM-associated variant, described her concern for her children and shared her thoughts on genetic testing:

“So you know if this is the way I’m made, this is part of the burden that I have to carry in life, then I’ll just carry it the best I can, and I would hope my children would make the same decision...if they know they have the gene, they might change a few things about how they take care of themselves, be more conscientious about check-ups and anything like that, catch it earlier and start treatment earlier, maybe get a better prognosis than me. But...it would be a relief for me mentally and emotionally to know that my kids are not going to have to go through this...I’ve been praying about this, they might have other issues, but they’d be free of this one. That’s my prayer.”
Pregnancy/Future Children

Symptomatic onset of heart failure associated with DCM can be observed during or soon after pregnancy in PPCM and PACM. Concerns of those participants that were currently pregnant centered on their personal health status and symptoms during pregnancy and the health of their baby. One participant (34-year-old Caucasian female affected with FDC and positive for a genetic variant) explained that she was more focused on her current heart health and ability to handle her pregnancy than her genetic status. Another (29-year-old Caucasian female with a family history of FDC and affected father) was concerned about the shortness of breath she was experiencing, and inquired if this was just due to her pregnancy or the onset of symptoms of DCM. One participant (50-year-old Caucasian female affected with IDC) described how her daughter was unwilling to participate in the study because she was pregnant and feared that she may be prescribed medications for her heart health that may be harmful to her unborn child. Another participant (25-year-old Hispanic female) that had been given a diagnosis of PPCM in a past pregnancy expressed that she was very interested in participating in the DCM Research Project and learning more information because she was concerned about not being able to have more children in the future. Other participants (n=3) expressed the need for information to make reproductive decisions and understand the possible risks to future children as a motivation for study participation and genetic testing. A few individuals (n=3) discussed how they might not choose to have children if they were to learn they had a genetic predisposition to DCM. One participant stated that they were
interested in genetic testing as both of their daughters were facing decisions about having children in the near future.

Screening and Genetic Testing

Although there are formal recommendations and consensus statements from both the Heart Failure Society of America and the HRS/EHRA, respectively, many participants had questions regarding the process of cardiac screening and genetic testing for DCM. They sought to gain more specific information on when relatives and children should be tested, how often, what screening involves, and where they should go to have these tests performed. They asked for recommendations on knowledgeable physicians in different areas of the country and the names of reputable laboratories to perform testing they may offer to their relatives. One participant (38-year-old Caucasian female with a family history of FDC and positive for a genetic variant) inquired about testing locations in their particular area of the country because they had family members that wanted to be screened to help ease their minds. One of the most frequently asked questions posed to study staff members was at what age children should start their screening or have genetic testing performed. They expressed concern for their children and wanted to do what they could to determine if their children are at risk for DCM and possibly prevent the onset of disease and maintain health. One mother (22-year-old Caucasian female affected with FDC with a history of ICD, heart transplant, and positive for a genetic variant) inquired if genetic testing for her young son made sense. He had regular cardiovascular screening, but the family had a history of early-onset DCM and she wanted to know if she should pursue testing for him to better evaluate his current and future risk. Another mother (38-
year-old Black female affected with FDC) inquired if having her 5-year-old daughter begin screening was appropriate, and if so, where should she go to have it performed. One participant (49-year-old Caucasian female affected with FDC and positive for a genetic variant) described how she was anxious for her children and grandchildren. She expressed understanding of the benefits of screening and testing but sought advice on when it was appropriate to pursue these tests in children.

**Emotional Adjustment**

14.2% of participants shared their personal emotional experience as well as the emotions of other family members in regards to a diagnosis of DCM, as well as genetic testing and screening for the disorder. Seven subthemes emerged under the category of emotional adjustment and include general adjustment (n=17), fear/anxiety/stress (n=16), denial (n=10), life choices (n=6), depression (n=5), anger/shock (n=4), and guilt (n=3).

**General Adjustment**

Participants described how both they and other family members were attempting to cope and deal with the knowledge that their families were at risk for DCM. One participant (41-year-old Caucasian female affected with FDC and positive for a genetic variant) described how she had not yet followed up with a physician as she was currently emotionally adjusting to the DCM diagnosis and needed some time before pursuing medical care. Another individual (64-year-old Caucasian female with family history of FDC and negative genetic testing) discussed how another family member was not adjusting well with the family diagnosis, stating they refused to see a doctor or get screened. This family member assumed they would develop heart problems in the future.
and did not want to pursue follow-up or care. One participant (57-year-old Caucasian male affected with FDC and a history of cardioversion and positive for a genetic variant) described his feelings of frustration surrounding the diagnosis of DCM and feeling that there was a lack of action he could take in regards to the prevention of the disease.

**Fear/Anxiety/Stress**

Feelings of fear, anxiety, and stress were expressed by individuals, both in regards to dealing with a diagnosis of DCM as well as contemplating genetic testing and potential results. One individual (34-year-old Black female unaffected with a family history of FDC and negative genetic testing) discussed her anxiety and stress surrounding her hypersensitivity of symptoms she felt she was experiencing. Any time she felt changes in her heartbeat or breathing she became concerned they were the onset of disease symptoms, even after negative genetic testing for a known genetic variant that was identified in her affected relatives. Another participant (50-year-old Caucasian female unaffected with a family history of FDC and negative genetic testing) explained how they were unsure if the fatigue and stress they were feeling were signs of the disease or just related to her emotional reaction to her brother’s recent death. Others described their emotional feelings in regards to screening and testing results. One individual (34-year-old Caucasian female with unknown FDC status but positive for a genetic variant) discussed her anxiety after learning of her abnormal screening results, while another (48-year-old Caucasian female with cardiovascular abnormalities not meeting criteria for DCM but a family history of FDC) discussed her hesitation and nervousness in participating in the study in regards to screening and genetic testing as she would prefer
just not to know if she was at risk at this time. Another participant (51-year-old Caucasian female unknown status and a family history of IDC) explained she was feeling hesitant to confront her personal risk for DCM after her mother’s sudden cardiac death. During a discussion in a follow-up interview, one participant (46-year-old Caucasian male affected with FDC with a history of ICD and positive for a genetic variant) expressed the fear his family members had prior to pursuing testing for a known genetic variant in the family, as well as the change after testing was completed:

“There used to be fear, but people didn’t want to be tested, but now they’re glad they know.”

One participant (57-year-old Ashkenazi Jewish female with unknown status and a family history of FDC) discussed their level of stress in regards to caring for other family members with declining health due to DCM. She discussed her stress issues surrounding caring for an ailing parent while taking care of her daughter and worrying about her own health, and explained that she was experiencing a lot of stress dealing with her own health while attending to other day-to-day family responsibilities. Some participants expressed a generalized fear and anxiety of just knowing they may be at risk for DCM, particularly in the presence of a family history of the disease. One individual (25-year-old Hispanic female unaffected with a family history of FDC) explained that after her two brothers were diagnosed with DCM at 18 and 22 and one passed away after heart transplant surgery, she was very scared for her risk to develop DCM even after normal screening results. After experiencing the death of both of his parents at a young age, his mother to sudden cardiac death and father to a reported heart-related issue, one
participant (52-year-old Caucasian male affected with FDC and a history of ICD, pacemaker, and heart transplant) described his concerns for his own health and life:

“I’ve lost both my dad [and mom]...I was a junior in high school when he [dad] passed away. I was a freshman in college when my mom passed away and back then they [physicians] just tell you ‘uh heart attack’ or ‘stroke’ or whatever. So I’ve always felt that I had a bomb ticking in my chest.”

Denial

Participants discussed how other family members may be in denial of their risk for DCM and how this impacted discussions and healthcare decisions for these individuals. When discussing family member participation in the DCM study, several people explained that they felt some would not be willing because they were thought to be in denial of the disease. One participant (47-year-old female of unknown race and ethnicity affected with FDC) described how, after her brother was diagnosed with DCM, it was recommended that she and her siblings all have cardiovascular screening performed. She talked about one brother who was in denial, and even though he was experiencing symptoms, refused to be screened. She explained that she herself had been offered to be a research participant in another study in the past but was in denial and did not participate at that time, and it was a genetic counselor she saw at one point that helped her choose to eventually join the DCM Research Project. Another (40-year-old Caucasian female affected with FDC with a history of ICD and heart transplant) discussed her brother who was given a diagnosis of DCM, but was in denial of the diagnosis, as he was not experiencing any symptoms at the time. One participant (43-year-old Black female
affected with FDC and positive for a genetic variant) discussed that she believed her
brother was in denial of being affected as he stated he did not have a heart problem even
though she knew he was taking medications for DCM. As part of a follow-up interview,
a participant (52-year-old Caucasian male affected with FDC and a history of ICD,
pacemaker, and heart transplant) described his experience with denial in his brother after
several family members were diagnosed with DCM:

“...we had a younger brother and he doesn’t talk about it. He would not talk about it.
He refused to talk about it. He refused to admit it. He just buried his head in the sand.
He was a little boy when my parents died [mother to sudden cardiac death and father to
a reported heart-related issue] He was still like 9-years-old by the time we lost both of
my parents. He’d kind of lost his childhood. He just didn’t know how to deal with this,
you know...he refused to talk about it...It was just denial.”

Life Choices

Knowledge that they may or may not have a genetic predisposition to DCM or be at
increased risk for the disease became a factor in making current and future lifestyle
decisions for some participants. A few participants discussed their concerns about how
active of a lifestyle they should lead after a diagnosis of DCM. One individual (64-year-
old Caucasian female with unknown status and family history of FDC and negative
genetic testing) described her concern that her affected brother was too active for his
condition, while another (50-year-old Caucasian female affected with IDC) discussed
how it was tough for her to be told to reduce her strenuous exercise routine, as it was a
part of her life she really enjoyed. Other participants discussed major life decisions that
may be impacted by knowledge they were at increased risk for DCM. One mother (35-year-old Caucasian female affected with FDC with a history of ICD, ablation, heart transplant, and positive for a genetic variant) explained that her high-school-age son did not want to pursue genetic testing due to the fear it may impact his ability to obtain a desired career in the military. Another mother (45-year-old Caucasian female affected with FDC and a history of a pacemaker and positive for a genetic variant) discussed her daughter’s desire to pursue genetic testing, as she wished to know if she carried the same variant identified in her mother. She wanted to pursue a residency in medical school, but felt she may change her plans and not attempt such a strenuous career path if her testing was positive. During follow up interview, this participant explained her daughter’s feelings about genetic testing and the decision she made after obtaining results:

“I had a bit of concern, she wanted to be a surgeon, specifically a pediatric surgeon, and she said ‘I will choose a different specialty that’s not so demanding, if I’m gonna end up like you, Mom’...a low energy, low stamina, chronic fatigue...that kind of thing. And so she wanted to know if she had the gene and then she would make a decision about residency. So I thought it was wise of her to ask, so she did the testing and she does not have the gene, which is an answer to my prayer. And she is now in a pediatric surgery fellowship and has two children!”

Depression

Depression was described by some individuals in regards to dealing with family illness and death due to DCM. One parent (66-year-old Caucasian female affected with FDC and positive for a genetic variant) described her feelings of depression and bewilderment
regarding the passing of their son due to DCM. Another individual (25-year-old Hispanic female unaffected with a family history of FDC) discussed feeling depressed in taking care of their ailing relatives but felt they had to remain strong for these individuals. Other participants discussed depression in other family members and their issues dealing with their diagnosis. One individual (65-year-old Caucasian male affected with FDC) described how his brother became reclusive and detached after his DCM diagnosis, eventually passing away while still in a depressive state. A participant (51-year-old Caucasian male affected with FDC and positive for a genetic variant) explained that his affected brother was currently hospitalized because he was battling severe depression, as he had to stop taking his depression medication after his DCM diagnosis. Another individual (45-year-old female with a family history of FDC and negative genetic testing) describes how her brother became depressed after his diagnosis and spent most of his time in bed, eventually committing suicide as a result of the diagnosis and subsequent depression. She also discussed how the hardest issue for the family to deal with was having a large number of affected individuals at one time.

Anger/Shock

A few participants discussed how anger was a reaction their family members were experiencing in regards to a DCM diagnosis. One (53-year-old Caucasian female affected with FDC and a history of ICD and positive for a genetic variant) explained that their brother had been angry about lifestyle changes he was advised to make after his diagnosis, and was also angry with her for encouraging family members to be screened, which is how he became diagnosed with DCM. Two other participants discuss feelings
of shock upon learning of a DCM diagnosis. One (69-year-old male affected with IDC) explained how the diagnosis came as a complete shock to him and his family as it was only discovered during a routine cardiovascular screening, without a known family history of symptomatic relatives. Similarly, another individual (52-year-old Caucasian female affected with FDC) stated how surprised she felt to be diagnosed with DCM, as she had never experienced any symptoms related to the disease.

**Guilt**

Three individuals discussed feelings of guilt surrounding the passing of genetic variants to their children. Two parents (64-year-old Caucasian female affected with FDC and positive for a genetic variant and 57-year-old Caucasian male affected with FDC with a history of cardioversion and positive for a genetic variant) specifically stated feeling guilty about passing down DCM-associated variants to their children, while a son (16-year-old Caucasian male affected with FDC with a history of heart transplant and positive for a genetic variant) described his mother’s fear that he may hold a grudge against her since he had tested positive for a variant that had been passed from her.

**Communication**

13.0% of participants described various issues regarding barriers to communicating information about DCM, screening, and genetic testing with other members of their family. Five subthemes emerged under the theme of communication including no contact (n=22), family dynamics (n=18), health issues (n=9), adoption/paternity (n=4), and location (n=3).
No Contact

In discussion with study staff regarding involvement of other family members, several individuals stated that there were members that they were no longer in contact with, and they were either unable or unwilling to have discussions with these individuals. The majority just made simple statements in regards to a particular family member or branch of the family they did not have contact with, but did not provide further details into the dynamics of these relationships. A couple participants discussed having minimal contact with ex-spouses after the end of the relationship. One person (56-year-old Caucasian female affected with IDC with a history of pacemaker and positive for a genetic variant) stated that her ex-husband is no longer in contact with her or her children, while another (17-year-old Caucasian female unaffected with family history of FDC) explained she is no longer personally in contact with her ex-husband, but she was able to relay information through her brother who still is in communication with him. Another individual (42-year-old Black male affected with FDC with a history of a pacemaker) simply discussed that his family was so large and there was some estrangement between relatives.

Family Dynamics

Several participants offered insight into family dynamics or issues that created a barrier in communication with other family members. One study participant (62-year-old Caucasian/Jewish female with cardiovascular abnormalities not meeting criteria for DCM and family history of FDC) requested that she not be contacted at home as her husband did not approve of her participation and felt she was making a big deal about something
that did not exist (genetic predisposition to DCM). Another (48-year-old Caucasian female affected with FDC and positive for a genetic variant) discussed how members of her family felt one relative was too pushy when it came to study participation, which had turned many from wanting to participate themselves, while that particular relative (65-year-old Caucasian female unaffected with a family history of FDC and negative genetic testing) separately expressed her frustration to study staff regarding those family members that refused to participate or have genetic testing performed. Another participant (50-year-old Caucasian female affected with IDC) simply felt her relatives were ignoring her when she tried to discuss screening recommendations with them. One man (46-year-old Caucasian male affected with FDC with a history of ICD and positive for a genetic variant) stated that he would only share his genetic testing results with those family members that requested them and would not voluntarily share this information otherwise. During a follow-up interview, one participant (52-year-old Caucasian male affected with FDC with a history of ICD, pacemaker, and heart transplant) described the difficulty he and his family had discussing the need to screen for DCM with an at-risk brother that was unwilling to have the conversation:

“We told my brother, you’d better go get yourself checked out...We actually talked to his wife, we put pressure on her. You need to get him in to have him looked at because if they find something before it gets bad they can start treating him and it might not get any worse. You know, there’s definitely something genetic, we don’t know what. So he was diagnosed with partially enlarged aorta, that was the only sign they had on him. But he
wouldn’t even talk about it, his wife would tell us about it. He still wouldn’t even talk about it.”

A couple participants discussed that it was their concern for the emotional impact a discussion of DCM and research participation may have on others that acted as a barrier to communication. One (53-year-old Caucasian female affected with FDC with a history of ICD and positive for a genetic variant) explained how her mother-in-law was very emotional regarding her husband’s death and she did not want to approach a discussion about participating in a research study for fear of upsetting her, while another (56-year-old Caucasian female affected with FDC with a history of heart transplant) stated she did not want to talk with her mother about obtaining medical records regarding her father’s heart-related death as she did not want to depress her by bringing up this sensitive topic.

Another dynamic that was presented by some participants was how best to approach the discussion of cardiovascular screening or genetic testing with children. One mother (64-year-old Caucasian female with cardiovascular abnormalities not meeting criteria for DCM with a family history of FDC and negative genetic testing) explained how she was unsure how to discuss the need for screening with her son who did not like to see doctors and had never pursued cardiovascular screening on his own in the past. Another mother (56-year old female with husband affected with IDC) discussed how she had downplayed her son’s risk for DCM in the past and never brought up the availability of genetic testing with him. She explained that she felt her children had enough to worry about as teenagers and were experiencing important milestones in their lives, and the timing of a DCM discussion was just not appropriate at the time.
Health Issues

When discussing communication of information to extended family, some participants relayed how the current health status of some family members made conversations difficult in light of their conditions. Two individuals (72-year-old Caucasian female affected with IDC and a history of cardioversion, heart transplant, and positive for a genetic variant, and a 61-year-old Caucasian female affected with FDC) explained how the declining mental status (i.e. dementia, senility) of older relatives hindered the discussion and retention of information. Others discussed family members with other debilitating diseases that impacted the ability to communicate. One (46-year-old Caucasian female affected with FDC) discussed a relative with multiple sclerosis, and two others (60-year-old Caucasian female affected with FDC with a history of cardiac transplant and positive for a genetic variant and a 57-year-old Caucasian male affected with IDC with a history of ICD) explained that relatives had impaired communication and comprehension abilities after suffering from strokes. One individual (55-year-old Caucasian female affected with FDC) explained how she would like her brother, affected with DCM, to participate in the study, but he had experienced brain damage due to sudden cardiac death, which made understanding difficult for him.

Adoption/Paternity

Four individuals discussed issues surrounding unknown or unclear family history as a barrier for further discussion or obtaining knowledge of health history. Two participants (69-year-old Caucasian male affected with IDC and a history of heart transplant and 13-year-old Caucasian/Asian affected with IDC with a history of heart transplant and...
positive for a genetic variant) discussed lack of knowledge and inability to identify other at-risk individuals due to parents being adopted out by their biological families. Two other families explained that there were potential family secrets regarding family history that hindered communication. One participant (55-year-old Caucasian female affected with IDC with a history of ablation, cardioversion, pacemaker, ICD, and positive for a genetic variant) discussed that two of her relatives were conceived by artificial insemination, but they were unaware of this fact themselves, while another (63-year-old Caucasian female of unknown status and FDC) discussed how she believes another family member may be her biological parent but that no one in her family was willing to discuss this topic with her, and hindered discussions regarding inheritance.

**Location**

Three participants (43-year-old Caucasian female affected with FDC and positive for a genetic variant, 22-year-old Caucasian male affected with IDC and a history of heart transplant, and 25-year-old Black female affected with IDC with a history of ICD) shared that family members were in locations that made it difficult to contact in order to have further discussion with. These locations include an assisted living home, homeless shelter, as well as prison, all of which hindered family discussion and participation in a research study.

**Research**

As participants of a study, individuals shared particular issues related to being part of research. Under the main theme of research, 11.9% expressed concerns, and five
subthemes emerged, including bloodwork (n=14), general issues with research (n=12), privacy (n=9), research versus clinical testing (n=8), and speed of return of results (n=8).

**Bloodwork**

For participation and testing as part of the DCM Research Project, a blood draw is required. Several individuals expressed issues and concerns regarding this request. Some simply explained that they did not like having their blood drawn for any reason as a potential barrier to participation, while others discussed their inability to travel to a location to have their blood drawn as a concern. Others were more concerned about the potential cost and/or reimbursement of having their blood drawn. Some received bills or were told by phlebotomy sites they would be financially responsible, and wanted assurance from study staff that these costs would be covered. One participant (53-year-old Caucasian male affected with FDC with a history of cardioversion and ICD with negative genetic testing) explained how he went to have his blood drawn at a convenient site, but was told he would have to pay $50. After discussing this with study staff, he chose to wait until he was near the location of the hospital in Portland, Oregon where the study was located to have his blood drawn to avoid this potential cost.

**General Issues with Research**

Participants offered individualized issues that were barriers to their, or other family member’s, involvement in research. Some discussed the amount of paperwork involved, time commitment needed, potential perceived financial costs, or the amount of travel that may be needed. Two participants explained that their relatives did not wish to participate because of general disinterest or distrust of research due to poor experiences in the past.
One (64-year-old Caucasian female with cardiovascular abnormalities not meeting criteria for DCM and family history of IDC) discussed how her husband did not want to participate in the study because he was not affected with DCM and saw no benefit to his involvement. Another (65-year-old Caucasian male affected with FDC) explained that his daughter did not wish to participate as she has distrust of research projects that are continually funded but never show significant results for the amount of money she believes they are granted.

Privacy
Several individuals discussed their concerns surrounding the privacy of health information as part of the study and who might be able to access any findings. Some participants did not want their physicians and insurance companies to be aware of their participation, and they were reluctant to request medical records to provide to the study. One participant (58-year-old Caucasian female unaffected with FDC) discussed how she wanted to participate but without informing her cardiologist. She wanted to keep her healthcare and research as separate as possible. Another individual (44-year-old Caucasian female affected with FDC with a history of heart transplant and positive for a genetic variant) wanted to ensure that any research findings would not be released to their doctor or insurance out of fear of discrimination and loss of coverage.

Research vs. Clinical Testing
As part of the DCM Research Project, any genetic testing results discovered through testing in the research laboratory required confirmatory testing in a clinical, CLIA-approved laboratory for medical use. Regarding this topic, 8 individuals (all found to be
positive for a genetic variant) sought clarification from the study staff as to why this confirmatory testing was needed, where they should go to have testing performed, and the potential cost of testing.

**Speed of Return of Results**

In regards to research genetic testing, several individuals contacted study staff to inquire on the length of time it took for results of genetic testing to be returned. The direct statement expressing lack of understanding the timeframe for return of testing results was presented by at least 4 individuals, and clarification was needed to explain the difference between testing in a research setting as opposed to clinical practice.

**Insurance**

Current guidelines recommend that those as risk for DCM undergo cardiovascular screening and genetic testing. 11.9% of participants shared both personal issues with insurance as well as those of other family members, and described how these issues were barriers for seeking medical care. Two subthemes emerged under insurance including coverage/lack of insurance (n=37) and concern for discrimination (n=14).

**Coverage/Lack of Insurance**

In the setting of cardiovascular screening, clinical genetic testing, and follow-up physician visits, several participants expressed concern and asked about their lack of insurance coverage or out-of-pocket costs of these procedures for both themselves and other family members. Several individuals discussed their lack of insurance as a motivator to join the DCM Research Project to allow them to have screening and testing they could otherwise not afford. One mother (50-year-old unaffected Caucasian female),
whose husband died from complications of DCM, expressed concern for her son who did not have insurance or funds to be screened and her desire for him to participate in the study. Another participant (45-year-old Caucasian female affected with FDC) was eager for her other family members to join the study as they had not had any cardiovascular screening due to lack of insurance. Other participants discussed issues with their existing insurance coverage in regards to the medical care they were seeking outside of the research study. One participant (50-year-old Caucasian female with cardiovascular abnormalities not meeting criteria for DCM and a family history of FDC, pacemaker, and positive for a genetic variant) states that after she was informed of her research testing results she had not followed-up with a physician due to lack insurance and she was unable to afford the out-of-pocket cost for confirmatory genetic testing. A mother (47-year-old Caucasian female affected with FDC with a history of cardioversion, pacemaker, and ICD) explained that her children were not seeking the recommended cardiovascular screening due to either lack of insurance or high deductibles. One individual (37-year-old Caucasian female affected with IDC) discussed her desire to talk with a clinical genetic counselor, but her insurance would not cover the visit and was requesting guidance of next steps for care and testing. In a follow-up interview, this participant explained her issues when attempting to seek counseling:

“...I asked him [physician] about it [genetic counseling] and he said ‘Okay, no problem’...and then when I tried to do it [genetic counseling] it was more of a problem with the insurance. They said, ‘Well we don’t do that,’ that I had to go through the study [DCM Research Project].”
One mother (61-year-old Caucasian female affected with FDC and positive for a genetic variant), in 2002, requested literature for her son to send to his insurance company to petition for coverage of cardiovascular screening that was recommended for at-risk first-degree relatives, while another (36-year-old Caucasian female affected with FDC with a history of ablation, ICD, heart transplant, and sudden cardiac death, and positive for a genetic variant) explained that her children had not been screened for DCM due to lack of insurance coverage or that their deductibles were too high. One participant (47-year-old Caucasian female with cardiovascular abnormalities not meeting criteria for DCM and a family history of FDC) that was contacted for follow-up interview discussed the issue of not being able to choose her desired provider due to insurance constraints:

“You kind of have to go where your insurance dictates, that’s the biggest problem right there. The insurance don’t allow you to go to just anybody you want to go to. You’ve got to go where they kind of tell you to go...I’m a hard person to get insured anyhow and so when the insurance says ‘oh yea go to this person’ and this person tells you ‘oh you have to go to this place’ and then you have to go to that place. Pretty soon you feel like cattle and you don’t want to have to go through that whole mess.”

Concern for Discrimination

Several participants shared their feelings of trepidation regarding screening and genetic testing due to fears of discrimination and loss of coverage from their insurance companies. One participant (70-year-old Caucasian male affected with FDC) explained that the younger members of their family were very concerned with insurance discrimination and this had been the largest hurdle to generate interest in the family in
regards to study participation and screening. A mother (45-year-old unaffected Caucasian female), whose husband (46-year-old Caucasian male) was affected with FDC, discussed balancing her concerns for her children’s health with potential insurance discrimination based on screening results. Another individual (45-year-old Caucasian female affected with FDC and a history of a pacemaker and positive for a genetic variant) explained that she was so concerned about insurance discrimination that she planned to pay out-of-pocket for confirmatory testing of the variant identified during the research project so her insurance would not be involved. Even after explanation of GINA, which legally protects individuals from insurance discrimination, this was still a barrier for some individuals and their family members to pursue clinical screening and testing. One participant (46-year-old Caucasian male affected with FDC) expressed understanding of GINA and its protections but was still concerned about potential discrimination for life insurance coverage, which is not currently a protected benefit under GINA. One participant (40-year-old Caucasian male affected with FDC) shared his experience with an insurance company denying him life insurance based on his DCM diagnosis. He inquired if the study staff knew of others with a similar experience, as he was going through an appeal process to get a policy in place.

Genetics

8.6% of participants also shared questions regarding genetics and genetic testing. Five subthemes pertaining to genetics emerged, including inheritance (n=13), reduced penetrance/variable expression (n=10), gene function (n=7), testing affected versus unaffected (n=5), and relevant genetic variants (n=2).
Inheritance

Upon learning of a genetic variant in a family that may put other family members and children at risk, several participants inquired for education and clarification on the potential risk and what relatives to be concerned for. One participant (36-year-old Caucasian male affected with FDC with a history of cardioversion and pacemaker), who had recently tested positive for an autosomal dominant variant, explained he knew his daughter was at a 50% risk to inherit the variant, but wanted to know, if she were to test negative, would her children still be at risk for inheriting the mutation. Another individual (34-year-old Caucasian male affected with FDC and positive for a genetic variant) explained that his wife was currently pregnant, and after his recent positive genetic testing results, he wished to know the risk to his child to inherit the same mutation. One participant (52-year-old Caucasian male affected with FDC with a history of cardioversion, pacemaker, ICD, and sudden cardiac death), who had two different DCM-associated variants identified upon research testing, inquired about the origin of these mutations. He wished to know if they both came from one parent, or each parent passed a variant separately, but both are deceased and unable to be tested.

Reduced Penetrance and Variable Expression

The fact that many of the DCM-associated variants can exhibit reduced penetrance and variable expression was also a topic of discussion among participants. They inquired about the likelihood DCM symptoms would manifest in an individual and comparison of disease severity between family members. One individual (49-year-old Caucasian female with cardiovascular abnormalities not meeting criteria for DCM and a family history of...
FDC and an ICD) explained that her physician had brought up the term “reduced penetrance” and she wanted more information on this concept, as she was very concerned about her risk and reproductive options. Another participant (46-year-old unaffected Caucasian female with negative genetic testing) sought clarification in explaining why one member of the family carried a variant but experienced no symptoms while that same individual’s daughter was symptomatic.

Gene Function

Some individuals wanted deeper insight to the meaning of their genetic testing results. They sought to better understand what function the genes performed in the body and what the consequences of variant in these genes may mean for them and their families. One participant (49-year-old Caucasian female with cardiovascular abnormalities not meeting criteria for DCM and a family history of FDC, a pacemaker and positive for a genetic variant) requested more information on missense versus nonsense mutations in a gene and their impact on gene function, DCM disease course, and relation to other potential health issues. A mother (38-year-old Caucasian female with cardiovascular abnormalities not meeting criteria for DCM and a family history of FDC and positive for a genetic variant) requested informational material for her and her daughter to better understand the meaning of positive genetic testing results. Other participants wished to have more detailed information on how genetic testing technology actually works and how variants lead to disease and the symptoms they are experiencing. During a follow-up interview addressing medical knowledge, a 45-year-old Caucasian female affected
with FDC with a history of a pacemaker and positive for a genetic variant discussed the need to provide balanced information when discussing genetics with patients:

“But I would say don’t overwhelm people with medical jargon. Make as much information about the disease and about its progression available to people and say, look if you want to get into the medical thing, here are the studies that show what we’ve been telling you, and make that kind of knowledge available. I think sometimes we assume people are not capable of processing that kind of information, when we’re a specialist talking to a non-specialist, and I think maybe we should trust people can handle more information.”

Testing Affected vs. Unaffected Individuals

When discussing genetic testing in the context of the family, questions arose regarding the best person to obtain genetic testing first and the reasoning behind this concept. When possible, testing individuals affected with disease is the desired starting point to potentially find a disease-associated mutation within a family, as they are the most likely to carry a gene change, if present, in a family. One mother (34-year-old Caucasian female affected with FDC and positive for a genetic variant), who desired genetic testing for her unaffected son, sought clarification of why testing should be performed on an affected family member first, and the difference between diagnostic testing in an affected individual versus pre-symptomatic testing in asymptomatic at-risk family members. Another participant (57-year-old Ashkenazi Jewish female with cardiovascular abnormalities not meeting criteria for DCM and a history of FDC) inquired why testing needed to be performed on one of her affected relatives prior to herself. A mother (52-
A year-old Caucasian female of unknown status and negative genetic testing sought an explanation regarding testing for her children, and why heart tissue from her affected husband, who had passed from DCM complications, was requested for testing prior to testing her children.

**Relevant Genetic Variants**

Two participants inquired about the meaning of their genetic testing results when a variant was discovered. The discovery of unique variants is common in families with DCM, and it can be difficult to understand the implications of these results when little or no information exists to determine the pathogenicity of these findings. One participant (23-year-old Caucasian female with cardiovascular abnormalities not meeting criteria for DCM and positive for a genetic variant) was unclear of the meaning of a variant identified in both her and her brother, and sought more clarification on it's significance, while another (52-year-old Caucasian male affected with FDC with a history of cardioversion, pacemaker, ICD, and sudden cardiac death and positive for 2 genetic variants) discussed with a study staff member the lack of understanding of disease causing versus neutral variants and that there may be other genetic changes besides the identified variants playing a role in the families’ disease.

**Physician Issues**

As participants shared their personal stories, 7.9% described issues they experienced when seeking medical treatment. They explained how they encountered inconsistencies in the understanding regarding the genetics of DCM as well as screening and testing recommendations. Three subthemes associated with physician issues emerged, including
lack of understanding (n=17), general dissatisfaction/no physician (n=12), and conflicting information (n=5).

**Lack of Understanding**

Half of the participants that expressed physician issues discussed the lack of understanding of DCM as a genetic disease and recommended screening and genetic testing guidelines. They explained how their physicians either outwardly expressed a lack of understanding or made comments that led them to doubt they would receive the care they felt they and their family needed. A few individuals requested educational material from the study staff that they could provide to their physician to help them explain the disease and associated genetics. One mother (47-year-old Caucasian female with cardiovascular abnormalities not meeting criteria for DCM and a family history of FDC) specifically requested because her son was currently hospitalized and felt she needed information from the research study to properly educate her child’s physicians to ensure proper care. One participant (47-year-old Caucasian female with cardiovascular abnormalities not meeting criteria for DCM and family history of FDC) explained that even when they had information to provide to their physician, in a letter from the DCM Research Project explaining FDC, they still encountered issues:

“He did not receive that well [letter explaining FDC]. The doctors we have around here are mostly vascular type doctors. They really don’t understand what cardiomyopathy is even if you take the information there. It’s like ‘Well…uh…what’s that got to do with it?’”
Two participants (57-year-old Caucasian male affected with FDC with a history of cardioversion and positive for a genetic variant and a 59-year-old Caucasian female affected with FDC with a history of ICD and heart transplant) stated that their physicians were not concerned about their family history of DCM, while two others (51-year-old Caucasian female affected with FDC and positive for a genetic variant and a 50-year-old Caucasian female affected with IDC) explained that even in the presence of family history, physicians felt their DCM was caused by a virus and not genetic, due to lack of clogged arteries on examination. One participant (37-year-old Caucasian female affected with IDC), after experiencing the onset of heart failure symptoms during and after pregnancy, described how she felt her doctors did not take her father’s death due to cardiomyopathy into consideration:

“I told them [physicians] my dad died of cardiomyopathy but they didn’t know it was genetic...my dad died when he was 49 and was sick for 10 years with this...It’s not like I’m going to leave that detail out. But most doctors when you tell them, they don’t even say anything. They’re like ‘Oh, Okay.’”

Another participant (52-year-old Caucasian male affected with FDC with a history of pacemaker, ICD, and heart transplant) explained a physician’s reaction when he had his wife take their children in for an initial cardiovascular screening after he was diagnosed with DCM and his daughter death from complications of DCM:

“Now I was diagnosed and we told everybody they should have themselves checked out and their kids checked out and everything. We didn’t want to wait...and my wife took them there [pediatrician] and they did all this and she says the doctor came up and says,
‘Can I ask you why you are doing this?’ and she says, ‘Well my husband’s oldest daughter passed away from cardiomyopathy, his brother’s diagnosed, he has it.’ And the doctor said, ‘Oh you misunderstood, this is not a genetic illness.’”

Several others felt that they or their family members were not receiving proper care or screening. One individual (56-year old Caucasian female affected with FDC and a history of cardioversion and positive for a genetic variant) explained they felt their doctor was treating them as they would a patient with atrial fibrillation, even though they had a confirmed DCM-associated variant in the LMNA gene, while another (56-year-old Caucasian male affected with FDC and a history of cardioversion and positive for a genetic variant) felt their siblings were not being followed correctly as their physician was only checking for high blood pressure. One participant (52-year-old Caucasian female affected with FDC) explained how her physician told her that children did not need cardiovascular screening if their parents screening results were normal and they did not exhibit symptoms. Others presented confusion around timing and frequency of cardiovascular screening. One father (52-year-old Caucasian male affected with FDC with a history of pacemaker, ICD, and heart transplant) explained that his children’s cardiologist did not understand why he brought his children in yearly for echocardiograms even with a family history of DCM:

“They tell us you only need to come back for more [cardiovascular screening] when they get to puberty...you really gotta look into this. They find in all of their programs they wanted for the first two years to go [for screening] every year. Then they say you don’t really need to come back until [your child] goes into puberty. We said, ‘We’d
rather if you catch it sooner. We’d rather know in advance. We don’t want to wait until it goes downhill. We want to catch it at the first sign of anything.”

Another woman (23-year-old Caucasian female with cardiovascular abnormalities not meeting criteria for DCM and positive for a genetic variant) who sought DCM screening after experiencing heart palpitations and fluttering was told there was no need to perform follow up screening unless these symptoms were really bothering her. One grandmother (64-year-old Caucasian female affected with IDC with a history of heart transplant and positive for a genetic variant) requested help from study staff to help educate her grandchild’s physician who was only performing EKG as screening method and not including an echocardiogram,. Another participant (37-year-old Caucasian female affected with IDC) wanted more information on how to order genetic testing as her physician was unfamiliar with the process.

General Dissatisfaction/No Physician

Some participants described a general dissatisfaction or trepidation in regards to physicians in general, either due to past negative experiences or general wariness or disillusion of the medical profession. One participant (48-year-old Caucasian male with cardiovascular abnormalities not meeting criteria for DCM and a family history of FDC), upon being counseled on the screening recommendations for DCM, explained that he is not a strong believer in doctors due to a poor medical experience his mother had in the past, while another (57-year-old Caucasian/Jewish female with cardiovascular abnormalities not meeting criteria for DCM and a family history of FDC) discussed her wariness and distrust of doctors and medicine and how this made decision making in
regards to the pursuit of medical treatment quite stressful. She explained that she felt her intellectually disabled brother underwent unnecessary brain surgery when he was young and she believes this ruined his life. Another individual (53-year-old Caucasian male affected with FDC and positive for a genetic variant) explained that he had seen so many doctors and had so many procedures performed in the past that he was not interested in pursuing any type of screening or treatment for his DCM. One participant (39-year-old Caucasian male with cardiovascular abnormalities not meeting criteria for DCM and a family history of FDC) simply stated he did not see a doctor on a regular basis, had no previous screening or care, and did not know where he could go to even find a cardiologist in his area.

Conflicting Information

Some participants discussed how they felt they had received conflicting information from their physicians regarding screening results or diagnoses and sought clarification from study staff. One woman (24-year-old Caucasian female affected with PPCM and positive for a genetic variant) was diagnosed with PPCM during a pregnancy 6 years prior, and was reportedly told to terminate the pregnancy and never get pregnant again, but a recent cardiovascular screening had revealed normal results, which she did not understand. Two other individuals (32-year-old Caucasian female with cardiovascular abnormalities not meeting criteria for DCM and a family history of FDC, 25-year-old Hispanic female unaffected with a family history of FDC) reported they were told by their physicians not to have children due to their family history of DCM even though both were asymptomatic and had no confirmed DCM diagnosis or genetic testing results. A mother (34-year-old
Caucasian female with cardiovascular abnormalities not meeting criteria for DCM and a family history of FDC and positive for a genetic variant) described how her son had a previously abnormal ejection fraction discovered by echocardiogram a year prior to his diagnosis of DCM, but was told the results were normal at the time. Another participant (52-year-old Caucasian female affected with FDC) reported that a physician told her brother that his children did not need cardiovascular screening as long as his personal screening results were normal, and she sought clarification regarding this topic.

**Disease/Medications/Treatment**

After a diagnosis of DCM, 5.8% of participants had questions concerning the medications they were taking or should take, available treatments, as well as the possibility of other health issues related to DCM. Four separate subcategories emerged including other related health issues (n=13), medications (n=6), supplements (n=3), and treatment (n=3).

**Other Related Health Issues**

After a DCM diagnosis, some participants had concerns that other health issues they were experiencing or exposures they experienced were related to the diagnosis, and sought information from the study staff. Two questioned whether medical issues they had experienced could be complications of DCM. One (43-year-old Caucasian female with some cardiac abnormalities that could not be interpreted due to low quality imaging data and a family history of FDC) was concerned her recent abnormal liver function test results could be a sign of DCM, while another (46-year-old Caucasian female of unknown status with a family history of FDC, an ablation, and positive for a genetic variant) inquired if both her and her sisters declining kidney function could be related to
DCM. Others were concerned that past exposures, medical events, or diagnoses had an impact on a DCM diagnosis. Two individuals (47-year-old Caucasian female affected with FDC and a history of cardioversion, pacemaker, and ICD, 55 year-old Caucasian female affected with IDC) wanted to know if their relatives’ drug and alcohol abuse could lead to DCM. Another (36-year-old Caucasian female affected with FDC with a history of ablation, ICD, heart transplant, and sudden cardiac death and positive for a genetic variant) was concerned that exposure to radiation as treatment for tuberculosis as a child could have contributed to her DCM. One individual (48-year-old Caucasian female affected with FDC and positive for a genetic variant) inquired if her brother’s HIV diagnosis may have contributed to his DCM. One participant (51-year-old Caucasian female affected with FDC) wanted to know if there was a genetic link between her scleroderma diagnosis and DCM, while another (65-year-old Black male affected with IDC) inquired if his chronic asthma was a symptom of DCM. One father (33-year-old Caucasian male affected with FDC with a history of ICD) explained that his DCM was brought on by “broken heart syndrome” as he had no previous symptoms until after the death of his young children. One died soon after birth due to reported “heart issues” while the other died in childhood soon after a cardiomyopathy diagnosis. The father reported he had reviewed research on health issues arising after tragic events, and felt this was true for him and his DCM symptom onset.

Medications

A few participants contacted study staff to inquire about what medications were recommended for DCM. Three individuals wanted information on possible prescription
medications for asymptomatic patients, with one (23-year-old Caucasian female with cardiovascular abnormalities not meeting criteria for DCM and positive for a genetic variant) specifically asking if there was a particular medication for those with a genetic predisposition to DCM. Two others (60-year-old Caucasian female affected with FDC and positive for a genetic variant, 57-year-old Ashkenazi Jewish female of unknown status with a family history of FDC) wanted to know what impact long-term use of their prescribed medications might have on their health, while one mother (37-year-old Caucasian female with cardiovascular abnormalities not meeting criteria for DCM and) was concerned that her son’s sudden cardiac death was related to his use of an antidepressant. During a follow-up interview, one participant (37-year-old Caucasian female affected with IDC) described her experience in attempting to gather more information about the medications she had been prescribed:

“Another thing they [physicians] did was they gave me all this medication and didn’t really go into...well I researched on my own what each one did. At a certain point I was like why am I taking this water pill? I don’t need it...They [physicians] also had me on a really high dose of Lisinopril...and I asked if I could cut that back. I asked and they’re like ‘Yeah...sure.’ Another medicine I had that I researched said it didn’t help women that is decreased their improvement. When I asked, he [physician] was like ‘Well just stop taking that then.’...So I’m on these five things when I really only need two. I asked one of them (physician), ‘Can I take half?’ and he said, ‘Yeah’ and it made a huge difference.”
Supplements

Three participants inquired about the use of natural supplements and possible effects in regards to their DCM diagnosis. One individual (49-year-old Caucasian female with cardiovascular abnormalities not meeting criteria for DCM and a family history of FDC, a pacemaker and positive for a genetic variant) made a general inquiry on what supplements may be helpful to reduce the severity and progression of DCM, while two other participants (70-year-old Caucasian male affected with FDC and a 67-year-old Caucasian female with DCM post Adriamycin chemotherapy exposure and positive for a genetic variant) specifically inquired about CoQ10, for which they had read studies indicating potential benefits for patients with DCM.

Treatment

Three other participants contacted study staff with questions about treatment for DCM. Two (59-year-old Caucasian male affected with FDC and positive for a genetic variant and a 57-year-old Caucasian/Jewish female with cardiovascular abnormalities not meeting criteria for DCM and a family history of FDC) inquired about the progress of treatment for DCM and wanted to know more information in regards to advancements in technology including gene therapy and stem cell treatment. Another participant (29-year-old Caucasian female affected with FDC) had a specific question regarding the appropriateness of treatment with medications only versus an invasive procedure such as ablation.
Correlational Results

After the major thematic categories were established, data analysis was performed to determine if any statistical significant (p<0.05) correlations could be identified between the thematic categories and available demographic and health-related data of participants. See Table 3 and Table 4 for data used for correlation with thematic results.

Participant Age

Analysis of participant ages (range 13-83 years) compared to thematic categories indicated that, as the age of participants increased, there was a decrease in expressed concerns for children (point-biserial coefficient=-0.1518, p=0.0195) and an increase in expressed concerns for research (point-biserial coefficient=0.1338, p=0.0396).

Participant Gender

Although the thematic cohort is predominantly female (n=152, 63.4%), phi coefficient analysis indicated that, of the males that did express concerns, they were less likely to present issues regarding insurance (phi coefficient=-0.1367, p=0.035), and less likely to discuss emotional concerns (phi coefficient=-0.1383, p=0.0329) when compared to females.

Participant Ethnicity

The majority of participants in the study are Caucasian (n=214, 89.5%). Analysis comparing the concerns expressed by other ethnic categories compared to Caucasians revealed that those of Hispanic ethnicity (n=8, 3.3%) were more likely to share emotional issues than those of other ethnicities (phi coefficient=0.1621, p=0.0121).
Family Status and Genetic Testing Results

Analysis of family status comparing those individuals whose families were identified as FDC (n=174, 72.8% and includes FDC and probable FDC) to those with IDC (n=65, 27.2% and includes IDC and possible FDC) indicated that individuals with a family status of FDC were more likely to express concerns about the genetics of DCM than those with IDC (phi coefficient=0.1587, p=0.014). Also, those individuals who had a genetic variant identified and were informed that research results were available (n=48, 20.1%) were more likely to present concerns regarding genetics (phi coefficient=0.2500, p=0.0001) when compared to participants that did not have an identified variant.

Health-Related Data

Analysis examining available health-related data including the circumstances leading to a diagnosis of participants and personal history of invasive cardiovascular procedures revealed that those individuals who were diagnosed through cardiovascular screening (n=32, 13.4%) were more likely to express concerns regarding both physician issues (phi coefficient=0.1773, p=0.006) as well as genetic concerns (phi coefficient=0.1702, p=0.0084). Also, participants that had a personal history of a heart transplant were more likely to share issues related to insurance (phi coefficient=0.1379, p=0.033) and also barriers to communication with family members (phi coefficient=0.2031, p=0.0016).
TABLE 2. Participant Demographics: Entire Cohort (n=1638)

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<td>75.5%</td>
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<tr>
<td></td>
<td>IDC (includes IDC and possible FDC)</td>
<td>401</td>
<td>24.5%</td>
</tr>
<tr>
<td>Genetic Research Results</td>
<td>Positive for genetic variant</td>
<td>300</td>
<td>18.3%</td>
</tr>
<tr>
<td></td>
<td>Negative for genetic variant</td>
<td>224</td>
<td>13.7%</td>
</tr>
<tr>
<td></td>
<td>Unknown (No research testing performed or recorded)</td>
<td>1114</td>
<td>68.0%</td>
</tr>
</tbody>
</table>

Table 2. Participant Demographics: Entire Cohort
<table>
<thead>
<tr>
<th>TABLE 3. Participant Demographics: Thematic Code Cohort (n=239)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (at time of consent)</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Gender</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Race</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Ethnicity</td>
</tr>
<tr>
<td>Family Status</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Genetic Research Results</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Family informed of results availability</td>
</tr>
</tbody>
</table>

Table 3. Participant Demographics: Thematic Code Cohort
<table>
<thead>
<tr>
<th>TABLE 4. Cardiovascular Medical History Data: Thematic Code Cohort</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Method brought to medical attention</strong></td>
</tr>
<tr>
<td>Screening</td>
</tr>
<tr>
<td>Asymptomatic</td>
</tr>
<tr>
<td>Unknown</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Symptomatic presentation</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Signs of heart failure</td>
</tr>
<tr>
<td>Shortness of breath</td>
</tr>
<tr>
<td>Fatigue</td>
</tr>
<tr>
<td>Dyspnea on exertion</td>
</tr>
<tr>
<td>Edema</td>
</tr>
<tr>
<td>Weight gain</td>
</tr>
<tr>
<td>Paroxysmal nocturnal dyspnea</td>
</tr>
<tr>
<td>Orthopnea</td>
</tr>
<tr>
<td>Signs of arrhythmia</td>
</tr>
<tr>
<td>Palpitations</td>
</tr>
<tr>
<td>Presyncope</td>
</tr>
<tr>
<td>Thrombosis</td>
</tr>
<tr>
<td>Syncope</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Total number of presenting symptoms per symptomatic individual</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
</tr>
<tr>
<td>1</td>
</tr>
<tr>
<td>2</td>
</tr>
<tr>
<td>3</td>
</tr>
<tr>
<td>4</td>
</tr>
<tr>
<td>5</td>
</tr>
<tr>
<td>6</td>
</tr>
<tr>
<td>7</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Cardiovascular procedures/events</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Implantable cardioverter defibrillator (ICD)</td>
</tr>
<tr>
<td>Transplant</td>
</tr>
<tr>
<td>Pacemaker</td>
</tr>
<tr>
<td>Cardioversion</td>
</tr>
<tr>
<td>Ablation</td>
</tr>
<tr>
<td>Sudden cardiac death</td>
</tr>
<tr>
<td>Biventricular pacemaker</td>
</tr>
<tr>
<td>Bypass</td>
</tr>
</tbody>
</table>

Continued
Table 4 continued

<table>
<thead>
<tr>
<th>Total number of recorded cardiovascular procedures/events per individual</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>136 (56.9%)</td>
</tr>
<tr>
<td>1</td>
<td>55 (23.0%)</td>
</tr>
<tr>
<td>2</td>
<td>25 (10.5%)</td>
</tr>
<tr>
<td>3</td>
<td>14 (5.9%)</td>
</tr>
<tr>
<td>4</td>
<td>9 (3.8%)</td>
</tr>
<tr>
<td>Subject ID</td>
<td>Date of Correspondence Leading to Coded Theme</td>
</tr>
<tr>
<td>------------</td>
<td>-----------------------------------------------</td>
</tr>
<tr>
<td>159</td>
<td>10/2/2013</td>
</tr>
<tr>
<td>197</td>
<td>9/10/2008 Documented phone number no longer correct</td>
</tr>
<tr>
<td>503</td>
<td>1/16/2003</td>
</tr>
<tr>
<td>504</td>
<td>6/2/2005</td>
</tr>
<tr>
<td>533</td>
<td>3/16/2006 Verbally agreed, but did not return the form despite two attempts</td>
</tr>
<tr>
<td>674</td>
<td>9/20/2005</td>
</tr>
<tr>
<td>707</td>
<td>2/13/2004</td>
</tr>
<tr>
<td>713</td>
<td>5/4/2006 Did not contact, deceased</td>
</tr>
</tbody>
</table>

Continued

Table 5. Interview Time Points
Table 5 continued

<table>
<thead>
<tr>
<th>Subject ID</th>
<th>Date of Correspondence Leading to Coded Theme</th>
<th>Re-Contact Date</th>
<th>Date of Re-Consent</th>
<th>Interview Date</th>
<th>Time Span From Original Correspondence to Interview</th>
</tr>
</thead>
<tbody>
<tr>
<td>762</td>
<td>4/10/2008</td>
<td>Did not contact, deceased</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>982</td>
<td>5/2/2012</td>
<td>Did not contact, deceased</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>1092</td>
<td>4/7/2008</td>
<td>Not contacted. Did not consent to future contact</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>1249</td>
<td>7/10/2006</td>
<td>9/17/2015</td>
<td>10/22/2015</td>
<td>10/30/2015</td>
<td>9.3 years</td>
</tr>
<tr>
<td>1257</td>
<td>4/25/2014</td>
<td>10/29/2015</td>
<td>11/10/2015</td>
<td>11/19/2015</td>
<td>1.6 years</td>
</tr>
<tr>
<td>1376</td>
<td>3/17/2009</td>
<td>9/18/2015</td>
<td>Did not respond to initial contact despite two attempts</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>1399</td>
<td>5/2/2008</td>
<td>9/17/2015</td>
<td>Did not respond to initial contact despite two attempts</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>1401</td>
<td>7/21/2008</td>
<td>9/17/2015</td>
<td>Did not respond to initial contact despite two attempts</td>
<td>N/A</td>
<td>N/A</td>
</tr>
</tbody>
</table>

Continued
Table 5 continued

<table>
<thead>
<tr>
<th>Subject ID</th>
<th>Date of Correspondence Leading to Coded Theme</th>
<th>Re-Contact Date</th>
<th>Date of Re-Consent</th>
<th>Interview Date</th>
<th>Time Span From Original Correspondence to Interview</th>
</tr>
</thead>
<tbody>
<tr>
<td>1545</td>
<td>Did not contact per recommendation of study staff (sensitive case)</td>
<td>11/9/2012</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>1615</td>
<td>Verbally agreed but did not return the form despite two attempts</td>
<td>2/18/2014</td>
<td>9/17/15</td>
<td>N/A</td>
<td>N/A</td>
</tr>
</tbody>
</table>

Average time span 5.2 years

---

**TABLE 6. Interviewed Participants: Demographic and Clinical Data**

<table>
<thead>
<tr>
<th>Participant ID</th>
<th>Gender</th>
<th>Race</th>
<th>Age at first consent</th>
<th>Family status</th>
<th>Gene status</th>
<th>Cardiovascular procedure/event</th>
</tr>
</thead>
<tbody>
<tr>
<td>14</td>
<td>F</td>
<td>Caucasian</td>
<td>47</td>
<td>FDC</td>
<td>UNK</td>
<td>None</td>
</tr>
<tr>
<td>159</td>
<td>M</td>
<td>Caucasian</td>
<td>46</td>
<td>FDC</td>
<td>POS</td>
<td>ICD</td>
</tr>
<tr>
<td>504</td>
<td>F</td>
<td>Caucasian</td>
<td>45</td>
<td>FDC</td>
<td>POS</td>
<td>Pacemaker</td>
</tr>
<tr>
<td>1249</td>
<td>M</td>
<td>Caucasian</td>
<td>52</td>
<td>FDC</td>
<td>UNK</td>
<td>Pacemaker ICD Transplant</td>
</tr>
<tr>
<td>1257</td>
<td>F</td>
<td>Caucasian</td>
<td>37</td>
<td>IDC</td>
<td>UNK</td>
<td>None</td>
</tr>
</tbody>
</table>

Legend: UNK (unknown testing status), POS (positive for genetic variant)

Table 6. Interviewed Participants: Demographic and Clinical Data
<table>
<thead>
<tr>
<th>Themes and Subthemes</th>
<th>No. Entries</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Concern for Children and Relatives</strong></td>
<td>115 (26.7%)</td>
</tr>
<tr>
<td>Screening/Genetic Testing</td>
<td>77</td>
</tr>
<tr>
<td>Children as Motivation</td>
<td>25</td>
</tr>
<tr>
<td>Pregnancy/Future Children</td>
<td>13</td>
</tr>
<tr>
<td><strong>Emotional Adjustment</strong></td>
<td>61 (14.2%)</td>
</tr>
<tr>
<td>General Adjustment</td>
<td>17</td>
</tr>
<tr>
<td>Fear/Anxiety/Stress</td>
<td>16</td>
</tr>
<tr>
<td>Denial</td>
<td>10</td>
</tr>
<tr>
<td>Life Choices</td>
<td>6</td>
</tr>
<tr>
<td>Depression</td>
<td>5</td>
</tr>
<tr>
<td>Anger/Shock</td>
<td>4</td>
</tr>
<tr>
<td>Guilt</td>
<td>3</td>
</tr>
<tr>
<td><strong>Communication</strong></td>
<td>56 (13.0%)</td>
</tr>
<tr>
<td>No Contact</td>
<td>22</td>
</tr>
<tr>
<td>Family Dynamics</td>
<td>18</td>
</tr>
<tr>
<td>Health Issues</td>
<td>9</td>
</tr>
<tr>
<td>Adoption/Paternity</td>
<td>4</td>
</tr>
<tr>
<td>Location</td>
<td>3</td>
</tr>
</tbody>
</table>

Table 7. Thematic Code Results
Table 7 continued

<table>
<thead>
<tr>
<th>Research</th>
<th>51 (11.9%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bloodwork</td>
<td>14</td>
</tr>
<tr>
<td>General Issues with Research</td>
<td>12</td>
</tr>
<tr>
<td>Privacy</td>
<td>9</td>
</tr>
<tr>
<td>Research vs. Clinical Testing</td>
<td>8</td>
</tr>
<tr>
<td>Speed of Return of Results</td>
<td>8</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Insurance</th>
<th>51 (11.9%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coverage/Lack of Insurance</td>
<td>37</td>
</tr>
<tr>
<td>Concern for Discrimination</td>
<td>14</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Genetics</th>
<th>37 (8.6%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inheritance</td>
<td>13</td>
</tr>
<tr>
<td>Reduced Penetrance/ Variable Expression</td>
<td>10</td>
</tr>
<tr>
<td>Gene Function</td>
<td>7</td>
</tr>
<tr>
<td>Testing Affected vs. Unaffected</td>
<td>5</td>
</tr>
<tr>
<td>Relevant Genetic Variants</td>
<td>2</td>
</tr>
</tbody>
</table>
Table 7 continued

<table>
<thead>
<tr>
<th>Physician Issues</th>
<th>34 (7.9%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lack of Understanding</td>
<td>17</td>
</tr>
<tr>
<td>General Dissatisfaction/No Physician</td>
<td>12</td>
</tr>
<tr>
<td>Conflicting Information</td>
<td>5</td>
</tr>
<tr>
<td>Disease/Medications/Treatment</td>
<td>25 (5.8%)</td>
</tr>
<tr>
<td>Other Related Health Issues</td>
<td>13</td>
</tr>
<tr>
<td>Medications</td>
<td>6</td>
</tr>
<tr>
<td>Supplements</td>
<td>3</td>
</tr>
<tr>
<td>Treatment</td>
<td>3</td>
</tr>
</tbody>
</table>
Chapter 4: Discussion

Psychosocial Themes

The primary aim of this study sought to identify the primary and recurring psychosocial concerns of DCM patients and their family members. We hypothesized that we would likely identify concerns in participants of the DCM Research Project that have been identified in other genetic disorders, including issues regarding personal distress, insurance and discrimination, concern for children and relatives, as well as barriers to communication. Through a systematic qualitative review of correspondence from participants during their involvement in the DCM Research Project, eight main themes emerged which included concern for relatives and children (26.7%), emotional adjustment (14.2%), communication (13.0%), insurance (11.9%), research (11.9%), genetics (8.6%), physician issues (7.9%), and disease/medications/treatment (5.8%). These findings reveal that the several of the main areas of concern expressed by patients and families affected with DCM, including concern for children and relatives, emotional adjustment, communication barriers, and insurance concerns, are similar to those reported in existing literature on the issues experienced by patients with other genetic disorders including other inherited cardiac and cancer-predisposition syndromes. Other emergent themes, such as questions regarding complex genetics, physician issues, and concerns regarding medications and treatments, may represent issues more unique to individuals
with DCM as well as other inherited cardiac disorders in association with the rapidly advances knowledge of genetic associations and cardiovascular disease.

**Concern for relatives and children**

Concern for relatives and children was the predominant theme that participants expressed. Similar to studies of patients at risk for other genetic cardiovascular disorders (Aatre & Day, 2011; Etchegary et al., 2015; Hendriks et al., 2005), individuals discussed that their decision to pursue genetic testing and screening for DCM was motivated more by their desire to inform their children and other relatives and not necessarily to satisfy their own autonomy. Participants discussed that results of predictive testing and screening may allow their children and family to make appropriate medical and lifestyle decisions to ensure better health and quality of life outcomes than they may have experienced themselves. Several individuals, with a strong family history of DCM, including the death of relatives due to the disease, as well as personal histories of invasive procedures, such as ICD or heart transplant, explained how these experiences impacted their desire to prevent their children and future generations from experiencing these traumatic events. One participant was quoted that her main hope in determining if her children were at risk was to allow them to be free of the fear of disease if they were to be negative for a genetic variant or make more informed lifestyle and healthcare decisions if they were to test positive. These findings support previous literature reported in other genetic disorders, including HCM, that many patients are motivated to seek genetic testing to relieve uncertainty regarding a familial diagnosis, to allay concerns for children and other family members, to guide future medical recommendations, and in the case of a family
history of sudden death, to find an explanation and meaning for their loss (Erskine et al., 2014). These findings highlight the importance of family-focused counseling for patients with DCM. Discussions during counseling appointments may shift more to the effects and risk of the disease for other members of the family, especially children, as opposed to the individual themselves. In depth discussions about the family’s personal experience with the disease and emotional impact it has had on family members and how this may effect personal motivation for seeking care and genetic testing should be explored with patients. Patient sessions should also include a detailed family history and pedigree construction, which would not only facilitate the conversation of personal disease experience, but also prompt the discussion on what family members are at risk for the disease allowing for review of existing practice guidelines for screening and genetic testing recommended by the HFSA and the HRS/EHRA, which include recommendations for screening and testing in children when they are at risk for DCM due to a significant family history or presence of a disease-associated genetic variant (Ackerman et al., 2011; Hershberger et al., 2009). This leads into another major area of concern for children presented by study participants. Several individuals inquired about the proper methods and timing of cardiovascular screening and genetic testing, especially for young children, to determine their risk for DCM. Unlike inherited cancer-predisposition syndromes in which it is often recommended that genetic testing be postponed until a child reaches legal adult age to provide consent, genetic cardiovascular diseases, including DCM, can affect young children, with approximately 50% of children affected with DCM before age 18 appearing to have a genetic cause, even in the absence of family history,
(Hershberger et al., 2009; Lakdawala et al., 2012), thus warranting cardiovascular screening and testing for underage children. When a pathogenic variant is identified in a family, questions emerge of what age to perform testing in children. Current professional recommendations indicate screening and testing in childhood, without dictating specific ages at which these should occur. In light of this, collaboration between cardiologists and genetic counselors is warranted to assess the appropriateness of genetic testing for at risk children, provide specialized pediatric care for those affected, and help families cope with the emotional impact this may have on parents and other family members (Morales & Hershberger, 2015).

As symptom onset of DCM may present or worsen during or after pregnancy, women who were pregnant during their participation in the DCM Research Project presented concerns unique to this subset of DCM patients. They discussed concerns regarding symptoms they were experiencing or medications they were prescribed and how they may impact their current pregnancy. They also inquired about the risk of DCM for future pregnancies, concern for the ability to carry children, and the desire to obtain information to make future reproductive decisions based on genetic testing results. These concerns exhibit the need for specialized counseling topics for this subset of DCM patients.

Collaborative efforts between cardiovascular genetic counselors and cardiologists with obstetricians and prenatal genetic counseling teams may be needed to provide comprehensive medical care during pregnancy as well as assisting in decision making pre and post-conception to assess risk, facilitate genetic testing, and guide informed decisions on reproductive options. In depth discussion should include prenatal diagnostic testing
and the availability of pre-implantation genetic diagnosis (PGD) as options for those concerned about future pregnancies and DCM.

**Emotional adjustment**

Clinical observations and research on the psychosocial adaptation to a DCM diagnosis, other inherited cardiac and cancer-predisposition syndromes, as well as chronic illness in general report that patients often experience similar emotional responses that include anxiety, stress, depression, denial, shock, anger, guilt, and general adjustment to living with a new diagnosis (Ingles et al., 2008; James et al., 2012; Livneh & Antonak, 2005; Meiser, 2005). Studies specifically focusing on individuals with DCM, have reported that patients experience feelings of anxiety, stress, and depression as factors that impact quality of life when emotionally adjusting to a diagnosis of DCM (Esplen et al., 2001; Hidayatallah et al., 2014; Rasoul et al., 2015; Steptoe et al., 2000; R. Teo et al., 2014). The current study corroborates these findings, as participants shared their experiences in dealing with a DCM diagnosis including feeling shock and denial in regards to an unexpected diagnosis, anxiety and stress about symptoms they had experienced, and guilt for possibly passing a genetic risk of DCM to their children. Participants in our study also provided additional depth by describing how emotionally adjusting to a diagnosis of DCM can also act as a barrier to pursuing medical care and screening for both themselves and family members, as well as affecting major life decisions patients may make based on genetic testing results, with some younger at risk individuals basing career decisions on genetic status. Others described how family members suffered severe depression after a diagnosis that negatively impacted their quality of life, one eventually committing
suicide suspected to be associated with their poor adjustment to their diagnosis. These findings emphasize that patients and families affected by DCM would benefit from emotion-focused counseling to help them cope with the adjustment to life with a diagnosis of DCM and attempt to reduce negative impacts these emotional responses may have on quality of life. Emotion-focused counseling has been recommended in other genetic disorders and demonstrates the importance of including genetic counseling in the care of patients with DCM (Biesecker & Erby, 2008; Erskine et al., 2014). Counselors should be aware of the possible emotional reactions that may be encountered to allow them to assist patients in recognizing and developing coping strategies to help them deal with a new DCM diagnosis. Reducing the emotional impact of a DCM diagnosis could then assist in facilitating decision making in regard to cardiovascular screening and genetic testing, as well as assist patients and family members work through lifestyle changes and consideration of future life choices in light of a DCM diagnosis. Those that may be experiencing more severe negative symptoms, including depression, might also benefit from a referral to a mental health specialist to help manage deeper psychological issues that may manifest after a DCM diagnosis. Studies have demonstrated that some individuals affected by a chronic illness may benefit from ongoing emotional support, to help them adapt to lifestyle changes and long-term effects of the disease (de Ridder, Geenen, Kuijer, & van Middendorp, 2008). Genetic counselors should be sensitive to the possible need for long-term psychosocial care in DCM patients to determine if a referral to a mental health specialist is warranted.
Communication

We also hypothesized that challenges in communicating genetic risk to family members including complex family dynamics and issues discussing complex genetic information would present as an issue for DCM families. Studies of individuals affected with other genetic disorders describe communication barriers including geographical distance, strained dynamics with relatives, concern that relatives will not understand, difficultly relaying complex genetic information, and desiring to protect others from worry and distress (Batte et al., 2015; Bleiker et al., 2013; Ormondroyd et al., 2014; van Oostrom et al., 2007). Our thematic findings revealed these same issues in the DCM cohort, but included deeper insight to some of the personal and unique barriers that were experienced by some individuals.

Participants discussed a lack of contact with relatives as a major issue to disseminating information about DCM and genetic risk to others in the family, either due to geographical distance or institutional barriers such as assisted living homes or imprisonment impeded communication with relatives. Other individuals discussed more emotional and social barriers to communication. A few participants discussed tentative contact with ex-spouses as an issue when discussion risks and recommendations. These findings demonstrate that impaired familial cohesion, either by geographical distance or emotional strain, has a negative impact on communication of health-related information, which has also been described in other genetic disorders (Rodriguez, Corona, Bodurtha, & Quillin, 2016). Other communication issues included parents who were uncertain of the timing of the discussion with children and how much information to even disclose,
while others were fearful of discussing the disease with family members that may have strong negative emotional reactions due to their past experience with DCM, including the death of a close relative. These findings are in agreement with other studies examining family discussion of disease when there is a risk for sudden cardiac death, including DCM (Wiley, Demo, Walker, & Osborne Shuler, 2015). Patients may find it challenging to discuss the seriousness of a diagnosis with a child without instilling an excessive amount of fear. This can also be a consideration when discussing risk with other family members that may be perceived as emotionally unable to handle such information. Other participants discussed that having family members with intellectual impairment due to age-related dementia or mental complications from other health-related issues impaired their ability to comprehend the complex nature of a genetic risk discussion. A few participants revealed that pre-existing family secrets regarding suspected or undisclosed non-paternity impeded open discussion of inherited disease risk.

As evidenced by the variety of issues presented by the DCM cohort in regards to family communication, discussion of health-related issues and genetic risk can be a complex task. The affected individual may feel an obligation to inform at risk relatives but may be unsure of how to navigate preexisting family dynamics and potential negative emotional reactions. Genetic counselors may need to inquire about family dynamics with patients to determine if communication barriers exist. Helping patients identify issues may help them develop or suggest communication methods that would be most appropriate for their individual family situations. Current genetic counseling practice often incorporates the use of a family letter to help patients share complex genetic and
disease-related information to ask risk relatives, but dissemination of these letters and uptake of recommendations is difficult to track once provided to a patient. An exploration of other options of family communication is warranted to provide varying methods of sharing information to address the multiple barriers that may be encountered. As society becomes more technology-based in their communication methods, even within a family, applications that utilize virtual methods of communication, including personal email, as well as web-based portals or social media applications, may help to improve dissemination of health-related information, as it negates geographical barriers and may improve uptake of information and recommendations, especially in adolescents and young-adult demographics which may be more comfortable with web-based education and communication. Even within the adult population, personal email has become a more utilized system of communication as well. Combining these two methods, some social media applications actually now employ functions that allow users to send messages not only to others using the same social media tool, but send that same message to personal email accounts to those that may not be members of the site. A study examining the potential benefits and limitations of the use of technology in the communication of health information postulates that the use of social media will be widely used to disseminate health information and will increase peer-to-peer and family discussion and support. They caution that a better understanding is warranted to expand our understanding of the use of social media and establish reliable methods to ensure the efficacy and accuracy of the health information that is shared through these electronic pathways (Mamlin & Tierney, 2016). Additional research is needed to determine the
benefits, limitations, and efficacy of such communication efforts and to explore other possible methods to conquer communication barriers that may be encountered when sharing healthcare information within a family.

Although letters and potential electronic tools may be useful to overcome geographical distance and some basic discomfort in the discussion of healthcare information, it does little to tackle some of the more complex emotional barriers that may exist within a family. It does not address people’s hesitation to discuss difficult topics and does not allow for the interpretation of tone-of-voice and body language cues in response to receiving this type of information for assessing the need for more in depth discussion to navigate complex emotional issues that may arise. Family counseling sessions can be recommended to help share information and facilitate testing for those that wish to seek these services and help navigate some of the emotional reactions to disease-risk, but more complex issues, including undisclosed non-paternity and other family secrets may need more in depth and delicate approach. These families may need referrals to other mental health and family-counseling professionals to help navigate communication methods in the context of complex family dynamics.

Insurance

Another major area of concern presented by study participants that served as a barrier to pursuing healthcare, screening, and genetic testing was the issue of insurance coverage and fears of discrimination. Insurance issues have been reported as one of the largest issues in pursuing genetic testing in DCM (Morales & Hershberger, 2015), and mirror the same concerns that have been reported by patients confronting the risk of other
genetic disorders (Aatre & Day, 2011; Klitzman, 2010; Peterson, Milliron, Lewis, Goold, & Merajver, 2002). Individuals in the DCM cohort discussed how a lack of insurance and concerns of coverage costs prevented not only themselves from pursuing screening and genetic testing, but also was an issue for many other members of their families. They also added additional insight explaining that even when they pursued recommended screening or testing, their insurance coverage did not allow them to see the providers they desired. Several discussed lack of insurance as a motivation to join a research study to gain access to screening and genetic testing they would otherwise be unable to obtain. Those with insurance coverage focused their concerns on the potential for discrimination based on screening and genetic testing results. Even with discussions of GINA and the protection this law provides, fear still existed that prevented individuals from pursuing recommended screening and testing. Participant stories not only reveal a shared issue for patients with DCM and those at risk for other genetic disorders, but also reveal the fact that those family members not currently seeking clinical care often hold these concerns. These individuals may not be aware of the legal protections covered by GINA or available research studies that may impact their decisions to pursue recommended healthcare. In addition, when a DCM-associated variant is identified in an individual, at-risk family members only then need to be tested for this causative variant. This testing is often cheaper than larger gene panels ordered on proband patients, and is often more likely to be covered under existing insurance coverage. Individuals that chose not to seek care for insurance reasons may not be aware of this information, believing that they simply cannot afford testing even when a genetic variant is identified in a
family. This highlights the importance of proper education and information dissemination regarding costs, insurance coverage, and protections to those family members that do choose to seek care, as they may be tasked with having these conversations with family members when sharing recommendations on screening and testing for those relatives at risk for DCM. Even with the protections of GINA, the fear and perception of discrimination can take many forms and can impact decisions for not only testing but treatment and results disclosure as well. It is important to determine if a patient, or family member, is making decisions based on perceptions of discrimination in order to help them navigate these concerns, explain existing protections, and determine the best course of action in seeking medical care (Klitzman, 2010).

**Research issues**

Due to the fact that the correspondence data used for this study was provided by individuals who voluntarily participated in research of DCM, we sought to uncover possible concerns unique to research participants during our investigation of themes. Participants presented varying issues regarding participation in the DCM Research Project. Providing a blood sample was an issue for some, as they did not wish to have their blood drawn or encountered logistic issues finding a draw site or issues with financial charges imposed by draw sites. Others discussed reluctance to participate due to perceived time commitments or distrust of research in general, including concerns for the privacy of personal information that was to be provided after enrollment. These issues highlight the importance of thorough discussions during the research consent process, highlighting the responsibilities of both the participant and the study, including
travel that may be necessary and any cost that may be incurred. Particular attention should be focused on privacy, including HIPAA provisions and institutional research review boards that serve to protect the anonymity of patients and research participants to help alleviate these potential concerns. Once enrolled in the DCM Research Project, participants inquired about the timeline of genetic testing and return of genetic testing results, as well as help understanding why research results must be confirmed in a clinical laboratory for official medical use. These recurring questions indicate a need for clear discussion early in the research process regarding realistic expectations and what information or results may or may not be provided to them. Discussion should also include the regulatory differences between research and clinical testing and the limitations placed on the scope of research results.

Genetics

Considering the locus and allelic heterogeneity, reduced penetrance, and variable expressivity of DCM-associated variant, it is not surprising that several participants contacted study staff to gain further knowledge of the genetic basis of DCM. Upon learning of positive results for a genetic variant, participants inquired about the risk to other family members, prompting discussions of inheritance patterns, and the fact that family members with the same variant may not present at the same age or experience the same symptoms as other affected family members. Others inquired about the reasoning behind testing those family members that are affected with DCM prior to testing others that may be at risk. Some wanted more detail on the biological function of the genes associated with DCM, and the consequences of a unique variant identified in their family.
One individual explained that she believed patients should be provided with more detailed genetic information without a lot of medical jargon, and medical professionals should not assume a patient cannot handle complex topics. With the complexity of DCM genetics and varying educational and intellectual backgrounds of the patient population, genetic professionals that are trained to understand these complex topics and convey them in a simple, concise manner are integral to the care of DCM patients. A challenge these genetic professionals face is balancing the needs of those who may desire more detailed medical information regarding a DCM diagnosis with those that may become overwhelmed with in depth discussion of genetic details and complex information. Providing personalized care is the major goal in the genetic counseling setting, so a discussion of the level of detail of information desired by patients on an individual basis can help to determine the amount of knowledge they need to make healthcare decisions and understand their diagnosis. Not all individuals may be able to comprehend highly technical information, and providing this data may detract from their understanding of more pertinent disease information needed to determine care as well as share with at risk family members. Sharing basic information for all patients, while directing those that desire more complex data to the proper resources may provide a balance in these situations.

Physician issues

Although DCM is a common form of cardiomyopathy encountered by many cardiovascular and medical professionals, the genetic etiology and complexity of discerning between those with non-ischemic, idiopathic, and familial disease may not be
fully understood or appreciated by all healthcare professionals. Anecdotal experience indicates that cardiologists often do not recognize FDC in their practices, and when they do, they may be unable or unlikely to collect proper family history or provide accurate genetic education and screening recommendations to at-risk patients (Burkett & Hershberger, 2005). The current study is the first to provide data, including personal stories, supporting that patients struggle with their providers’ lack of appreciation of DCM genetics. Participants in the DCM Research Project shared stories of the issues they and their family members experienced when seeking care outside of the research project. Although this theme has not been extensively discussed in existing literature and was not a hypothesized potential finding at the start of our study, data from this study supports lack of genetic DCM knowledge among some physicians, including cardiovascular specialists. A study performed by Ruiter et al. (2010), comparing practices between general hospitals and university based medical centers, indicated that DCM patients seeking care at a general hospital were less likely to be told their disease could be genetic and less likely to be referred to a genetics specialist when compared to those that received care at a university medical center. Another study that surveyed general practitioners about their knowledge and management of patients with genetic cardiac disease showed, that even though a majority had seen at least one patient with a genetic cardiac disorder, they had limited confidence in the appropriate management of these patients and were dependent on guidance from knowledgeable cardiologists on which patients to refer for genetic counseling (Marathe, Woodroffe, Ogden, & Hughes, 2015). In our study, participants reported that their physicians had a lack of
understanding of the genetics of DCM and they received conflicting information regarding the disease and screening recommendations. Individuals reported they were told that DCM was not genetic or had family history disregarded during discussions of their family experience with the disease. Others questioned if their family members were receiving specialized care as individuals with DCM as opposed to other cardiovascular diseases, and some received questions from physicians regarding the need for cardiovascular screening for them and their relatives. Although professional guidelines exist from the HFSA and the HRS/EHRA, providing recommendations for when to screen and perform genetic testing, not all medical professionals may be aware of these recommendations or have understanding of the emerging knowledge of the genetic etiology of DCM that has evolved rapidly over the past few decades. Alternatively, they may disagree with the recommendations or simply lack the incentives to conduct a genetic evaluation. A few research participants even requested educational information from the DCM Research Project staff they could provide to their physicians to help educate them and improve the care they or their family members were receiving. These findings, in combination with the reports by Ruiter et al. (2010) and Marathe, Woodroffe, Ogden, & Hughes (2015), highlight the need for further education of those medical professionals that may encounter patients with DCM, as well as the importance of referring these patients to a center where they can meet with an integrated team of cardiology specialists and genetic professionals, including genetic counselors, to provide the proper care and management of patients with cardiomyopathy as well as their families. This becomes especially imperative for those individuals and family members
that may have DCM-associated genetic variants in genes such as *LMNA* that convey a greater risk for arrhythmia and possible sudden cardiac death. Identifying these individuals and their at-risk family members can facilitate pre-symptomatic care and treatment and help preserve the health and prolong the lives of those with DCM. The need for proper medical care is also apparent in the issues presented by other study participants who shared how their past negative healthcare experiences made them now reluctant to seek medical care even after a DCM diagnosis. They chose to forgo care to avoid perceived negative impacts of entering the medical care system again. These findings also shed light on the fact that many patients must become their own advocate in the medical field, and proper patient education may be imperative to ensure appropriate care for themselves or family members to help avoid negative outcomes due to improper treatment. This is especially important for those that may not have access to specialty clinics and must seek care at a facility that may not have expertise in caring for those with DCM.

**Disease, medications, and treatment**

Also in the context of medical care, participants inquired about medications, treatments, and other health care issues in relation to a diagnosis of DCM. This theme was not initially expected since the purpose of correspondence within the study was not to provide medical care or recommendations, but this information provides additional insight to concerns DCM patients have when seeking and receiving medical care. Some were concerned that other health issues they were experiencing were associated with a DCM diagnosis or signs of symptomatic onset of the disease. Also, as there are different
medications and treatments that may be utilized by those with DCM, it is not surprising that patients would have questions regarding possible strategies of care. More specific questions regarding advanced treatments, such as stem cell therapy, the availability of specific medications for those with a genetic variant, and the effectiveness of natural supplements for those with DCM showcase the desire for knowledge beyond the basic information typically provided to patients. One participant specifically discussed their need for more in depth knowledge of the reasoning and purpose of her prescribed medications, taking it upon herself to gather more information. This again highlights the importance of education for patients, not only regarding the disease but also potential symptoms they may experience as well as the available treatments and medications that may be utilized in their care. Again, as patients are often their own advocates as they enter the medical system, providing them material to help not only educate themselves but also provide to other health care professionals may also be warranted to ensure proper treatment of those affected with DCM.

**Data Correlations**

The second aim of this study was to correlate the emergent psychosocial concerns with demographic data from the DCM Research Project database including age, gender, ethnicity, family diagnosis status, cardiovascular information, and genetic testing results. After the major thematic categories were established, data analyses were performed, using phi coefficient and point-biserial analysis, to determine if any statistically significant (p<0.05) correlations could be identified between the thematic categories and available demographic and health-related data of participants. Results showed that
concerns expressed by participants differed with regard to age, gender, ethnicity, family status, genetic variant results, reason participants were brought to medical attention, as well as invasive procedure history, indicating these factors may play a role in the expression of concerns in the DCM population.

**Participant Age**

Participant ages of consent spanned from 13-85 years among those who expressed concerns. Analysis comparing individual ages to their concerns indicated that, as the age of participants increased, there was a decrease in expressed concerns for children.

Examining the group that presented concerns for children, the average age was 44.8 years with only 13.3% being over age 60, while the entire thematic cohort had an average slightly higher at 47.7 years, 23.3% of those participants were over age of 60. Since the predominately expressed concern for children in this study was the appropriateness and timing of cardiovascular screening and genetic testing for the young, the fact that the professional recommendations are well defined for adults, as opposed to when to begin these tests for young children, may reduce the frequency for those older participants with adult-aged children to discuss this topic. DCM patients of more advanced age may be experiencing more active symptoms associated with the disease that may shift their primary concerns to their current healthcare needs. As these results may indicate differing levels of concerns based on patient age group, care should be taken in predicting topics of concern based on age alone. Assessment of patient issues in a clinical setting should be based on individual discussions and assessment.
As participant age increased, analyses also showed older individuals were more likely to express concerns for research. This may be due to differences in perception of the purpose of research between those of younger or older generations. Among those who expressed concerns, the average age was 47.7 years, but in the group that discusses research concerns, the average age was 56 years with a mode of 65. In an investigation of public attitudes toward research participation, Trauth, Musa, Siminoff, Jewell, and Ricci (2000) explained that those aged 65 and older were the least willing to participate in medical research, with middle-aged and younger being more likely to voluntarily enroll in research studies (Trauth, Musa, Siminoff, Jewell, & Ricci, 2000). A study performed in the UK examining the attitudes of older adults toward genetic testing revealed that individuals of more advanced age were more wary of research results being used for the gain of private companies and expressed concerns for the ethical use of findings. But with a more in depth discussion of genetic research and intended ethical purpose, elderly individuals saw benefit to genetic studies that would benefit society and future generations (Skirton, Frazier, Calvin, & Cohen, 2006). Other barriers to the enrollment for participants of advanced age are described in a study by Basche, et al. (2008), in which 60% of participants aged 65 and older reported one or more barriers to participation in clinical trials that included logistical barriers, time demands, or reluctance to be treated at a university medical center (Basche et al., 2008). Results of the study for the DCM cohort align with this existing research, in which those of older ages expressed research issues that included general distrust of medical research and concerns of logistics and time commitments. These results, in combination with
existing literature, highlight the importance of in depth consent discussions that include the intended purpose of a research project, including the use of potential results, as well as what requirements are necessary for participation focusing on any necessary travel, especially if individuals of advanced age are a desired demographic.

**Participant Gender**

Prior to thematic analysis, the gender totals were nearly equivalent in the original cohort of eligible participants with 51.4% being female. After review for emergent themes, it was shown that more concerns were expressed by women (63.4%) in comparison to men (36.6%) in this cohort. This aligns with existing literature explaining that the communication of health related information, including genetic risk, was a task primarily performed by women within a family (Batte et al., 2015; d'Agincourt-Canning, 2001). Men who are found to carry a disease associated genetic variant are likely to share this information to their immediate family, including spouses, children and siblings, but they are less likely to discuss this information with their extended at risk family (d'Agincourt-Canning, 2001). In these instances, women often take the role of family spokesperson, disseminating health related information, even if they are not part of the affected kindred (d'Agincourt-Canning, 2001). This knowledge becomes important when discussing disease-related information and genetic risk with patients in a clinical setting. It may be important to identify the family spokesperson, or the individual who may have a history of maintaining and communication family health information within a kindred. Although it is important to ensure the affected patient is provided an in depth education of their disease, it may also be just as important to ensure proper education of the individual who
may bear the responsibility of explaining this information to others. Also, male patients may need to be counseled about the importance and benefits of communicating genetic risk outside of their immediate family, and may benefit from a deeper discussion about methods to which this information may be shared, more so than some female patients. Correlational analysis of patient gender and thematic findings in the current study showed that males were less likely to express concerns related to insurance. At first this may seem surprising, as historic gender roles often place matters of finance as the responsibility of men within a family. However, research has shown that women within a family are not only more likely to be the primary communicators, but they are often responsible for negotiating professional health care within a family (d'Agincourt-Canning, 2001). Again, this highlights the importance of identifying the family spokesperson, who may not only be responsible for sharing health-related information, but also information regarding insurance coverage for screening and genetic testing. Knowledge that these individuals, who may have coverage themselves, may be having discussions with family members with more issues pertaining to healthcare coverage may warrant a more in depth discussion of out-of-pocket costs for gene panel testing as well as single-site testing for known familial variants, as well as financial assistance programs, that can assist the spokesperson in providing more detailed information to those that may be reluctant to pursue healthcare or testing due to perceived costs. Data analysis also demonstrated that men in this cohort were less likely to share emotional issues related to a DCM diagnosis. This finding follows existing gender stereotypes in which it may be more socially acceptable for women to share their
emotional experiences than men. With the presence of a FDC diagnosis within a family, men may feel a responsibility to play a more stoic supportive role and allow women to play a more emotional nurturing role. A study examining social emotional sharing demonstrated that, although both men and women experienced similar emotional responses when experiencing similar situations, women were more likely to share their emotions with a broader network of individuals, while men tend to share only with spouses or close companions (Pennebaker, Zech, & Rimé, 2001). Denial was an emotional response described for some male relatives in the DCM cohort, and may lead to those individuals being less likely to share their emotional experiences as emotional avoidance of the diagnosis take precedence. Other stories show that, though they may not share their emotional experiences, men can suffer severe emotional consequences to a diagnosis, with two male individuals described as suffering severe symptoms of depression after a DCM diagnosis. A study examining gender and racial differences is psychosocial responses in heart failure patients described that men, particularly non-white men, were more likely to have poor health perception and suffer more depressive symptoms than women (Macabasco-O'Connell, Crawford, Stotts, Stewart, & Froelicher, 2010). It is important to attempt to identify those that may be at risk for more severe psychological issues, in a clinical setting, and provide them or their family members with contact information for mental health professionals that may be needed while adjusting to a DCM diagnosis.
Participant Ethnicity

As the majority of participants in the study are Caucasian (89.5%), other ethnic groups were not highly represented. Data analysis comparing the concerns expressed by other ethnic categories compared to Caucasians did reveal that those of Hispanic ethnicity (3.3%) were more likely to share emotional issues than non-Hispanics. Hispanic participants in the DCM cohort shared a variety of emotional responses that include anxiety and fear of screening and genetic testing with a family history of young death due to DCM complications. One participant discussed the emotional toll having several affected relatives had on her personally, and described family members feeling of guilt and anger for passing down or inheriting a genetic variant that had been identified in the family. Another discussed the need to stay strong and support others that were affected in the family. A study examining emotional support for Hispanic and non-Hispanic women with cardiovascular disease reported that emotional support had a direct correlation to perceived success in managing disease for Hispanic women (Andrea, May 2014). The identification and presence of a strong emotional support system may be helpful to increase individuals, especially those of Hispanic ethnicity, to successfully manage a DCM diagnosis. The identification of a strong support system may be particularly important in families, such as those in the DCM cohort, with many affected relatives or a history of disease related death in young family members. Although the number of Hispanic individuals represented in the DCM cohort is small, it may be beneficial to openly discuss emotional reactions to a DCM diagnosis and available support systems in
a clinical setting. Further studies involving a larger cohort of Hispanic individuals are warranted to validate these findings.

Family Status and Genetic Testing Results

Analysis of family status comparing those individuals whose families were identified as FDC to those with IDC indicated that individuals with a family status of FDC were more likely to express concerns about the genetics of DCM than those with IDC. Also, those individuals who had a genetic variant identified and were informed of their genetic status through the research study were more likely to present concerns regarding genetics when compared to participants that did not have an identified variant, did not undergo testing, or were not informed of their testing results. In the presence of a family history of DCM in multiple relatives, it is not surprising that individuals with an FDC status are more likely to bring up questions or concerns about the genetics of DCM. The finding that those that are informed of the presence of a disease-associated genetic variant also follows logic that these individuals would then be motivated to learn about the identified variant and the risks for them and their family members. Questions that arose for DCM study participants spanned several topics including inheritance patterns, reduced penetrance and variable expression of DCM-associated variants, and the functions of genes in the body. They also sought deeper explanations of the meaning of relevant genetic variants identified through testing and the importance of testing relatives affected with DCM prior to testing unaffected at-risk relatives. The complexity of the genetics of DCM can be a difficult subject for some individuals to understand, but these are important concepts for DCM patients to comprehend, as they often then assume the
responsibility of educating other at-risk relatives of this information. A study of family communication of genetic risk in a cohort of HCM patients revealed that a higher comprehension of genetic concepts, including autosomal inheritance, was a significant predictor to the communication of risk information to other family members (Batte et al., 2015). These findings in combination with the breadth of genetic questions present by the DCM cohort highlight the importance of genetic education for affected and at-risk patients. This emphasizes the importance of the inclusion of genetic counselors in the care of patients with DCM, especially in the presence of a family history, as they are specifically trained to communicate complicated genetic information in a manner that can be understood by individuals of varied levels of education. A solid understanding of genetics can not only help DCM patients better understand their own diagnosis, but may also increase the chance that they will share this information with at-risk relatives.

Health-Related Data

Health-related information, confirmed by medical records, for participants of the DCM Research Project that included the reason individuals were brought to medical attention and personal histories of invasive cardiovascular procedures were also available for analyses. Correlational analyses of this data with emergent themes revealed that those individuals who were diagnosed through cardiovascular screening were more likely to discuss issues they experienced with physicians as well as questions regarding the genetics of DCM. The physician issues presented in the DCM cohort often centered on conflicting information associated with the timing, frequency, and need for cardiovascular screening for DCM. Thus, those individuals who came to be diagnosed
through screening may have experienced issues during this process. These individuals may also be more likely to request screening for at risk children, which may have prompted conversations with physicians on the appropriate timing and need for this screening when physicians may not have been knowledgeable of existing recommendations. These patients may need to be provided with more support and information to help educate providers on the screening recommendations for those at risk for DCM, especially young children.

Those brought to medical attention through screening also show an increase in questions regarding genetics. In examining this particular subset, over a quarter (26.5%) of the patients identified by screening were informed of having a genetic-variant through research testing, and almost all (87.5) had a family status of FDC. These other factors may have led to this correlation, and again, those with identified variants or with a family history of DCM may require further education of the genetics of DCM and genetic testing. More research is necessary to see if genetic concerns still exist in those identified through screening in the absence of a genetic variant or family history.

In examining participant histories of invasive cardiovascular procedures and emergent themes, data analyses indicated that those individuals with a personal history of a heart transplant were more likely to share issues with insurance as well as discuss barriers to communication with family members. Patients with a transplant history presented concerns in both insurance subthemes of discrimination and issues with coverage or lack of insurance. It may be that those who had already experienced a major medical procedure have previous experience with insurance coverage or issues that may prompt
them to be more likely to ask questions when faced with additional medical procedures such as genetic testing. Due to the fact that participants often shared concerns for other family members that lacked proper insurance coverage, it may be speculated that having a history of such a major surgery, due to a DCM diagnosis, may prompt more concern for at-risk relatives to seek screening or treatment causing them to be more likely to inquire about insurance options and coverage for these individuals.

Also, having a personal history of a major surgical procedure such as a heart transplant may prompt individuals to attempt communication to relatives about the potential risk of DCM so others may avoid potential surgery or other invasive procedures in the future. Because they may be more likely to attempt communication with family members, they may encounter more barriers to the process, and thus may be more likely to share these communication issues. These findings may warrant a discussion of personal motivations to communicate with at-risk relatives, particularly when there is a history of invasive disease-related surgery. It is also important to discuss barriers to communication individuals feel they may encounter within their kindred to help provide tools or suggestions to ensure proper dissemination of health information. Further investigation is needed to determine if these correlations are present in larger DCM cohorts with heart transplants or other invasive procedures.
Chapter 5: Implications

Current statements provided by the HFSA and HRS/EHRA recommended that expertise in cardiovascular genetics be utilized to ensure proper initiation, interpretation, and implementation of cardiovascular screening and genetic testing for patients and family affected with or at risk for DCM (Ackerman et al., 2011; Hershberger et al., 2009; Somers et al., 2014). The results of the current study demonstrate that the concerns and issues experienced by DCM patients vary widely and may be influenced by demographic differences as well as family history and personal histories of invasive cardiovascular procedures. Patients may experience an array of emotional concerns regarding a DCM diagnosis as well as have questions about the genetics of DCM, risk to family members, and methods of screening and treatment. Existing studies on those affected with a genetic cardiovascular disease have determined that patients who are satisfied with their understanding of disease, including the genetic etiology and risk to family members, are more likely to adjust well to living with a chronic disorder and more likely to share information with at risk family members (Batte et al., 2015; Ingles et al., 2008). This highlights the importance of incorporating specialized cardiovascular genetic counselors as part of the integrated healthcare team needed to provide comprehensive service to DCM patients and their families. Prior knowledge of the primary emotional concerns and educational needs of DCM patients can allow for more directed counseling of these
individuals and facilitate more personalized care to help ensure proper education allowing patients to better understand their diagnosis and promote dissemination of information to extended family. The results of the current study reveal several opportunities for genetic counselors to use their existing skills for education and psychosocial support when counseling patients with DCM. Strategies for counseling techniques for each emergent theme and correlations identified in this study are summarized in Table 8.
<table>
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<tr>
<th>Main Theme Identified in Current Study</th>
<th>Suggested Strategies</th>
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| Concern for Children and Relatives    | • Family-focused counseling (concern may shift more to other family members, especially children)  
• Discussion of family “disease story” to ascertain emotional impact and patient motivation  
• Discussion of existing screening/testing recommendation including children  
• Discussion of prenatal testing and reproductive options for patients that are or may become pregnant |
| Emotional adjustment                  | • Emotion-focused counseling methods  
• Help patient develop coping strategies to living with chronic illness and potential lifestyle changes  
• Open discussion of how diagnosis or genetic results may impact future life decisions, especially in the young  
• Allow open discussion of emotional adjustment, with special attention to male patients that may require more prompting to share personal information  
• Recognize that some ethnic groups may be more apt to share emotional reactions and inquire about existing support systems  
• Referral to mental health professional for those who may experience or are at risk for severe psychological issues including depression and anxiety |

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<th>Main Theme Identified in Current Study</th>
<th>Suggested Strategies</th>
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| Communication                        | • Inquire about existing family dynamics to identify existing barriers to communication and family dynamics.  
• Identify family spokesperson and ensure proper education for family discussion.  
• Discuss implications for communication of genetic results and risk to female spouse of male patients, as they be likely to act as primary communicator.  
• Consideration of communication methods based on individual or family preference including family letter as well as electronic and social media outlets.  
• Family counseling sessions to allow for education of several at risk family members in one setting.  
• Referral to mental health professional for family or personal counseling to navigate delicate issues of family secrets including non-paternity. |
| Insurance                            | • Assess if patient decision making is highly influenced by insurance concerns for coverage or privacy.  
• Explanation of GINA protections and exceptions.  
• Discussion of financial assistance programs by institution or commercial laboratory when applicable.  
• Identify family member acting as healthcare coordinator that may bear responsibility for insurance claims.  
• Determine past history with insurance claims and existing issues, especially with when there is a history of invasive cardiac surgery.  
• Proper education and literature to allow patients to facilitate insurance discussion with other at risk family members. |
Table 8 continued

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<tr>
<th>Main Theme Identified in Current Study</th>
<th>Suggested Strategies</th>
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| Genetics                              | • Ensure patient understanding of inheritance and risk to relatives in the presence of a genetic variant or family history of disease  
• Determine level of detail desired by patient and educate accordingly  
• Provide additional literature or resources for patients who desire a higher level of education  
• Spend additional time eliciting concerns of patients with non-familial cases to identify issues unique to this population |
| Physician Issues                      | • Ensure understanding of existing recommendations for screening and genetic testing provided by the HFSA and HRS/EHRA  
• Determine desired location of continued care of patient (community hospital vs. academic medical center)  
• Provide educational literature for patients to share with other healthcare providers to ensure proper screening and care  
• Participate in educational activities and publications that target cardiologists and physicians to enhance knowledge |
| Disease/Medications/Treatment          | • Referral to appropriate physician or cardiologist for discussion of proper medications and treatment options and changes to current regimens  
• Provide educational literature for patients to share with other healthcare providers to ensure proper treatment |

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<tr>
<th>Main Theme Identified in Current Study</th>
<th>Suggested Strategies</th>
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| Research                             | • Thorough discussion of HIPAA and IRB protections for privacy and use of research data  
• Clarification and alleviation of travel requirements and financial burden for participants  
• Discussion of realistic expectations for research results at the time of consent, including turnaround time as well as ample discussion about the requirements of result confirmation in a clinical laboratory  
• Targeted discussions of perceived barrier to participation especially for participants of older ages |
Chapter 6: Limitations and Future Research

A major strength of the study is the unbiased nature of the presentation of concerns from a large cohort of participants with DCM and their family members. Details of the issues expressed by participants were not elicited through interviews or questionnaires, but presented through voluntary communication with staff members of the DCM Research Project. This allowed for the unique opportunity to organically identify a wide spectrum of psychosocial issues experienced by patients and families affected with DCM. Although these unsolicited interactions provide a unique opportunity to identify recurring concerns disclosed organically by this patient population, it may not allow for the identification of all concerns and/or psychiatric issues that may be experienced by DCM patients. Also, a limitation of this correspondence data is that it only includes what is overtly expressed by participants during their participation in the DCM Research Project. Issues that individuals may have been unwilling to discuss, or did not have the opportunity to share, could not be addressed as part of this study. This cohort also only represents individuals who willingly participated in medical research. The concerns of those individuals and families affected with DCM that may not be willing to participate in research are not represented in this data. In addition, correspondence data recorded by study staff was not intended for use in this particular study and some recorded data included paraphrases and basic transcriptions of conversations that may not have
included thorough details pertaining to the psychosocial issues of participants. Future studies examining the concerns of other patients with DCM that have been diagnosed and undergone genetic testing in a clinical setting would allow for greater generalization of emergent issues to the DCM patient population, particularly in regards to the theme of physician issues, as this has not been widely discussed in existing literature of DCM patients.

Demographic similarities in those with expressed concerns should be noted as well. The majority of participants were white female adults, with a smaller representation of men, individuals of other races and ethnicities, as well as individuals of younger age. Although young children and adolescents were eligible for participation in the study, there was a lack of recorded correspondence for this group as parents and guardians were more likely to be the primary communicators for underage participants. Future studies are warranted to include a larger variation in ethnic and racial background as well as men and children with DCM to determine if differences in psychosocial issues are similar to those reported in this study.

Detailed demographic, genetic, and cardiovascular data was available for participants including genetic testing results and medical procedure histories, which allowed for correlation of this data with emergent themes. There was a lack of some demographic information such as socioeconomic status and educational background that may have provided more insight to differences in psychosocial concerns in relation to these variables. Researching the issues experienced by individuals of different socioeconomic
and educational levels may allow for deeper insight in regards to particular areas such as insurance, access to care and understanding of genetics.

Participant correspondence data used in this study was presented over a period of time during individual enrollment in the DCM Research Project. Some individual’s interactions with study staff spanned several years as family members were enrolled and research genetic testing was performed. The current study sought to identify the major psychosocial concerns of this group, but further research could be performed to identify specific points in time where issues were presented to study staff and correlate this data with hallmark changes in the healthcare of patients with DCM such as the introduction of genetic testing and the establishment of screening and testing consensus recommendations. Results of such research could create a timeline that depicts the evolution of concerns of DCM patients over time how changes in healthcare recommendations may have impacted these issues.

Although the current study explored issues families experienced when dealing with a DCM diagnosis, focus was centered on the concerns of family members as individuals. Further research exploring how aspects such as family size and number of affected individuals in a kinship would help to gain a better understanding of the issues DCM families may experience. This may provide more detail on how a family’s physical and emotional closeness as well as familial disease history may impact issues such as communication of screening recommendations and genetic risk.

For the purpose of this study, a small number of follow-up interviews were performed for the purpose of clarification of issues that were expressed in the existing correspondence.
and to better describe emergent themes. Future studies could include more detailed structured interviews and/or questionnaires to further refine the themes described in this study as well as explore psychosocial issues that may not have been identified during participation in the research project. Also, there was an average of 5.2 years between original concern expression and participant interview, which may have effected recollection of past experiences. Detailed follow-up interviews may allow for the examination of how psychosocial concerns of individuals have evolved over a time and how it has impacted their life. It may also help to determine what may be needed to help patients adjust to issues faced while living with a diagnosis of DCM. Data analysis examining correlations between identified psychosocial themes with demographic data and health-related information provide insight into potential trends that may exist for different subgroups of DCM patients. Based on findings in this study, concerns expressed by participants differed in regards to age, gender, ethnicity, and personal and family health history which possibly influence the concerns and issues expressed by patients and families affected with DCM. Additional research is necessary, examining larger cohorts of individuals with shared demographic backgrounds and health history to determine if these same psychosocial issues are truly influenced by these differences.
Chapter 7: Conclusion

The primary aim of this study sought to identify recurring psychosocial concerns of DCM patients and their family members, as well as correlate the emergent psychosocial themes with demographic data including age, gender, ethnicity, family diagnosis status, health-related information, and genetic testing results. After completion of both the thematic and correlational analyses, our hypothesis that we would likely identify concerns in participants of the DCM Research Project that have been identified in other genetic disorders was confirmed. This cohort discussed issues regarding personal distress, insurance concerns, concern for children and relatives, as well as barriers to communication that have been experienced by patients with other genetic disorders. This cohort also expressed concerns in other areas that are not as well documented in the existing literature, including particular research concerns and issues encountered when seeking medical care and treatment for DCM. Comparing thematic findings to participants’ demographic and health-related information revealed that these factors could also impact the type of concerns presented and the level of expression of particular issues. These findings add insight into the psychosocial impact a DCM diagnosis can have on patients and their families, which has not been the subject of extensive research in the past. The knowledge of issues experienced by these patients can help to inform health care providers, especially genetic counselors, on what concerns may need to be
addressed when caring for and counseling DCM patients and aid in the implementation of methods to best care for these individuals and their families.

The knowledge of DCM and its genetic etiology has rapidly advanced over the past few decades, and the availability of genetic testing has become increasingly available to those affected by or at risk for DCM. In more recent years, recommendations have been provided by the HFSA and HRS/EHRA to provide guidance for screening and genetic testing for those at risk for DCM, but these recommendations may not be well known or utilized by all healthcare professionals who may encounter patients with DCM. The complex nature and genetic heterogeneity of DCM requires an integrated healthcare team that includes cardiologists and genetic counselors trained to care for these patients. The current study reveals that there are several psychosocial issues that can arise in patients with DCM that can also be influenced by differences in ethnicity and gender as well as family and personal medical history, and exemplifies the need for a multidisciplinary healthcare team in the care of DCM patients and their families. Providing both appropriate medical care with proper education on the genetics of DCM and emotional support for those affected with disease is required to ensure proper personalized care for those affected with DCM. Proper education on the risk to family members, especially children, and a discussion of the recommendations for screening and predictive testing can help patients better adjust to a diagnosis and facilitate communication within families, with the ultimate goal of identifying those individuals at risk for DCM and provide early intervention and treatment to prevent or delay the onset of disease.
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Appendix A: Phone Interview Script
Hello my name is _________________________, and I am part of the Dilated Cardiomyopathy research group at The Ohio State University. We are currently researching the major concerns patients enrolled in the study have had regarding the diagnosis of DCM in their family. Do you have a few minutes to answer a few questions?

If no, schedule another time: _____________________________

If yes:

Great! So you are aware, we will be recording our call to make sure we are collecting the right information from you.

According to our records, on (date), you expressed concern/asked questions regarding _____________________________. Would you be willing to discuss this concern in further detail?

If yes:

1. Can you explain your concern in more detail and what may have prompted it?

2. During that time you used the word/phrase ____________________________. Can you elaborate on your feelings at that time?

3. Do you still feel concern in this area or have pending questions?
   a. If no, what or who helped you work through this issue?
   b. If yes, what would have been helpful to assist you with your concern/question?

4. Have you had any new questions or concerns arise since your last contact with the DCM research team?

5. Is there anything else you would like to discuss with us concerning our conversation?

Thank you so much for your participation and your help. Your comments will be used to improve our work together.