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## Engagement in Family Screening for Hypertrophic Cardiomyopathy

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Engagement in Family Screening for Hypertrophic Cardiomyopathy

A Dissertation Presented By

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University of Massachusetts Medical School

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*Engagement in Family Screening for Hypertrophic Cardiomyopathy*

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## Table of Contents

Abstract .....	1
Dissertation Proposal .....	2
Summary of Changes from Proposal .....	40
Slide Presentation.....	42
Dissemination Plan.....	86
Appendix A .....	87
Appendix B .....	88

### Abstract

**Background:** Despite consensus guidelines, only about half of at-risk relatives in families with Hypertrophic Cardiomyopathy (HCM) undergo clinical screening and even fewer undergo predictive genetic testing, leaving those unscreened at risk for sudden cardiac death. The use of qualitative inquiry to examine family communication and complex factors influencing uptake of screening may inform interventions to increase uptake and prevent sudden cardiac death.

**Purpose:** The purpose of this study was to describe the engagement of at-risk relatives in family screening for HCM.

**Specific Aims:** The specific aims were to (1) Describe the experience of communication of genetic risk of HCM in families with a causative variant for HCM; (2) Use the Theory of Engagement to identify facilitators and barriers to family screening in families with a causative variant for HCM; and (3) Identify strategies to increase uptake of clinical screening and predictive genetic testing in families with a causative variant for HCM.

**Framework:** The Theory of Engagement, adapted from McAllister, was used as an initial framework for the study.

**Methods:** A qualitative descriptive design with purposive and snowball sampling was used and data were analyzed using qualitative content analysis.

**Results:** The overarching theme of Bringing Genetic Risk to the Foreground was comprised of three major themes: Cues to Action, Preferences for Knowledge and Gateways to Screening, reflecting factors that affect engagement with genetic risk and family screening throughout the lifespan.

**Conclusions:** Integrated longitudinal care and access to genetic specialists are needed for patients and families with a causative variant for HCM.

**Key Words:** Hypertrophic cardiomyopathy, engagement, family screening, qualitative

Dissertation Proposal

Engagement in Family Screening for Hypertrophic Cardiomyopathy

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### **Introduction to the Problem and Specific Aims**

Hypertrophic Cardiomyopathy (HCM), a disease of the sarcomere characterized by unexplained left ventricular hypertrophy, is the most common inherited cardiovascular disorder, affecting at least 1 in 500 individuals in the general population (Maron et al., 1995; Semsarian, Ingles, Maron, & Maron, 2015). Although most with this clinically heterogeneous familial disease may be without disabling symptoms throughout their lifetime, an important subset experience severe sequelae such as heart failure, atrial fibrillation with risk of stroke, and sudden cardiac death (SCD) (Ho, 2012). HCM is the most common cause of SCD in the young, accounting for approximately one-third of SCD in high school and college athletes in the United States (Maron, Doerer, Hass, Tierney, & Mueller, 2009). Although the annual mortality rate from HCM is less than one percent per year in the general population (Gersh et al., 2011), SCD may be the first manifestation of the disease, with devastating consequences.

The implantable cardioverter defibrillator (ICD) has been shown to effectively prevent SCD in a cohort of high-risk patients with HCM by terminating lethal ventricular arrhythmias at a 2-4% appropriate discharge rate per year for primary prevention (O'Mahony et al., 2012). At present, the ICD is the only therapy available to prevent SCD and alter the natural history of HCM, making family screening of vital importance to identify as many relatives at risk for SCD as possible to consider them for ICD implantation. Subsequently, professional societies recommend family screening, beginning with clinical screening for risk stratification and predictive genetic testing (PGT) once a pathogenic mutation has been identified in the proband to exclude at-risk family members who test negative from unnecessary and costly longitudinal surveillance (Ackerman et al., 2011; Elliot et al., 2014; Gersh et al., 2011).

Despite published consensus guidelines that clearly recommend use of specialized genetics services including genetic counseling, uptake (the proportion of those eligible who complete clinical screening or PGT) by at-risk relatives in HCM families remains low (See Table 1). Since HCM is transmitted in an autosomal dominant fashion, 50% of the patient's first degree relatives (parents, siblings, children) are at risk for the disease which may be present in those without symptoms. Failure to engage in clinical screening for HCM leading to potential consideration for ICD therapy leaves those at-risk relatives who remain unscreened vulnerable to SCD.

In studies of facilitators and barriers to uptake in HCM families (See Table 2), commonly identified reasons to seek out PGT were ruling out risk for self and children (Khouzam et al., 2014; Christiaans et al., 2009; Ormondroyd et al., 2013; Smart, 2010) and relief of uncertainty (Smart, 2010). Potential barriers to the use of PGT included issues related to communication and family responsibility, (Ormondroyd et al., 2013; Smart, 2010), reduced risk perception in the absence of symptoms (Ormondroyd et al., 2013), ambivalence about the value of PGT, (Khouzam et al., 2014; Ormondroyd et al., 2013; Smart, 2010), anticipated anxiety regarding test results, and issues pertaining to access to testing and insurance coverage/discrimination (Khouzam et al., 2014). Similar barriers have been reported by those seeking to improve uptake of clinical screening without PGT (Finch, Russell, Kumar, and Yousef, 2011; Olausson et al., 2014).

Qualitative research, which is designed to capture the human experience related to a phenomena of interest via purposive sampling of information rich cases (Sandelowski, 1995), can provide valuable contextual information to inform clinical genetics practice (Bernhardt, 2008). Inviting the voices of patients with variant positive HCM mutations and their at-risk relative(s) to be heard will provide further insight into complex, multifactorial issues affecting uptake including family responsibility, communication of genetic risk, and disclosure brought to

light by previous qualitative (Geelen, Van Hoyweghen, & Horstman, 2010; Ormondroyd et al., 2013; Smart, 2010; Subasic, 2013) and survey studies (Batte et al., 2015; Christiaans et al, 2009; Khouzam et al., 2014).

To protect patient privacy and autonomy, communication of genetic risk and initial recommendations for screening must occur from the proband or index case in the family to their at-risk relative(s). The process of engagement, which is defined as “the degree of cognitive and emotional involvement with one’s increased risk of developing HCM as a result of one’s family history of HCM” (adapted from McAllister, 2003, p. 180) of at-risk relatives has not been well described. Further exploration of this experience may lead to increased understanding of communication from proband to family members and engagement in screening in HCM families, improving uptake and therefore preventing SCD.

The purpose of this study is to describe the engagement of at-risk relatives in family screening for hypertrophic cardiomyopathy.

**The specific aims of the study are:**

**Aim 1:** Describe the experience of communication of genetic risk from the perspective of a) the at-risk relative(s) and b) the index case in families with a pathogenic variant for HCM

**Aim 2:** Utilize McAllister’s Theory of Engagement to identify facilitators and barriers to engagement in family screening for HCM and expand the theory to the HCM population

**Aim 3:** Identify strategies to improve engagement in family screening including a) cardiac screening and b) predictive genetic testing for families with a pathogenic variant for HCM

## **Background and Significance**

### **Molecular basis of HCM**

Sarcomere mutations cause HCM, which is transmitted in an autosomal dominant pattern, with 50% of offspring of an affected individual at risk for inheriting the sarcomere gene mutation (Seidman & Seidman, 2011). HCM is characterized by incomplete penetrance, indicating that not all individuals who carry the mutation develop the phenotype, and variable expressivity, with different clinical manifestations of the disease among patients with the same mutation (Deo & MacRae, 2010). Since the discovery of the first mutation of the sarcomere gene in 1990, the genetic heterogeneity of the disease has become evident with over 1500 individual mutations (90% missense mutations) in 11 or more genes identified (Seidman & Seidman, 2011). The majority of mutations involve the cardiac  $\beta$ -myosin heavy chain (MYH7) and cardiac myosin binding protein C (MYBPC3) (Ho, 2010).

### **Genetic Testing for HCM**

Over the past twenty-five years, advances in DNA sequencing have led to commercially available DNA testing for HCM beginning in 2003 (Ackerman et al., 2011; Ho, 2012). Over time, the cost of commercial testing has decreased and the number of genes covered has increased and will likely further expand with whole exome/genome sequencing in the future (Judge, 2015). Due to the genetic heterogeneity of HCM, classification of a particular DNA variant is probabilistic rather than binary (mutation positive/negative) and variants can be reclassified as new information becomes available, which poses a challenge to clinical decision making (Ho, 2012).

Diagnostic or comprehensive genetic testing begins in an initial member of the family seeking out genetic services, who is often referred to as the proband or index case – (see Figure 1) with clinically expressed HCM. Identification of a pathogenic DNA (i.e., disease causing or variant) mutation in the proband does not alter medical management, but can aid in differential

diagnosis between HCM and other causes of hypertrophy such as hypertension, athlete's heart, and metabolic storage diseases (Ho, 2012). Approximately 50% of genetic tests of the proband yield a negative result, and variants of unknown significance (VUS) are reported in about 15% of tests (Maron & Maron, 2014). A pathogenic variant is identified in approximately 35% of genotyped patients (Maron & Maron, 2014).

Family members of probands in whom a pathogenic variant has been identified have the option of predictive genetic testing (PGT), sometimes referred to presymptomatic genetic testing, or cascade screening. In those families where the proband has not had a pathogenic variant identified, (negative result or VUS), PGT is not an option and continued clinical surveillance is recommended (Ho, 2012). In instances where one or more variants of unknown significance have been identified, testing of additional family members (when available) may be suggested to look for co-segregation of the variant(s) in those clinically affected (Gersh et al., 2011).

Currently, the greatest clinical utility of genetic testing for HCM is PGT of pre-symptomatic, first degree relatives after testing in the proband confirms a genetic mutation (Ingles & Semsarian, 2014). PGT then entails a targeted sequencing of the genes associated with the family mutation in these individuals (see Figure 2) (Ingles & Semsarian, 2014). A negative result in the at-risk family member spares them a lifetime of continued surveillance in the absence of symptoms and the disease is also ruled out in their offspring. A positive mutation status in an asymptomatic individual may result in increased surveillance, and where HCM is ultimately diagnosed, avoidance of high risk activities (Maron et al., 2015), and risk stratification for SCD (Deo & MacRae, 2010). Furthermore, knowledge of mutation status in the at-risk relatives can assist in family planning, with the option of pre-implantation genetic testing in

embryos created through in vitro fertilization for those who do not wish to pass on the disease-causing allele (Ho, 2012).

Increased availability of and access to genetic testing for HCM has led to identification of a new category of patients who are genotype positive but phenotype negative, without evidence of left ventricular hypertrophy (Maron & Maron, 2014). Targeted medical therapies to modify disease before irreversible structural damage to the heart occurs are currently being tested in genotype positive patients prior to diagnosis of clinical disease and represent an innovative prospect in treatment enabled by PGT (Ho, Charron, et al., 2015; Ho, Lakdawala, et al., 2015). As advances in genetic technology continue to contribute the ultimate goal of prediction and prevention of HCM (Ho, 2010), the potential benefits and harm of preclinical disease detection should be considered (Ingles, Burns, Barratt, & Semsarian, 2015).

### **Clinical Screening**

Clinical screening, with or without genetic testing, is a Class I recommendation (should be performed) for first degree relatives (i.e., children, siblings, and parents) of patients with phenotypic HCM per the American College of Cardiology and American Heart Association (Gersh et al., 2011) and the European Society of Cardiology (Elliott et al., 2014). Clinical screening for HCM consists of imaging tests (primarily echocardiography) and an electrocardiogram in conjunction with a history and physical and three generation family pedigree. Suggested criteria for confirmation of phenotypic expression of HCM include an unexplained left ventricular wall thickness greater than 15 mm in the absence of a dilated left ventricle as visualized by 2D echocardiography (Maron et al., 2014).

Historically, left ventricular hypertrophy (LVH) in HCM was felt to appear most commonly during adolescence but can also appear in infancy or early childhood as well as

during later adulthood (Maron et al., 2004). Conversions from normal wall thickness to LVH have been described in later adulthood and the variable onset of phenotypic expression associated with HCM guide current clinical screening practices (Maron et al., 2004). Recent observations in genotyped cohorts have indeed shown that middle age adult onset disease is the norm (Page et al., 2012), emphasizing the importance of screening at-risk individuals well into adulthood.

Clinical screening recommendations with ECG and echocardiogram begin at age 12 in the absence of other indices of suspicion, and continue every 12 to 18 months until ages 18 to 21, after which screening every 5 years is typically recommended (Maron et al., 2004). In instances where echocardiogram is inconclusive due to suboptimal imaging, cardiac magnetic resonance imaging (CMR) may be used to confirm diagnosis and phenotype (Gersh et al., 2011). There is also evidence to suggest that late gadolinium enhancement (LGE) associated with CMR may play a role in risk stratification for SCD in HCM patients (Chan et al., 2014).

An improvement in clinical screening rates for first degree relatives of patients with HCM following implementation of a specialized HCM clinic has been reported by Finch, Russell, Kumar and Yousef (2011) in the UK and Olausson et al. (2014) in Australia. Both groups identified barriers to clinical screening, including lack of understanding of the mode of inheritance, strained family relations, and personal preferences of family members to opt out. Finch et al. (2011) also listed geographical and logistical issues as impediments to screening. In discussing similar barriers identified by both groups, Olausson et al. (2014) comment that the “paucity of literature explaining barriers to clinical HCM screening rates necessitates inferences from other diseases, such as colonoscopies in patients with a family history of colorectal cancer” (p. 668).

### **Risk Stratification**

The rationale for clinical screening of at-risk relatives of patients with a confirmed diagnosis of HCM is to identify family members with undetected disease who are at risk for SCD which may occur as the first indication of the potentially lethal disorder. Following clinical screening, risk stratification for patients with a confirmed diagnosis of HCM involves identifying those at highest risk for SCD, which is most common in individuals under 30 years of age (Maron & Maron, 2013). Risk for SCD is comparable in both genders (Olivotto et al., 2005), and not particular to race.

For HCM patients deemed to be at high risk for SCD, implantation of an ICD is the only reliable prevention strategy resulting in prolongation of life, with proven efficacy in terminating lethal ventricular arrhythmias (Page et al., 2012). Five established risk factors for SCD in HCM which inform the decision to implant an ICD are 1) family history of HCM-related SCD; 2) unexplained recent syncope; 3) massive LV hypertrophy ( $\geq 30\text{mm}$  thickness); 4) non-sustained VT on serial ambulatory Holter; and 5) hypotensive or attenuated blood pressure response to exercise (Ho, 2012). These risk factors and other characteristics to guide decision making such as LGE, are used to identify HCM patients who would benefit most from ICD therapy although the process remains imprecise, largely due to the low positive predictive value of each risk factor (Ho, 2012).

### **Communication of genetic risk**

Information acquired via clinical screening and genetic testing provided by a genetic counselor or clinician confers an estimate of genetic risk that may be communicated from the index case to at-risk family members. However, the body of research on communication of risk for monogenic cardiovascular disorders is less well established than in other populations where

commercial genetic testing has been available for a longer period of time. Systematic reviews of studies of communication of genetic risk highlight research conducted primarily in families with late onset disorders, including hereditary cancers such as Hereditary Breast and Ovarian Cancer and Hereditary Non-Polyposis Colorectal Cancer (Seymour, Addington-Hall, Lucassen, & Foster, 2010) and in families with Huntington's Disease grouped with other hereditary cancers and disorders (Gaff et al. 2007; Wiens, Wilson, Honeywell, & Etchegary, 2013; Wiseman, Dancyger, & Michie, 2010).

Descriptive studies of the experience of probands (Gaff, Collins, Symes, & Halliday, 2005) and both probands and at-risk relatives (Roshanai, Lampic, Rosenquist, & Nordin, 2010) around disclosing cancer genetic information cite lack of contact and social and geographical distance, in addition to perceptions of irrelevant information, as barriers to communication. Roshanai et al. (2010) speculate that a lack of clear understanding of the genetic information and subsequent transfer of the message negatively impact communication, although enhanced information at cancer genetic counseling by the same group was not shown to improve knowledge, risk perception, or number of relatives informed (Roshanai, Rosenquist, Lampic, & Nordin, 2009). Similarly, a communication skills intervention was not shown to affect sharing of breast cancer genetic test results (Montgomery et al. 2013), although other genetic counseling interventions to improve family communication have been developed (The Socio-Psychological Research in Genomics (SPRinG) Collaboration et al., (2015) and are being tested prospectively (Hodgson et al., 2014).

Similar research of other hereditary conditions that differ by age of onset, pattern of inheritance, and prognosis is needed (Wiseman, Dancyger, and Michie, 2010). Although HCM shares an autosomal dominant inheritance pattern with Hereditary Breast and Ovarian Cancer,

Hereditary Non-Polyposis Colon Cancer and Huntington's Disease, the varied age of onset of HCM and the risk of SCD distinguish it from other types of oncogenic and neurodegenerative conditions. Therefore, a descriptive study of communication of genetic risk in families with HCM will expand the literature in this area.

The experience of communication of genetic risk in families with HCM has not been described in depth, particularly from the perspective of the at-risk relative. In an online survey of a national sample of patients with HCM recruited from the Hypertrophic Cardiomyopathy Association (HCMA), female gender and higher comprehension of autosomal dominant inheritance significantly predicted communication of HCM risk information to 100% of the participants' siblings and children (Batte et al., 2015). Patients cited lack of contact and lack of closeness with their relatives as barriers to communication. However, survey data may not completely capture the contextual issues surrounding communication of genetic risk in HCM families. Further exploration of this experience may inform an intervention tailored to the cardiovascular genetic population.

### **Nursing Implications**

There is a need for further research on the human experience of genetic disorders to uncover the complexities of patient and family engagement in the context of family screening. As providers of health care, nurses are obligated to understand how to assist the growing number of patients and families who receive genetic test results (Hamilton, Bowers, & Williams, 2005) and facilitate communication leading to engagement in family screening for genetic cardiovascular disease. This focus on health promotion and disease prevention for the client (patient, family, community) corresponds with an area of genomic nursing research recommended by the Genomic Nursing State of the Science Advisory Panel (Calzone et al.,

2013). The proposed study is also congruent with suggested research in categories of risk assessment, communication, and decision support further delineated by the panel. This research will contribute to the advancement of nursing science by extending the Theory of Engagement from an oncology population to a cardiovascular population and help to guide future studies, thereby assisting in translation of genetics and genomics into health care.

### **Theoretical Framework**

The Theory of Engagement (McAllister, 2002) will serve as a starting point to guide the study by framing the interview questions to explore causal and intervening factors affecting engagement, which has been defined as “the degree of cognitive and emotional involvement with one’s increased risk of developing HCM as a result of one’s family history of HCM” (adapted from McAllister, 2002, p.180). Accordingly, an adapted version of the model (see Figure 3), wherein the cancer specific factors have been modified will be used. Following traditional content analysis, the theory will serve as the basis for directed content analysis of data to compare findings from the HCM population to those from the Hereditary Non-Polyposis Colon Cancer population (HNPCC).

Engagement originated as the core category best suited to describe the data that emerged from a grounded theory study of families with HNPCC conducted by UK genetic counselor and researcher, Dr. Marion McAllister (McAllister, 2001, 2002). This study was undertaken to develop a theoretical model with explanatory power for behavior around predictive genetic testing, particularly in high risk families where conventional health behavior models may not always apply (McAllister, 2002). McAllister’s model suggests that engagement affects attitudes towards PGT (McAllister, 2002).

True to the paradigm model of grounded theory (Strauss & Corbin, as cited in McAllister, 2001), the theory is composed of causal conditions, which are psychosocial factors that facilitate engagement, such as being at an age where one's relative was known to be first affected. On the opposite pole there are intervening conditions, which are psychosocial factors that prevent engagement or interfere with the impact of causal conditions, such as ignorance of family history. Other components in the theory include individual psychological factors such as personal theories of inheritance and coping factors which interact with one another and the degree of engagement in a recurrent fashion.

Engagement is the central concept, or hub of the wheel, around which the McAllister's Theory of Engagement is built. McAllister defines engagement as "the degree of cognitive and emotional involvement with one's increased risk of developing cancer as a result of one's family history of cancer" (2003, p. 180). She also delineates partial engagement as "at the cognitive level only" and intense engagement as "at cognitive and emotional levels" (2003, p. 180). Since engagement at the affective level only was not observed in the study, McAllister posits that cognitive engagement is an antecedent of affective engagement.

McAllister likens disengagement to avoidance/denial and defines it as "no current engagement at either cognitive or affective levels" (McAllister, 2002, p. 501). She differentiates disengagement from un-engagement, which she explains is when "engagement has not yet occurred" (McAllister, 2002, p.496). McAllister defines partial engagement as "thoughts about family history of cancer", and intense engagement as "thoughts *and* feelings" about family history of cancer." (McAllister, 2002, p.501). She further elaborates that the feelings expressed by the intensely engaged include fear and anxiety (McAllister, 2003, p.180).

Engagement is depicted on a continuum from un-engagement through partial engagement to intense engagement (See Figure 4). When intense engagement is too emotionally painful, such as when a participant experiences a family member dying from the disease, disengagement, which is reversible, may occur. McAllister postulates that individuals move back and forth between varying degrees of engagement along the continuum. She also states that a critical degree of engagement (which she acknowledges is not defined in the study) is required for an individual to take any action, such as seeking out genetic counseling, undergoing screening, and considering PGT.

The final theory, according to McAllister, is a set of hypotheses about ways in which the different components relate or interact around the process of engagement. In her study, McAllister (2003) noted an association between the degree of engagement and action in relation to cancer risk. She also noted that engagement was a dynamic process that could change over time. As HNPPC family members became more aware of their risk, they became more intensely engaged. Eventually, intensity of engagement lessened over time, which McAllister hypothesized may have occurred after they passed the age at which a family member was affected. Those who were intensely engaged prior to predictive genetic testing tended to accept mutation carrier status than more readily those who were partially engaged prior to testing.

## **Methods**

### **Research Design**

A qualitative descriptive design will be used to describe the engagement of at-risk relatives in family screening for hypertrophic cardiomyopathy in mutation positive families. Qualitative description, which is a form of naturalistic inquiry, provides a data-near, comprehensive summary of the phenomena of interest without pre-selection or manipulation of

variables (Sandelowski, 2000). The qualitative descriptive design enables the researcher to begin with a theory (such as The Theory of Engagement) as a framework for collecting or analyzing data, while allowing alternate paths of inquiry as the study unfolds (Sandelowski, 2000).

Qualitative description is an appropriate design to obtain answers to clinically germane questions such as “What reasons do people have for using or not using a service or procedure? Who uses a service and when do they use it?” (Sandelowski, 2000, p. 337).

### **Population/Setting**

Approximately 350 to 400 patients with HCM or those at risk for HCM due to a family history of the disease receive longitudinal, comprehensive care by clinicians at the Cardiovascular Genetics Center (CVGC) at the study site, which is a major tertiary care facility and academic medical center in the Northeast. Specialized care including clinical evaluation, treatment, and genetic counseling along with access to advanced imaging, and genetic testing are provided at this center. This site has two databases which will be used to select participants. The Standardized Clinical Assessment and Management Plan (SCAMP) database was designed by the Cardiovascular Genetics Team to optimize patient outcomes and help to identify reasons for variation in behavior around utilization of resources. This database tracks the percentage of at-risk first degree relatives who have been evaluated by echocardiogram under each index case, which could inform maximum variation sampling for the study. The CVGC clinical database contains all patients seen at the BWH CVGC clinic, including those not followed longitudinally in the SCAMP.

### **Sample**

**Inclusion criteria.** Participants are eligible for the study if they meet the following criteria:

1a. First degree (i.e., parent, sibling, child) (preferentially) or in the absence of first degree, second degree relatives (aunt, uncle, niece, nephew, grandparent, half-sibling) of patients with a confirmed pathogenic mutation for HCM known for more than three months, and

1b. Patients with a confirmed pathogenic mutation for HCM known for at least three months who have at least one first degree at-risk relative (parent, sibling, child) preferentially or second degree at risk relative in the absence of first degree (aunt, uncle, niece, nephew, grandparent, half-sibling).

Both patients and at-risk relatives must be:

- Able to speak and read English
- Between the ages of 18 and 65
- Able to provide informed consent

**Exclusion criteria.** Patients are ineligible for the study if they meet the following criteria:

- Above index cases without first or second degree relatives

Both patients and relatives are ineligible for the study if they are:

- Under 18 or over 65 years of age
- Unable to speak and read English
- Unable to provide informed consent

## **Procedures**

**Study approval.** Approval from the Institutional Review Board (IRB) at the institution will be obtained prior to conducting the study and all participants will undergo informed consent.

Federal Health Information Privacy and Accountability Act (HIPAA) standards will be upheld throughout the study and the researcher will act responsibly to safeguard sensitive genetic information. To maintain confidentiality, data will be coded and de-identified and stored securely as detailed in the data management section below. Participants will be made aware of resources available to them should they develop any psychological distress as a result of the interview or participation in this study.

**Recruitment.** The researcher will recruit eligible participants identified in the SCAMP and CVGC databases and their first or second degree relatives (in the absence of first degree relatives) over an approximate 6 to 9 month period. The researcher will identify potential participants via the two databases in conjunction with a CVGC physician or genetic counselor and obtain a HIPAA waiver of authorization to access the medical record of these patients to obtain their contact information. The researcher will send a letter signed by their CVGC health care provider describing the study with the researcher's contact information should they wish to contact the researcher directly or opt out of a recruitment phone call via phone or email. The researcher will then follow up each letter to each potential participant (with the exception of those who have opted out) with a phone call to describe the study and ask patients for their participation. Fliers containing a brief description of the study will also be placed in the CVGC clinic.

Recruitment of first or second degree relatives of the index cases will occur through snowball sampling. The investigator will ask the index case participant to identify up to 3 relatives who might be interested in participating in the study. The index case participant will be given study fliers to be distributed to these relatives with the investigator's contact information. The relative can choose to either contact the investigator directly or may ask the index case to

provide his/her contact information to the investigator. Additional recruitment sites will be used if enough participants are not recruited during the first 6 month time period. Participants will be mailed a \$25 gift card for taking part in the study.

**Sampling.** Purposive sampling from the homogeneous subgroup of mutation positive families within the databases will be used to assist in minimizing the number of sampling units required to produce analytically meaningful results (Sandelowski, 1995). A maximum variation approach (Sandelowski, 1995), will be used to recruit the index cases with the goal of achieving demographic variation as well as variation in percentage of family members informed by the index case as identified by the SCAMP database. This strategy is designed to seek out representative coverage of the phenomena of interest (Sandelowski, 1995). Snowball sampling (Creswell, 2013) of the index cases will be used to identify first or second degree relatives for participation in the study. A minimum of 20 participants will be recruited (N = 5-8 index case participants; N = 12-15 relatives). Recruitment will continue until informational redundancy is achieved for both groups.

**Data collection.** Following informed consent of the participant, semi-structured interviews will be conducted either in person (face to face or via Skype) preferentially or by telephone if video conference technology is unavailable, travel distance too long, or per participant preference. Flexible interview questions (and open-ended probes) guided by the Theory of Engagement will be used as a starting point for the interview. Separate interview guides will be used for the index cases and their first or second degree relatives to capture both perspectives. Interviews will last approximately 60 minutes and will be audiotaped. Interviews conducted via Skype will not be videotaped.

Participants will be asked to provide demographic information including age, sex, race, ethnicity, socioeconomic status, and time since genetic testing. The researcher will record the information manually on the data collection form without use of an audiotape. Three generation family pedigrees of the index cases and accompanying clinical notes created by CVGC clinicians (genetic counselor and/or MD) will also be obtained via chart review when available.

As an additional demographic measure, participants will be verbally administered the Genetic Literacy and Comprehension Measure (Hooker et al., 2014, with permission), which has been adapted from the Rapid Estimate of Adult Literacy in Genetics (REAL-G) (Erby, Roter, Larson, & Cho, 2008). The REAL-G has demonstrated strong concurrent validity with the rapid estimate of adult literacy in medicine (REALM), and strong predictive validity for patients using genetics services (Erby et al., 2007). Educational packets on clinical screening and genetic testing given to HCM patients and the link to the Vidscrip (web-based educational video which index cases may send via email to their at-risk relatives) will be used to triangulate interview data to help establish credibility (Lincoln & Guba, 1985).

**Data analysis.** Qualitative content analysis of the interview data with concurrent collection and analysis of data will be performed and codes generated from the data (Sandelowski, 2000). Content analysis will be carried out in two phases. First, a conventional content analysis will be performed to achieve a full description of the phenomena without preconceived categories (Hsieh & Shannon, 2005).

Steps for content analysis will be conducted as outlined by Miles, Huberman, and Saldana (2014) which include 1) coding of data from various sources; 2) noting insights and reflections on the data; 3) sorting through the data to identify similar phrases, patterns, themes, sequences and important features; 4) looking for commonalities among the data and selecting

them for further consideration and analysis; 5) gradually streamlining the data to a group of generalizations that are true for the data; and 6) examining these generalizations in light of what is already known.

In the second phase, a directed content using analysis (Hseih & Shannon, 2005) using predetermined codes based on the Theory of Engagement will be performed to validate and potentially extend the theory for the HCM population.) If predetermined codes do not fit the data, a new category will be assigned. Results will either support or not support applicability of the Theory of Engagement to the HCM population (Hseih & Shannon, 2005). To establish credibility, negative case analysis (exploring cases that appear to counter the theory) will be performed (Lincoln and Guba, 1985). Ongoing peer review and debriefing by a dissertation chair/committee will take place throughout the study and a reflexive journal will be kept by the investigator cataloging rationale for methodological decisions to maintain an audit trail (Creswell, 2013; Lincoln & Guba, 1985).

**Data management.** Interview data and field notes will be entered into a Word document and demographic data will be entered into IBM SPSS v. 23® Statistics with verification of the latter through double entry of data. Each participant's data will be assigned a code number known only to the researcher and only these numbers will appear on data collection forms. All paper data will be stored in a locked file cabinet accessible only to the investigator and electronic data will be stored on an encrypted, password protected computer on a secure UMMS Research drive. All data with patient identifiers will be de-identified prior to entry in a non-Partners computer system.

### **Limitations**

The study will be performed in at a single specialized genetics clinic in an academic medical center in the Northeast where those who seek care are largely Caucasian, middle to upper socioeconomic status, and well educated, which is not necessarily representative of the larger population. Since recruitment of at-risk relatives will be done via snowball sampling, reaching an adequate sample size to achieve informational redundancy may be problematic. If participants are recruited via national support groups outside of the BWH Cardiovascular Genetics Clinic, self-reported information will be unable to be confirmed by medical record. There may also be sampling bias on the part of the index case to refer those relatives who are more likely to be open to participation. The accessible population who agree to participate may be more engaged at baseline than those who do not and therefore not representative of the true sample. Interviewing by telephone (and to a lesser extent, Skype) limits the researcher's ability to read non-verbal cues.

### **Summary**

HCM is a clinically and genetically heterogeneous inherited cardiovascular disease which may lead to adverse sequelae including SCD in a small subset of individuals, including those without symptoms or prior evidence of the disorder. Once a patient is diagnosed with HCM, clinical screening of first degree family members, with or without genetic testing, is recommended by professional societies to identify as many relatives as possible who may benefit from ICD therapy to prevent SCD. However, clinical screening and PGT for HCM in at-risk relatives remain underutilized and a deeper understanding of communication between family members and barriers and facilitators to family screening, particularly from the viewpoint of the at-risk relatives, is needed. A theoretical framework of engagement will be used as a starting point for this qualitative descriptive study to describe the engagement of at-risk relatives in family screening with the goal

of informing development of interventions and future quantitative research for the cardiovascular genetic population.

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Table 1

*Studies of Uptake of Genetic Services*

<b>Author/Year/ Country</b>	<b>Method</b>	<b>Aim</b>	<b>Population/Sample</b>	<b>Uptake</b>	<b>Factors Affecting Uptake</b>
Charron et al. (2002)  France	Observational Retrospective	1. Discuss HCM genetic testing questions  2. Propose guidelines  3. Report on preliminary experience	HCM/clinic based 29 adults with pathogenic mutation in family  9 sets of parents  22 couples prenatal counseling  10 adults for diagnostic testing	*19/29 = 66% for PGT adult  1/9 = 11% for PGT child (via parents)  *not reported as a percentage in original study	N/A
Christiaans et al. (2008)  The Netherlands	Observational Retrospective	Assess uptake of GC, PGT in HCM families within 1 yr. of identification of a	HCM /clinic based 97 HCM families with pathogenic mutation	39% for GC 38.6% for PGT 99% Conditional uptake PG	No difference in uptake in GC by gender of proband or relatives, SCD in families, or

Author/Year/ Country	Method	Aim	Population/Sample	Uptake	Factors Affecting Uptake
				(immediately post GC)	young age of relative
Miller et al. (2013)  United States	Observational Retrospective	1. Assess uptake of CS and PGT for at-risk relatives 2. Test the hypothesis that uptake of PGT similar to other genetic conditions 3. Evaluate factors impacting uptake of CS and GT among relatives	HCM/DCM clinic based 57 probands (46 HCM/ 11 DCM)  40 with pathogenic mutation  302 relatives for CS 213 relatives for PGT	173/302 = 57% CS 84/213 = 39% PGT  Comparable to 44% uptake PGT in HBOC population	1st degree relatives more likely to have CS and PGT than 2 <sup>nd</sup> degree relatives  Number of living affected relatives impacted the uptake of CS  No proband or family specific factors impacted the uptake of PGT

HCM = Hypertrophic Cardiomyopathy; DCM = Dilated Cardiomyopathy; GC = Genetic Counseling; PGT = Predictive Genetic Testing; CS = Cardiac Screening; SCD = Sudden Cardiac Death; HBOC = Hereditary Breast and Ovarian Cancer

Table 2  
*Qualitative and Survey Studies of HCM families and genetic testing*

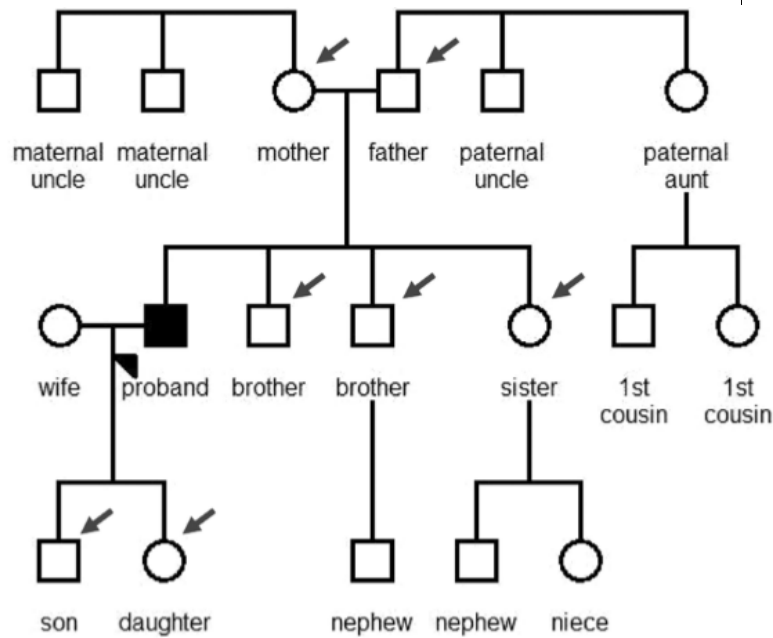
Author/Year Country Method	Aim	Population/Sample	Facilitators and Barriers to Testing	Themes	Other
Smart (2010)  United Kingdom  Qualitative Exploratory	To investigate the experience of people who had been offered GT  Explore 3 key areas: Disorders and treatment Genetic testing process Sharing information in family groups	27 participants who had undergone a DNA test:  Disorders: HCM (14); LQTS (13)  Type of Testing: Proband (15) Cascade (9) Research (3)  Genetic Test Results: Pathogenic (17) Non-pathogenic (7) VUS (3)	Facilitators: 1. Reduce uncertainty 2. Predict those at risk, especially children  Impediments: 1. Issues of communication and family responsibility 2. Ambivalence around test results 3. Burden of knowing one is at risk for SCD	N/A	Recommendation:  Facilitate CS by identifying ways to share information in families and to support patients with family communication

Geelen et al. (2011) The Netherlands Qualitative Longitudinal	To study how families deal with the genetic risk of HCM	6 HCM families involved in genetic testing followed over 3.5 years  57 members interviewed  Not all relatives underwent PSGT	N/A	Key areas:  1. Becoming aware of a familial disease 2. Making it known/disclosure 3. Experiencing the family disease	Findings:  Each family experienced the 3 key areas according to established patterns of family life which were not altered by genetic testing or HCM diagnosis
Ormondroyd et al. (2013) United Kingdom Qualitative Thematic analysis	1. To explore the process of PSGT 2. To understand how people learn about risk and make decisions re: PSGT 3. To evaluate psychosocial impact of PSGT	HCM/LQTS clinic based 22 (18 HCM, 4 LQTS) > 18 yrs. who had undergone PSGT since 2004 but not within the preceding 6 months.	Facilitators: Need to know for children first, then self Barriers: Low risk perception (self); Insurance, Heavy burden, Effect on marriageability (kids)	N/A	Barriers to informing family:  Resentment Estrangement Ambivalence about PSGT
<b>Author/Year</b> <b>Country</b> <b>Method</b>	<b>Aim</b>	<b>Population Sample</b>	<b>Facilitators and Barriers to Testing</b>	<b>Themes</b>	<b>Other</b>
Subasic (2012) United States Qualitative Phenomenological	Provide an insider's account of living with HCM: 1. How HCM impacts family and guides	15 adults with HCM; 13 via HCMA 2 via word of mouth 45 interviews over 3 years  7 (46.6%) underwent genetic testing but	Facilitator: Determine future risk for children  Barriers:	1. It's in the family (disclose?) (have GT?)  2. Finding a new normal	Diagnostic versus predictive genetic testing not delineated within the study

Longitudinal	decision re: GT 2. How physical limitations associated with HCM alter being-in-the-world 3.How HCM alters social relationships	only 3 (20%) received conclusive results	Financial concerns Lack of awareness re: availability of GT No children Not recommended by MD	3.HCM and relationships
Christiaans et al. (2009) The Netherlands Questionnaire Cross-Sectional	Evaluate counselee's views and opinions on GC PGT, and cardiac follow up and identify associations between demographics, clinical characteristics and attitude towards cardio-genetic care	Relatives of 95 HCM probands in mutation carrying families who disclosed DNA test results at least 18 months ago  123/146 who did PGT (86% response rate)  76% of carriers received regular cardiac follow up within an avg. time span of 3 years post test results	Facilitators: Hereditary nature of the disease Need to know for self and children  Barriers (to follow up): No symptoms Not necessary per MD Cardiac tests normal	Further research needed into why some mutation carriers not receiving regular follow up  Carriers who had manifest HCM, were older and male likely to have positive attitude towards care; GC valued Ok to receive genetic test results via phone/mail
Khouzam et al. (2015) United States Web-based Survey Cross-sectional	Uncover experience of HCM by assessing the impact of select demographic and familial factors, and attitudes and beliefs toward GT on uptake	306 individuals from HCMA diagnosed or at risk for HCM including those who had and had not participated in GT	Facilitators: Learn risk for family/kids Make better decisions Satisfy curiosity Provide reassurance Barriers: Insurance Access to GT Results useless, worrisome	More likely to have GT/PGT if:  Offered/discussed by clinician Saw genetics professional for HCM Professional advised testing Genetic mutation in family

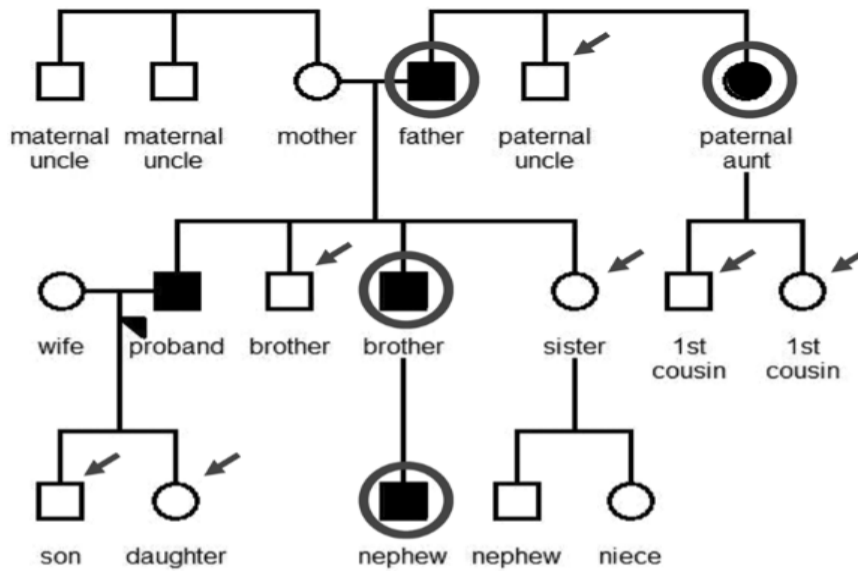
HCM = Hypertrophic Cardiomyopathy; HCMA = Hypertrophic Cardiomyopathy Association; GC = Genetic Counseling; PGT = Predictive Genetic Testing; LQTS = Long QT Syndrome; VUS = Variant of Unknown Significance; PSGT = Pre-symptomatic Genetic Testing; SCD = Sudden Cardiac Death

Figure 1. Three Generation Family Pedigree (From Cirino and Ho, 2013, with permission)



**Figure 1.** Pedigree. A pedigree is a family tree. Squares indicate male family members; circles, female family members. Solid symbols indicate people who have the family’s disease. The arrowhead indicates the proband, that is, the person who is being evaluated for an inherited heart disease. His family members are also at risk for developing the condition. The arrows point to his first degree family members (children, siblings, parents) who need periodic clinical evaluation.

Figure 2. Cascade Family Screening (From Cirino and Ho, 2013, with permission)



**Figure 2.** Cascade family screening. The circled shapes show family members from Figure 1 whose symbols are now darkened because they were diagnosed with heart disease in the process of family screening. The arrows point to the first degree family members of all affected individuals. These immediate family members need to be examined periodically because they are at risk for developing the family’s heart condition.

Figure 3. Process of engaging with HCM risk (adapted from McAllister, 2002)

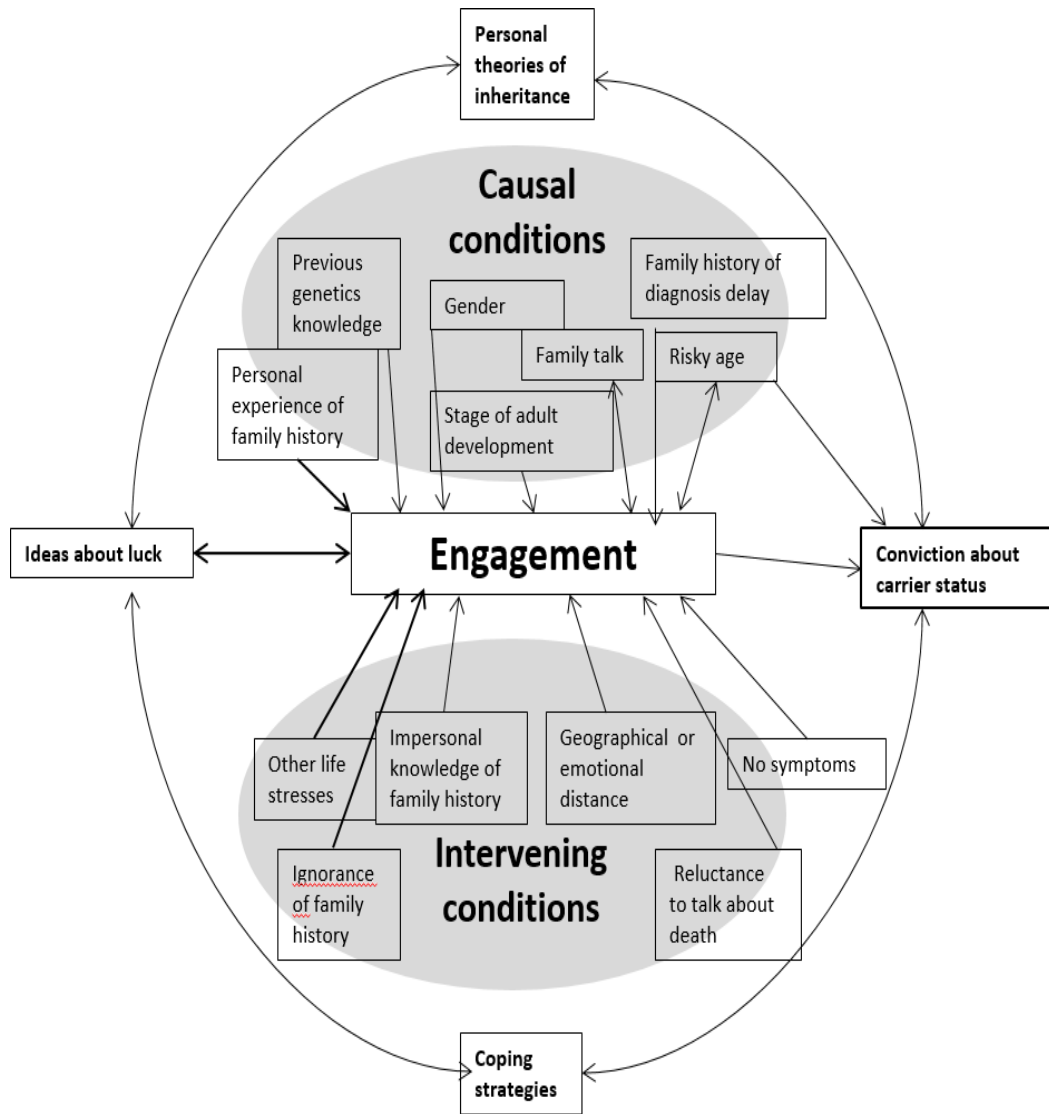
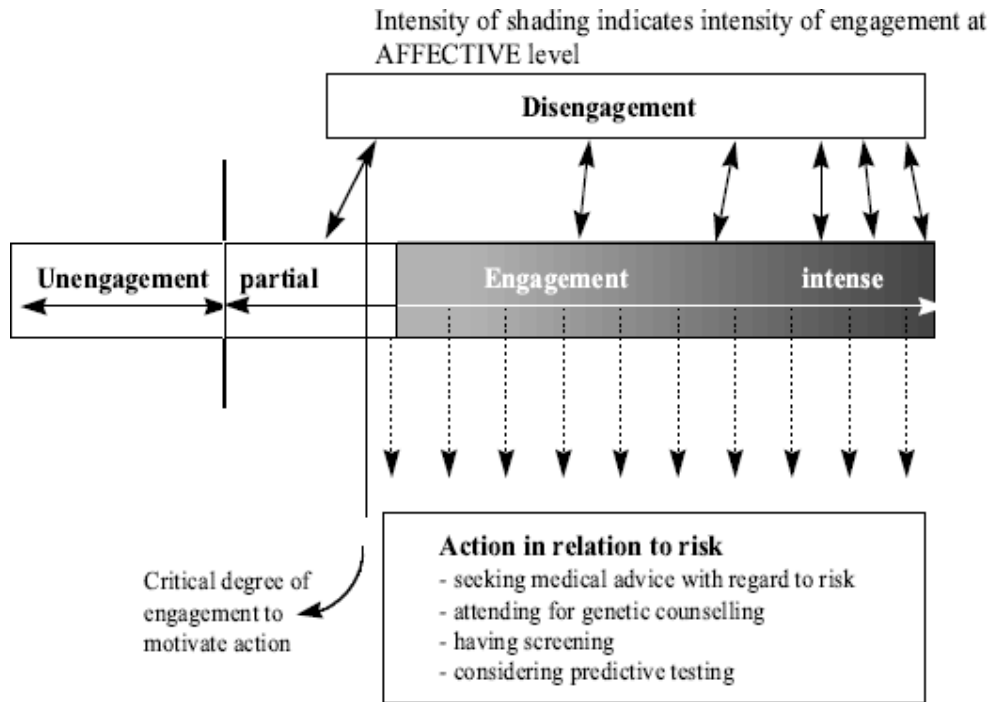


Figure 4

Engagement and Action in Relation to Risk (McAllister, 2002, p.497, permission pending)



## Summary of Changes from Proposal

The research approach, featuring a qualitative descriptive design using purposive sampling with maximum variation of the probands and snowball sampling of the at-risk relatives in families with a positive mutation for hypertrophic cardiomyopathy (HCM), was carried out per the proposal with the following exceptions:

1. After the original proposal was submitted which included use of the Standardized Clinical Assessment and Management Plan (SCAMP) database in addition to the clinical institutional database at the study site, institutional support for the SCAMP was withdrawn. This database had been used to track percentage of first degree relatives screened and reasons screening had not be completed. Subsequently the researcher lost access to this database and relied solely upon the clinical database of patients seen in the Cardiovascular Genetics Center (CVGC) at the study site.
2. After receiving responses from potential participants following recruitment via letter with the option to opt out, those interested who met criteria were interviewed after providing their verbal informed consent. To perform subsequent purposive sampling following the initial round of interviews, an amendment was filed with the IRB to obtain a HIPAA waiver of authorization to view the medical records of patients seen in the CVGC. This enabled the researcher to streamline recruitment to those with unscreened at-risk relatives.
3. In the original proposal, second degree relatives were only to be recruited in the absence of first degree relatives. In order to be able to interview a second degree relative of a proband who already had a first degree relative participating in the study, an amendment was filed. This decision was made to pursue an anticipated rich description of a scenario where second degree relatives became closer in the context of communication about HCM in the family.
4. In the original proposal, potential participants meeting inclusion criteria were ages 18-65 years. After subsequent discussion with the content expert on the dissertation committee and members of the CVGC group at the study site, a decision was made to change the age criteria to 18 years and older. Again this decision was made to pursue the valuable experience of older probands and at-risk relatives in the database.

5. After interviewing the first six participants, it was clear to the researcher that some participants had either forgotten information about the genetic component of HCM or had limited information. After discussion with the content expert on the committee, a decision was made to file an amendment to be able to offer interested participants the email link to the Vidscript, a web based educational video about HCM that had been made by genetic counselors in the department. If after being told about the Vidscript a participant expressed interest, it was sent via email as a follow up to the interview.
6. In the original proposal, the language “mutation positive” was used to describe the subset of HCM patients that would be the focus of the study. After receiving the list of patients within the mutation positive subset from the study’s Principle Investigator, letters were sent to recruit participants from this list and interviews were conducted. After reviewing the charts of some of the participants, it became clearer that the mutation positive subset consisted of patients with genetic test results of both “likely pathogenic” and “pathogenic” mutations. I later revised the description of the participants to include the terms “likely pathogenic” and “pathogenic” to be clearer about the subset.
7. As per the original protocol, all 29 participants were verbally administered the Genetic Literacy Assessment of Comprehension (GLAC) measurement scale at the conclusion of the semi-structured interview. However, after multiple unsuccessful attempts to contact the researchers who adapted the scale from the Rapid Assessment of Genetic Literacy (REAL-G) to obtain permission to use the scale and to gain clarity around proper scoring of the scale, a decision was made in conjunction with the dissertation chair to omit the GLAC measurement scale results from the manuscript.
8. After submitting a draft of the results of the study to the content expert on the committee, additional information from the medical record was requested for the results such as atrial fibrillation and the number of visits the participant had with a genetics MD and genetic counselor prior to the time of interview. This information was collected from the medical record and added to the results section.

# Engagement in Family Screening for Hypertrophic Cardiomyopathy

## Bringing Genetic Risk to the Foreground

Slide Presentation

Michelle G. Glowny MSN, RN  
University of Massachusetts Worcester  
Graduate School of Nursing  
December 19, 2018

## Acknowledgements

### Dissertation Committee

Carol Bova, PhD, RN (Chair)

Donna Perry, PhD, RN

Neal Lakdawala, MD

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- Lily Kravitz Nursing Studies Award, Brigham and Women's Hospital
- Nurses Educational Fund, Inc.

# Introduction

- Hypertrophic Cardiomyopathy (HCM)
  - 1 in 500 (~ 600,000 in US)
  - Autosomal dominant
  - Incomplete, age-related penetrance
  - Variable expressivity
  - Sudden cardiac death may be first manifestation
  - Consensus guidelines for screening (Gersh, 2011)

# Background and Significance

- Uptake of family screening for HCM by at-risk relatives is low (Miller, Wang and Ware, 2013)
  - Cardiac screening **57%**
  - Predictive genetic testing **39%**
  - Those unscreened remain at risk for sudden cardiac death
- 
- Why Aren't the Guidelines Being Followed?

# First Step Towards Family Screening

- Communication of genetic risk to family members
- Direct contact of at risk relatives prohibited
- Proband as a proxy for genetics clinician

# What is Known: Family Communication of Genetic Risk

- Oncology and neurodegenerative disease cohorts
- Contributing factors – Rs and Cs
- In families with HCM
  - Follows pre-existing patterns of family communication
  - Female sex and comprehension of autosomal dominance

# What is Known

## Facilitators and Barriers to Family Screening

### Facilitators

- Determine future risk for children
- Reduce uncertainty
- Satisfy curiosity, inform decisions
- Recommended by MD
- Saw genetics professional for HCM
- Known family mutation
- Relatives with HCM

### Barriers

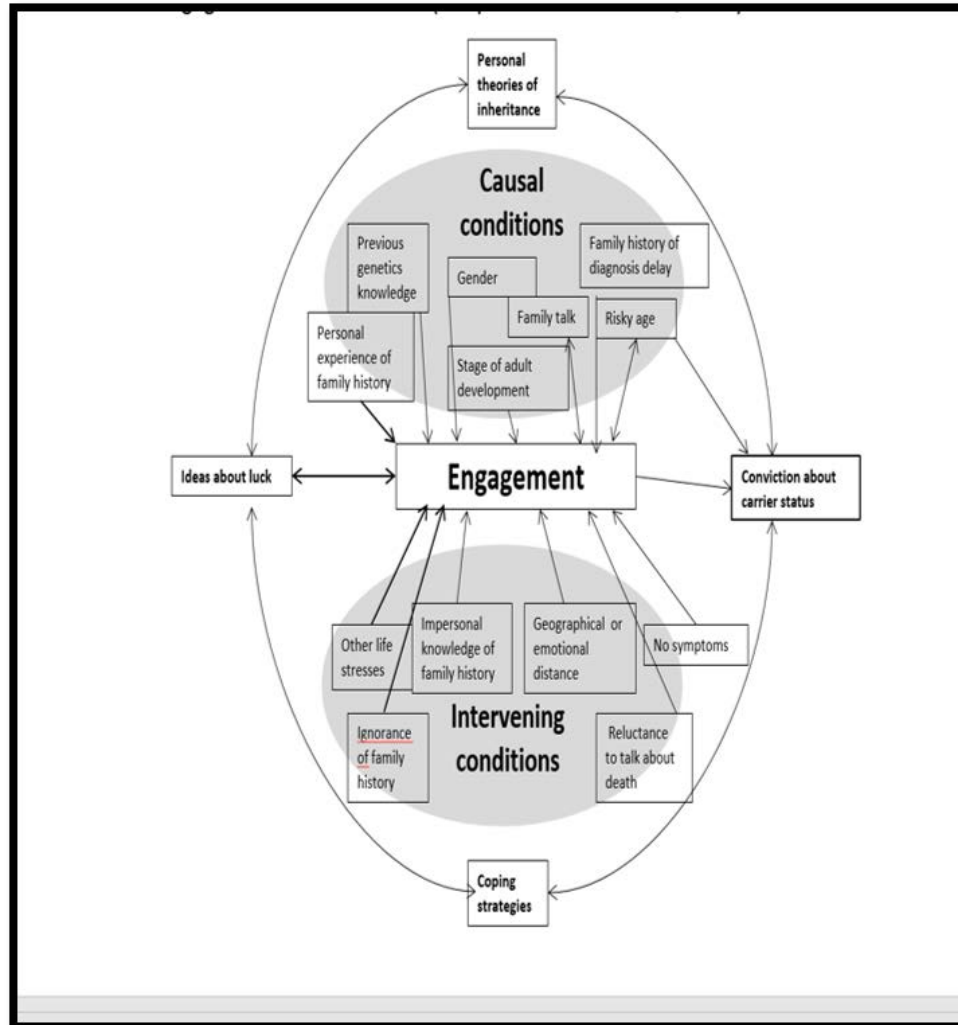
- Ambivalence about the DNA test
- Burden of knowing
- Family communication and responsibility
- Low risk perception
- Insurability and marriageability
- Not recommended by MD
- No children, no access to testing

## Gaps in the Literature

- Few studies of communication of genetic risk have included families with HCM
- A deeper understanding of the perspectives of the stakeholders is needed to inform interventions to increase uptake of family screening and help prevent sudden cardiac death

# Theory of Engagement

(Adapted from McAllister, 2002)



Definition:

The degree of cognitive and emotional involvement with one's increased risk of developing HCM as a result of one's family history of HCM"

# Purpose

To describe the engagement of at-risk relatives in family screening for hypertrophic cardiomyopathy

## Specific Aims

1. Describe the experience of communication of genetic risk from the perspectives of a) the at-risk relatives and b) the probands in families with a causative mutation for HCM
2. Use the Theory of Engagement to identify facilitators and barriers to family screening for HCM and expand the theory to the HCM population
3. Identify strategies to improve engagement in family screening including a) cardiac screening and b) predictive genetic testing in families with a causative mutation for HCM

# Methods

- Qualitative descriptive design
- Purposive sampling with maximum variation
- Snowball sampling of at-risk relatives
- Partners IRB approval; HIPAA waiver
- Trustworthiness
  - Peer debriefing and review
  - Analytic and reflexive memoing
  - Triangulation of data
  - Member checking

# Inclusion Criteria

- Age 18 and over
- Able to speak and read English
- Able to provide informed consent
- First degree relative or second degree relative of patients with a causative mutation for HCM known for more than 3 months
- Patients age 18 and over with a causative mutation for HCM known for more than 3 months

# Sampling and Recruitment

- Institutional database of HCM patients
- Families with a causative mutation for HCM
- Letter, followed by phone call
- Probands identify and reach out to at-risk relative with researcher contact info
- \$25 gift card compensation

# Data Analysis

- Demographic data: IBM SPSS v. 24<sup>®</sup> Statistics
- Audiotaped, transcribed semi-structured interviews
- Qualitative content analysis (Miles and Huberman, 2014)
- Conventional and directed analyses (Hsieh and Shannon, 2005)

## Participant Characteristics (N = 29)

	Probands (n=16)	At-risk relatives (n=13)	Clinical Database (N=623)*
Female (n, %)	10 (62.5%)	8 (61.5%)	242 (38.4%)
Age in yrs median (range)	57.5 (36-89)	35 (18-74)	48.38 ± 15.90
White (n,%)	16 (100%)	13 (100%)	448 (81.2%)
Less than high school	2 (12.5%)	0	
HS/GED/some college	4 (25%)	2 (15.4%)	
4 yr. college or higher	10 (62.5%)	11 (84.6%)	
Relationship to proband			544 (87.3%) probands
Child	...	7 (53.8%)	
Sibling/half-sibling	...	6 (46.2%)	
*Database of all HCM pts			

## Clinical Characteristics – HCM Status

HCM Status	Probands (n=13)	At-risk relatives (n=16)
P(+)G(+)	16(100%)	3(23.1%)
P(-) G(+)		3(23.3%)
P(-) G(-)		1 (6.3%)
P(+) G unknown		2 (12.6%)
P(-) G unknown		3 (23.1%)
LVH G unknown		1 (6.3%)
P= Phenotype G=Genotype LVH=Left Ventricular Hypertrophy		

## Clinical Characteristics (N = 29)

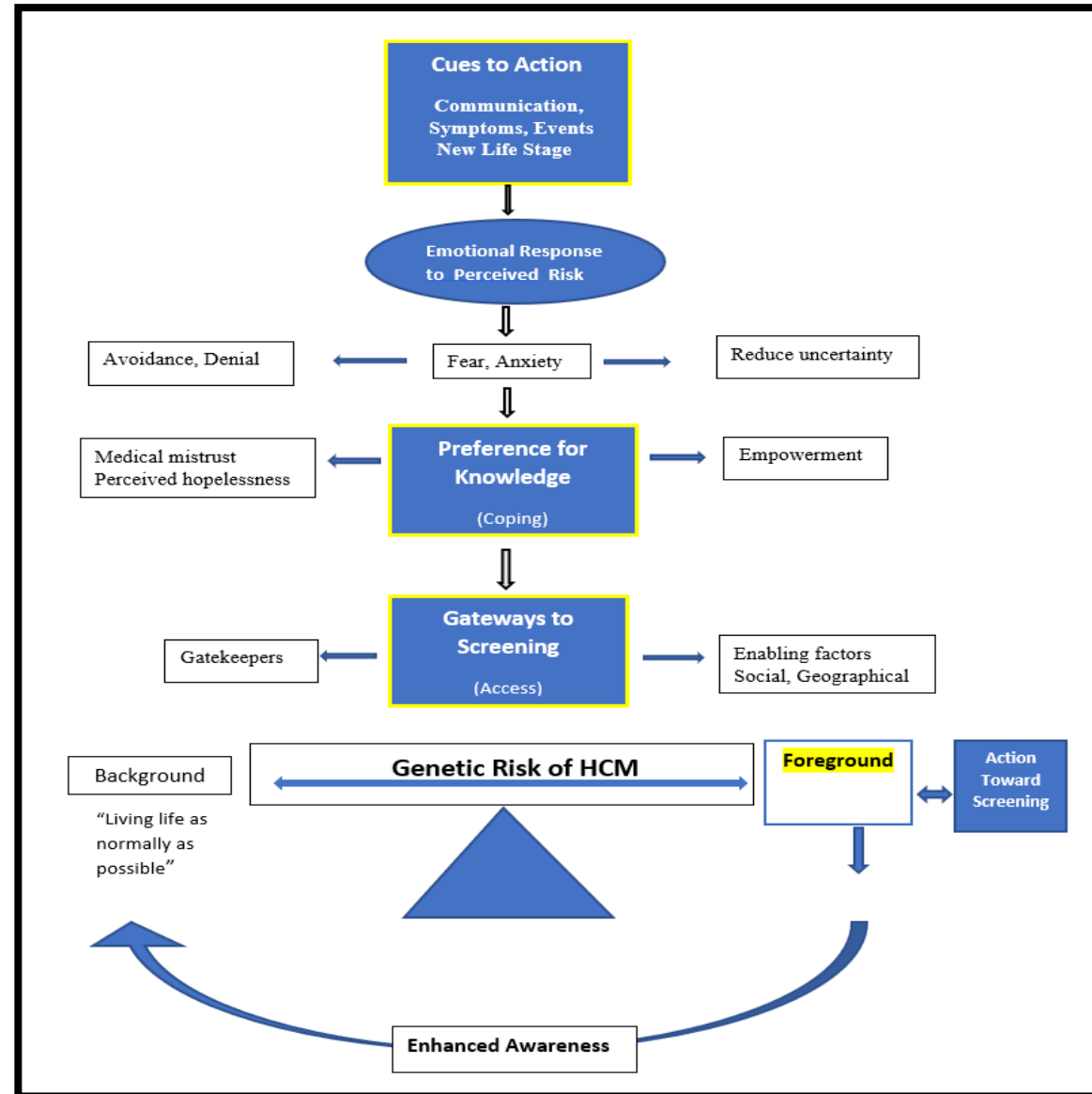
<b>Time since diagnosis yrs. (median, range)</b>	<b>15 (7-33)</b>	<b>10 (5-17)</b>	
Time since genetic testing yrs. (median, range)	6 (1-11)	6.5 (1-10)	
Atrial fibrillation (n,%)	6 (37.5%)	1 (7.7%)	169 (27.1%)
Current ICD (n,%)	7 (43.8%)	3 (23.1%)	217 (34.8%)
Heart transplant (n,%)	3 (18.8%)	0	17 (2.7%)
# CVGC MD/GC visits (median, range) ICD = Implanted Cardioverter Defibrillator; CVGC = Cardiovascular Genetics Clinic GC = Genetic Counselor	7.4/1.5 (1-15/0-2)	2.1/0.46 (0-9)/(0-2)	

# Overarching Theme and Major Themes

- Bringing Genetic Risk to the Foreground
  - Cues to Action
  - Preferences for Knowledge
  - Gateways to Screening

Overarching  
Theme  
Bringing  
Genetic Risk  
to the  
Foreground

“Yeah, you bet I did [notify siblings about HCM in the family]. Because knowledge is power and when I, when I was educated and identified that this was, that you could detect this through DNA, and really looked at the doctor,...we really looked at our family, my family tree and it really became, this whole scenario became more in full color for me.” (Proband)



# Major Theme: Cues to Action

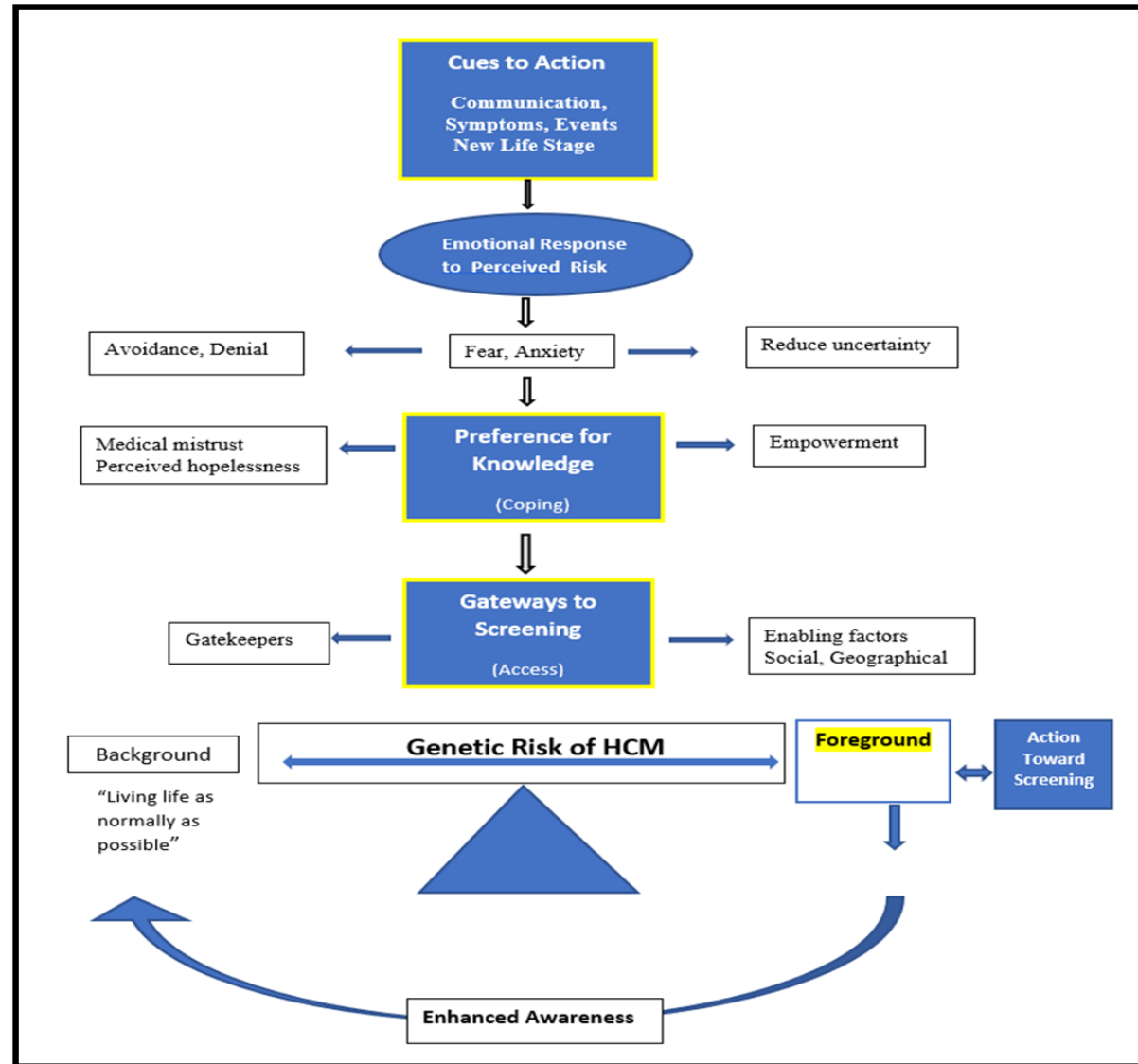
- 4 Dimensions:
  - Communication (family, HCPs)
  - Symptoms (family, self)
  - Transition to new life stage
  - Key events

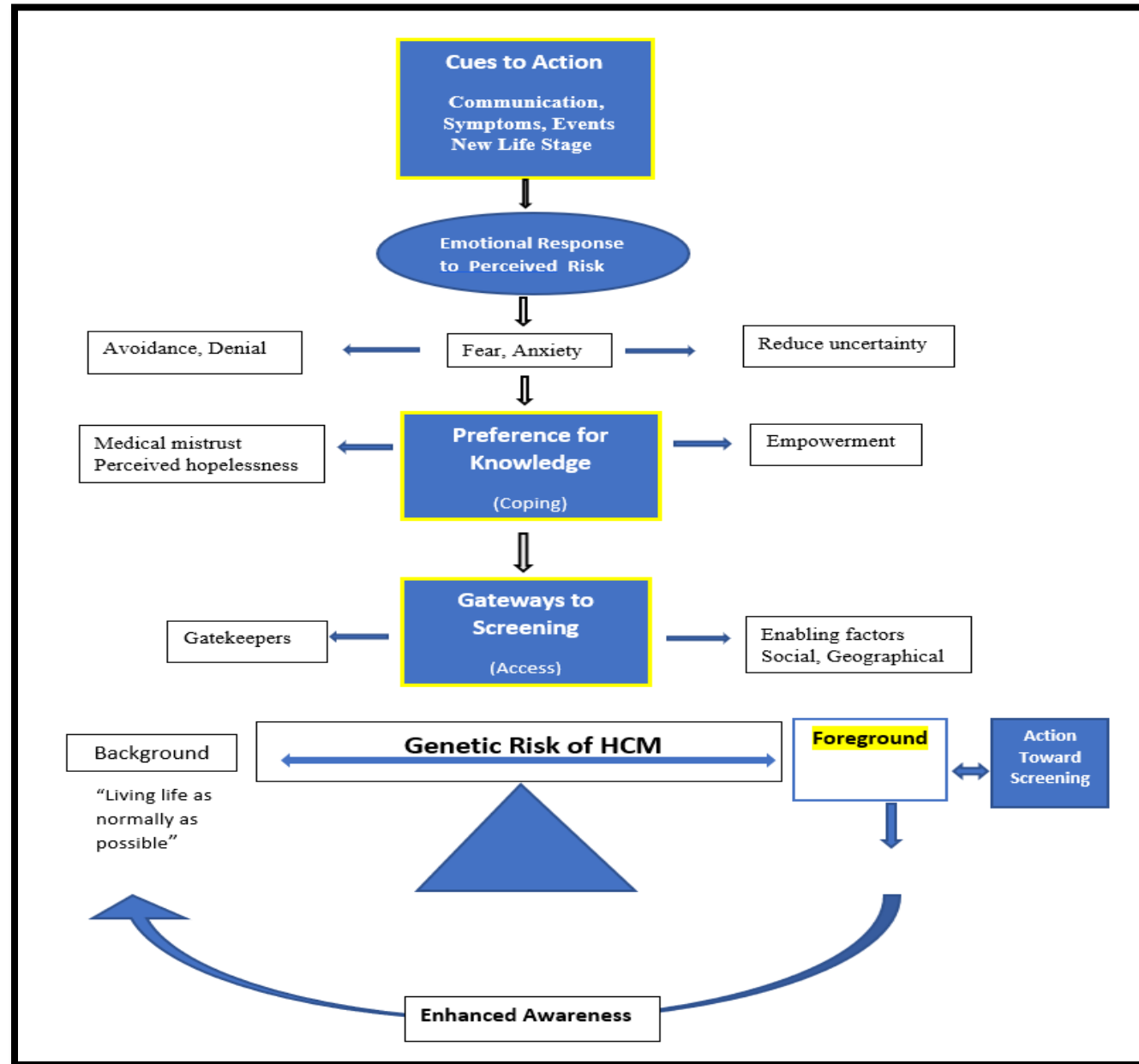
# Cues to Action: Key Event

- “She had it [the DNA kit] on her desk for about a year, and I said, ‘When are you going to send that in?’ And I think she had some kind of mental block about it, but she was visiting up here... and she sat down and just flopped back her head and I said, ‘Let me have your wrist’ and her heart was beating like crazy. And we hadn’t been doing anything strenuous...So she sent, I guess she...they had to send her a new one or something, a new test, but she did send it in” (Proband)

## Cues to Action: Transition to New Life Stage

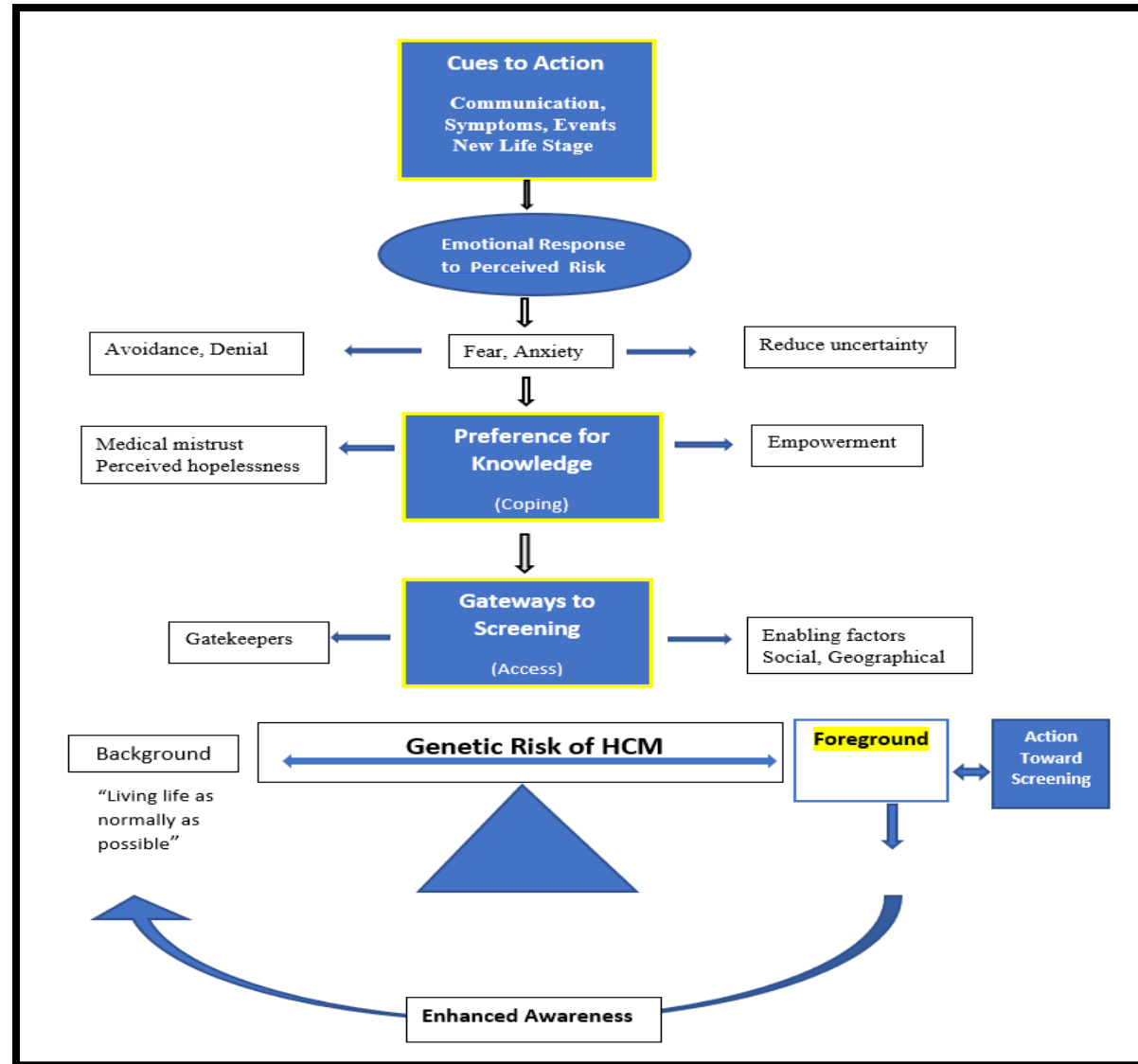
- “Yeah, I just think the biggest thing for me really is that they’re still treating this disease, or [me] with kid gloves in a way because they’re not talking about it with me...there’s only so much Googling I can do and only so many searches I can really do to find out ways I can reduce my risk. But I, I would like someone who this is their job to talk to me about it, and not just think I’m this fragile middle schooler and I care about my health and I wanna be proactive.” (At-risk relative)





# Major Theme: Preferences for Knowledge

- “So, my brother and I, the fact that we are able to know that there’s a potential for us and we’re monitored and people are looking out for that specifically makes me feel grateful so that we’re no one’s surprise ever...”  
(At-risk relative)
- “Well I think the doctor probably suggested it but then they both, both my parents wanted me to get the genetic testing done. Just to know I guess...I think I just wouldn’t want to know and have it hovering over, you know.”  
(At-risk relative)



## Gateways to Screening

“Um and then recently a couple of years ago, I started seeing an [electrophysiologist] and he is the one that encouraged me to uh, consider genetic testing. And I told him, ‘Well my girls had been tested. They’ve had echos and we were told we were okay’ And, um, but he, he suggested that I, I pursue it.” (Proband)

## Communication of HCM in the Family

- Varied and inconsistent
- Factors influencing the timing and content of the message
  - Understanding of HCM as a genetic condition
  - Timing and severity of clinical onset of HCM for the proband
  - Age of the at-risk family member
  - Familial culture

## Discussion: What This Study Adds

- Bringing genetic risk to the foreground –Insight into events that shift attentiveness towards genetic risk in the HCM population
- Cues to action - Contextualized information to complement results of existing studies
- Identification of individual, family, provider and systems factors for further study/interventions

## Discussion – Comparison to What is Known

- Bringing genetic risk to the foreground – evolving awareness
  - Patterns of “becoming aware of a familial disease” (Geelen et al, 2011)
  - Patterns of awareness and disclosure (Atkinson et al.,
  - “Foregrounding inherited disease risk” Theory of Genetic Vulnerability (Hamilton and Bowers, 2007)
- Cues to action - HCP recommendations important (Khouzam et al., 2015)
- Challenges with communication of risk and understanding of the spectrum of probability of genetic risk consistent with existing literature

## How Did The Theory of Engagement Work in the HCM population?

- Exemplars of causative and intervening factors were identified in the current study population
- Evidence to support shared phenomena across genetic conditions
- Direct comparison precluded – method, timing
- HCM specific codes: Fear of sudden cardiac death, activity intolerance impacting sports, career choices

# Implications by Theme

Theme	Implication
Cues to Action	<ul style="list-style-type: none"> <li>• Longitudinal care/support</li> <li>• EHR for reminders for serial screening</li> <li>• Family letter, educational video</li> <li>• Exploration of direct contact</li> </ul>
Preferences for Knowledge	<ul style="list-style-type: none"> <li>• Further exploration of the relationship between coping, information seeking and processing, genetic/health literacy</li> </ul>
Gateways to Screening  *Nursing in a collaborative/coordinating role given shortage of genetic counselors	<ul style="list-style-type: none"> <li>• Education of HCPs (PCPs, specialty)</li> <li>• Referral pathways</li> <li>• Virtual visits, telegenetics</li> <li>• Reimbursement for family-based screening</li> </ul> <p>EHR = Electronic health record</p>

# Further Research Needed

- Longitudinal studies using theoretical frameworks encompassing the elements of time and life stage
  - Family Systems Genetic Illness model (Rolland and Williams, 2005)
  - Life Course Perspective (LCP) (Hamilton, Innella & Bounds, 2016)
- Experience of genotype positive, phenotype negative persons “at-risk population” over the life course

# Further Research Needed

- Interventions to assist in education re: understanding of basic genetic principles and support communication of genetic risk in families with HCM
- Experience of communication of risk and engagement in family screening for HCM in diverse populations

# Limitations

- Single academic medical center
- Caucasian, middle to upper class, well-educated
- Recall bias
- Family referral bias
- No completely unscreened at-risk relatives

# Conclusion

- Engagement with genetic risk is a lifelong, recursive process.
- An integrated, longitudinal approach to care including appropriate referral and access to genetic counseling is needed throughout the continuum.
- Interventions targeting mutable factors such as understanding of genetic risk, personal risk perception and communication to family are a logical next steps to help increase uptake of screening.

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My family, my co-workers and my village

# Special Dedication

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- Dorothy L. Sexton, EdD, RN

## Dissemination Plan

The primary description of the dissertation work was submitted as a manuscript on February 28, 2019 to *Circulation: Cardiovascular Quality and Outcomes* for review and consideration for publication.

Appendix A

Glowny Interview Guide **Index Case**

Interview Questions	Probes (as needed)
<p><b>1. Can you tell me how heart disease has affected you and your family?</b></p>	<p>What is the name of the condition?</p> <p>Can you tell me more or give me more detail?</p> <p>What do you understand is the risk of inheriting the disease for your siblings, children, parents?</p>
<p><b>2. Can you describe how you communicated with your relative to discuss this heart condition and the need for screening?</b></p>	<p>What did you tell them? How did you tell them?</p> <p>When did you tell them?</p>
<p><b>3. Did they have any emotional reactions to the discussion?</b></p>	
<p><b>4. What do you believe were things that helped you to discuss the disease with your relatives?</b></p>	<p>Personal experience of the disease</p> <p>Genetic knowledge Family talk Geographical distance Family relationships</p> <p>Biggest motivation to tell? Did you feel pressure to tell them?</p> <p>Other important reasons to tell?</p> <p>Biggest barrier to communication? Any other obstacles?</p>
<p><b>5. Have they been screened? What tests have they done?</b></p>	<p>Echo, ECG, CMR PGT?</p>
<p><b>6. Is there anything your health care providers could have done to assist you in the process of communicating with your relatives about the disease?</b></p>	<p>More education?</p> <p>More psychosocial Support? Other?</p>
<p><b>7. I would like to speak to your family members too. Is there anyone in your family who would be interested in speaking with me? Anything you say to me will remain confidential.</b></p>	

Appendix B

Glowny Interview Guide **Relative**

Interview Questions	Probes (as needed)
<p><b>1. Can you tell me how heart disease has affected you and your family?</b></p> <p><b>2. How did you first learn you were at risk?</b></p>	<p>What is the name of the condition?</p> <p>Can you tell me more or give me more detail?</p> <p>What do you understand is your risk of inheriting the disease?</p>
<p><b>3. Can you describe how your relative told you about this heart condition and the need for screening?</b></p>	<p>What did they tell you? How did they tell you? When did they tell you?</p>
<p><b>4. Did you have any emotional reaction to the news?</b></p>	
<p><b>5. What do you believe were things that helped you to proceed or not proceed with getting screened?</b></p>	<p>Personal experience of the disease Genetic knowledge Family talk Geographical distance Family relationships Biggest motivation to get screened? Did you feel pressure to get screening? Other important reasons to get screening? Biggest barrier to getting screening? Any other obstacles?</p>
<p><b>6. Have you been screened? What tests have you done?</b></p>	<p>ECG, Echo, CMR, PGT?</p>
<p><b>7. Is there anything your health care providers could have done to assist you in the process of getting screened?</b></p>	<p>More Education? More Psychosocial Support? Other?</p>