ADDRESSING BREAST CANCER RISK FOR WOMEN IN FAMILIES WITH INDETERMINATE NEGATIVE *BRCA1* AND *BRCA2* GENETIC TEST RESULTS

by

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ABSTRACT

The purpose of this research was to describe calculated risk, risk perceptions of future breast cancer, and accuracy of risk perceptions of relatives (sisters or daughters) of women who have breast cancer and received genetic counseling regarding indeterminate negative *BRCA1/2* test results. A secondary purpose was to evaluate breast cancer screening recommendations from relative's primary care providers (PCPs) and recent screening participation. We assessed the type and amount of information about genetic counseling/testing that was shared among family members and with PCPs. Latent variable modeling was used to assess the influence of perceived amount of shared information on the accuracy of relative's own risk perceptions about breast cancer. Using a cross-sectional design, surveys and telephone interviews were conducted with 85 female relatives. Most estimated their risk to be higher than calculated estimates, yet calculated risk demonstrated that most were at average-risk (operationalized as < 20% lifetime risk by Claus and BRCAPRO risk calculators). A majority of average-risk relatives (87%) reported receiving recommendations for annual mammography from their PCP, and having a mammogram within the past 1-2 years. However, 10% of women were identified as being at elevated-risk ($\geq$20% lifetime risk by Claus or BRCAPRO), warranting annual breast magnetic resonance imaging (MRI) screening according to national guidelines; none of these women received recommendations for MRI screening. Regarding sharing of information, nearly 20% of relatives reported that nothing was

shared with them about their family member's genetic counseling; most (76.5%) did not discuss their family member's genetic testing or test results with their PCP. Further, relatives were generally unaware of the existence of a genetic counseling summary letter provided as part of standardized genetic counseling. Those who perceived more information was shared with them about their relative's genetic counseling had more accurate perceptions of their own risk for breast cancer (correlation = 0.748 (p=0.000) than women who perceived less information was shared (correlation = 0.346 (p=0.05). Our findings underscore the need for effective strategies that facilitate sharing of genetic counseling information with relatives and PCPs.

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CHAPTER 1

INTRODUCTION

Breast cancer is the second leading cause of cancer death in women (American Cancer Society, 2012). Genetic influences play a crucial role in breast cancer development. Best practices for breast cancer screening and prevention vary based on an individual's risk. Risk is influenced by genetic makeup as well as lifestyle and personal health history. Recently, annual magnetic resonance imaging (MRI) has been suggested as an adjunct to annual mammography for women ages 30 and above who are at elevated-risk for breast cancer with a lifetime risk of equal to or greater than 20% (American Cancer Society, 2014; Kuhl et al., 2010; National Comprehensive Cancer Network, 2013b; Saslow, 2007). Women at average-risk are encouraged to have mammography every 1-2 years beginning at age 40 or 50 depending on the guideline followed (see Table 1.1) (American Cancer Society, 2014; National Comprehensive Cancer Network, 2013b; U.S. Preventive Services Task Force, 2012). Despite advances in knowledge about screening and reducing risk for breast cancer in family groups with elevated-risk, many women with lifetime risk for breast cancer $\geq$ 20% are not receiving mammography and MRI screenings based on these guidelines (Cohen, 2010; Guerra, Sherman, & Armstrong, 2009).

Whether or not a woman receives a screening test depends on many factors, including availability of the test, recommendations by her primary care provider, and a

woman's decision to be screened (Price et al., 2010; Rauscher, Hawley, & Earp, 2005). Women's perceived risk for breast cancer plays a role in her decision to be screened (Katapodi, Lee, Facione, & Dodd, 2004; McCaul, Branstetter, Schroeder, & Glasgow, 1996). Women with higher perceived risk are more likely to seek information about cancer screening either on their own or from their health care providers (Dillard, Couper, & Zikmund-Fisher, 2010). Many behavioral frameworks such as the health belief model (Rosenstock, Strecher, & Becker, 1988) and the Precaution Adoption Model (Weinstein, 1988) include the concept of susceptibility to disease or perceived risk as antecedents to the uptake of healthy behaviors (Smerecnik, Mesters, Verweij, de Vries, & de Vries, 2009). Tilburt et al. note, "perceived risk is an important subjective psychological phenomenon related to threat appraisal that is closely intertwined with judgments about susceptibility to disease as well as the probability of benefit from interventions" (2011, p. 1). Thus, it is important to understand perceived risk as a component of women's decisions to participate in breast cancer screenings. Ideally, a major component of perceived risk for breast cancer is a woman's objective level of risk. Objective risk is influenced by family history of breast cancer, which is a manifestation of family genetics among other things.

Familial cancer is a term used to represent a cluster of cancers that occur within a family due to a combination of genetic and environmental factors where a mutation in a single gene has not been identified or is not likely (Fisher Center for Familial Cancer Research, 2012). A family cluster may be identified in the absence of multiple cancers if one cancer is suspicious, for example a woman with just one sister who was diagnosed at 45 years of age. Hereditary cancer is a term used to describe cancer where a mutation in

a single gene is present and thought to contribute strongly to the cancer (Fisher Center for Familial Cancer Research, 2012). Occasionally, a woman who has had breast cancer that is suspected of being hereditary, because of family history, age of onset, or other factors, will seek genetic testing to determine if a DNA mutation is present. If testing is undertaken, the most common result is that no mutation is identified (van Dijk, 2005). The terms uninformative, inconclusive, and indeterminate negative have been used in the literature to describe such a negative test when there is a family history of breast and/or ovarian cancer and no currently known mutations in breast cancer predisposition genes (Cypowyj et al., 2009; Dorval et al., 2005; Mannis, Fehniger, Creasman, Jacoby, & Beattie, 2013; Patenaude et al., 2006; van Dijk, 2005). For the purposes of this dissertation, a nonpositive *BRCA1/2* test result will be termed an indeterminate negative test result. Such a result simply means that the woman does not have a known mutation in any of the breast cancer predisposition genes. This result should not be interpreted to mean the family is not at increased risk for breast cancer based on genetic factors. Such a family may be described as having familial cancer rather than hereditary cancer. Women without breast cancer in the family should still obtain breast cancer screenings, based on the specific pedigree and other risk factors (see Table 1.1). If a woman's lifetime risk for developing breast cancer is 20% or greater, screenings may include annual magnetic resonance imaging (MRI) exams in addition to annual mammography. Appropriate screening with MRI and mammography can lead to early detection and possibly more effective treatment in these women (Kriege et al., 2004; Kuhl et al., 2010; Lee et al., 2010).

Genetic testing is often offered in the setting of genetic counseling. Counselors complete a risk assessment by compiling a family pedigree (diagram of family relationships with medical history) and asking the counselee about other personal risk factors. Counselors then provide personalized genomic information including information about risk of cancer (or risk of a second primary cancer). Cancer risk may be presented in terms of lifetime risk, 5-year risk, or qualitative descriptors of risk. Many risk assessment calculators exist to help health care providers attain these numbers. Two commonly used models include the BRCAPRO statistical model and the Claus model (Amir, Freedman, Seruga, & Evans, 2010; Gail & Mai, 2010). In addition to risk information, counselors also provide information about prevention and early detection methods. They may also provide general information about risk and prevention that may apply to the extended family.

Goals of providing personalized genomic information include offering better health care for patients and allowing them to make informed decisions based on the most accurate and applicable information available (Weitzel, Blazer, Macdonald, Culver, & Offit, 2011). Families in which a member has undergone genetic counseling are a special population. The family pedigree has been evaluated by an expert in risk assessment. Counselors are knowledgeable about hereditary cancer syndromes, risk assessment instruments, and risk-specific screening recommendations. While these principles apply to many types of cancer, this research addresses breast cancer in particular. In a systematic review and meta-analysis about the psychological impact of genetic counseling for familial cancer, Braithwaite, Emery, Walter, Prevost, and Sutton (2006) note that one outcome of effective genetic counseling is accuracy of perceived risk. In

cases of familial cancer, they assert, "…the goal is to communicate information regarding personal risk of cancer so that individuals can make informed choices regarding options for risk management, principally cancer surveillance and predictive genetic testing" (p. 62). Tilburt et al. (2011) note, "misperception of risk has been shown to both increase and decrease use of preventive health services and therefore can have significant implications for the health of those at greater than average-risk of developing cancer" (p. 2).

Genetic counseling sessions for breast cancer may involve a single family member or many family members; however, a family assessment is always included. If a DNA blood test is indicated within a family, it is best to test an affected family member first, especially a family member who had early onset cancer, bilateral breast cancer, or multiple primary cancers because that family member has the highest likelihood of having a positive test (National Comprehensive Cancer Network, 2013c, pp. MS-15). Regardless of the DNA test outcome, counselors often write a summary letter to the counselee providing information about the counseling session, testing that was done (if any), and also providing general information about the potential risk of other family members. The individual who receives the counseling (most often the individual who has had breast cancer) is encouraged to disseminate information to other family members and to encourage them to, in turn, share the information with their primary care providers. Genetic counselors typically do not contact family members who were not involved in the counseling session to share risk information, especially in the event of indeterminate negative DNA test results. This places the burden on the cancer survivor to disseminate this technical and sometimes complex information, which she herself often does not fully understand. Results from previous research suggest that this information is not

consistently and reliably communicated to family members (L. E. Forrest, Curnow, Delatycki, Skene, & Aitken, 2008; Seymour, Addington-Hall, Lucassen, & Foster, 2010; Vos, Jansen, et al., 2011; Vos, Menko, et al., 2011). As such, the genetic counseling summary letter can be a key piece of written information that is available for reference when sharing risk information with close family members. National guidelines identify the need to provide counselees with tools to inform and educate family members about genetic counseling information such as a letter, website, or referral to a genetic counselor (Riley et al., 2012).

Purpose

The purpose of the proposed cross-sectional descriptive study was to understand the impact of information shared about genetic counseling sessions by close relatives on the accuracy of risk perception for women potentially at increased familial risk of breast cancer. Participating women had biological first-degree relatives with a personal history of breast cancer who have received genetic counseling, received an indeterminate negative *BRCA1/2* test result, and who have received genetic counseling summary letters suggesting that their close relatives may be at increased risk for breast cancer. This study intended to describe the contribution of a woman's self-reported understanding of information shared about genetic counseling sessions by close relatives on her accuracy of risk perception about her own breast cancer risk (ultimately we replaced the variable of self-reported *understanding* of information with self-reported *amount* of information shared by close relatives about their genetic counseling sessions). Further, in this study we calculated the lifetime breast cancer risk estimates for women, whose first-degree female relatives have undergone genetic counseling and testing with indeterminate

negative results, comparing the calculated objective risk with the woman's self-described screening plan and self-report of breast cancer screenings to determine whether screening plans and screening participation are in alignment with risk-based guidelines of the American Cancer Society (ACS) and the National Comprehensive Cancer Network (NCCN).

Conceptual Model

This study drew upon Leventhal's Common Sense Model of Self-regulation as a broad framework for exploring women's responses to risk information (Leventhal, Brissette, & Leventhal, 2003). The Common Sense Model proposes that people will respond to situational stimuli such as an illness symptom or a health threat or stressor with the parallel processes of developing cognitive representations of the danger and developing representations of fear. As a result of cognitive and emotional responses, coping mechanisms are developed to control the danger and fear associated with the situational stimuli. Marteau and Weinman (2006) propose that Self-regulation theory can likewise be used to predict and understand behavioral response to genetic risk information (see Figure 1.1). Risk perceptions are part of the cognitive representation of a health threat that are influenced by both preexisting representations of the health threat as well as emotional responses to the health threat (Leventhal et al., 2003; Marteau & Weinman, 2006).

Impact

This study helped identify women who may be receiving inappropriate levels of screening or who may have inaccurate risk perceptions. Women make health and lifestyle

choices based on perceptions of personal risk. The data gleaned may inform future intervention research that will help health care professionals work with a population that would benefit from increased awareness about their individualized risk for breast cancer and personalized screening/ prevention strategies. More timely screening of women with familial risk for breast cancer may help identify cancer earlier. Conversely, avoiding unnecessary screening may save health care dollars and avoid false positive screens and downstream effects. Additionally, the knowledge gained about how women perceive their individual risk of developing breast cancer may provide insight as to how genetic health information is received, understood, and acted upon when delivered to extended family by their sisters and mothers who received genetic counseling.

Specific Aims

The specific aims for this study relate to women who have mothers or sisters who have received genetic counseling (counselees) and indeterminate negative *BRCA1/2* test results. Upon completion of genetic counseling, counselees were provided with summary letters encouraging them to share genetic information with their close relatives. The women described in the following aims are those close relatives.

Specific Aim 1

Specific aim 1 was to calculate an estimate of women's lifetime risk for breast cancer and compare this estimate to women's perceived risk about developing future breast cancer. This aim included three research questions:

1. What is the average calculated risk for breast cancer using the Claus model, the BRCAPRO model, and the Gail model for women (with sisters or mothers

who received genetic counseling and indeterminate negative *BRCA1/2* results)?

2. What percent of women (with sisters or mothers who received genetic counseling and indeterminate negative *BRCA1/2* results) qualify for annual MRI breast screenings based on NCCN guidelines (a lifetime risk for breast cancer ≥ 20%) based on the Claus or the BRCAPRO risk calculators?
3. What percent of women (with sisters, mothers, or daughters who have received genetic counseling and had indeterminate negative *BRCA1/2* results) over-estimate vs. underestimate their risk as compared to their calculated risk for breast cancer?

Specific Aim 2

Specific aim 2 was to determine whether self-reported screening plans and self-described screening practices are in alignment with risk-based guidelines in women whose first-degree female relatives have received genetic counseling and indeterminate negative *BRCA1/2* test results. This aim includes two research questions:

1. What percent of women whose first-degree female relatives have received indeterminate negative test results **report that they are screening for breast cancer according to risk-based guidelines**, i.e., are women who have ≥20% lifetime risk of developing breast cancer, receiving both annual mammogram and MRI (as recommended by the National Comprehensive Cancer Network (NCCN) and the American Cancer Society (ACS))?
2. What percent of women whose first-degree female relatives have received indeterminate negative test results **report receiving recommendations for**

breast cancer screening from their primary care physicians or from another source that are consistent with the National Comprehensive Cancer Network (NCCN) and American Cancer Society (ACS) guidelines based on the level of risk (i.e., annual mammography if < 20% lifetime risk and ≥ 40 years of age; mammography with MRI if ≥ 20% and ≥ 30 years of age)?

Specific Aim 3

Specific aim 3 was to determine the contribution of a woman's self-rated understanding of genetic health information, shared by her first-degree female relative about genetic counseling sessions, to her risk perception and to the accuracy of her perception of individual lifetime risk for breast cancer while controlling for confounding influences of factors known to contribute to risk perception, including age, education, health literacy, numeracy, knowledge about breast cancer genetics, and self-reported distress related to family history of breast cancer and perceived personal risk for breast cancer. This aim includes the following research questions:

1. What is the magnitude of the relationship between calculated lifetime risk for breast cancer and perceived lifetime risk for breast cancer?
2. Does a woman's self-rated understanding of genetic health information shared by her first-degree relative moderate the accuracy of risk perception?
3. Does a woman's self-rated understanding of genetic health information shared by her first-degree relative predict risk perception?

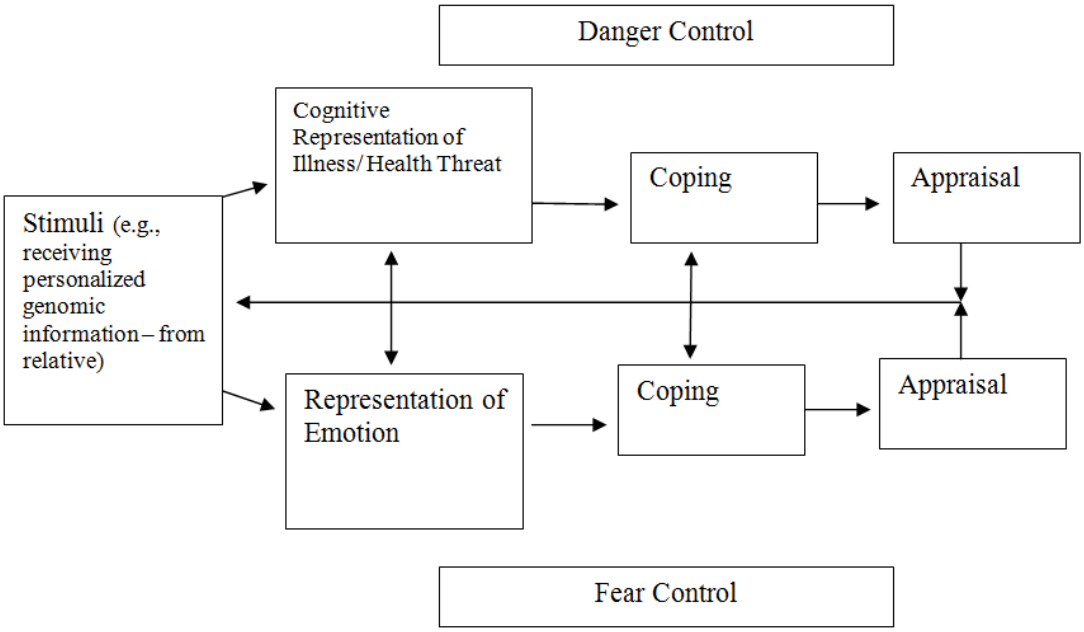


Figure 1.1
Leventhal's Common Sense Model of Self-regulation of Health and Illness to explain responses to health risk information. Permission to print this adaptation of the Common Sense Model has been obtained by Linda Cameron and Howard Leventhal.

Table 1.1 Screening mammography and breast MRI guidelines for average- and high-risk women by organization

Organization	Risk Group	Mammography	Breast MRI
NCCN[a]	Average-risk	Annual beginning at age 40 – end age not given	Not recommended
	>20% lifetime risk by models largely dependent on family history	Annual beginning at age 30 – end age not given	Consider annual beginning at age 30 – end age not given
American Cancer Society[b]	<15% lifetime risk (average-risk)	Annually beginning at age 40, continue as long as in good health	Not recommended
	>20% lifetime risk	Annually beginning at age 30, continue as long as in good health	Annually beginning at age 30, continue as long as in good health, consult with HCP
	15%-20% lifetime risk	Annually beginning at age 30, continue as long as in good health	Talk to doctor about limitation/ benefit screening MRI
ACOG[d]	Average-risk	Annually beginning at age 40, end age not given – consider medical comorbidity and life expectancy for women 75 years and older	Not recommended
	≥20% lifetime risk	Annually	Annual – no begin or end age given
USPSTF[c]	Average-risk	Every 2 years begin at age 50, end at age 74	Not recommended
	Elevated-risk	No specific recommendations for mammography – women should be referred to genetic counseling	No specific recommendations for MRI – women should be referred to genetic counseling

[a] (National Comprehensive Cancer Network, 2013b)
[b] (American Cancer Society, 2014)
[c] (U.S. Preventive Services Task Force, 2012)
[d] (American College of Obstetricians and Gynecologists, 2011)

CHAPTER 2

BACKGROUND AND LITERATURE REVIEW

Breast Cancer Etiology

Breast cancer is the second leading cause of cancer death in women (American Cancer Society, 2012). All breast cancers are genetic; however, not all cancers are inherited (Daly et al., 2010). In other words, all cancers are the result of genetic and epigenetic alterations, for example, when the cell loses its ability to repair itself or when cell growth goes unchecked (Hanahan & Weinberg, 2000). These alterations, or mutations, may stem from a variety of factors, including age, environment, and lifestyle; they may also be inherited, that is, present in a person's genetic make-up from conception. Because the development of cancer requires a series of several mutations over years, having one or more mutations present at birth (inherited mutations) dramatically increases the chances of developing cancer and increases the likelihood of early onset cancer. However, less than 10% of breast cancers are due to a single, inherited, dominant gene mutation (Foulkes, 2008).

Breast Cancer Risk Stratification and Screening Recommendations

A variety of organizations have issued breast cancer screening guidelines and risk reduction measures that are based on a woman's level of risk, including the American

Cancer Society (ACS) (American Cancer Society, 2014), the National Comprehensive Cancer Network (NCCN) (2013b), and the National and the American College of Obstetricians and Gynecologists American College of Obstetricians and Gynecologists (2011). These organizations recommend annual MRI for women at certain levels of elevated-risk; see Table 1.1 for a summary of guidelines. Level of risk is therefore important and impacts decisions about screening and prevention. Level of risk is estimated in several ways. First, if an inherited germline gene mutation is identified, then risk is estimated based on the profile of the specific gene mutation (A. Antoniou et al., 2003). The most common and well-known autosomal dominant gene mutations that can cause breast cancer are part of the syndrome called Hereditary Breast and Ovarian Cancer (HBOC). The genes that cause HBOC, the *BRCA1* and *BRCA2* genes confer a lifetime risk for breast cancer of between 31% and 78% by age 70 (A. Antoniou et al., 2003). Besides the *BRCA1/2* genes, other autosomal dominant gene mutations that can cause breast cancer exist (see Table 2.1).

In the absence of a known mutation, risks may be calculated through the use of risk calculators that take family history, age, and other elements of personal medical history into account (Afonso, 2009; Amir et al., 2010). The risk may be presented numerically or qualitatively with terms such as average, elevated, high, or very high. Numeric risk may be presented in terms of lifetime risk (percent chance that a woman will develop breast cancer in her lifetime), 5-year risk (percent chance that a woman will develop breast cancer in the next 5 years), or relative risk (the odds of developing breast cancer compared to the general population or to women their same age, race/ethnicity who do not have a family history); for example, a relative risk of 2.0 indicates that an

individual has twice the risk to develop breast cancer of the general population. A lifetime risk for breast cancer of 20% means that 20 out of 100 women with similar risk factors are predicted to be diagnosed with breast cancer at some point in their lifetime.

Classifying Family Patterns of Breast Cancer

Because heredity plays a role in breast cancer risk, health professionals examine family pedigrees to determine if there is a pattern of breast and/or ovarian cancer in the family that could represent a hereditary syndrome. Cancers in a family might be classified as sporadic, familial, or hereditary. This categorization can help in determining what type of screening and prevention measures might be undertaken, assist families in understanding their risk, and help health care professionals determine whether genetic testing might be warranted (Berliner & Fay, 2007). Unfortunately, the classification is not always clear cut. In addition, as more family history becomes available or as more cancer cases present themselves, categories may shift over time.

Sporadic Breast Cancer

The majority of all breast cancers are sporadic. They arise from mutations that occur later in life and are not present at birth (National Human Genome Research Institute, 2012). Cancers in a family are termed sporadic if they occur at the typical age of onset (over 50) and demonstrate no particular pattern of inheritance (Berliner & Fay, 2007). These cancers are likely due to nonhereditary causes and there is very little chance that genetic susceptibility testing would reveal a deleterious mutation in a dominant gene (Berliner & Fay, 2007). Lifestyle and environment factors are known to contribute to sporadic breast cancers. Women who belong to families with a sporadic breast cancer but

no other striking familial or personal risk factors for breast cancer are said to be at "population risk" or "average-risk." In the general population, it is commonly reported that 12% of women, or 1 out of 8, will develop breast cancer at some time during their lives (National Cancer Institute, 2014a); however, Pharoah et al. (2002) note that if those with familial and hereditary cancer are removed from the "general population," the remaining women have a significantly lower risk than 12%

Sporadic breast cancers may be associated with multiple, common low-risk gene alleles that have been identified in genome-wide association studies (Foulkes, 2008); however, testing women for these low-risk alleles has not yet proven to be clinically useful (Winstead, 2010).

Hereditary Breast Cancer

Hereditary breast cancer refers to those cancers related to specific gene mutations that were inherited from a parent and thus, the mutations are found in all somatic cells and are present from birth. Inherited mutations are rare and account for approximately 5-10% of all breast cancers (American Cancer Society, 2012) . Families who possess highly penetrant autosomal dominant genes generally have members with cancers occurring at younger ages, bilateral cancers, and/or a greater number of cancers in the family. Cancer in these families often demonstrate an autosomal dominant pattern of inheritance (National Comprehensive Cancer Network, 2013c). The most common genetic mutations associated with breast cancer are in the *BRCA1* and *BRCA2* genes. Other autosomal dominant genes exist that confer high risk (see Table 2.1). Individuals carrying these types of high-risk gene mutations have a lifetime risk for breast cancer that is

approximately five times that of the general population (National Cancer Institute, 2014a).

Familial Breast Cancer

The distinction between familial breast cancer and hereditary cancer can be difficult. Berliner and Fay (2007) note that individuals should be referred for cancer risk assessment when either personal or family history suggests familial or hereditary cancer. The NCCN describes familial cancers as follows:

> Familial cancers share some but not all features of hereditary cancers. For example, although familial breast cancers occur in a given family more frequently than in the general population, they generally do not exhibit the inheritance patterns or onset age consistent with hereditary cancers. Familial cancers may be associated with chance clustering of sporadic cancer cases within families, genetic variation in lower penetrance genes, a shared environment, or combinations of these factors. (National Comprehensive Cancer Network, 2013c, pp. MS-1)

While other authors distinguish between hereditary and familial cancers in a similar fashion to NCCN (Berliner & Fay, 2007; Fisher Center for Familial Cancer Research, 2012), it should be noted that some have used the term "familial" to refer to cancers that may be or are known to be caused by inherited mutations (Foulkes, 2008). For example, a Cochrane Review describing cancer genetic risk assessment for those at risk of familial breast cancer includes studies about the care of *BRCA1/2* carriers (Hilgart, Coles, & Iredale, 2012). Figure 2.1 presents an illustration of the amount of breast cancer attributed to sporadic, familial, and hereditary causes as well as common terms used to describe the risk level of each category and lifetime risk estimates for each category.

For the purposes of the proposed study, the NCCN definition of familial cancer is utilized. The population of interest in this study includes women who have not had cancer, but have close family members who have had cancer and genetic testing with

indeterminate negative results. It is possible, therefore, that these women may have patterns of inheritance that appear to be familial or hereditary. Some of these women may be found to have levels of risk that are equal to or above 20% lifetime. Because these women have not received genetic counseling themselves, information that they have obtained about their risk for breast cancer and screening that should be done would likely have been obtained through self-study, through information from their primary care providers, or possibly through their relatives who have received genetic counseling.

Breast Cancer Prediction Models

Several computer-based statistical models have been developed to estimate lifetime and 5-year risks of breast cancer and/or the risk of carrying a *BRCA1/BRCA2* mutation in individuals and populations. These models vary in which risk factors are taken into account. They also differ in the epidemiological data which were used in their development. This in turn defines the population for that the specific model is appropriate. Each computer model has strengths and weaknesses.

Evaluating Validity of Breast Cancer Prediction Models

To evaluate the usefulness of a particular model, calibration and discrimination are commonly assessed indicators (S. W. Fletcher, 2013). Calibration describes the ability of a model to accurately predict cancer occurrence at the population level. It is measured by comparing the number of women in a particular group that are estimated (E) to develop breast cancer with the number who are diagnosed with breast cancer, or the observed (O) number. If E/O is near 1.00, then a model is deemed to have good calibration (S. W. Fletcher, 2013). Well-calibrated models that accurately predict

population risk are important when developing policies or guidelines that are based on populations; health care policy makers can use these models when conducting cost/benefit analysis in a large group (Amir et al., 2010, p. 681).

For the primary care clinician, a more useful model will accurately assess individual risk so that prevention and detection activities may be individualized (Amir et al., 2010). Discrimination is a measurement of how well a model stratifies individual women into those who do and those who do not develop breast cancer in a given period; discrimination is a measure of how well models perform at an individual level (S. W. Fletcher, 2013).The concordance rate or the c-statistic is a method used to assess the discrimination of a model. The c-statistic is the proportion of randomly selected pairs in a group where one woman has a diagnosis of breast cancer and one does not in which the woman with cancer is given a higher calculated risk by the model than the woman without cancer. Values for the c-statistic can range from 0.50 (where the women with cancer were given higher risk 50% of the time– odds similar to a coin toss) to 1.00 (where the model discriminates perfectly – always assigning higher risk to those with cancer) (S. W. Fletcher, 2013; Parmigiani et al., 2007).

Gail model. The Gail model is the most widely used tool for assessing breast cancer risk. It was developed at the National Cancer Institute by Dr. Mitchell Gail (Gail et al., 1989). This model calculates an individual woman's risk of developing breast cancer over the next 5 years as well as lifetime risk to age 90, based on seven risk factors: current age, age at menarche, age at first live birth, number of first-degree relatives with breast cancer, number of previous breast biopsies, history of atypical hyperplasia, and race. Age at first live birth and the age at menarche are proxies for hormone exposure.

The Gail model has been modified since its original inception; the modified version is sometimes referred to as the NCI-Gail model (Amir et al., 2010) or as the Breast Cancer Risk Assessment Tool (BCRAT) (S. W. Fletcher, 2013). This instrument is easily accessible to health care providers and patients. It can be assessed online at www.cancer.gov/bcrisktool/.

Fletcher (2013) presents an overview of studies using the Gail model. The Gail model demonstrates good calibration ranging from 0.94 to 1.03, indicating that it has good accuracy at a population level. However, it does not discriminate well for individual women with c-statistics calculated between 0.58 and 0.63 in different studies (S. W. Fletcher, 2013). These c-statistics indicate that in randomly selected pairs of women (one with and one without a breast cancer diagnosis), the woman with breast cancer had a higher Gail score in 58 to 63% of cases. These numbers are slightly better than a coin toss, but not a lot. In a study or 55,301 women, the sensitivity of the Gail model (proportion of all women who developed breast cancer over a 5-year follow-up who had an estimated 5-year risk $\geq$1.67%) was found to be 44% (Rockhill, Spiegelman, Byrne, Hunter, & Colditz, 2001). The specificity of the Gail model in that same sample (proportion of women who remained free of breast cancer over a 5-year follow-up with an estimated 5-year risk <1.67%) was 66% (Rockhill et al., 2001).

In addition to the poor concordance rate (discrimination), another weakness of the Gail model is that it has performed poorly when used in higher-risk populations (Amir et al., 2010). The Gail model does not include family history beyond the first-degree relatives, and does not take into account age at diagnosis or types of cancer besides breast. Because it does not emphasize family history, it is not the type of model that the

ACS or the NCCN advocates for use when recommending more intensive breast cancer screenings. When following the NCCN guidelines or the ACS guidelines for screening and evaluating breast abnormalities, the Gail model should not be used to determine lifetime risk; NCCN guidelines rely on models that are largely dependent on family history (National Comprehensive Cancer Network, 2013b; Saslow, 2007). The Gail model is more easily accessible and easier to use than the models that take more family history into account, which may account for its more widespread use than other models. Health care providers may not be aware that it has limited ability to assess risk in families where there is a strong history of breast cancer.

Breast Cancer Prediction Models Emphasizing Family History

For patients with a family history that includes multiple cases of breast cancer, early onset breast cancer, or a family member with ovarian cancer, models that focus more on the extended pedigree are valuable for predicting breast cancer risk. Models that emphasize family history will provide risk estimates of developing breast cancer in a certain number of years and over a lifetime. This information is helpful in tailoring screening and prevention plans to individual women. These models also provide an estimate for risk of carrying a deleterious *BRCA1* or *BRCA2* gene mutation. These estimates are used to help decide whether or not to test a woman for gene mutations. Many models are available that emphasize family history include the Claus Model, the BRCAPRO Model, and the IBIS or Tyrer-Cuzick Model presented here.

Claus model. The Claus model estimates both 5-year and lifetime risks for developing breast cancer. It includes both maternal and paternal family history of breast cancer as well as ages of onset. The updated model includes family history of ovarian

cancer (Amir et al., 2010). The Claus model takes into account both first-degree and second-degree relatives. Amir et al. (2010) identify several limitations to the Claus model. First, the model does not include nonhereditary risk factors such as hormonal exposure. Second, the risk is calculated based on lifetime risk tables derived from North American women in the 1980s, which are lower than current North American risk or European risk. The Claus model is only for use with women who have at least one female first- or second-degree relative with breast cancer (Afonso, 2009).

BRCAPRO *model.* The BRCAPRO model provides both 5-year and lifetime risks for developing breast cancer. It also provides probabilities for carrying a *BRCA1* and *BRCA2* mutation. It was developed at the University of Texas Southwestern Medical Center at Dallas and the BayesMendle Group at Johns Hopkins University. The CancerGene software that runs this model is publically available for downloading at www4.utsouthwestern.edu/breasthealth/cagene/. This model incorporates other predictive models for heritable breast cancer, including the Claus model, the Couch model, the Shattuck-Eidens model, the Frank model, and a Bayesian probability model added by the developers of the BRCAPRO model (S. W. Fletcher, 2013). The BRCAPRO model includes information about both affected and unaffected relatives; thus, two cases of breast cancer in a family where there are only two females in a single generation are more significant than two cases of breast cancer in a family where there are 30 females in a single generation. This model, like the Claus model, does not take into account non-hereditary risk factors for breast cancer and is therefore likely to underestimate risk (Amir et al., 2010).

Other models. More than a dozen models exist to estimate the likelihood of developing breast cancer and/or that a *BRCA1/2* mutation is present (Parmigiani et al., 2007). Models vary by the specific family and personal history data used for the calculations, and for the different source populations the resulting estimations of risk will differ. Other models include Breast and Ovarian Analysis of Disease Incidence and Carrier Estimation (BOADICEA), the family history assessment tool (FHAT), Finnish, Myriad, NCI, University of Pennsylvania (Penn), and Yale University (Yale) (A. C. Antoniou et al., 2008; Parmigiani et al., 2007). The Tyrer-Cuzick model is also referred to as the IBIS model (Tyrer, Duffy, & Cuzick, 2004). The Tyrer-Cuzick model predicts 10-year risk for cancer development. This model is unique in that it takes into account both personal risk factors (as the Gail model) as well as the family history of breast and ovarian cancer (as the Claus model). The personal risk factors included in this model are age at menarche, parity, age at first childbirth, age at menopause, atypical hyperplasia, lobular carcinoma in situ, height, and BMI (Tyrer et al., 2004). This model includes the most comprehensive set of personal and family variable models and unlike the other models, it allows for the possibility of multiple genes of differing penetrance (Amir et al., 2010). The software for this model is available for download at www.ems-trials.org/riskevaluator/ with a disclaimer that the instrument is for research purposes only (S. W. Fletcher, 2013)

With the exception of the Gail model, models that use computer programs to calculate risk are not likely to be used by a woman herself. Given that these computer models are not designed with the intention of being used solely by the lay public, it is

likely that women will turn to their primary care providers to help understand risk and make informed decisions about surveillance options for breast cancer.

Breast Cancer Risk Assessment by Primary Care Providers

Medical doctors (MDs), nurse practitioners (NPs), and physician assistants (PAs) who specialize in primary care are on the front line in health care. Most often, matters of primary prevention and promotion of cancer screening tests fall to primary care providers. Primary care providers have a great opportunity to identify patients at elevated-risk for breast cancer and refer them for a formal risk assessment and possible genetic counseling as well as recommend appropriate risk-based prevention and early detection interventions. For many women who are at increased risk for breast cancer, their primary care provider is the main source of information about their breast cancer risk and what screening methods are appropriate (Keogh, McClaren, Apicella, & Hopper, 2011). Most primary care providers agree that assessing breast cancer risk is a primary care provider's responsibility (Sabatino, McCarthy, Phillips, & Burns, 2007). However, not all primary care providers assess a woman's risk for breast cancer or recommend risk-appropriate screening tests.

Primary care providers rarely use software to calculate breast cancer risk scores. In a cross-sectional survey of a nationally representative sample of 351 internists, family practitioners and obstetrician-gynecologists (OB-GYNs) Guerra, Sherman, and Armstrong (2009) found that although 88% of providers had discussed breast cancer risk at least once during the past 12 months, only 18% had used a software program to calculate the breast cancer risk. Physicians in the sample who were more likely to use software were OB-GYNs and those who had a family member with breast cancer, or who

had a greater knowledge of breast cancer risk. Similar findings are presented by Sabatino, McCarthy, Phillips, and Burns (2007), who found that 76% of primary care providers report they almost never calculate Gail scores; only 3% reported that they usually or always calculate risk by Gail score. It should be noted that of the software models presented, the Gail model is the most easily accessed and used. It does not require entering a pedigree or downloading specialty software. This study did not evaluate the use of models that rely heavily on family history such as the Claus model and the BRCAPRO model; therefore, it is unknown whether health care providers in this sample may have been calculating breast cancer risk using other models, but the likelihood of this is low. Models that rely heavily on family history are recommended for use in evaluating the need for more intensive screenings. These family history intensive models such as the Claus and the BRCAPRO are available to primary care providers; however, they are more difficult to use and require that software be downloaded. Literature in primary care journals explains the use of software for predicting risk such as the Gail model, the Claus model, and the BRCAPRO model (Afonso, 2009). Still, Berg et al. note in their discussion that physicians have less experience with these calculations (Berg et al., 2010).

Primary care providers are more likely to collect family history and information about personal risk factors as a means of assessing breast cancer risk rather than use computer software to quantify risk. In a study by Sabatino, McCarthy, Phillips, and Burns (2007), 71% of primary care providers report that they usually or always ask about family history. Fewer report asking about nonhereditary risk factors, including parity (48%), history of biopsies (40%), or age at menarche (35%)(Sabatino et al., 2007). Burke,

Culver, Pinsky, Hall, Reynolds, Yasui, and Press (2009) assessed primary care physicians' skills in assessing family history for breast cancer risk using unannounced standardized patient visits. They found that physicians collected sufficient family history to assess breast cancer risk 48% of the time when encounters involved a scenario with an anxious standardized patient at moderate risk, 100% of the time when encounters involved a patient with a strong maternal history of breast cancer, and 45% of the time when the patient had a strong paternal history of breast cancer (Burke et al., 2009). In other words, physicians frequently did not ask all of the family history questions they needed to ask in order to make an adequate risk assessment, and may not understand the dominant inheritance of breast cancer predisposing gene mutations (i.e., that paternal history is as important as maternal history). Furthermore, collecting sufficient data is not synonymous with interpreting it correctly and making correct recommendations.

Once a primary care provider has collected risk assessment, information may be shared with the patient (risk education and counseling), used to form recommendations for prevention and screening, used as a basis for ordering a genetic test, or used as a basis to make a referral to an oncology specialist or genetic counselor who can provide education and recommendations. In the study by Burke et al. (2009), 20% of primary care providers offered a numeric assessment of lifetime risk for breast cancer. Most often, however, primary care providers presented risk to their patients in words rather than numbers. Researchers found that physicians may convey the risk assessment in terms of "no increase," "slight increase," or "significant increase"; however, the most frequent way of describing risk was to state that it was "increased" without specifying the degree of increase. The authors note that the general statements about risk, "may reflect an

appropriately cautious approach to estimating risk-based on a single primary care visit; [i]t could also reflect a style of practice that is focused less on defining risk than on determining appropriate preventive strategies" (Burke et al., 2009, p. 355).

A common response by primary care providers to a patient's concern about breast cancer is to order a mammogram. In the study by Burke et al. (2009) where standardized patients presented for an unannounced visit, the physicians frequently recommended mammograms based on their interpretation of the patients' risk level. It is noteworthy that in the two high-risk cases, with a family history possibly indicative of a heritable high-risk mutation, physicians recommended mammography in 93% of patient encounters where the breast cancer was present in the maternal side of the family but only in 63% of the encounters where early onset breast and ovarian cancer was on the paternal side of the family (2009). The scenario with both breast and ovarian cancer on the paternal side of the family was a more concerning family history, yet mammography was not recommended 37% of the time. It should be noted that recommending magnetic resonance imaging (MRI) was not included as an outcome of the study because data collection was completed before MRI was added to guidelines for screening women at elevated-risk (Burke et al., 2009).

Screening Mammography and Magnetic Resonance Imaging (MRI)

Screening mammography is currently the most effective population-wide secondary prevention strategy to prevent morbidity and mortality related to breast cancer (Bleyer & Welch, 2012; Hellquist et al., 2011) Screening mammograms are x-rays of the breast used to detect breast cancer in women who are asymptomatic as opposed to

diagnostic mammograms that are used to diagnose breast cancer when a woman has breast symptoms or when she has had an abnormal screening mammogram. Mammography may be recorded using images created on standard x-ray film or digital images. Both methods use x-rays to produce the images; the difference is in the way the images are recorded. Digital mammography yields better results for women who have dense breasts and are pre- or peri-menopausal (Pisano et al., 2005).

Screening mammography is recommended for women as a method to discover breast cancer in earlier stages when treatment has a greater chance of success. Breast cancers found before they begin to cause physical symptoms are more likely to be smaller and less likely to have regional node involvement (American Cancer Society, 2014). In the U.S., recommendations vary about when average-risk women should begin screening and how often they should screen. The U.S. Preventive Services Task Force Services recommends mammography screening every other year beginning at age 50 and continuing until age 74 (U.S. Preventive Services Task Force, 2009). Other organizations, including the ACS, NCCN, and the American College of Obstetricians and Gynecologists (ACOG), recommend average-risk women participate in mammography annually beginning at age 40 (see Table 1.1). For women with elevated-risk for breast cancer, typically defined as $\geq$ 20% lifetime risk, many organizations recommend beginning mammography sooner and offering annual breast MRI as an adjunct to mammography (see Table 1.1).

Images created through magnetic resonance imaging (MRI) are created using magnetic fields rather than x-rays. MRI breast screenings have been found to have significantly higher sensitivity than mammography (Saslow, 2007). The evidence for

MRI screening recommendations is still emerging. In one large study involving women at elevated-risk for breast cancer, many of whom had dense breast tissue, the supplemental yield of MRI in detecting breast cancer was 14.7 per 1000 women; 68 MRI screenings would be needed (after negative mammography and ultrasound results) to detect one cancer (Berg et al., 2012). One concern about MRI breast imaging is that while there is a higher rate of cancer detection, there is also a higher rate of false-positive findings (Berg et al., 2012). As would be expected based on higher prevalence rates in high-risk women, false-positive rates with MRI screening are lower for women who have had breast cancer or for those with a family history of breast cancer (Berg et al., 2012; M. E. Brennan et al., 2009; S. Brennan, Liberman, Dershaw, & Morris, 2010). The current trend in guideline creating bodies has been to reserve MRI screening for women at elevated-risk.

Whether a woman who is at elevated-risk for breast cancer obtains an MRI screening or not depends on whether MRI screening is ordered by a prescriber and whether the woman follows through to get the test. Even in high-risk populations, health care provider recommendations for MRI are low (Cohen, 2010). Similarly, uptake of MRI testing by women is low. In a study of 1215 women at increased risk for breast cancer who were offered MRI screening free of charge as part of the study, 512 (42%) declined participation (Berg et al., 2010). Women in this study were more likely to participate if they had Gail or Claus lifetime risk estimates $\geq$ 25%; the most frequent reasons they gave for not participating in MRI were claustrophobia (25.4%) and time constraints or other priorities (18.2%) (Berg et al., 2010). Participants were told that their insurance provider would be billed if their personal physician agreed to provide a referral and that the study would cover any costs for MRI screening not covered by insurance; 47

women (9.2%) did not participate because the physician either would not provide a referral or did not believe that MRI screening was indicated (Berg et al., 2010). Screening for breast cancer with MRI appears to be less tolerable to women than mammography.

Communicating Information about Risk to At-risk Relatives

When a woman (counselee) receives genetic counseling and testing for potential hereditary breast and ovarian cancer syndrome (HBOC), a family pedigree is usually taken. A risk assessment is completed to determine if the woman would be a good candidate to have a blood test to look for a genetic mutation (Riley et al., 2012). After the blood test is completed, the counselor discusses with the woman her risk of developing cancer based on whether the test came back as positive, true negative, or indeterminate negative. Counselees are then encouraged to share that information with potentially at-risk family members. The National Society of Genetic Counselors (NSGC) has published guidelines for cancer risk assessment and counseling (Riley et al., 2012). They declare that an essential element of disclosure is to "identify at-risk family members and provide [the] patient with tools to inform and educate family members" (p. 158). Examples of tools that can be used to inform and educate family members include a family contact letter, website information, or referrals to genetic professionals (Riley et al., 2012).

While most genetic counselors consistently teach counselees about the implications of genetic health information for their close family members, most counselors do not contact family members directly. Generally, to preserve the autonomy and privacy of their patients, genetic counselors will leave it to the counselee to share information with family members. If family members refuse to share information with

relatives, then the genetic counselors should consider whether they have a duty to warn and consult with the ethics committee or HIPAA compliance officer at their institution (Riley et al., 2012, p. 158).

Summary letters and letters written specifically for at-risk family members are tools that counselees can use when sharing information with their at-risk relatives. In a study of 626 genetic health professionals, it was found that 79% always send a summary letter to the counselee after a consultation and 90% consistently share information about the familial implications of the pedigree; however, 41% never write letters specifically for at-risk family members (L. E. Forrest, Delatycki, Curnow, Skene, & Aitken, 2010).

Women often report sharing test information with their close relatives. In a study of 1,103 women who were tested for *BRCA* mutations, 97.5% reported communicating the test result to at least one blood relative within 4 months of testing. Of women who were positive for *BRCA* mutations, 99.5 reported telling at least one family member, of women who were true negative, 99.0% reported sharing, and of those who were uninformative, 96.7% reported telling at least one family member (Cheung, Olson, Yu, Han, & Beattie, 2010). While this study seems to indicate a high degree of information sharing, self-report by the counselees was the main outcome of interest. Researchers did not verify the outcomes with the family members themselves. Further, this study only asked counselees if they told family members about their own risk. It did not ask whether they explicitly stated how that information may apply to the close relative.

Close family members may be told about test results by the counselee; however, the information may not be transmitted with much accuracy. In a study of families where a member was tested for *BRCA 1/2* mutations, researchers followed the transmission of

information from the genetic counselor, to the counselee, and finally, to close family members. It was discovered that there is very little correlation between the information actually communicated and the recall and interpretation of that information by counselees and their family members (Vos, Menko, et al., 2011). Because counselees have a difficult time understanding risk information themselves, let alone interpreting it and teaching it to relatives, there have been calls for genetic counselors to guide counselees in the communication process or even inform relatives directly about test results and their risk if possible (Godard, Hurlimann, Letendre, & Egalite, 2006; Seymour et al., 2010; Stol, Menko, Westerman, & Janssens, 2010; Suthers, Armstrong, McCormack, & Trott, 2006; Vos, Jansen, et al., 2011). Further, there is some evidence that family members would prefer receiving risk information from a health care provider rather than from their family member (Tunin, Uziely, & Wolosik-Wruble, 2009).

Although in the future, different methods of delivering genetic risk information to at-risk family members may be employed, presently, the most common method of information dissemination within a family involves genetic counselors encouraging their counselees to spread the word within the family. The National Society of Genetic Counselors states that a counselor identifies disclosure as a key element in cancer risk assessment and counseling, noting that counselors should, "identify at-risk family members and provide [the] patient with tools to inform and educate family members (i.e. family contact letter, website information, referrals to genetic professionals)" (Riley et al., 2012). Family members who receive risk information from a close relative who has received genetic counseling then have the opportunity to respond to that information. The sharing of risk information within a family can influence risk perceptions. In the present

study, we evaluated the accuracy of risk perception in potentially at-risk family members when an extended member of the family has received genetic counseling.

Women who learn information from their close relatives about the relative's genetic counseling session may or may not share that information with their primary care providers. Kinney et al. (2006) found that counselees with uninformative results were much less likely to discuss their BRCA test results with their primary-care providers than those with positive results.

It is beyond the scope of the present study to assess actual knowledge transferred from counselees to sisters and daughters. This study focused on sisters' and daughters' self-rated understanding of genetic information that was shared. Ultimately, self-rated understanding of genetic information shared by a relative who received genetic counseling is a general sense that one has a working knowledge of the information, or that the information would be available for use. In this study, we aimed to determine whether self-rated understanding of genetic information contributes to accuracy of risk perception.

Theoretical Foundations: Self-regulation Theory and Response to Risk Information

This study was broadly based on the Common Sense Model of Self-regulation as presented by Leventhal et al. (2003) (see Figure 1.1). The constructs of the Common Sense Model were identified as the strongest among theoretical frameworks to help researchers understand "the process of developing and coping with perceptions of risk-based on family history information" (Sivell et al., 2008, p. 53). According to the Common Sense Model of Self-regulation, when faced with health threats (termed

stimuli), people will take actions (termed coping procedures) that result from their cognitive representations of danger and their emotional representations of fear (Leventhal et al., 2003). These actions are taken with the intent of controlling danger and fear and are considered to be parallel actions – occurring simultaneously and interacting with one another. Coping actions are then evaluated for their success in reducing the negative emotions cause by the health treats (fear control) and in reducing the threats themselves (danger control) (Leventhal et al., 2003).

Building on the Common Sense Model, Marteau and Weinman (2006) present an interpretation of the model that DNA risk information is a stimulus that can lead to coping actions that are dependent upon both cognitive and emotional representations. Marteau and Weinman use Self-regulation theory to "explain and predict the characteristics of risk information that are more and less likely to motivate behavior change" (2006, p. 1361). They propose that with DNA risk information as the stimulus, a main component of the cognitive representation of the health threat is perceived risk. The authors further propose that perceived risk is influenced by how well the risk information "fits" with people's preexisting ideas about the threat to health. Thus, people are more likely to take actions including risk reducing behaviors for a health threat with a genetic component if they understand that health threat to be genetic in origin.

In the proposed study, receiving DNA risk information was operationalized as the reported amount of information shared by her first-degree relative about the relative's genetic counseling session. This is the stimulus that results in cognitive representations – including risk perception and emotional representations of the health threat.

Other constructs known to influence risk perception were also taken into account. Tilburt et al. (2011) recently completed a systematic review of the literature related to risk perception in high-risk populations. The review included 53 studies, 64% of which focused on women at increased risk for breast cancer and most of which looked at women who had not personally been tested. This review has helped guide the selection of constructs that can influence risk perception and several were evaluated as covariates in the proposed study. The Tilburt model illustrates important demographic, clinical, and psychosocial factors (cultural, affective, personality, motivational, and cognitive) that are associated with perceived risk for cancer in populations at elevated-risk for cancer (see Figure 2.2). In this study, measured cognitive factors included health literacy, numeracy, and knowledge about breast cancer genetics. The affective factor distress was measured as the fear representation of the health threat. Demographic factors taken into account included age and education as these have been shown to influence perceived risk.

Perceived Risk and Accuracy of Risk Perception

Perception of risk plays a role in decisions people make about how to care for their health. Collins and Street (2009) define risk perception as, "a socially constructed perception about the likelihood of an adverse event built upon prior experiences and interactions" (p. 1507). The concept of risk perception is multifaceted, influenced by scientific, psychological, social, economic, and cultural factors (Collins & Street, 2009, p. 1506). Risk perceptions may be developed through both analytic reasoning and experiential reasoning, and while health care providers are more likely to rely on analytic reasoning, patients are more likely to rely on experiential reasoning (Collins & Street, 2009). Lipkus (2007) notes, "a comprehensive understanding of risk requires knowledge

of precursors (e.g., risk factors), likelihoods (probabilities), consequences, and the pros and cons of preventive actions necessary to control/ avert the harm if possible" (p. 696). Lipkus further notes that, "most recent conceptualizations of risk view risk as a combined function, often multiplicative, of the probability of loss and consequence of loss (e.g., severity of loss in the physical, psychological, social and economic realms" (2007, p. 697). This paper will focus primarily on the probability dimension of risk, especially comparative verbal and numeric risks and the accuracy of risk (see variable definitions and measures).

A primary goal of genetic counseling is to assist people to attain a more accurate perception of risk. It is believed that if people more accurately understand their risk, they are better prepared to take appropriate actions to reduce that risk (Haas et al., 2005). More studies have focused on risk perception than on accuracy of risk perception (Smerecnik et al., 2009; Tilburt et al., 2011).

Risk perceptions can be influenced either upwards or downwards when health care providers share information about likelihoods of disease. Information about risk can be shared using numeric, verbal, and visual formats (Lipkus, 2007). Health care providers tend to view risk communication as the effective transmission of precise information that is completed effectively if the patient understands risk as the health care provider does (Collins & Street, 2009, p. 1507). Patients, on the other hand, may focus more on experiential reasoning to understand risk communications drawing upon personal life experience and emotion (Collins & Street, 2009). Indeed, many women have difficulty interpreting risk information, especially when it is presented in a numeric format (Leventhal, Kelly, & Leventhal, 1999; Schwartz, Woloshin, Black, & Welch,

1997). Women tend to underestimate risk when using verbal comparative scales but over-estimate using numeric scales (Lipkus et al., 2000; Woloshin, Schwartz, Black, & Welch, 1999). This study used measures of both comparative numeric and comparative qualitative risk estimates to evaluate risk perception (see variable definitions and measures in Chapter 3).

Younger women who are at increased risk for breast cancer are more likely than older women to have accurate risk perceptions compared to the Gail model (Haas et al., 2005). An initial evaluation of the Gail model of 3,165 women found that women with the highest relative risk for breast cancer had the highest risk perceptions (Bondy, Vogel, Halabi, & Lustbader, 1992). These were the women with one or more first-degree relatives with breast cancer. Genetic counseling has been shown to increase accuracy of risk perception in counselees (Bjorvatn et al., 2007) and improvements may be maintained for at least 12 months (Watson et al., 1999). Women who received a written summary of genetic counseling results had greater accuracy of risk perceptions based on counselors' categorizations risk (Lobb et al., 2004).

In the age of personalized medicine, people are increasingly seeking information about their risk for a variety of conditions. While genetic counseling is one way to obtain information about risk, a variety of risk calculators are readily available on the internet including a calculator for estimating risk for disease, including risk for heart disease from the Mayo Clinic: http://www.mayoclinic.com/health/heart-disease-risk/HB00047, a calculator to estimate colorectal cancer risk from the National Cancer Institute: http://www.cancer.gov/colorectalcancerrisk/ , and a type II diabetes risk calculator from the American Diabetes Association: http://www.diabetes.org/diabetes-

basics/prevention/diabetes-risk-test/ . The intent of providing risk information through these tools is to motivate users to act to reduce their risk (Cameron, Marteau, Brown, Klein, & Sherman, 2011). People are also willing to pay for their own DNA risk information. According to their web page, over 200,000 people have been genotyped using 23 and me: https://www.23andme.com/.

Health Literacy

Health literacy is defined as the "degree to which individuals have the capacity to obtain, process, and understand basic health information and services needed to make appropriate health decisions" (U.S. Department of Health and Human Services, 2000). Analysis from the 2003 National Assessment of Adult Literacy found that 36% of U.S. adults have limited health literacy. Nationally, higher levels of education are associated with higher levels of health literacy, and living below the poverty level is associated with lower levels of health literacy (Kutner, United States Dept. of Education., & National Center for Education Statistics., 2006). Low health literacy has been associated with poor health outcomes, including more hospitalizations, greater use of emergency care, and lower ability take medications as directed (Berkman, Sheridan, Donahue, Halpern, & Crotty, 2011). Differences in health literacy are consistently associated with lower use of mammography (Berkman et al., 2011).

Adequate health literacy is necessary for women to understand their genetic risk and make decisions about which prevention and screening measures they would like to undertake (McBride, Koehly, Sanderson, & Kaphingst, 2010). Brewer, Tzeng, Lillie, Edwards, Peppercorn, and Rimer, (2009) studied posttreatment female breast cancer survivors (N=163) finding that women with lower levels of health literacy give higher

estimates for recurrence risk for a hypothetical scenario about women with early-stage breast cancer. Additionally, their estimates were more variable when provided in a numeric format (0% to 100%) but less variable when provided in a verbal format ("low" or "high"). Health literacy affects the variability in numbers chosen to interpret verbal descriptions of risk, even when controlling for age, income, race, and actual recurrence risk (Brewer et al., 2009).

Numeracy

Health numeracy is considered by many to be an important subcomponent of health literacy (Squiers, Peinado, Berkman, Boudewyns, & McCormack, 2012). Health numeracy is defined as the "degree to which individuals have the capacity to access, process, interpret, communicate, and act on numerical, quantitative, graphical, biostatistical, and probabilistic health information needed to make effective health decisions" (Golbeck, Ahlers-Schmidt, Paschal, & Dismuke, 2005, p. 375). Increasingly, people are presented with numerical health information for the purpose of making health decisions that will reduce risk and improve health outcomes (Reyna, Nelson, Han, & Dieckmann, 2009).

Low health numeracy has been shown to distort risk perceptions and understanding of risks and benefit of screenings, reduce medication adherence, impede access to treatments, and hamper risk communication (Reyna et al., 2009). Innumeracy has been associated with overestimation of risk for breast cancer (Schapira, Davids, McAuliffe, & Nattinger, 2004).

Measurement of Numeracy

Health numeracy has been measured in a variety of ways. Some scales ask participants to rate their own numeracy skills for a self-assessed numeracy measure (Fagerlin et al., 2007). However, other researchers have proposed that these types of scales may be measuring individual difference in confidence as opposed to the ability to understand and use numeric information (Weller et al., 2012). One of the original ability-based measures of numeracy was developed by Schwartz, Woloshin, Black, and Welch (1997) and included three items that assessed individuals' abilities to use the mathematical concepts of probability, proportions and percent. Lipkus, Samsa and Rimer, (2001) saw the need for an expanded instrument to assess health literacy because many people including highly educated individuals scored poorly on existing numeracy instruments. A longer instrument was needed to capture a broad range of abilities. Others have added questions and developed more instruments in an attempt to measure numeracy. In 2012, Weller et al. published the results of a psychometrically improved measure of numeracy developed through a Rausch analysis of 18 items pulled from existing numeracy scales. The resulting eight-item scale purports to assess a broader range of ability than previous skills while at the same time avoiding keeping subjective perceptions. The Rausch-based numeracy scale combines five questions from a numeracy instrument developed by Lipkus, Samsa, and Rimer (2001), expanded one of the original measures of numeracy developed by Schwartz, Woloshin, Black, and Welch (1997), and two questions from the cognitive reflection test (CRT) developed by Frederick. Less numerate individuals report higher risk perception (Dieckmann, Slovic, & Peters, 2009). Numeracy has been shown to correlate with a patient's ability to interpret numerical

estimates of breast cancer treatment effectiveness (Lipkus, Peters, Kimmick, Liotcheva, & Marcom, 2010)

Knowledge About Breast Cancer Genetics

Knowledge about the hereditary nature of cancer in the family has been positively associated with risk perception in families at risk for bowel cancer (Glanz, Grove, Lerman, Gotay, & Le Marchand, 1999). Tilburt et al. (2011) identify awareness of hereditary risk as a cognitive factor that influences perceived risk. Key outcomes of genetic counseling for breast cancer include improved knowledge about personal risk and knowledge about breast cancer heredity (Braithwaite, Emery, Walter, Prevost, & Sutton, 2006). As noted above, although extended family members do not always attend genetic counseling sessions, a summary letter is sent with the person who received counseling and instructions that they should share information with extended family members, and encourage them to seek care from health care providers to help them understand their risk for breast cancer (Hayat Roshanai, Lampic, Rosenquist, & Nordin, 2010). Recommendations of the National Society of Genetic Counselors specify that an essential element of genetic cancer risk assessment counseling includes identifying at-risk family members, regardless of whether genetic test results came back as positive, negative, or indeterminate negative (Riley et al., 2012). In addition, genetic counselors are to provide their patient with the tools they need to inform and educate family members about breast cancer and their personal risk; examples of tools include website information, a family contact letter, and referrals to genetic professionals (Riley et al., 2012, p. 158). Therefore, it can be expected that genetic counseling may have an impact on knowledge about breast cancer heredity and breast cancer risk among other family members at risk. Indeed, most

people who attend genetic counseling report that they do share information with their close relatives (Hayat Roshanai et al., 2010). In the present study, counselees who received genetic counseling through the REACH study were provided with pamphlets containing information about breast cancer genetics. These pamphlets could be used by counselees to educate themselves or family members about breast cancer genetics.

According to the Common Sense Model of Self-regulation of Health and Illness Behavior by Leventhal (2003), people respond to an internal or environmental stimuli with the parallel processes of cognitive and emotional responses in attempt to make sense of the health threat. In the present study, we are looking at the genetic counseling of a first-degree relative as a stimulus. When a family member who received genetic counseling shares the results of the counseling sessions and results of genetic tests with their close relatives, they are sharing personal genomic information that pertains to both themselves and their close family members. Close family members then will respond to that genetic risk information with both cognitive and emotional responses (Marteau & Weinman, 2006). In this study, knowledge about breast cancer heredity was assessed as a cognitive response to receiving DNA risk information. Further, awareness of hereditary risk is an important cognitive component of perceived risk (Tilburt et al., 2011).

Cancer-related Distress

The construct of distress relates to responses including intrusive thoughts and avoidance reactions experienced as a result of a particular life event or particular life circumstances (Zakowski et al., 1997). A variety of terms have been used to indicate distress about cancer, including cancer, worry, cancer anxiety, fear of cancer, cancer-related distress, and cancer-specific distress (Hay, Buckley, & Ostroff, 2005). Some have

differentiated worry and fear by noting that worry pertains to feelings and thought processes whereas fear includes physiologic responses (Champion et al., 2004). The terms worry and distress are used fairly interchangeably; for example, researchers have measured distress with worry scales (Henderson et al., 2008) and worry with scales developed to measure distress (Patenaude et al., 2013). It is thought that worry and distress are highly interrelated because worry promotes intrusive thoughts (distress) therefore distress is a product of worry (McCaul & Goetz, 2008)

Cancer-related distress and increased perception of risk for future breast cancer have been found to be associated with one another (Tilburt et al., 2011). Cancer-related distress has also been prospectively associated with increased uptake of screening mammography (Erblich, Bovbjerg, & Valdimarsdottir, 2000; Hay, McCaul, & Magnan, 2006). In women with a family history of breast cancer, perceived risk has been positively correlated with anxiety and both the intrusion and avoidance subscales on the impact of events scale (Erblich et al., 2000). Breast cancer-specific distress in women who are at increased risk for hereditary breast cancer is significantly related to having at least one sister affected with breast cancer and to being involved with a family member's breast cancer diagnosis and treatment (van Dooren et al., 2005).

Summary

A primary function of cancer genetics services is to provide patients with risk information. Accurate perceptions are a basis for informed decision making. Women who underestimate their risk for breast cancer may choose not to discuss their family history and risk with their primary care providers or may not take advantage of screenings that can catch breast cancer in earlier stages when it is more easily and successfully treated.

Alternatively, women who over-estimate their risk may experience higher levels of anxiety or push for inappropriate screenings.

When a woman receives genetic counseling for breast cancer, she is encouraged to share genetic information, including risk information, with her relatives. Counselees are instructed that close family members may be at increased risk for developing breast cancer and that they should discuss risks and screening plans with their primary care providers. This cross-sectional study explored how close relatives of counselees perceived their risk. Using a statistical analysis with latent variables, we assessed whether genetic information shared by the counselee contributed to accuracy of risk perception above and beyond other factors known to contribute to risk perception. This study also examined self-reported screening behaviors and report of screening recommendations received from PCP by women who are close relatives of counselees. We calculated risk estimates using BRCAPRO and Claus models to determine how many women were at elevated-risk for breast cancer and of those, how many have received recommendations for breast screening with MRI. Additionally, historical data were collected to describe when, how, and what genetic information was shared within the family and with primary health care providers (see Appendix C).

Study results have advanced our knowledge about close family members of women who have received genetic counseling for breast cancer. This important population may carry higher than average-risk for breast cancer and may not have accurate understanding of recommended screenings based on their level of risk. Increased understanding about information needs in this population will inform future intervention

research aimed at providing family members with tools and information needed to make informed decisions based on personalized genetic information.

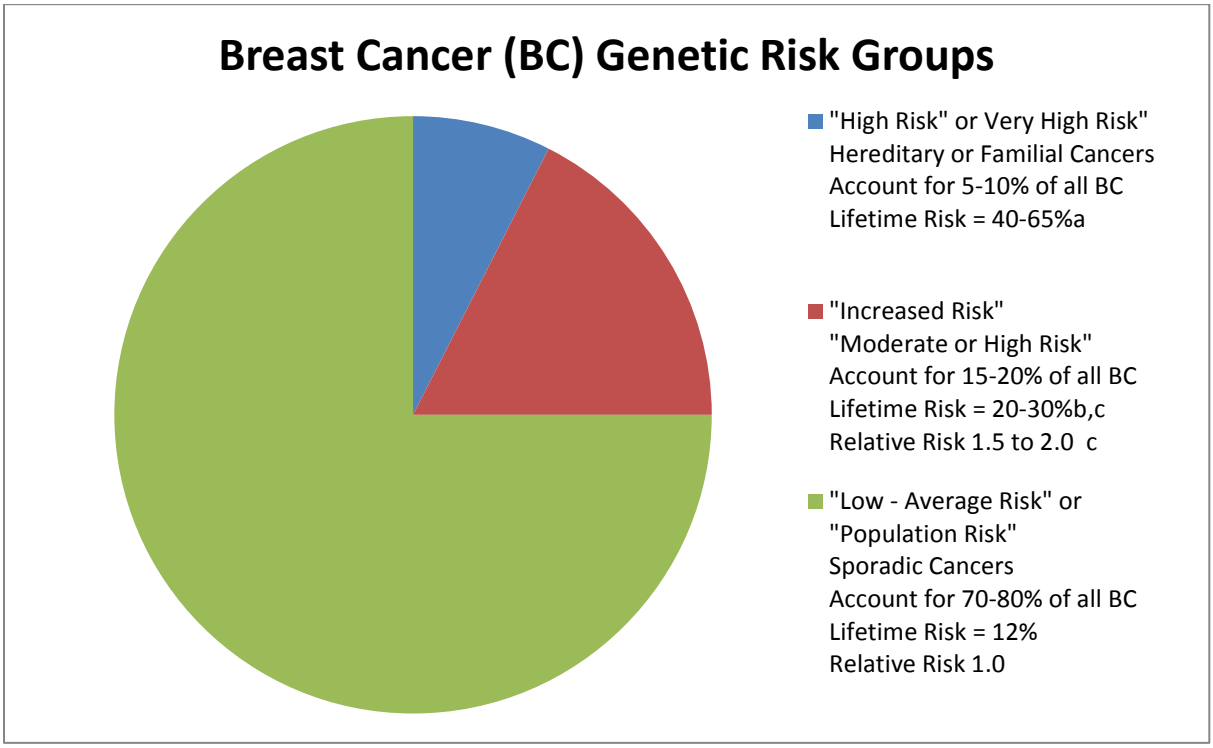


Figure 2.1
Breast cancer genetic risk groups
[a] (Hilgart et al., 2012)
[b](National Cancer Institute, 2014b)
[c](National Cancer Institute, 2012a)
[d](Foulkes, 2008)

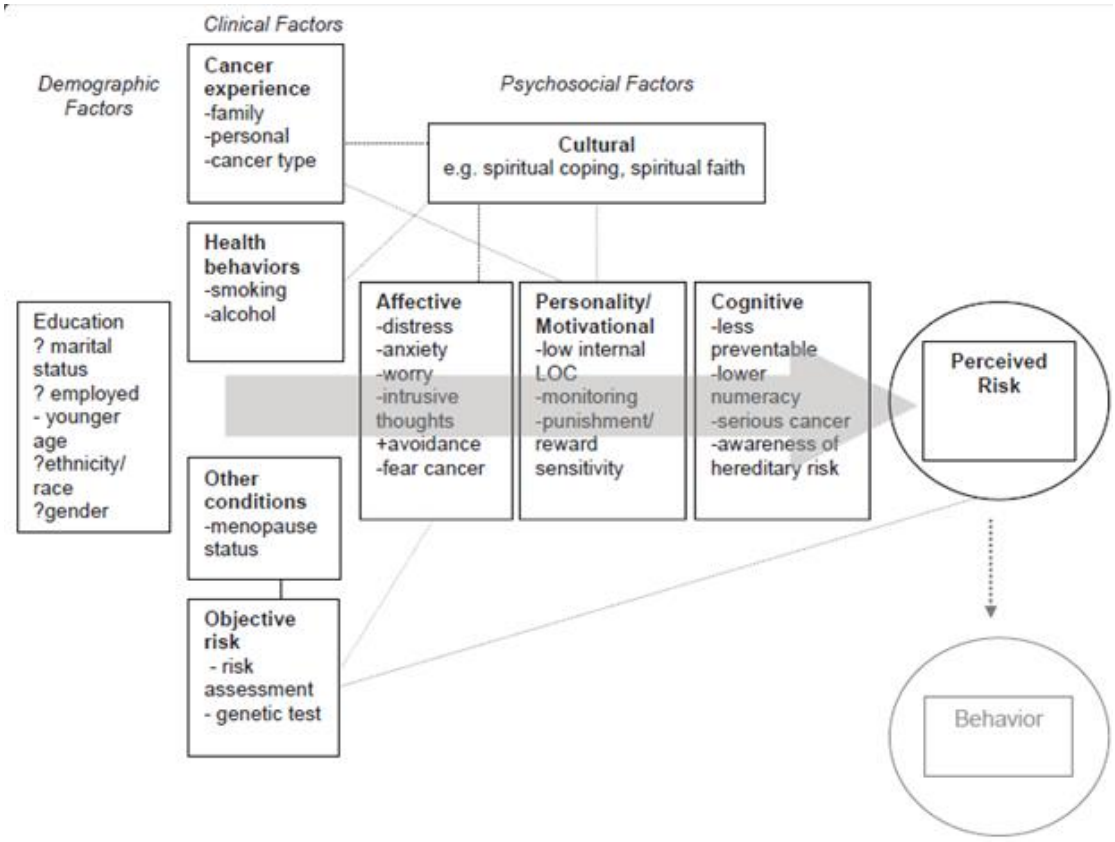


Figure 2.2
Tilburt's model of risk perception in high risk populations (Tilburt et al., 2011, p. 11)

Table 2.1

Genes associated with heritable breast cancer

Syndrome Name	Germline Mutations in (gene):	Breast Cancer Risk % by age	Associated Cancers/ Disorders
Hereditary Breast and Ovarian Cancer (HBOC)	*BRCA1*	44-78% by age 70[a]	Early-onset breast cancer Ovarian cancer Pancreatic cancer Male breast cancer Testicular cancer Early-onset prostate cancer
Hereditary Breast and Ovarian Cancer (HBOC)	*BRCA2*	31-56% by age 70[a]	Early-onset breast cancer Male breast cancer Ovarian cancer Prostate cancer Melanoma Pancreatic cancer
Li-Fraumeni Syndrome	*P53*	50% by age 50 [b]	Childhood sarcoma Brain tumors Leukemia Adrenocortical carcinoma [b]
Cowden Syndrome	*PTEN*	25-50% Lifetime [b]	Multiple hartomas Breast cancer Gastrointestnal malignancies Endometrial cancer Thyroid disease Trichilemmomas Oral fibromas Papillomas Acral, palmar, plantar keratosis
Peutz-Jeghers Syndrome	*STK11*	32-54% by age 60-70	

[a] (A. Antoniou et al., 2003)
[b] (National Cancer Institute, 2012b)
[c] (Foulkes, 2008)

Table 2.2

NCCN criteria for referral to cancer genetics professional

Affected individuals with one or more of the following:

- A known mutation of breast cancer susceptibility gene in family
- Early-age-onset breast cancer
- Triple negative (ER-, PR-, HER2-) breast cancer
- Two breast cancer primaries in a single individual
- Breast cancer at any age, and
    - ≥1 close blood relative with breast cancer <50 y, or
    - ≥1 close blood relative with epithelial ovarian cancer at any age, or
    - ≥2 close blood relatives with breast cancer and/or pancreatic cancer at any age
    - From a population at increased risk
- ≥1 family member on same side of family with a combination of breast cancer and ≥1 of the following (especially if early onset): pancreatic cancer, aggressive prostate cancer (Gleason score ≥7); sarcoma, adrenocortical carcinoma, brain tumors, endometrial cancer, leukemia/lymphoma; thyroid cancer, dermatologic manifestations and/ or macrocephaly, hamartomatous polyps of GI tract; diffuse gastric cancer
- Ovarian cancer
- Male breast cancer.

An unaffected individual with a family history of one or more of the following:

- A known mutation in a breast cancer susceptibility gene within the family
- ≥2 breast primaries in a single individual
- ≥2 individuals with breast primaries on the same side of the family (maternal or paternal)
- First- or second-degree relative with breast cancer ≤45 y
- ≥1 family member on same side of family with a combination of breast cancer and ≥1 of the following (especially if early onset): pancreatic cancer, aggressive prostate cancer (Gleason score ≥7); sarcoma, adrenocortical carcinoma, brain tumors, endometrial cancer, leukemia/lymphoma; thyroid cancer, dermatologic manifestations and/ or macrocephaly, hamartomatous polyps of GI tract; diffuse gastric cancer
- Male breast cancer

(National Comprehensive Cancer Network, 2013c, pp. BR/OV-1)

CHAPTER 3

RESEARCH DESIGN AND METHODS

Sample

The sample was recruited from relatives of breast cancer patients enrolled in a pilot study who have agreed to be contacted for cancer-related research studies. The objective was to include 100 women ages 40 to 74, of all races and ethnicities, who are fluent in English and live in any state in the United States. Participants did not have a personal history of breast or other type of cancer besides nonmelanoma skin cancer, and did not have had a bilateral mastectomy. Women who participated in this study had biological sisters or mothers who had previously been diagnosed with breast cancer, received genetic counseling, and had a *BRCA1/2* genetic test with indeterminate negative results. From here forward, the relatives who had breast cancer and received genetic counseling and testing will be referred to as the counselees. Counselees were not the participants in the proposed study; however, it is important to understand the background of the counselees because they are the women who received genetic counseling and may have shared that information with the proposed study participants. The counselees are also the ones who referred their relatives into the pilot study from which the proposed study will sample. The following paragraphs describe the counselees.

The study recruited relatives from two groups of counselees. The first group of counselees included women who participated in the *Risk Education & Assessment for*

Cancer Heredity (REACH) study (P.I. Anita Kinney, PhD, RN) and had *BRCA1/2* testing with indeterminate negative results. REACH study participants were identified through the Utah Population Database (UPDB) and recruited through the Utah Cancer Registry. The REACH study provided standardized in-person or telephone genetic counseling to those who met the NCCN criteria for referral for genetic counseling for *BRCA1/2* testing (National Comprehensive Cancer Network, 2013c). These women were offered genetic testing if appropriate. All women received an educational brochure about *BRCA1/2*-related cancer risks, genetic testing, hereditary and familial risk, and recommended medical management (e.g., screening guidelines) for women who underwent testing. Posttest counseling was provided along with standardized summary letters alerting them to the possibility that close relatives may be at increased risk for breast cancer and may need more intensive breast cancer surveillance, (possibly including MRI) and encouraging counselees to share this information with their close relatives and to encourage the close relatives to, in turn, share that information with their primary care providers.

The second group of counselees included patients who received genetic counseling and testing through the Family Cancer Assessment Clinic (FCAC) at Huntsman Cancer Institute. The High Risk Breast Cancer Clinic also follows the practice of sending genetic counseling summary letters. First-degree female relatives of counselees who attended genetic counseling through FCAC may be different from relatives of women contacted through women who received genetic counseling through the REACH study. Women attending FCAC have either self-referred for genetic counseling or have been referred by a concerned clinician. Women who self-refer for

genetic counseling may have a stronger concern about their family history of cancer and concern for how it may affect other family members and thus may be more likely to share information about risk than women enrolled through the REACH study. It was thought it would be helpful to have women in the study who have been referred by counselees from both settings because one group is likely to be representative of families who either are not aware of their family history, not as concerned, or do not have the resources to seek out specialized counseling, whereas the other group is likely to be more representative of women who were either concerned themselves, or had a primary care provider concerned enough, to refer them to the clinic, and had access to the resource.

Counselees from both recruitment sources received their counseling between the fall 2010 and 2013. Therefore, participants in the present study had family members who received counseling a few months prior to our contact with them to up to 2 1/2 years prior to our contact with them. Most of the participants received counseling at least a year or more prior to our contact with them. Data about the time of the family member's counseling was to be collected as a part of this study and evaluated in terms of its effect on self-reported understanding about genetic information shared by the counselee as well as accuracy of risk perception. We expected that most of the participants in the proposed study would have talked with their relatives about the relatives' genetic counseling because they were referred into the study by their relatives. Participants in the present study (women with a family history of cancer) may not have gone immediately to their primary care providers to discuss their risk for breast cancer upon hearing about the counselee's genetic counseling session. They may have waited until their next physical exam if they discussed the counseling at all. Many women have physical exams every 1

to 2 years. If a primary care provider makes a recommendation for screening mammography or screening breast MRI for a participating woman with a family history of breast cancer, she may not immediately obtain the test. The cross-sectional design of present study was intended to allow for analysis of the effect of time since relatives' counseling on variables such as accuracy of risk perception, self-report of discussing genetic information with primary care provider, and self-report of screening plans and screening actions. Information gathered about the effect of time on these variables was intended to future studies designed to assess the impact of receiving personalized genetic information.

Counselees from both groups described above were asked by REACH investigators to provide contact information for their sisters and daughters. Those sisters and daughters were then asked to participate in a survey that aimed to collect preliminary data for a planned breast cancer prevention study involving genomic risk information targeting at-risk women who have relatives with a personal history of breast cancer who received indeterminate negative *BRCA1/2* results. Unaffected women with a family history of breast cancer who agreed to participate completed a single questionnaire. Participants were asked if they would be willing to be contacted in the future for cancer-related research. Only women who indicated they would be willing to have future contact were invited to participate in the proposed study.

Inclusion and Exclusion criteria

Included participants were of any race, aged 40-74 years, fluent in English, had a mother or sister who received genetic counseling during 2010-2013 for possible hereditary breast cancer, and had indicated that they would be willing to be contacted for

future research. The counselee's mother or sister(s) were tested for *BRCA1/2* mutations, received indeterminate negative results, and received a genetic counseling summary letter. Potential participants were excluded if they had a personal history of any type of cancer (except nonmelanoma skin cancer), had received genetic counseling or testing themselves, had bilateral mastectomy, lived outside the USA, or were incarcerated.

Human Subjects Protections

Institutional Review Board (IRB) approval for the REACH Project and the pilot study (P.I. Anita Kinney) was granted through the University of Utah. Additionally, both studies (from which participants for the present study were recruited) were approved by the University of Utah Clinical Cancer Investigations Committee (CCIC), Utah Cancer Registry (UCR), and Resource for Genetic and Epidemiologic Research (RGE).

For the present study, IRB approval was obtained from the University of Utah and was considered primary. Additionally IRB deferral was obtained from Brigham Young University because of Deborah O. Himes' employment. Two research assistants were hired to assist with data collection and data entry. All study personnel completed appropriate Collaborative Institutional Training Initiative (CITI) and HIPAA training. All data collected from participants are stored in a locked office and on encrypted key drives stored in locked file cabinets. Only approved research personnel have access to this data.

Procedures

After IRB approval, REACH staff provided Deborah O. Himes P.I. with a list of REACH-pilot participants who have indicated they would be willing to participate in future research. Names and contact information were sent via the encrypted email system

approved for transferring personal health information. Data were collected from two sources: a mailed packet and a telephone interview. The following sections describe the procedures in more detail. The initially conceived timeline is illustrated in Figure 3.1: Initial Project Timeline.

Recruitment

Once contact information for potential participants was obtained, an introduction and consent cover letter was sent to potential participants (see Appendix A). The letter introduced the study and alerted the women to expect a telephone call within about a week. During the telephone call, verbal consent to participate was obtained. Those declining to participate were asked to provide the primary reason that they declined participation and to provide their age, education, and self-described race/ethnicity so that differences between participants and nonparticipants can be evaluated. Women who completed the study were thanked for their time with a $25.00 visa gift card once all data were collected.

Data Collection

Data were collected from two sources: a paper and pencil packet that will be mailed and a telephone interview (see Appendix B for the survey packet and Appendix C for the telephone interview). Women who agreed to participate were instructed that a survey packet would be sent in the mail. The packet included written survey questions that took approximately 15 minutes to complete based on testing with two women in ages 50 and 60. A stamped and addressed return envelope was included for women to mail the survey back. Participants were asked to fill it out and mail it back quickly after

receiving it. If women agreed to participate during the recruiting telephone call, an appointment for the telephone interview was for 2 to 3 weeks in the future at a mutually agreed upon day and time. Two to 3 weeks was selected to allow enough time for the woman to receive the packet in the mail, fill out the forms, and mail them back. A reminder telephone call was placed if the survey has not been received back by 7 days ahead of the scheduled interview. If the packet was received back prior to the telephone interview, it was be reviewed for accuracy so that unanswered questions could be clarified during the telephone interview, if possible, to minimize missing data. The packet included questions about demographics, perceived risk, distress, health literacy, numeracy, and knowledge about breast cancer genetics. Additionally, the packet included a family history form that women were asked to mail back. This form helped facilitate obtaining pedigree information during the telephone interview (see Appendix B).

During the telephone interview, answers to any unanswered survey questions were obtained if possible and answers to questions were clarified if needed. Data were collected about women's understanding of information shared by their sisters or mothers about their genetic counseling sessions, breast cancer screening plan and recommendations, and the pedigree and health history information necessary to complete the Gail, Claus, and BRCAPRO instruments (see Appendix C). The reason for collecting pedigree and screening information on the phone was to ensure accuracy and completeness of the data. The telephone interviews took approximately 40 minutes to complete. The initial plan was to audio tape the telephone if participants agreed and that participants would not be excluded if they refused audio taping. At the conclusion of the telephone interview, women were instructed that estimates of lifetime risk for breast

cancer would be calculated based on the pedigree information they provided. Women were asked if they would like to have information about personal risk for breast cancer once the calculations were completed. If women wanted the information, a letter was be sent with the lifetime risk calculations along with the thank you letter (see Appendix D). Participants who received risk information were encouraged to share that information with their primary care providers. After all data were collected from both the survey and the telephone interview, a $25.00 visa gift card and thank you letter was sent as a thank you. The thank you letters included a web address published by the National Society of Genetic Counselors that can be used to find a genetic counselor by zip code as well as contact information for the Family Cancer Assessment Clinic in case participants wanted more information.

Variable Definitions and Measures

Guided by the Common Sense Model of Self-regulation (see Figure 1.1), a structural equation model (see Figure 3.2) was developed to determine the contribution of understanding of information shared about genetic counseling sessions to the accuracy of a woman's perception of individual risk for breast cancer controlling for the confounding influences of demographic, cognitive, and emotional factors known to contribute to risk perception. Variables were selected for the model based on important constructs identified in Tilburt's Model of Risk Perception in High Risk Populations (see Figure 2.1). The following sections describe variables and measures that will be used in the proposed study.

Perceived Risk

The latent variable, perceived lifetime risk for breast cancer, was measured using two instruments that evaluate comparative quantitative and qualitative estimates of lifetime risk for breast cancer. The reliability of these instruments as a measure for the overall construct of perceived risk was to be deemed good if the measurement error is small. If the coefficients of the relationships between the measured variables and the constructs are high, then these instruments would be deemed valid measures of the construct. The qualitative item was asked first based on work by Taylor et al. (2002), which found that asking for qualitative comparative rating of risk before asking for other estimates of risk resulted in more accurate risk perceptions. In that study, the other questions about risk included numeric estimates for quantitative population risk and quantitative personal risk without anchors. Using an anchor of population risk has been shown to increase accuracy of risk estimates (Apicella et al., 2009; Dillard, McCaul, Kelso, & Klein, 2006).

Qualitative risk perception. To evaluate qualitative risk perception, we asked, "In your opinion, compared to other women your age, what are your chances of getting breast cancer?" with five Likert type options ranging from "much lower" to "much higher." A "don't know" option was also be included. This is the same question format used in the REACH study when women were asked about their risk of getting breast cancer or having it recur. This will allow for potential future secondary analysis of concordance of risk perception between first-degree relatives.

***Comparative quantitative risk perception*.** To measure comparative quantitative perceived risk, women were presented with a graphic of 100 women (see Appendix B).

Twelve women were shaded. The question read, “On average, 12 women out of 100 will get breast cancer in their lifetime. This is a picture with 12 women shaded dark.” This statement offers women a basis for comparison or an “anchor” for what is normal or average. The question went on to state, “Picture yourself in a room with 100 women exactly like you. How many of you will get breast cancer in your lifetime? Please pick a number between 0 and 100. ” This latter half of this statement used wording by Schapira et al. (2004, p. 666). A frequency format with a graphic has been shown to have a lower risk estimation error when compared to the percentage scales when estimating lifetime risk for breast cancer (Schapira et al., 2004, p. 668). This format has been used in recent work; Cameron et al. (2011) purport that “individuals may comprehend risk estimates better when they are presented graphically” (para. 11). Providing women with the graphic with 12 of 100 women shaded and providing them with the information that “on average 12 women out of 100 will get breast cancer in their lifetime” provides an anchor or a context within which women can make their estimates. This method was used by Cameron et al. (2011) in a study of communication strategies related to genetic risk .

Calculated Risk

Calculated risk was assessed using three models: Claus, BRCAPRO, and Gail. Questions related to risk calculations were asked over the telephone as these are more difficult questions with some foreign terminology that may need to be explained. Only the Claus and BRCAPRO models were be used as indicators of the latent variable calculated risk because participants had family histories for breast or ovarian cancer significant enough to warrant genetic counseling and testing in the family. A discussion of these risk calculators can be found in Chapter 2.

Accuracy of Perceived Risk

Studies operationalize accuracy of perceived risk in many ways. In the present study, the accuracy of perceived risk were be assessed as the coefficient of the path between the latent variable "calculated lifetime risk for breast cancer" measured by the three breast cancer risk models and the latent variable "perceived lifetime risk for breast cancer" as measured by the comparative quantitative estimate and the comparative verbal estimate of risk. A beta weight of 1.0 would be perfect accuracy (see Figure 3.2).

Demographics

Demographics included age, marital status, highest education level attained, race/ethnicity, income, health insurance coverage, type of primary health care provider (if any), and historical questions about how information related to the genetic counseling session and summary letter was shared between the relatives. Demographics to be included in the initial path analysis include age and education because they have been shown to be associated with perceived risk (Tilburt et al., 2011).

Health Literacy

Self-assessed health literacy was measured using the Set of Brief Questions developed by Chew, Bradley, and Boyko (2004). This instrument was selected because it offers a practical way to identify patients with low health literacy. Being only three questions, it will not add a great deal to participant burden. Questions ask individuals to rate their difficulty understanding written and verbal information in the health care setting on a five-point Likert scale. The questions about how often help is needed to read hospital materials and how often one has problems learning about a medical condition

range from “never” to “always.” The question about confidence in filling out medical forms ranges from “not at all” to “extremely” (see Appendix B).

Content validity for this instrument is supported because investigators based questions on domains of health literacy described in qualitative research (Baker et al., 1996; Chew et al., 2004). Both reliability and criterion-related validity has been supported using areas under the curve receiver operating characteristic (AUROC) when compared to the two most commonly used measures of health literacy, the Rapid Estimate of Adult Literacy in Medicine (REALM) and the Short Test of Functional Health Literacy in Adults (STOFHLA) (Baker, 2006; Davis et al., 1993; Parker, Baker, Williams, & Nurss, 1995). The instrument was compared to the STOHFLA in a population of 332 Veterans’ Administration clinic. The three questions, (1) “How often do you have someone help you read hospital materials?”, (2) “How confident are you filling out medical forms by yourself?”, (3) “How often do have problems learning about your medical condition because of difficulty understanding written information?”, had areas under the receiver operating characteristic curves (AUROC) of 0.87 (95%CI=0.78-0.96), 0.80 (95% CI= 0.67-0.93), and 0.76 (95%CI=0.62-0.90), respectively (Chew et al., 2004). When compared to the REALM in 305 English-speaking adults in a university-based primary care clinic, the single question “How confident are you in filling out medical forms by yourself?” had an AUROC of 0.82% (95% CI=0.77to 0.86) in detecting limited or marginal health literacy. Adding one or both of the other screening questions did not significantly increase the AUROC for limited or marginal health literacy (Wallace, Rogers, Roskos, Holiday, & Weiss, 2006).

Numeracy

Numeracy was measured using the Rausch-based numeracy scale recently developed by Weller, Dieckmann, Tusler, Mertz, Burns, and Peters (2012). This instrument includes eight items that assess the users' ability to understand, manipulate, and use numerical information including probabilities (see Appendix B). Questions reauired participants to answer mathematical questions and analyze information from a table.

Reliability for the Rausch-based numeracy scale is supported by a Cronbach's alpha of .71 in three separate samples recruited to reflect ranges of education levels (total n=1970). Because this Rausch-based numeracy scale is newly developed, there are not further studies with Cronbach's alpha to report. However, this newly created instrument is a compilation of questions from previously developed instruments for measuring numeracy. This instrument with eight items had higher alpha values than any of the earlier instruments when administered to the same sample (Weller et al., 2012). Internal consistency is further supported with a mean interitem correlation of r=.24 (Weller et al., 2012). This level of interitem correlation is near optimal when measuring a broad, higher-order construct (Clark & Watson, 1995, p. 316).

Predictive validity is supported because the Rausch-based numeracy scale was able to predict performance on tasks that involved understanding and application of mathematical principles (Weller et al., 2012). An advantage of this scale over previously developed instruments is that it approached normal distribution in the two large samples in which it has been tested, allowing numeracy to be treated as a continuous rather than a dichotomous variable.

This new scale represents a composite of four previously developed scales (Frederick, 2005; Lipkus et al., 2001; Peters, Dieckmann, Dixon, Hibbard, & Mertz, 2007; Schwartz et al., 1997). The scale was developed to address limitations of the previous instruments. Previous instruments were skewed and less successful at predicting various levels of numeracy with some being more difficult and some being too easy. For example, when the cognitive reflection test was administered to a group of highly numerate students from highly respected universities, over 60% of students scored either zero or one on the three-item test (Frederick, 2005). With the Lipkus et al. (2001) instrument on the other hand, nearly a third of participants were able to answer all eight items correctly, indicating an inability of the Lipkus instrument to discriminate at the upper levels of the latent trait. This Rausch-based numeracy scale is able to discriminate among a broader range of numeracy, and yields a more normal distribution of results (Weller et al., 2012). This instrument is an objective measure of numeracy as opposed to instruments that ask participants to describe their comfort/ ability to use numbers in a subjective way. The Rausch-based numeracy scale assesses a range of numeracy abilities with minimal subject burden.

Knowledge About Breast Cancer Genetics

In this study, breast cancer genetic knowledge was be measured using the 27-item Breast Cancer Genetic Counseling Knowledge Questionnaire (BGKQ) (Erblich et al., 2005). Twenty-three items may be answered as either “true,” “false,” or “don’t know,” four items are multiple choice items with five to six options (see Appendix B). This instrument was developed to assess knowledge of information that is typically included during genetic counseling for breast cancer. This questionnaire has been chosen because

it has been shown to distinguish between women who have received genetic counseling information from those who have not. Although the participants in the present study had not received genetic counseling at the time of their participation, the expectation was that their first-degree relatives who have received genetic counseling will have had the opportunity share knowledge gained counseling sessions with them.

Items for the Breast Cancer Genetic Counseling Knowledge Questionnaire (BGKQ) were developed following a detailed content analysis of genetic counseling pretest sessions that followed guidelines. Potential questions were developed from these sessions then assessed by four genetic counselors for appropriateness. Three of the four genetic counselors needed to agree (interrater agreement of 0.75) that the questions were appropriate for them to be included. Items were reevaluated; some were dropped and some were modified until a 45-item version of the questionnaire was formed with an IR of 0.93, indicating high levels of content validity (Erblich et al., 2005). Once initial items were developed, a second phase of development involved administering the questionnaire to 75 people, including nurses with and without oncology certification, and healthy women with and without family histories of breast cancer, as well as people who had attended genetic counseling. These groups with supposed differing levels of knowledge of information presented in genetic counseling were given the 45-item version of the BGKQ along with the Breast Cancer and Heredity Knowledge Questionnaire (BCHK), an 11-item instrument previously validated for use in lower risk women. Based on this work, items were dropped if they were too simple or too difficult. The remaining 37 items were then evaluated by confirmatory factor analysis, which indicated that 27 items loaded onto a single factor. An ANOVA was conducted to compare scores of the five groups

controlling for demographics; a main effect of group was observed ($P < 0.0001$), indicating support for good criterion-related validity within this sample. With the 27-item GBKQ, women who had received counseling scored higher than all other groups, indicating that the instrument measures knowledge obtained through genetic counseling.

The GBKQ has been used to detect genetic counseling knowledge obtained in part through the family member who received the counseling as reported in the study by Patenaude et al. (2013). In this study, daughters of mothers with *BRCA 1/2* mutations were administered the GBKQ an average of 3.1 years following the mother's *BRCA1/2* test result and genetic counseling. Daughters scored an average of 61.9% correct on this questionnaire (Patenaude et al., 2013). In the study by Erblich et al. (2005), women who had received genetic counseling themselves scored an average of 76.6% on the questionnaire and women who had not had breast cancer nor received genetic counseling scored an average of 35% and 41% for those who had a positive family history of breast cancer and those who did not, respectively.

Reliability for this instrument has been demonstrated by a Cronbach's alpha of 0.92 in a study of 75 women (Erblich et al., 2005). This instrument was also used in a study of 40 daughters of mothers with *BRCA* 1/2 mutations to assess knowledge of the daughters who had not attended genetic counseling (Patenaude et al., 2013); however, internal consistency was not assessed in this study (A.F. Patenaude, personal communication, March 10, 2013).

Distress

The concept of distress related to a family history of breast cancer and personal risk for breast cancer was measured using the 15-item Impact of Event Scale (IES),

which was designed to measure current subjective distress during the prior week in reaction to a defined stressor (Horowitz, Wilner, & Alvarez, 1979). This instrument was adapted for the REACH study (P.I. Anita Kinney) so that the potentially stress-inducing event is the state of having a certain risk for breast cancer related to family history (see Appendix B). Because the same adapted instrument was used in REACH as well as the proposed study, future comparisons in secondary analysis will be able to be made between counselees and their unaffected first-degree female relatives. This self-report instrument is intended to measure "the current degree of subjective impact experienced as a result of a specific event." (Horowitz et al., 1979, p. 209). Participants rate the frequency of certain psychological, physiological, and behavioral responses to the event on a four-point scale. Weights are applied to the responses as follows: not at all = 0, rarely = 1, sometimes = 3, often = 5. The full Impact of Events Scale is 15 items including one subscale related to intrusion and one subscale related to avoidance. Intrusive phenomena include experiences like thinking about a stressful event, or having dreams about it. Avoidance phenomena include actions like trying to stay away from reminders or trying not to talk about the event. A total score can be calculated for the complete IES or for the subscales. The range for the full scale is 0-75. Based on multiple examples from the literature, a score of $\geq$ 40 on the full scale is indicative of a significant stress response.

The intrusion subscale of the IES has demonstrated satisfactory internal consistency in samples of relatives of women with breast cancer with a Cronbach's alphas for the total scale of 0.91 (Thewes, Meiser, & Hickie, 2001), for the avoidance subscale of .84 - .87 (Kim, Duhamel, Valdimarsdottir, & Bovbjerg, 2005; Thewes et al.,

2001) and for the intrusion subscale of .81 to .83 (K. E. Fletcher et al., 2006; Kim et al., 2005; Thewes et al., 2001). Test-retest reliability for the intrusion subscale of the IES was found to be r=0.75, suggesting a moderate agreement between scores from one administration to another (Thewes et al., 2001).

To assess face validity for women at increased risk for breast cancer, a small group was asked to describe what they believed the IES measured and to assess the clarity of the instructions and the items. Women felt that the items were about anxiety, worry, or emotional well-being. For the most part, they thought the instructions and items were clear and easy to understand. Perhaps most importantly, they felt that the items were pertinent for women with a family history of breast cancer (Thewes et al., 2001).

The IES was assessed for construct validity in a sample of women at risk for familial breast cancer; a component factor analysis yielded a two-factor solution, consistent with the two subscales in the instrument (Thewes et al., 2001). The IES was assessed for convergent validity in the same sample by calculating point-biserial correlation coefficients between scores on the IES and two other measures of generalized distress: the Beck Depression Inventory (BDI) and the state component of the State-Trait Anxiety Inventory (STAI-State), the General Health Questionnaire (GHQ-28), as well as breast-cancer related attitudes and events. Breast cancer-related events and attitudes included contemplation of prophylactic mastectomy, a breast-cancer related live event within the past year, and the total number of first- and second-degree relatives who have either been diagnosed with or died from breast cancer (Thewes et al., 2001). Scores on the total IES were significantly related with breast cancer-related attitudes and events supporting the idea that the IES is a useful measure of breast cancer-related distress in

women at increased risk for breast cancer due to family history (Thewes et al., 2001, p. 465).

Reported Amount of Information Shared About Genetic Counseling Session

A question was asked about how much women felt was shared with them by their sister or mother who attended genetic counseling. The variable "amount of information shared" was assessed by asking the question, "Would you please rate on a scale of 0-5 how much information your sister or mother shared with you about what she learned in her genetic counseling session. With zero being she shared nothing about the session to five being she shared a great deal" (see Appendix C).

Self-rated Understanding of Genetic Health Information

Historical questions about how information was shared from the genetic counseling session were asked during the telephone interview (see Appendix C). Questions were tailored based on the relative who received genetic counseling. The variable, "understanding of genetic counseling information" was assessed by asking the question, "To what degree do you understand the information she shared with you about her genetic counseling session? Please rate how well you understand the information she shared on a scale of 0-5 with zero being you don't understand it at all to five being you understand a great deal." This is an ordinal level question that was intended to be used in the path analysis to assess whether self-rated understanding of genetic counseling information provided to a close relative mediates accuracy of risk perception (see Figure 3.2).

Screening Recommendations/ Screening History

To obtain information about what types of breast screenings have been done (mammography and/or MRI) and what screenings have been recommended, we used an adaptation of questions developed by Vernon et al. (2004) and the questions developed for the Behavioral Risk Factor Surveillance System (BRFSS) by a working group of the CDC and BRFSS state coordinators, which can be accessed at http://www.cdc.gov/brfss/questionnaires/english.htm .

The BRFSS is a state-based health survey that "collects information on health risk behaviors, preventive practices, and health care access primarily related to chronic disease and injury" (Office of Surveillance Epidemiology and Laboratory Services, 2013). This questionnaire is administered annually and collects data on mammography but not on breast MRI. The questions related to mammography on the BRFSS include:

1. A mammogram is an x-ray of each breast to look for breast cancer. Have you ever had a mammogram?

    a. Yes
    b. No
    c. Don't know/ not sure
    d. Refused

2. How long has it been since you last had a mammogram?

    a. Within the past year (anytime less than 12 months ago)
    b. Within the past 2 years (1 year but less than 2 years ago)
    c. Within the past 3 years (2 years but less than 3 years ago)
    d. Within the past 5 years (3 years but less than 5 years ago)
    e. More than 5 years ago

    (Office of Surveillance Epidemiology and Laboratory Services, 2013)

The instrument presented by Vernon et al. (2004) was developed by members of the Division of Cancer Control and Population sciences sponsored by the National Cancer Institute (NCI). Researchers in the field of colorectal screening had identified a

problem with data collection: patients often did not know the difference between colonoscopy and sigmoidoscopy. Therefore, this group worked over several years to develop a core set of colorectal screening measures and standardized descriptions of the tests. The instruments measure whether patients are aware of, or have participated in, various screenings for colon cancer. The questions also focus on whether the tests are for screening or diagnostic purposes. Cognitive testing was performed on the questions to assess whether people could comprehend and interpret the questions and to assess the strategies people used to recall the information (Vernon et al., 2004). Performing cognitive testing helps improve "reliability and validity of self-reports of retrospective information by identifying and reducing sources of response error that may go unnoticed in field tests of survey instruments" (Vernon et al., 2004, p. 900).

The advent of MRI screening recommendations for women at elevated-risk of breast cancer is relatively new (Saslow, 2007). Because MRI breast screening may be less familiar to women, it was thought that a description of the screening should accompany the questions about the screenings to yield more accurate results when asking about screening participation. Therefore, the Vernon instrument was adapted and used to measure screenings related to breast cancer. The introduction to the questions vided a brief description explaining mammography and breast MRI exams are. The description for mammography was modeled after the BRFSS questionnaire. The description for breast MRI was adapted from patient information posted on the website RadiologyInfo.org, which was developed by the Radiological Society of North America and the American College of Radiology. After explaining each type of screening, the questions asked whether or not the woman had "ever heard of" the test, "ever had" the

test, and if so, what was the date of the "most recent?" These questions were used initially by Vernon (2004) in a face-to-face interviewer-administered mode, but they were written with the intent that they could be adapted to use in telephone interviews or in self-administered questionnaires. Additional questions added for the purpose of this study asked related to mammography and breast MRI tests included whether or not "anyone ever recommended it?" if so, "how often was it recommended that you receive it?" and "do you plan to get" the screening and if so, "how often do you plan to get" the screening? These additional questions were used to help determine if the woman had a screening plan that is in agreement with the NCCN guidelines based on her risk level.

Analysis

Sample

The sample was described using percentages for categorical measures. Additionally, measures of central tendency were used to assess the distribution continuous variables including. Risk was calculated and reported based on the Claus, BRCAPRO, and Gail models. Accuracy of lifetime risk perception was reported for each model; women will be considered accurate if their estimate falls within +/- 3% of a given scale. Kurtosis and skewness were assessed. An absolute value less than two was considered to not be overly skewed or kurtotic. Psychometric performance of instruments was assessed. Internal consistency was calculated using Cronbach's alpha where appropriate. Internal consistency is not appropriate for measures that are not based on a redundancy (internal consistency model). Numeracy, for example, might not be appropriate for internal consistency evaluation. For such scales, we will use communality estimates as lower bounds of reliability from exploratory factory analyses.

Analysis of Specific Aim 1

Specific aim 1 was to calculate an estimate of women's lifetime risk for breast cancer and compare this estimate to women's perceived risk about developing future breast cancer. This aim included three research questions:

4. What is the average calculated risk for breast cancer using the Claus model, the BRCAPRO model, and the Gail model for women (with sisters or mothers who received genetic counseling and indeterminate negative *BRCA1/2* results)?
5. What percent of women (with sisters or mothers who received genetic counseling and indeterminate negative *BRCA1/2* results) qualify for annual MRI breast screenings based on NCCN guidelines (a lifetime risk for breast cancer $\geq$ 20%) based on the Claus or the BRCAPRO risk calculators?
6. What percent of women (with sisters, mothers, or daughters who have received genetic counseling and had indeterminate negative *BRCA1/2* results) over-estimate vs. underestimate their risk as compared to their calculated risk for breast cancer?

Risk scores were calculated for the Claus and BRCAPRO models using Cancer Gene software and for the Gail models using the NIH website. Because the Gail model is the most commonly used risk calculator by primary care providers, for purposes of comparison, a Gail estimate of risk was calculated along with Claus and BRCAPRO. Average calculated risk was reported using percentages and frequencies. We did not categorize women as qualifying for MRI breast screening based on Gail scores. Frequencies and percentages were reported about the number of women above and below

the 20% lifetime risk threshold for each model. Over- and under-estimation will be reported for each risk calculator. Over- and under-estimation was defined as a woman's perceived risk estimate that is (+/-) 3% from the score produced by the risk calculator. Three percent was chosen as the cut off for over- or under-estimation because average-risk is 12% and the ACS uses 15% (a difference of 3%) as a starting point for suggesting discussions about MRI screenings with primary health care providers. Therefore a difference of 3% can have clinical significance. Because the risk calculators provide different lifetime risk estimates for breast cancer, it was possible for a woman's estimate to be categorized as an over-estimate for one calculator and an underestimate for another. Over- and under-estimates were provided for risk perceptions vs. both the Claus, BRCAPRO, and Gail models.

Analysis of Specific Aim 2

Specific aim 2 was to determine whether self-reported screening plans and self-described screening practices are in alignment with risk-based guidelines in women whose first-degree female relatives have received genetic counseling and indeterminate negative *BRCA1/2* test results. This aim includes two research questions:

1. What percent of women whose first-degree female relatives have received indeterminate negative test results **report that they are screening for breast cancer according to risk-based guidelines**, i.e., are women who have $\geq$20% lifetime risk of developing breast cancer, receiving both annual mammogram and MRI (as recommended by the National Comprehensive Cancer Network (NCCN) and the American Cancer Society (ACS))?

2. What percent of women whose first-degree female relatives have received indeterminate negative test results **report receiving recommendations for breast cancer screening** from their primary care physicians or from another source that are consistent with the National Comprehensive Cancer Network (NCCN) and American Cancer Society (ACS) guidelines based on the level of risk (i.e., annual mammography if < 20% lifetime risk and ≥ 40 years of age; mammography with MRI if ≥ 20% and ≥ 30 years of age)?

To answer these questions, two dichotomous variables were computed, one for whether or not women self-report screening according to NCCN and ACS guidelines and one for whether or not women report being recommended to screen according to NCCN and ACS guidelines. Women were considered as screening according to NCCN and ACS guidelines if they had a risk less than 20% and received their most recent screening mammogram within the past year. If women have a risk of 20% or greater, they were considered to be screening according to NCCN and ACS guidelines if they received both a screening mammogram and screening breast MRI within the past year. Likewise, they average-risk women were considered to have received recommendations for screenings in accordance with guidelines if they reported recommendations to screen annually with mammography. Women at elevated-risk were considered to have received screening recommendations according to guidelines if they were instructed to receive annual screening mammograms and breast MRI. Questions about self-reported screening practices and self-reported screening recommendations by primary care providers ask women about the most recent mammogram and MRI as well as the one(s) before the most recent one(s). We intended to count women as screening annually if both intervals

were 1 year or less and procedures were done for screening and not diagnostic purposes. The exception was intended to be women of average-risk who are exactly 40 years of age since 40 is the age to begin mammogram screenings. These women would not be expected to have received two mammograms to be screening according to guidelines.

After the telephone interview was completed, a lifetime risk estimate for breast cancer was calculated using the pedigree information obtained. If lifetime risk in either Claus or BRCAPRO was found to be $\geq$ 20%, then a woman was be considered to be up-to-date with the screening guidelines if she had received a screening mammogram and a screening breast MRI within the past 1 year. For women whose lifetime risk for breast cancer did not exceed 20% in the Claus and BRCAPRO models, women were counted as "screening according to guidelines" if they had received a screening mammogram within the past year. A similar assessment was made of the women's reports of recommendations by their providers. Additionally, we intended to report on whether women were over-screening. The items assessing MRI and mammography screening asked whether each test was for diagnostic or screening purposes. Diagnostic tests were excluded when assessing for over- or under-screening.

Note that the following is the initial conception of specific aim 3. We altered the aim slightly as the study progressed.

Analysis of Specific Aim 3

Specific aim 3 was to determine the contribution of a woman's self-rated understanding of genetic health information, shared by her first-degree female relative about genetic counseling sessions, to her risk perception and to the accuracy of her perception of individual lifetime risk for breast cancer while controlling for confounding

influences of factors known to contribute to risk perception, including age, education, health literacy, numeracy, knowledge about breast cancer genetics, and self-reported distress related to family history of breast cancer and perceived personal risk for breast cancer. This aim includes the following research questions:

1. What is the magnitude of the relationship between calculated lifetime risk for breast cancer and perceived lifetime risk for breast cancer?
2. Does a woman's self-rated understanding of genetic health information shared by her first-degree relative moderate the accuracy of risk perception?
3. Does a woman's self-rated understanding of genetic health information shared by her first-degree relative predict risk perception?

These questions were to be answered using structural equation modeling (SEM) to look at the strengths of associations among latent and measured variables. A provisional recursive SEM model was used to estimate these relationships (Figure 3.2). In this initial model, predictor variables, which are exogenous (unexplained), included age, education, health literacy, numeracy, knowledge of breast cancer genetics, distress, and understanding of information shared about the relative's genetic counseling session. All of these exogenous variables except self-reported understanding of genetic health information from a close relative's genetic counseling session are known to influence risk perception and were treated as covariates in the predictive relationships (that is, all regression relationships were conditioned statistically on the exogenous variables). The correlation between the latent constructs "Calculated Risk" and "Risk Perception" related to lifetime risk for breast cancer is, in essence, accuracy of risk perception – it could be viewed as the validity of the perceptions. The latent variable "Calculated Risk" was

estimated using the Claus and the BRCAPRO models. The latent variable "Risk Perception" was estimated using comparative quantitative and qualitative risk perceptions. It was intended that if understanding about genetic health information shared by the counselee was found to increase the regression coefficient of the path between calculated and perceived risk, then we would have been able to state that self-reported understanding about the genetic health information shared by the counselee had a positive moderating effect on the accuracy of risk perception. It was intended that if the direct effect of self-reported understanding of genetic health information improved prediction of a woman's perceived risk above and beyond the other covariates in the model, then the understanding about the genetic health information shared by the counselee could have been said to contribute to a woman's risk perception.

Power

Unlike simple planned comparisons between groups, power computations for multivariate structural equation models are complex, with different power for every parameter and relationship and requiring assumed specific values for every unique model parameter. Therefore, generic approaches have been developed in terms of global fit statistics (e.g., Root Mean Squared Error of Approximation or RMSEA) that are appropriate for more realistic scenarios where this degree of theoretical specific knowledge is lacking. For the Figure 3.2 structural equation model, a sample size of 100 would give a power of .88 to reject the null hypothesis that the population RMSEA is <= .06 when the true RMSEA is .10 (df=90) and alpha = .05 (MacCallum, Browne, & Sugawara, 1996).

Software

IBM SPSS version 21 was be used to run statistical analysis on specific aims 1 and 2. M*plus* software by Muthen and Muthen was used to run the structural equation model for specific aim 3.

Missing Data

Missing data were expected to be minimal. Most packets were received back by mail before the telephone portion of data collection and they were reviewed for completeness. Incomplete information was collected over the telephone when possible. In some instances, the telephone interview took place before a completed packet was received. The proportion of missing data was reported. The analysis under maximum likelihood estimation is valid under the usual assumptions of ignorable missingness (missingness not dependent on the unobserved value of the censored observation). Missing data bias was intended to be reviewed by computing a dummy variable reflecting the presence or absence of missing data for each variable in the model and then the dummy variable will be correlated with all other variables in the model as well as selected demographic and historical variables.

Linearity and normality assumptions were assessed for all variables using all of the usual diagnostics. We also tested for conditional independence in the measurement relationships, which states that measures of the same construct will be correlated only because of the underlying true construct.

Non-normality

In structural equation modeling, non-normal data increases the likelihood of rejecting models that may not be false and well as committing a type I error. Multivariate normality was intended to be tested using Mardia's test for multivariate normality. Univariate indicies of skewness and kurtosis were examined to determine if the absolute value is greater than 2.0. If non-normality is pronounced, then bootstrapping was intended to be undertaken to derive standard errors and confidence intervals. With bootstrapping, the data are treated as the population; a sample is taken with replacement. Each sample with replacement produces a different set from the samples. The number of bootstrap replicates will be 2000. Bootstrap standard errors do not require the assumption of normality.

Indices of Fit

Although historically structural equation models have been evaluated according to several global fit indices (Bollen & Long, 1993), modern practice strongly favors the Root Mean Squared Error of Approximation (RMSEA) as the primary criterion. It subsumes the common chi-square test of model lack of fit in the special case where the null RMSEA = 0. The Root Mean Square Error of Approximation (RMSEA) should be less than 0.08 for satisfactory fit for the model as a whole), the *p* value for the test of close fit (should be statistically nonsignificant). If the model does not fit satisfactorily (i.e., RMSEA >.08), then modification indices for omitted relationships can suggest additional relationships that will necessarily improve the model fit by the stated amount; these were planned to be added only if consonant with theory and substantive knowledge. Significance of each path was computed via likelihood ratio test of the difference in chi

square between two tested models, one with and one without the path in question, evaluated at one degree of freedom. The coefficient having the largest *p*-value greater than .05 by this test was deleted. The significance of the remaining paths was recalculated. This process was followed until all remaining paths are significant by the likelihood ratio test.

Steps		Recruitment & Data collection			Follow Up & Thank You		Completion		
	Start	+1 Week	+10 days	+2-3 Weeks		All Data In			
Mail introductory letter to potential participants	X								
Call potential participants one week after introductory letter mailed (recruitment/ set interview time)		X							
Mail survey – same day as recruitment phone call		X							
Reminder phone call 10 days after survey mailed if survey not received back			X						
Conduct participant interviews at pre-arranged time (2-3 weeks after initial call)				X					
Calculate Risk (Gail Claus *BRCA* Pro)					X				
Send risk summary letter to those who requested it					X				
Mail participant incentive (after packet received)						X			
Data cleaning and data entry							X		
Data Analyses								X	
Complete dissertation chapters and articles									X

Figure 3.1
Initial project timeline

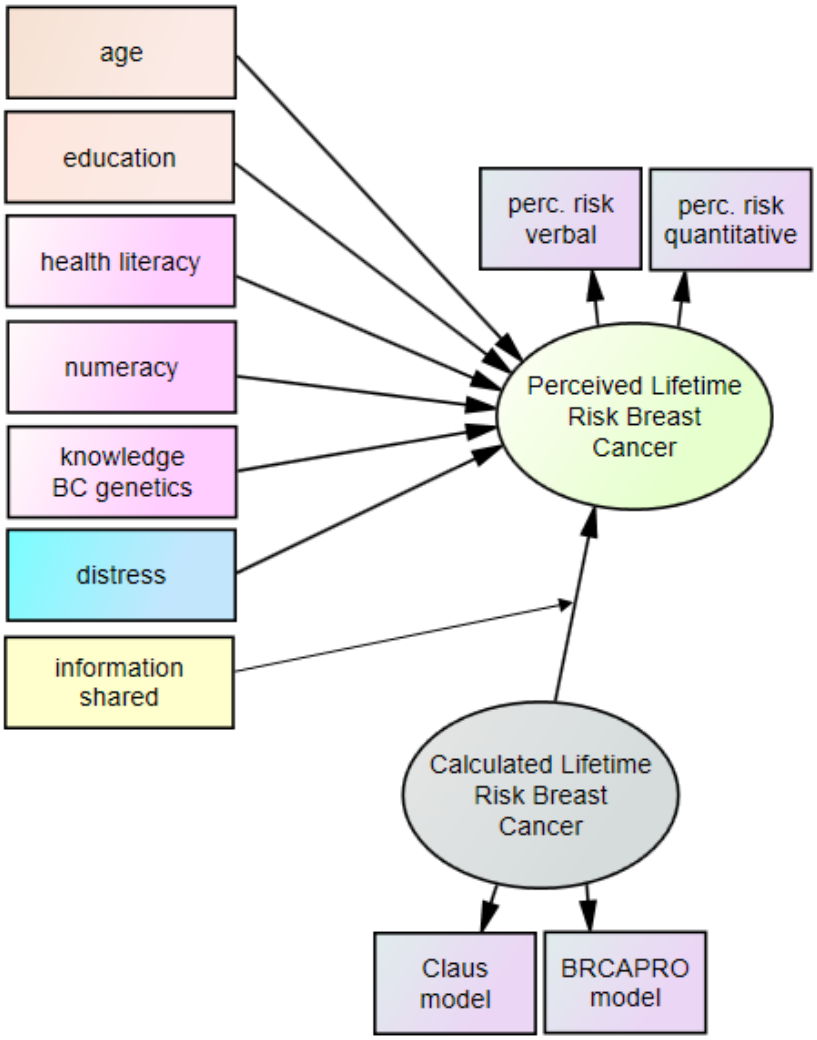


Figure 3.2
Initial latent variable model

CHAPTER 4

RESULTS MANUSCRIPT 1: RISK FOR BREAST CANCER AND SCREENING BEHAVIORS IN WOMEN WHOSE FIRST-DEGREE RELATIVES HAVE RECEIVED INDETERMINATE *BRCA1/2* GENETIC TEST RESULTS

Two manuscripts have been prepared for publication based on the results of the present study and are presented in Chapters 4 and 5 for the purposes of the Results and Discussion sections of the dissertation and comprise Chapters 4 and 5. Figures and tables in each manuscript are specific to the research questions outlined in each manuscript and correspond to the dissertation research aims and are presented at the end of each chapter/manuscript. References for each manuscript are included in the references at the end of the dissertation as a whole. Further results that were beyond the scope of these manuscripts are presented in Chapter 7.

The first results manuscript presented here in Chapter 4 has been prepared for a primary care provider audience and addresses the results pertaining to specific aims 1 and 2. The second manuscript, presented in Chapter 5, has been prepared for an audience of genetic counselors and presents the findings related to specific aim 3.

Abstract

Purpose

The purpose of this study was to describe calculated risk, risk perceptions, recent screening recommendations, and practices for women whose first-degree female relative was diagnosed with breast cancer and received genetic counseling and *BRCA1/2* testing with indeterminate results. We also assessed whether women shared their family members' indeterminate test results with their primary care providers.

Methods

This cross-sectional study utilized survey and interview techniques to assess comparative verbal and quantitative risk perceptions among women with a first-degree relative with breast cancer who received an indeterminate *BRCA1/2* test result. Five-year and lifetime risks were calculated using the Gail, Claus, and BRCAPRO models; differences between the calculations and women's own estimates of lifetime risk are presented. Breast cancer screening behavior was assessed using questions from the Behavioral Risk Factor Surveillance System questionnaire. Women were asked what information they shared with their primary care providers (PCP).

Results

Eighty-five women participated. Most women estimated their risk to be higher than estimates calculated by the Gail (42.9%), Claus (73.8%), and BRCAPRO (78.6%) models. Most (86.8%) women at average-risk (operationalized as < 20% lifetime risk by Claus and BRCAPRO) reported receiving recommendations for annual mammography from their primary care provider and had received a mammogram within the past 1-2

years. Approximately 10% of women were identified as being at elevated-risk for breast cancer based on their family pedigree, warranting annual breast MRI screening according to national guidelines, yet none of these women had received recommendations for enhanced screening. Most women (76.5%) did not discuss their family member's genetic testing with their PCP.

Conclusions

Women tended to over-estimate their risk for breast cancer and women at elevated-risk did not receive recommendations for annual breast MRI. Primary care providers are encouraged to calculate pedigree-based individualized risk for breast cancer, refer to genetics specialists as needed, and follow risk-based screening guidelines.

Introduction

For most women, including those at increased risk for breast cancer, primary care providers (PCPs) are a main source of information about breast cancer risk and appropriate screening methods (Keogh et al., 2011). Guidelines for screening and risk reduction are based on estimated level of risk for a woman and vary by organization (see Table 4.1) (American Cancer Society, 2014; Mainiero et al., 2013; National Comprehensive Cancer Network, 2013a, 2013b, 2013c; The American College of Obstetricians and Gynecologists, 2011). Women with first-degree relatives with breast cancer may fall into the category of average-risk, or elevated/high risk. Assessing risk for breast cancer is a complex process requiring the evaluation of a family pedigree and personal risk characteristics (Berliner & Fay; National Comprehensive Cancer Network, 2013b). Several organizations stratify breast cancer screening guidelines based on a

woman's percent chance of developing breast cancer over her lifetime; women with higher levels of risk should be offered annual screening breast MRI in addition to mammography (see Table 4.1). To calculate lifetime risk estimates for breast cancer, a risk prediction model must be used.

Risk Prediction Models

Many risk prediction models exist. Some models are better in certain populations and for certain purposes. Complicating matters, different models provide different calculations for the same woman. The Gail model (Gail et al., 1989) (more recently updated and referred to as the NCI-Gail model or the Breast Cancer Risk Assessment Tool (BCRAT) (S. W. Fletcher, 2013) is the most commonly used risk prediction model; however, the Gail model takes into account limited family history and is not appropriate for determining need for annual MRI (American Cancer Society, 2014). The Gail model may estimate risk higher than other models based on personal risk factors (Ward & Smith, 2010). It tends to perform poorly in higher-risk populations (Amir et al., 2010). The Gail model is, however, used to determine the appropriateness of chemoprevention for women >35 years of age based on 5-year risk calculations (Freedman et al., 2011; U.S. Preventive Services Task Force, 2013).

The Claus, BRCAPRO, and Tyrer-Cuzick (also called IBIS) models assess an extended family cancer history and are appropriate to use in determining the need for annual screening breast MRI. Both the ACS and NCCN suggest that women should consider annual screening breast MRI if lifetime risk for breast cancer exceeds 20%. The ACS has suggested that there is not enough evidence to recommend for or against MRI between 15 and 19% but recommend against MRI below 15%. The Claus and

BRCAPRO models have been widely used in research as well as genetic counseling practice (Amir et al., 2010; National Cancer Institute, 2014b) and can be helpful for women without a known cancer-associated gene mutation with one or two first- or second-degree relatives with breast cancer (Claus, Risch, & Thompson, 1994). The BRCAPRO model estimates the chance of carrying *BRCA1/2* mutation and a women's individualized lifetime risk for breast cancer (National Comprehensive Cancer Network, 2013a, 2013b; Parmigiani et al., 2007).

Genetic Testing

When the family history of cancer looks as if a potentially harmful mutation in breast cancer susceptibility genes could be present, a risk assessment should be performed by a trained health professional, including trained PCP or genetic counselor, to determine whether genetic testing is warranted (Moyer, 2013). Genetic testing can be done to identify mutations that predispose a person to cancer. Published guidelines list criteria to be considered for *BRCA1/2* testing, including but not limited to a cancer diagnosis at age 45 or younger, or a diagnosis at age 50 with 1 or more close relatives with cancer at any age, diagnosed at any age with one or more close relative with breast cancer diagnosed younger than age 50, having a close male relative with breast cancer at any age, having two primary breast cancers including bilateral disease or two separate cancers with one diagnosed prior to age 50 (National Comprehensive Cancer Network, 2013c). Ideally the first testing in a family is performed in an individual with breast cancer because lack of a positive result in an unaffected individual is difficult to interpret. If a positive result is found, then other family members should be tested to determine if they carry the mutation. Family members who carry the mutation are considered to be at

high risk; those who do not have the mutation are considered to be at average-risk. A test result can only be considered a *true negative* if there is a known familial mutation and the tested individual does not carry this exact mutation.

Indeterminate Test Results

The most common outcome of genetic testing in a family without a known *BRCA1/2* mutation is an indeterminate test result. In the absence of a known familial mutation, failure to find a deleterious mutation is referred to as an "*indeterminate*" test result (National Comprehensive Cancer Network, 2013c). This type of language is used because (1) there is the possibility that a mutation not yet identified in the *BRCA1/2* genes is present, (2) there could be a mutation in a gene not tested (e.g., *PTEN*-Cowden's Syndrome or *P53*-LiFraumeni's Syndrome), and (3) we do not want to give the impression that the family cancer history does not include hereditary causes. Other terms used in the literature to describe a negative *BRCA* test in the absence of a known family mutation include "*indeterminate negative*"(Patenaude et al., 2006), "*inconclusive*" (Cypowyj et al., 2009; Dorval et al., 2005), "*uninformative*"(Mannis et al., 2013; National Comprehensive Cancer Network, 2013c; van Dijk, 2005; Vos, Menko, et al., 2011), or "*uninformative negative*"(Riley et al., 2012). The terms "*inconclusive*" and "*uninformative*" have also been used to describe variants of unknown significance that are mutations that have not at this time been shown to affect breast cancer risk, but could be labeled as deleterious in the future as more research is made available (National Comprehensive Cancer Network, 2013c; Vadaparampil, Malo, de la Cruz, & Christie, 2012).

Purpose

The purpose of this cross-sectional, study was to determine whether sisters and daughters of women who received indeterminate *BRCA1/2* test results were at elevated-risk for breast cancer and whether they had received screening recommendations from their PCP and breast cancer screening congruent with their level of risk. Additionally, we evaluated women's risk perceptions and compared them to individual calculated risks. Finally, we asked women about the extent to which they shared their family history of breast cancer and the fact that they had a sister or mother who received genetic testing and counseling with their PCPs. This population of women is important to study because their family pedigree has already been evaluated by a genetic counselor and found suspicious enough to warrant a *BRCA1/2* test in a family member affected by cancer and may have a greater proportion of women at elevated-risk for breast cancer than the general population.

Methods

We had two sources of probands, (1) REACH participants who were identified through the Utah Population Database (UPDB) and recruited through the Utah Cancer Registry, and (2) patients who received genetic counseling and testing through the Family Cancer Assessment Clinic (FCAC) at Huntsman Cancer Institute. These probands (women who had previously received genetic counseling and testing following their own breast cancer) referred their female family members without cancer to the Risk Education and Assessment for Cancer Heredity (REACH)-Pilot Study. Women who completed the REACH-Pilot Study and agreed to be contacted for future cancer-related research were contacted for the present study. Information sent to us by REACH-pilot included only

name, contact information, and family grouping variable. We do not know whether our participants' family member was counseled through REACH or through FCAC.

Following IRB approval, introductory letters were mailed to 135 women. The final sample consisted of 85 women who met inclusion criteria: age 40–74 years, fluent in English, and had a mother or sister with a personal history of breast and/or ovarian cancer who received *BRCA1/2* genetic counseling and testing between 2010 and 2013 who had an indeterminate negative *BRCA1/2* result. Women were excluded if they had a personal history of any type of cancer (except nonmelanoma skin cancer), ever received *BRCA1/2*-related genetic counseling or testing, have had a prophylactic bilateral mastectomy or oopherectomy, lived outside the United States, and/or were incarcerated. Women of Ashkenazi Jewish descent were not included because of very a small number of women in this category and because their relatives may have had testing based on descent only as no additional family history is required to perform genetic testing for founder mutations in this subgroup (National Comprehensive Cancer Network, 2013c) . Participating women were mailed a survey packet with a consent cover letter and a future date and time was set for a telephone interview. Interviews were conducted from October to December 2013. A more detailed description of the study protocol can be found in Himes et al. (in process).

Measures

Women provided written, three-generation family cancer histories. We created pedigrees from these histories and reviewed them with participants during the telephone interview if any clarification was needed (e.g., if they had not written an age of death for a family we asked them to provide an estimate). Pedigrees with family cancer histories

were entered into CancerGene software to obtain BRCAPRO and Claus model estimates of 5-year and lifetime risk for breast cancer. Gail risk estimates were calculated using the Breast Cancer Risk Assessment Tool on the NIH website.

Women were asked in the survey to rate their risk of developing breast cancer using verbal descriptors (such as lower, higher), and to estimate a percent lifetime risk in comparison to other women of the same age. Information about screening behaviors and screening recommendations was obtained during the telephone interview using questions from the Behavioral Risk Factor Surveillance System (BRFSS) questionnaire developed by state coordinators and the CDC (Office of Surveillance Epidemiology and Laboratory Services).

Additional questions were asked in the interview about what information women shared with their PCP, including (1) their family history of cancer, (2) having a sister or mother that received genetic counseling, and (3) *BRCA1/2* test result of their sister or mother. All data were analyzed using IBM SPSS version 21.

Results

Study Population

Of the 122 women who were contacted, 98 were eligible and 85 completed the study. Participants were mostly married, non-Hispanic White, and highly educated with a mean age of 52.2(*SD* 8.9) (see Table 4.2).

Risk Calculations

Calculated risks are presented in Table 4.3. Of importance, 10.6% of the participants (*n* = 9 of 85) had a lifetime risk as calculated by the Claus model that was

20% or higher; 16.7% had a risk that was 15% or higher. We operationalized being at elevated-risk as having a lifetime risk for breast cancer of 20% or greater by either the Claus or BRCAPRO models because these models take a larger amount of family history into account and are the type of model used to determine appropriateness of annual screening breast MRI based on ACS and NCCN guidelines. None of the women had a lifetime risk equal to or greater than 20% using the BRCAPRO model; therefore, when we refer to women at elevated-risk in our study, we are referring to those with an lifetime risk estimate >20% based on the Claus model. The ACS adds a third risk group called "moderate risk" for women with a lifetime risk between 15% and 20%, noting that there is not enough evidence to advise for or against screening MRI at this risk level.

Notably, 78.8% of participants had Gail 5-year risk higher than 1.67%, the risk generally considered sufficient to justify chemoprevention. We did not collect data about chemoprevention.

Risk Perception

Most women rated their chances of developing breast cancer in their lifetime as "higher" or "much higher" than other women their own age (see Table 4.4). Women provided quantitative estimates for their personal lifetime risk for breast cancer ranging from 1% to 95% (mean 20%, *SD* = 20). Most women described their risk as being between 5 and 30%; however, a few selected very high numbers. One woman described her lifetime risk as being 95% (Claus estimate = 12.1%), and 2 women thought their risk was 90% while their Claus model estimates were 16.9% and 13.1%, respectively. More women perceived their numeric risk as 12% than any other number (*n*=15 of 84), mirroring information they were provided in the stem of the question: "On average 12

women out of 100 will get breast cancer in their lifetime." The 9 women with risk calculations 20% or greater had estimated their risk as being 12-70% with verbal scores ranging from "higher" to "much higher."

Congruence Between Risk Calculations and Women's Estimates

Differences between women's quantitative risk perceptions and their calculated scores were obtained for each of the three risk models. We considered women's self-reported estimates as congruent with a particular model if their estimate was within +/- 3% of the model's calculated estimate. As can be seen in Table 4.5, the percent of women who estimated their risk to be higher or lower than a particular model varied. A difference of 3% was selected because average-risk is often reported to be 12% and according to the ACS, women with 15% lifetime risk may be offered annual screening breast MRI, thus 3% can make a clinical difference.

Screening Recommendations - Mammography

All women at elevated-risk ($\geq$20% lifetime), and 86.8% of women at average-risk (<20% lifetime) reported receiving screening recommendations for annual mammography from their PCP. One woman in her 40s with a lifetime risk <20% by the Claus model indicated that she received a recommendation to have screening mammography every 2 years. Table 4.6 delineates women's reports of mammography recommendations from their PCPs according to risk strata and age. According to NCCN and ACS, all women over 40 years of age should receive annual mammograms. The shaded cell in Table 4.6 indicates that 86.8% of women report they have received recommendations for annual mammography in accordance with NCCN/ACS guidelines.

According to the USPSTF (2012), women should discuss with their health care providers the pros and cons of breast cancer screening based on personal risk factors and values, but in general should begin biennial mammography screening at age 50. The boxed cells in Table 4.6 indicate that no women reported receiving a provider recommendation for minimum USPSTF population-based guidelines, most received recommendations to screen more frequently than USPSTF minimum recommendations.

Screening Recommendations – Breast MRI

The USPSTF does not have published screening guidelines for women at elevated-risk. NCCN and ACS recommend that women at ≥ 20% lifetime risk by models that take extended family history into account receive annual MRI in addition to annual mammography. None of the elevated-risk women, defined by having a Claus calculation ≥20%, reported receiving a PCP recommendation for annual MRI; therefore, none of the elevated-risk women are considered to have received screening recommendations from their PCP in accordance with risk-based guidelines. Two women reported receiving recommendations for annual screening breast MRI; however, these women did not fall into an elevated-risk category by the Claus model. They had lifetime risks of 7.7% and 12.3%.

Recent Screening Practices – Mammography

Most women (80.0%) at all levels of risk reported receiving a screening mammogram within the past 1-2 years. Table 4.7 illustrates the most recent screening mammogram for women based on age and risk categories. Seven of the 76 average-risk

women (9.2%) received their most recent mammogram for diagnostic reasons and therefore were not included in this table.

Recent Screening Practices - MRI

None of the women at elevated-risk had received breast MRI screening according to risk-based guidelines. Only 7 (8.2%) women reported receiving a breast MRI at any time. Five of these were diagnostic tests and 2 were done for screening purposes. The 2 women who had breast MRI for screening purposes were not considered to be at high risk according to the Claus and BRCAPRO models.

Information Shared with PCP

A large number of women (89.4%) reported that they shared information about their family history of cancer with their PCP. Far fewer shared information about their sister or mother's genetic counseling (24.7%) or their sister or mother's test results (22.4%).

Discussion

Calculation and interpretation of breast cancer risk is a complex task. When a *BRCA1/2* mutation has not been previously identified in a family, the most common outcome of *BRCA1/2* testing in a cancer patient is an indeterminate result. If a family member tests positive for a *BRCA1/2* mutation, other family, members can be tested to determine risk level. In contrast, in families where there is an indeterminate result, other members' risk must be quantified based on the patient's family history for appropriate medical management. PCPs are challenged to assess cancer risk, help patients understand their risk, and recommend appropriate risk-based screenings for these patients.

Recommendation of appropriate screening is made even more challenging by the differing guidelines, including the ACS (American Cancer Society, 2014), NCCN (National Comprehensive Cancer Network, 2013b), and USPSTF (2012) and by the fact that various risk calculators provide different estimates of risk for the same woman.

Women in our study comprised a unique group because (1) these women had mothers or sisters that met consensus-approved guidelines *BRCA1/2* testing and received indeterminate test results; (2) at the conclusion of the genetic risk notification counseling session, our participants sisters/mothers received a standardized summary letter informing them that their female relatives could be at elevated-risk and may meet the requirements for breast MRI screening or chemoprevention; and (3) these women are typically followed by primary care providers rather than genetics professionals because they have not had cancer themselves and are not in a family with an identified high risk gene.

We suspected that this group might have a greater proportion of women at elevated-risk than the population at large. Indeed, 10.6% of our sample was found to be at $\geq$20% lifetime risk by the Claus model and would meet guidelines for annual screening breast MRI. In contrast, approximately 1% of the U.S. female population is at $\geq$ 20% lifetime risk for breast cancer (Graubard, Freedman, & Gail, 2010). ACS guidelines indicate that there is insufficient evidence to recommend against MRI in the 15-20% lifetime risk range; 16.5% of our sample would qualify for annual MRI based on a risk of $\geq$15% lifetime risk. The Gail model is not for use in determining need for annual screening breast MRI. As can be seen in Table 4.3, if PCPs were to rely on the Gail model to identify women for MRI, many more women would qualify. As mentioned, 2

women in our study received recommendation for annual screening MRI from their PCP. Although their risk was not elevated by Claus, we do not have enough information to infer that these screening recommendations indicate over-screening. There could be other reasons their PCP recommended annual MRI including increased breast density.

The Gail model is important in assessing the need for chemoprevention. The FDA has approved Tamoxifen and Raloxifene for women with 5-year risk >1.67% according to the Gail model, although it has recently been suggested that higher cut-offs should be used for women over 50 (Freedman et al., 2011). We did not ask women whether they had received recommendations for chemoprevention; however, nearly 80% of our study population with an average age of 52.2 years had 5-year risk for breast cancer $\geq$1.67% by the Gail model. Thus, our sample had a much higher proportion of women who meet the criteria for chemoprevention than women in the general population where elevated 5-year Gail estimations range between 4-36% depending on age (Graubard et al., 2010).

Women who receive genetic counseling and testing receive personalized genetic information, which has implications for close biological relatives. Practice guidelines for cancer genetic risk assessment encourage genetic counselors to share familial implications of the assessment with their patients so that their patients may share that information with family members (Riley et al., 2012). Ninety percent of genetic counselors report that they consistently do so (L. E. Forrest et al., 2010). Women who have received counseling are encouraged to share risk information with their families and encourage family members to share that information with their PCPs. Our findings suggest that women are not consistently sharing information with PCPs about their sister's and mother's genetic counseling and test results. It could be that the women in

our study were evaluated too close to the time of their family member's test and had not yet had the opportunity to share this information with their PCPs. We did not have the test dates for relatives of our participants. It could also be that they did not understand the information or perceive it as pertinent to their care.

To enhance care delivery, it is important that genetic specialists communicate with counselee's PCPs (Nelson et al., 2014). Many PCPs have expressed a lack of confidence in basic knowledge of cancer genetics (Cox et al., 2012). Research has shown that women at elevated-risk may not be receiving appropriate mammography and MRI recommendations (Cohen, 2010). Close relatives of women in our sample had extensive pedigrees created and analyzed by professionals in cancer risk assessment, yet they may have never known it, because they had not received information about the genetic counseling and testing from their relatives. Previous research indicates that women who have received counseling may have difficulty understanding the implications of an indeterminate test result (Cypowyj et al., 2009). Additionally, information is often lost as messages go from genetic counselor to patient and from patient to other family members (Vos, Menko, et al., 2011). If those who have received counseling do not understand the implications of an indeterminate result, they cannot explain it adequately to their family members, and the family members may not explain it well to their care providers. Based on our results, PCPs should not assume that women will volunteer information about their family's genetic counseling and testing. Similarly, if a patient reports that her close relative had a *BRCA1/2* test showing her family member's cancer was "not genetic," her risk should not be assumed to be low or average. PCPs should also not assume that if a

woman is at elevated-risk she, would have been told by her family member who received an expert risk assessment.

Most of our study participants were considered to be at average-risk and had received mammography screening recommendations from their PCP in line with national guidelines. It is concerning, however, that more than 10% of the women were found to be at increased risk for breast cancer, yet none had received a recommendation for annual MRI in accordance with ACS and NCCN guidelines. Our findings are consistent with national patterns, indicating that breast MRI screening is under-utilized among elevated-risk women (Miller et al., 2013).

Many PCPs do not use risk calculating software. When they do, it is more likely to be the Gail model than more complex software based models that can be used to determine risk level for and the need for MRI screening (Afonso, 2009; Berg et al., 2010; Edwards, Maradiegue, Seibert, Saunders-Goldson, & Humphreys, 2009; Guerra et al., 2009; Sabatino et al., 2007). In a busy primary care practice, it can be challenging to find the time to perform a comprehensive breast cancer risk assessment (Wood, Flynn, & Stockdale, 2013). However, there is an opportunity for interdisciplinary collaboration. Registered nurses and other supportive staff working in primary care often assume the roles of collecting, organizing, and assessing patient history, including family history. These health care staff members often coordinate referrals and could be effectively trained in cancer risk assessment to identify women at increased risk and help coordinate risk-appropriate care.

The USPSTF recently issued new guidelines encouraging PCPs to identify women with family histories that may be associated with mutations in breast cancer

susceptibility genes with simple screening tools. It is recommended that high-risk women receive genetic counseling and be offered *BRCA1/2* testing if warranted, from a health care provider trained in breast cancer risk assessment, including genetic counselors or trained primary care professionals (Moyer, 2013). The USPSTF has classified the screening and referral of women to genetic services for counseling and testing if appropriate as a level B recommendation. The Affordable Care Act deems that preventive measures rated level A or B are to be covered without copayment by the patient(Centers for Medicare & Medicaid Services, (ND)).

We suggest PCPs use two levels of screening for breast cancer risk assessment. First, women who need in-depth risk assessment need to be identified. The USPSTF has identified several screening tools that could serve this purpose (Moyer, 2013); studies have also looked at using self-administered online screening tools that can be incorporated into the electronic health record to help PCPs collect this type of data (S. M. O'Neill et al., 2009; Ruffin et al., 2011). Second, for women who screen positive - indicating the need for an in-depth risk assessment, PCPs should assess risk using risk estimating models that take extensive family history into account or refer patients to health care providers including genetic counselors who are trained in breast cancer risk assessment to make these calculations. Armed with evidence-based lifetime risk estimates, PCPs will be able to recommend guideline concordant breast cancer screening, including MRI for women at elevated-risk.

Primary care providers (including physicians, nurse practitioners, physician assistants, and the nurses in their practices) as well as our colleagues in genetic counseling apply judgment, skill, and compassion when assessing and explaining risk to

women. A multidisciplinary approach is helpful when caring for women whose families have a suspicious but indeterminate genetically based risk for breast cancer.

Table 4.1

Risk-based cancer screening guidelines for women without breast cancer

Organization	Risk Categories & Definition	Mammography Screening Recommendations	Breast MRI Screening Recommendations
American Cancer Society[a]	**Average-risk** (<15% lifetime risk)	Annual beginning at age 40 and continuing as long as in good health	Not Recommended
	Moderately increased risk (15 - 20% lifetime risk)	Annual beginning at age 40 and continuing as long as in good health	Not enough evidence to recommend against or for annual MRI
	High Risk (about 20-25% or greater lifetime risk[b])	Annual beginning at age 40 and continuing as long as in good health	Annual MRI Recommended - no starting age suggested
U.S. Preventive Services Task Force[c]	**Average-risk** (no known genetic mutation or history of chest radiation)	**Aged 40-49 -** Individualize decision about screening based on circumstances and values. **Aged 50-74** every 2 years **Aged ≥75** no recommendation	Insufficient Evidence
National Comprehensive Cancer Network (NCCN)[d]	**Average-risk** (as defined by qualitative and quantitative assessment)	Annual beginning at age 40	
	Increased Risk (> 20% lifetime risk[e])	Annual beginning at age 30	Consider annual MRI beginning at age 30

Note: Risk categories are presented using labels and definitions as defined by each organization.
[a]ACS Guidelines 2014
[b]"according to risk assessment tools that are based mainly on family history such as the Claus model"
[c]USPSTF Guidelines 2009
[d]NCCN Guidelines 2013
[e]"as defined by models that are largely dependent on family history (e.g., Claus, BRCAPRO, Tyrer-Cuzick)"

Table 4.2

Characteristics of study population
(*n*=85)

Variable	*n*	(%)	*M*	*(SD)*
Age, years			52.2	(8.9)
Race/ ethnicity				
Non-Hispanic White	84	(98.8)		
Asian	1	(1.2)		
Education				
High school/ GED	13	(15.3)		
Some college	15	(17.6)		
Vocational	8	(9.4)		
2 year college	9	(10.6)		
4 year college	28	(32.9)		
Master's degree	11	(12.9)		
Professional degree	1	(1.2)		
Marital status				
Married	67	(78.8)		
Member unmarried couple	1	(1.2)		
Separated	3	(3.5)		
Divorced	10	(11.8)		
Widowed	2	(2.4)		
Never married	2	(2.4)		
Religion				
Protestant Christian	5	(5.9)		
Roman Catholic	3	(3.5)		
Latter-day Saint	61	(71.8)		
None	13	(15.3)		
Other[b]	3	(3.5)		
Insurance				
Insured	78	(91.8)		
Not Insured	7	(8.2)		
Primary Care Provider				
Physician	69	(81.2)		
Nurse Practitioner	5	(5.9)		
Physician Assistant	4	(4.7)		
None	7	(8.2)		

[b] Open responses for "other" religion included "atheist, nondenominational, Spiritual."

Table 4.3

Calculated risk

Model		[Range %]	*M*	(*SD*)	Lifetime ≥15%risk *n*	(%)	Lifetime ≥20% risk *n*	(%)	5-year ≥1.67% risk *n*	(%)
Gail										
	5-year	[0.6-12.0]	3.14	(2.3)					67	(78.8)
	Lifetime	[8.3-38.8]	20.07	(6.6)	72	(84.5)	29	(34.1)		
Claus										
	5-year	[0.2-5.7]	2.15	(1.2)						
	Lifetime	[2.0-38.3]	11.84	(6.7)	14	(16.5)	9	(10.6)		
BRCAPRO										
	5-year	[0.8-2.2]	1.24	(0.5)						
	Lifetime	[4.0-14.7]	9.53	(2.0)	0	(0.0)	0	(0.0)		

Table 4.4

Self-reported perceived relative risk (*n*=85)

Response	*n*	(%)
Much lower	2	(2.4)
Lower	9	(10.8)
The same	27	(32.5)
Higher	40	(47.1)
Much higher	5	(5.9)
Don't know/ No Answer	2	(2.4)

Compared to women of similar age

Table 4.5

Congruence between risk calculator and women's estimates

Model		*n*	(%)
Gail			
	Women estimated higher risk	36	(42.9)
	Women congruent with risk calculation	15	(17.8)
	Women estimated lower risk	33	(39.3)
Claus			
	Women estimated higher risk	62	(73.8)
	Women congruent with risk calculation	13	(15.5)
	Women estimated lower risk	9	(10.7)
BRCAPRO			
	Women estimated higher risk	66	(78.6)
	Women congruent with risk calculation	13	(15.5)
	Women estimated lower risk	5	(6.0)

Note: Percent calculations are based on women who gave estimates of their lifetime risk for breast cancer (*n*=84). One woman did not provide a numeric estimate. Women were considered to provide estimates congruent with each risk calculator if their estimate came within 3% (+/-) of the risk calculator result.

Table 4.6

Mammography recommendations from PCP for average and elevated-risk women by age

	Average-risk (*n*=76)						Elevated-risk (*n*=9)	
	age 40-49		age ≥50		All Ages		All Ages	
	n	(%)	*n*	(%)	*n*	(%)	*n*	(%)
Every year (annually)	26	(86.7)	40	(87.0)	66	(86.8)	9	(100.0)
Every two years	1	(3.3)	0	(0.0)	1	(1.3)	0	(0.0)
Just one time	1	(3.3)	0	(0.0)	1	(1.3)	0	(0.0)
Never recommended	0	(0.0)	1	(2.2)	1	(1.3)	0	(0.0)
Don't Know	0	(0.0)	1	(2.2)	1	(1.3)	0	(0.0)
Other	2	(6.6)	4	(8.7)	6	(8.0)	0	(0.0)
Total	30	(99.9)	46	(100.1)	76	(100.0)	9	(100.0)

Boxed cells represent minimum mammography screening recommendations by USPSTF. Shaded cell represents minimum mammography screening recommendations by ACS and NCCN. Primary care providers may recommend screenings earlier than guidelines based on other risk factors.

Table 4.7

Most recent screening mammogram for women by risk category and age

	Average-risk Women						Elevated-risk Women	
	Ages 40-49		Ages 50-74		All Ages		All Ages	
	n	(%)	*n*	(%)	*n*	(%)	*n*	(%)
A year ago or less	20	(69.0)	27	(67.5)	47	(68.1)	6	(0.75)
More than 1 but not more than 2 years ago	6	(20.7)	7	(17.5)	13	(18.8)	2	(0.25)
More than 2 but not more than 3 years ago	0	(0.0)	1	(2.5)	1	(1.5)	0	(0.0)
More than 3 but not more than 5 years ago	0	(0.0)	3	(7.5)	3	(4.3)	0	(0.0)
More than 5 years ago	2	(6.9)	2	(5.0)	4	(5.8)	0	(0.0)
Has never had a mammogram	1	(3.4)	0	(0.0)	1	(1.5)	0	(0.0)
Total:	29	(100.0)	40	(100.0)	69	(100.0)	8	(100.0)

Note: women whose most recent mammograms were performed because of a symptom or as a follow-up from a previously abnormal test are not included in this table. The boxed data represent the 35 women who are considered to have received their most recent screening mammogram in accordance with USPSTF guidelines. The shaded box represents the 47 women who received their most recent screening mammogram in accordance with ACS and NCCN guidelines. Note that women screening outside USPSTF guidelines are mostly receiving screenings earlier than suggested. Women screening outside of ACS and NCCN guidelines are mostly receiving screenings less frequently than suggested. No women in the elevated-risk category are considered to be screening by guidelines because none have received screening breast MRI.

CHAPTER 5

RESULTS MANUSCRIPT 2: BREAST CANCER RISK PERCEPTIONS AMONG RELATIVES OF WOMEN WITH INDETERMINATE NEGATIVE *BRCA1/2* TEST RESULTS: THE MODERATING EFFECT OF AMOUNT OF SHARED INFORMATION

Abstract

The most common result of *BRCA1/2* mutation testing when performed in a family without a previously identified mutation is an indeterminate negative test result. Women in these families may have an increased risk for breast cancer because of mutations in non-*BRCA* breast cancer predisposition genes, moderate- or low-risk genes, or shared environmental factors. Risk estimates, therefore, must be based on family history and other risk factors. We evaluated 85 sisters and daughters of women who received an indeterminate negative *BRCA1/2* results and found that most of them reported receiving very little information from their family member about her counseling session. When participants perceived that more information was shared about their relative's genetic counseling session, they had more accurate perceptions (correlation = 0.748 (p=0.000) of their own risks for breast cancer than those who perceived that less information was shared (correlation = 0.346 (p=0.05), where perfect accuracy is operationalized as a correlation of 1.00 between calculated and perceived lifetime risk). Overall, very little information was shared between close relatives who received genetic

counseling and our study participants; nearly 20% reported that nothing was shared with them about their mother or sister's genetic counseling. Family members were generally not aware of the existence of a genetic counseling summary letter that their relatives received following the session. Our findings underscore the need for effective strategies that facilitate counselee's to share information about their genetic counseling sessions with their relatives. Such communication may help their relatives better understand their cancer risks and enhance risk appropriate cancer prevention.

Introduction

Breast cancer risk assessment has implications for both patients and their family members. A cancer risk assessment includes evaluating the patient's family history and other risk factors, as well as providing individualized interpretation of genetic test results. Genetic counselors can help their patients understand what test results mean to them as well as their family members in terms of risk for future cancer and appropriate medical management. Counselors typically encourage their patients to share information and genetic test results with family members and to encourage family members, in turn, to share information with their primary care providers (Riley et al., 2012). The purpose of this study was to determine whether the accuracy of sisters' and daughters' perceptions of their own risk for future breast cancer are improved when more information is shared by their family members who received *BRCA1/2* genetic counseling and received indeterminate negative results. We hypothesized that the level of family communication influences the accuracy of breast risk perceptions among counselee's at-risk relatives.

Background

Genetic counselors play a key role in identifying at-risk family members and helping their patients communicate risk information to family members. The National Society of Genetic Counselors (NSGC) recommends that an essential element of disclosure is to "identify at-risk family members and provide [the] patient with tools to inform and educate family members" (Riley et al., 2012, p. 158). Because of concerns about patient privacy, the most common method counselors use to disseminate risk information within the family is to suggest that patients share the information with relatives (L. E. Forrest et al., 2010). Although patients are often willing to share information, research has shown that information is often not disseminated to all family members who may benefit from receiving it and the information that is shared is often inaccurate (K. Forrest et al., 2003; Hayat Roshanai et al., 2010; MacDonald et al., 2007; Vos, Menko, et al., 2011). Thus, many at-risk relatives lack critical information that could help them better understand their cancer risks and be aware of appropriate preventive and screening measures (Ersig, Williams, Hadley, & Koehly, 2009; Vos, Jansen, et al., 2011).

Much of the research on communication and risk perception among families at risk for breast cancer has focused on families with a known *BRCA1/2* mutation. Yet the most common outcome of *BRCA1/2* testing is an indeterminate negative result, meaning a negative result in the absence of a known family mutation. Members of these families may still be at increased familial cancer risk. In the absence of an identified mutation, it is recommended that familial risk be estimated based on a family history evaluation including the types and ages of onset of cancer in a family (National Comprehensive

Cancer Network, 2013c). Some families have more cases of cancer than would be expected due to chance. Women in these so-called family clusters may have an increased risk for breast cancer because of inheritance of another high- or moderate-risk gene mutation, shared environmental factors, or a combination of the two (Berliner & Fay, 2007). While these families may not carry the same level of risk as *BRCA1/2* positive families, risk may still be high enough earlier onset of screening, screening breast MRI, and/or chemoprevention (Freedman et al., 2011; National Comprehensive Cancer Network, 2013b). Thus, risk assessment and individualized communication about genetic test results by the counselor are important to family members beyond the counselor's immediate patient, even in the presence of an indeterminate negative *BRCA1/2* test result.

A primary goal of genetic counseling is to help people accurately understand risk and make informed decisions based on personal risk (Hilgart et al., 2012; Riley et al., 2012; Smerecnik et al., 2009). It is believed that if people more accurately understand their risk, they are better prepared to take appropriate actions to reduce and manage this risk (Haas et al., 2005). Research assessing accuracy of risk perception related to breast cancer in families at elevated-risk has primarily focused on women who received genetic counseling rather than their family members (Hilgart et al., 2012; Tilburt et al., 2011). In the presence of an indeterminate negative test result within the family, family members do not often seek genetic counseling. If they receive information about their family member's test results, they must generally rely on second-hand information shared by the counselee. Women with indeterminate negative test results are less likely to share information obtained during genetic counseling sessions than those who tested positive for mutations (Patenaude et al., 2006).

Risk perceptions can be measured using verbal or numeric estimates. Health care providers tend to view successful risk communication as the transmission of precise information, expecting that patients should understand their risk as the health care provider does (Collins & Street, 2009, p. 1507). Patients, on the other hand, may focus more on experiential reasoning to understand risk communications, drawing upon personal life experiences and emotions (Collins & Street, 2009). Indeed, many women have difficulty interpreting risk information, especially when it is presented in a numeric format (Leventhal et al., 1999; Schwartz et al., 1997). Often women's verbal and numerical risk estimates are not congruent (Smerecnik et al., 2009). Women tend to underestimate risk when using verbal comparative scales but over-estimate their numeric risk (Lipkus et al., 2000; Woloshin et al., 1999). The terms "over-estimate" and "underestimate" suggest that there is an accurate estimation, but varying risk models may give quite different risk estimates.

To assess accuracy of risk perception, an objective or "gold standard" measure of risk is needed against to compare subjective risk perceptions. Researchers typically set arbitrary breaks between categories of accuracy vs. overestimation or underestimation of risk using either numeric or verbal categories (Smerecnik et al., 2009). For example, some have required women's perception to fall within two categories of counseled risk on a six-point scale to be counted as accurate (Bjorvatn et al., 2007), or to fall within one category of counseled risk estimate (Lobb et al., 2004). Haas et al. (2005) categorized women as "high-risk" if they had a Gail score of more than 1.67%, all other women were determined to be "average-risk," and women's risk perceptions were deemed inaccurate if they did not choose the verbal category (high or average) that corresponded with their

Gail scores and the numeric cut-points selected by the authors. Metcalfe et al. (2013) calculated lifetime risk of breast cancer in sisters of breast cancer patients using the Tyrer-Cuzick model and categorized women as overestimating or underestimating if they did not select the exact same percent of lifetime risk for breast cancer that the model generated; they reported the average degree of overestimation. Thus, definitions of accuracy in the literature are not consistent. A woman may have an accurate estimation of her personal risk in relation to one objective measure of risk but have an inaccurate estimation of her risk when compared to another measure. Even when using the same objective measure of risk (e.g., the Gail model or the Claus model), researchers have categorized overestimation, underestimation and accurate estimation in different ways (Bjorvatn et al., 2007; Domanska, Nilbert, Soller, Silfverberg, & Carlsson, 2007; Haas et al., 2005; Lobb et al., 2004; Rimes, Salkovskis, Jones, & Lucassen, 2006)

Methods

Study Population

Participants included biological sisters and daughters of women who had a personal history of breast cancer and received indeterminate negative *BRCA1/2* test results from a board certified genetic counselor. Participants were between the ages of 40-74. Women were excluded if they ever received breast cancer-related genetic testing, had received a prophylactic bilateral mastectomy or oopherectomy, had a personal history of any type of cancer other than nonmelanoma skin cancer, and/or if they were of Ashkenazi Jewish descent as the associated high-risk status with this ancestry necessitates special consideration in evaluating risk.

Participants were referred to the study by their sisters or mothers with breast cancer who had received genetic counseling either as part of the *Risk Education & Assessment for Cancer Heredity* (REACH) study, a population-based randomized equivalency/noninferiority cluster randomized trial of remote in-person vs. telephone *BRCA1/2* counseling and testing or through the clinical genetic counseling service at Huntsman Cancer Institute. It is unknown which of the current study participants were referred by counselees from the two sources. All counselees who referred participants to our study had received pre- and posttest genetic counseling along with standardized summary letters alerting them to the possibility that close relatives may be at increased risk for breast cancer and may need more intensive breast cancer surveillance, possibly including breast MRI. Counselees were encouraged to share this information with their close relatives (our potential participants) and encourage their relatives to share that information with their primary care providers.

Procedures

All procedures were approved by the University of Utah Institutional Review Board. Potential participants were mailed introductory letters followed by telephone calls to assess for eligibility and invite them to participate. Eligible women who agreed to participate were sent a packet in the mail with a survey and a family history collection tool. They also completed a telephone interview to review their family history data and ask additional questions. Prior to the telephone interview, a pedigree was drawn from the self-reported family history. Women were asked if they wanted to receive their 5-year and lifetime risk estimates by the three models used. Women who completed the study

were thanked with a mailed $25.00 prepaid gift card and for those who desired, their breast cancer risk estimates.

Measures

Risk perception. The mailed survey included two questions about perceived risk for breast cancer. The initial question asked women to rate their perceived risk verbally stating, "In your opinion, compared to other women your age, what are your chances of getting breast cancer?" Women could respond on a five-point scale ranging from "much lower" to "much higher." The second question first presented women with a graphic showing 12 of 100 women shaded dark and stating, "On average 12 women out of 100 will get breast cancer in their lifetime." Then the question instructed, "Picture yourself in a room with 100 women exactly like you (same risk-factors). How many of you will get breast cancer in your lifetime?" This question was accompanied by a picture of 100 women with none shaded and the statement, "You can pick any number between 0 and 100." A frequency format with graphic has been shown to have a lower risk estimation error when compared to the percentage scales when estimating lifetime risk for breast cancer (Cameron et al., 2011; Schapira et al., 2004). Asking the qualitative question first and providing an anchor population has been shown to increase accuracy of risk perception (Apicella et al., 2009; Dillard et al., 2006; Taylor et al., 2002).

Calculated risk. Five-year and lifetime risks were calculated using the Claus, BRCAPRO, and Gail models. Claus and BRCAPRO lifetime risk estimates were used as indicators for the latent variable calculated risk.

Accuracy of risk perception. Some refer to the agreement between perceived risk and calculated risk as accuracy. Inherent in this terminology is the assumption that the

calculations are correct and women are "accurate" if their perceptions are close to the estimates. However, every model calculates risk-based on different factors and estimates may vary widely between models. Therefore, we use the term "accuracy" recognizing that it is a common term in the literature, but the term "agreement" may hold less bias. We operationalized the concept of accuracy of risk perception as the level of agreement, or in statistical terms, the path coefficient, between the latent variable "calculated lifetime risk" for breast cancer and "perceived lifetime risk" (see Figure 5.1). We chose not to include the Gail calculations in the model because it does not take extensive family history into account and is therefore not an appropriate model to use for lifetime risk calculation when determining medical management (American Cancer Society, 2014). The Gail model considers risk factors beyond the family history and is the most frequently used model.

Information shared. Women were asked to rate how much information their sister or mother with breast cancer shared about her genetic counseling session on a scale of 0-5 with 0 indicating that the family member shared no information and 5 indicating a great deal of information shared. Similarly women were asked to rate how well they understood the information shared on a 0-5 scale with 0 indicating that she understood none of the information and 5 indicating that she understood a great deal. We also asked whether women were aware of the posttest counseling summary letter, or the informational pamphlet that was provided to their sisters/mothers following their relative's posttest genetic counseling session.

Numeracy, knowledge, and health literacy. We assessed three cognitive variables known to influence risk perception including numeracy, knowledge, and health literacy

(Tilburt et al., 2011). Numeracy was measured using the eight-item Rausch-based numeracy scale that assesses the users' ability to understand, manipulate, and use numerical information including probabilities. Possible scores range from 0-8 with higher scores indicating higher levels of numeracy (Weller et al., 2012). The 27-item Breast Cancer Genetic Counseling Knowledge Questionnaire (BGKQ) was used to assess knowledge about breast cancer genetics. Scores could range from 0-8 with higher scores indicating higher levels of knowledge (Erblich et al., 2005). We assessed health literacy using the Set of Brief Questions developed by Chew, Bradley, and Boyko (2004). Each of the three questions has five response options that were scored from 0-4. Questions included, "How often do you have someone help you read hospital materials?" ("never" to" always"), "How confident are you filling out medical forms by yourself? ("not at all" to "extremely"), and "How often do you have problems learning about your medical condition because of difficulty understanding written information?" ("never" to "always"). Total scores could range between 0-12 with higher levels indicating higher levels of health literacy.

Cancer-related distress. Cancer-related distress was measured to assess the emotional response to being at risk for breast cancer. We used the 15-item Impact of Event Scale (Horowitz et al., 1979), which asks about how frequently certain statements were true for the participant during the past 7 days ranging from "not at all" to "often." Instructions to women were, "thinking about your family history of cancer, how often would you say…" followed by a list of comments made by people after stressful life events that are thought to be indicators of distress.

Statistical Analyses

Descriptive statistics (percents and frequencies) were calculated using IBM SPSS software version 21. Latent variable modeling was completed using M*plus* software; version 7 was employed to test the hypothesis that the amount of information shared by women's sisters or mothers who received genetic counseling would increase the accuracy of perceptions about their personal breast cancer risk.

Latent variable models are built on theory and clinical experience (Borsboom, Mellenbergh, & van Heerden, 2003; Byrne, 2012). Our study/ model was based broadly on the Common Sense Model of Self-regulation (CSM) by Leventhal et al. (2003). The CSM proposes that people respond to health threats with both cognitive and emotional reactions. Cognitive and emotional responses simultaneously influence one another and are key drivers of actions that people take to control the threat and control fear. It has been proposed that the CSM provides a strong framework for studying risk perception based on family history information (Marteau & Weinman, 2006; Sivell et al., 2008). We view risk perception as a cognitive response to the health threat of breast cancer (having a close family member with breast cancer who has received genetic counseling and testing). This cognitive response can be simultaneously influenced by other cognitive factors (numeracy, knowledge, health literacy) as well as emotional factors (cancer related distress). Our primary aim was to evaluate perceived risk while controlling for cognitive and emotional factors known to influence risk perception (Tilburt et al., 2011)

We selected a novel approach to measuring accuracy of risk perception that does not require the calculation of a difference score or an arbitrary break in categories. Using latent variable modeling we were able to consider both calculated risk and perceived risk

as latent variables. Latent variables are constructs that are measured by other indicators. The individual measurement items can be modeled as manifestations of the underlying latent construct and error terms for each measurement item can be estimated (Kline, 2010). Accuracy of risk perception was defined as the level of agreement (i.e., as a continuous variable) between risk perception and calculated risk. In our study, the construct of perceived lifetime risk for breast cancer was operationalized with both a verbal and numeric estimate provided by the participant (see Figure 5.1). Using a combination of both numeric and verbal measures allowed a more comprehensive view of a woman's risk perception. The concept of calculated risk was measured by the lifetime risk calculations produced by Claus and BRCAPRO models. Although we calculated Gail scores, we did not include those as indicators of calculated lifetime risk because medical management for familial cancer risk is primarily based on selected features of a patient's family history (National Comprehensive Cancer Network, 2013a, 2013b). This approach allowed us to examine the impact of amount of information shared on accuracy of risk perception, simultaneously accounting for verbal and quantitative risk perceptions and multiple measures of calculated lifetime risk.

Given that risk perception is a complex concept, our goal was to control for significant covariates that could complicate interpretation of our results. Selection of initial covariates was informed in part by Tilburt et al. (2011). Only significant covariates were included in the final model. Covariates that were evaluated but ultimately not included in the final model included age, education, and health literacy. Significant ($p < 0.5$ by Wald test) covariates that were retained include numeracy, knowledge about breast cancer genetics, and distress (see Figure 5.1).

Results

Demographics

Of the 135 women who were mailed introductory letters, 98 were ultimately eligible and 85 completed both the survey and the telephone interview (see Figure 5.2). Participant ages ranged from 40-71 with a mean of 52.2 (*SD* = 8.9). Nearly all women (98.8%) reported their race and ethnicity as non-Hispanic White with 1 woman reporting her race as Asian. Age, race/ethnicity, and educational level were similar between nonparticipants who shared demographic information (*n* = 11) and study participants (see Table 5.1).

Risk Perceptions

More women perceived their lifetime risk for breast cancer as being "higher" or "much higher" (53%) than other women their age as opposed to "the same" (32.5%), or "lower" or "much lower" (13.2%) using verbal measures. On average women estimated their quantitative lifetime risk to be 25.62% (*SD*=19.94) with a range of 1-95%.

Calculated Risk

Calculated 5-year and lifetime risk estimates by risk prediction model are presented in Table 5.2. Additionally, the percentage of women with lifetime risks equal to or greater than 15% and 20% are delineated. These cut-points are significant because both the NCCN and the ACS suggest that women screen with annual screening breast MRI in addition to mammography when lifetime risk is estimated to be greater than 20% using models that take extended family history into account. The ACS has suggested that

there is not enough evidence to determine whether to recommend for or against annual screening breat MRI in women with risk estimates between 15% and 20%.

Summary Letter and Informational Pamphlet

Women were asked whether they were aware that their sister or mother received a summary letter about their genetic counseling session. Only 12 women (14.3%) reported that they were aware of such a letter. Of those who were aware of a letter, 7 women saw the letter and 2 were given a copy to keep. Only 3 women reported that they shared information about the letter with their primary care provider. Two women reported that they provided their primary care provider with a copy of the letter. Women were asked to rate on a 0 to 5 scale whether some of the information in the letter applied to them with zero indicating that none of the information applied to them, and 5 indicating that some of the information applied strongly to them. Of the 12 women who were aware of the letter, 58% rated the letter's applicability to them as a 4 or 5 on the 0-5 scale. Four women reported that they were aware of an informational pamphlet that their sister or mother received as a part of the genetic counseling session. Two women reported that they saw the pamphlet and 1 reports that she read it.

Covariates of Perceived Risk

Family pedigree, distress, knowledge, health literacy, numeracy, age and education were all considered as variables that could influence perceived risk. As shown in Table 5.3, overall, women had low levels of cancer-related distress, high levels of health literacy, and average levels of numeracy and knowledge about breast cancer genetics. Health literacy, age, and education were not significantly associated with risk

perception and therefore were not included in the final latent variable model. The relationships between retained covariates and perceived risk are illustrated in Figure 5.1 as the standardized path coefficients. Numeracy and distress were associated with higher risk perception, but knowledge was inversely associated with risk perception. Standardized path coefficients less than 0.10 indicate weak relationships, values around 0.30 represent a moderate association, and values of 0.50 or more represent a strong relationship between constructs (Kline, 2010).

Amount of Information Shared and Understanding

Overall, women rated the amount of information shared by their sisters and mothers about their genetic counseling sessions as low (see Table 5.4). Only 18.8% of women reported that their sisters or mothers did not share information; these women were not asked how well they understood information shared. Women generally reported high levels of understanding the small amounts of information shared. As 1 woman stated, "all she told me was 'I'm negative, but you should still get your mammograms' – so that's not hard to understand." The families from which we recruited were not identified as having any *BRCA1/2* mutations; therefore, none of the sisters or mothers were likely to have a *true negative* test result. All of their relatives' test results were *indeterminate negatives*.

Moderating Effect of Information Shared on

Accuracy of Risk Perception

To evaluate the moderating effect of information shared between relatives on associations between perceived and calculated lifetime risk for breast cancer, we

compared two models: one with moderation (allowing different slopes and intercepts for the regression of perceived risk on calculated risk) and one with no moderation (with slopes and intercepts equal across levels of information shared). We hypothesized that the amount of information shared by sisters and mothers about genetic counseling would moderate the relationship between a woman's perception of her risk and objectively calculated risk (accuracy of risk perception).

The variable "amount of information shared" was stratified into high and low groups based on the amount of information women reported their family member had shared with them about the genetic counseling session. The "low shared information" group (n=68) included women who responded between 0 and 3 and the "high information shared" group (n=17) included women who responded 4-5 on the Information Shared scale. Stratifying on the basis of all six options (0-5) was not feasible due to the small sample size.

A chi square test was conducted to assess significance of the difference of deviance between the models. A difference in chi-square between the model with moderation and the model where the groups were constrained to be equal was 4.79 (df=1) (p = 0.287). This indicates significant improvement in model fit when the high and low amount of information shared groups is not constrained to be equal. Fit indices for the alternative model assessing moderation effect of amount of information shared were Chi-Square Test of Model Fit 22.550 (df=28, p=.7552), RMSEA = 0.0000, 90% CI [0.000-0.086]. A nonsignificant chi-square indicates that the model–implied covariance matrix is consistent with the population covariance matrix and supports the model; in other

words, the model and the data are not significantly different (Kline, 2010). RMSEA is below 0.05, indicating good model fit.

In summary, the amount of information shared by sisters and mothers about their genetic counseling sessions had a significant moderating effect on the accuracy of risk perception in their sisters and daughters who did not attend genetic counseling (see Figure 5.1). Perfect correlation between perceived and calculated risk (perfect accuracy) would yield a path coefficient of 1.0 between the two latent variables. In our sample, women who rated the amount of information shared as high had nearly twice the accuracy (standardized path =0.707, p=0.000) as those who rated the amount of information as low (standardized path = 0.326, p = 0.003) while controlling for distress, numeracy, and knowledge about breast cancer genetics. Thus, having a high amount of information shared more than doubled women's accuracy of risk perception.

Discussion

A familial cancer risk assessment by its very nature produces information that is valuable to the entire family. Our study is among the first to demonstrate that the accuracy of risk perceptions is better among counselee's relatives when they share more information about their genetic counseling session with them. In fact, with high amounts of information sharing, accuracy of risk perception in family members more than doubled. The salience of this finding is underscored given that genetic counselors often encourage their patients to share information with family members. Our study provides evidence that sharing makes a difference. It is noteworthy that the majority of our study's participants reported that limited information was shared with them. Nearly 20% reported that nothing at all was shared about their family member's genetic counseling session and

over 80% were considered in the *low amount of information shared group*. Thus, our findings suggest that communication could be improved in families where an indeterminate negative *BRCA1/2* test has been found. These findings are consistent with other literature, indicating that women with indeterminate negative *BRCA1/2* results are less likely to share their test results with family (Cheung et al., 2010; Patenaude et al., 2013). Our study is unique in that it elicited information about perceptions of the amount of information shared and did not focus specifically on test results.

The low amount of shared information does not necessarily mean that families do not communicate. Indeed, our participants were referred to the study by their sisters and mothers, indicating that they had some contact with or knowledge about their family members. It is possible that the low amount of information shared about genetic counseling could indicate that the information provided during genetic counseling was not something counselees deemed worth sharing with their close biological relatives because the genetic test result might have been perceived as "negative." Some women reported that their sisters or mothers told them the cancer was "not hereditary." The observed low level of information sharing in our study may be because the information was perceived as too complex to share in depth, or much of the information was shared but our participants had limited recall.

The sisters and mothers of our participants received genetic counseling according to a standardized protocol. A summary letter and an informational pamphlet were provided as part of test disclosure. Previous clinic patients had expressed the desire for an informational pamphlet specifically to help them explain cancer genetics to their family members. We initially thought that family members who were aware of or read the

summary letter and the informational pamphlet might have more accurate risk perceptions. However, few women were aware of the letter (14.1%) or pamphlet (3.5%), and even fewer reported reading them; therefore, we did not include these variables in our structural equation model. Although very few women were aware of a summary letter per se, we cannot rule out that the summary letter may have helped women convey information to their family members. Genetic counseling summary letters are not necessarily intended to be shared with family members; they are typically written for the woman herself, perhaps with a section that applies to the extended family.

It has been suggested that misperception of risk can increase or decrease use of screening and preventive services (Tilburt et al., 2011). Higher risk perceptions are generally associated with higher levels of screening (Katapodi et al., 2004). However, the ultimate goal is not to undiscerningly increase screening, but to achieve screening congruent with risk-based guidelines. The ACS and the NCCN recommend that women with lifetime risk for breast cancer of greater than 20% be screened annually with breast magnetic resonance imaging (MRI) in addition to mammography when risk is calculated with models that depend largely on family history. The ACS further suggests that breast MRI may be considered when a woman's estimated lifetime risk levels exceed 15%. Over 10% of our participants were considered to be $\geq$20% lifetime risk according to the Claus model, yet none of them had been offered or received screening breast MRI (Himes et al., in preparation). Thus, whether they had high or low levels of accuracy or high or low amounts of information shared, the highest risk women in our study had not been offered risk-appropriate breast cancer screening.

Practice Implications

It is important that genetic counselors consider disclosure methods that balance confidentiality with obligation to identify and inform family members that may be higher risk (Godard et al., 2006). The duty to warn would suggest that at least for close biological relatives in whom high levels of risk are suspected, the genetic counselor should act (Offit, Groeger, Turner, Wadsworth, & Weiser, 2004; Stol et al., 2010; Suthers et al., 2006). Practice recommendations for genetic cancer risk assessment, counseling, and testing published by the National Society of Genetic Counselors suggest that, "If a patient refuses to share information with relatives, the genetic counselor should evaluate his/her potential legal and/or ethical duty to warn. This evaluation should include a consultation with their institution's HIPAA compliance officer and/or ethics committee" (Riley et al., 2012, p. 58). Our findings suggest that encouraging patients to share information with family members and providing a summary letter is not enough. Women with an elevated lifetime risk for breast cancer been shown to benefit from more intensive screening including annual MRI (Berg et al., 2012; Kriege et al., 2004). Yet most women at high risk are not receiving annual MRI (Cohen, 2010). Approximately 10% of sisters and daughters in our study population were considered at high risk but had never received an MRI nor had one recommended by their primary care provider (Himes et al., in preparation). Women with indeterminate negative *BRCA1/2* tests may require more active psycho-educational interventions about what information to share with family members and strategies for sharing it. If family members are not aware of their risk, they may not be aware of all screening and prevention options available to them. Evidence-based genetic counseling interventions are needed to promote effective family

communication, and readily provide consultation to family members and their primary care providers.

Research Recommendations

While current practice guidelines suggest a duty to warn family members when counselees refuse or are incapable or sharing information, some clinicians have taken the duty to warn a step further (Suthers et al., 2006). It has been suggested that because many women have a difficult time understanding familial cancer risk information, interpreting it, and communicating this information to relatives, counselors should routinely guide their patients in the communication process or even inform relatives directly about test results and their risk if possible (Chan-Smutko, Patel, Shannon, & Ryan, 2008; Godard et al., 2006; Seymour et al., 2010; Stol et al., 2010; Suthers et al., 2006; Vos, Jansen, et al., 2011). There is some evidence that family members prefer receiving risk information from a health care provider rather than from their family member (Tunin et al., 2009). Future research is needed to determine the feasibility, acceptability, and effectiveness of these strategies in the presence of indeterminate negative *BRCA1/2* results when pedigree analysis indicates family members may be at elevated-risk. Genetic counselors might consider a letter addressed to family members that can be copied and hand delivered or mailed by the counselee or request consent from the counselee for a direct mailing of this information to their at-risk relatives.

Study Limitations

Our study population was virtually all non-Hispanic White and well educated, limiting the generalizability of our findings to more underserved populations. Whenever

family history is used to assess risk, there is the potential for inaccurate or incomplete cancer information. However, the women in our study had sufficient time to collect the required family history data. Further, many participants conferred with other family members to obtain data as accurately as possible, enhancing validity of family history information. Studies comparing self-reported family history with verified cases have yielded a high sensitivity for breast cancer when compared to validation by chart review (83-97%) (Kerber & Slattery, 1997; Parent, Ghadirian, Lacroix, & Perret, 1997). Because our study participants had participated in a previous study about breast cancer prevention and that we asked them to collect family history information for pedigree analysis, it is possible that they may have heightened awareness of breast cancer, yielding higher distress scores and inflated risk perceptions. However, this does not appear to be the case given that risk perceptions and distress scores were relatively low.

Conclusion

The most common result of *BRCA1/2* mutation testing when performed in a family without a previously identified mutation is the indeterminate negative test result. Women in these families may have an increased risk for breast cancer based on family history. We evaluated sisters and daughters of women who received an indeterminate negative *BRCA1/2* results and found that most of them reported receiving very little information about the counseling session from their sister or mother. When more information was shared about the genetic counseling session, sisters and daughters had more accurate perceptions of their own risks for breast cancer. However, our study participants reported that very little information was shared. At-risk female relatives of counselees are generally not aware of the existence of a genetic counseling summary

letter. It is important for genetic counselors to explore new ways to help their patients share information with family members to help family members perceive their risk for breast cancer more accurately, which could potentially allow family members to pursue risk-appropriate prevention and screening measures.

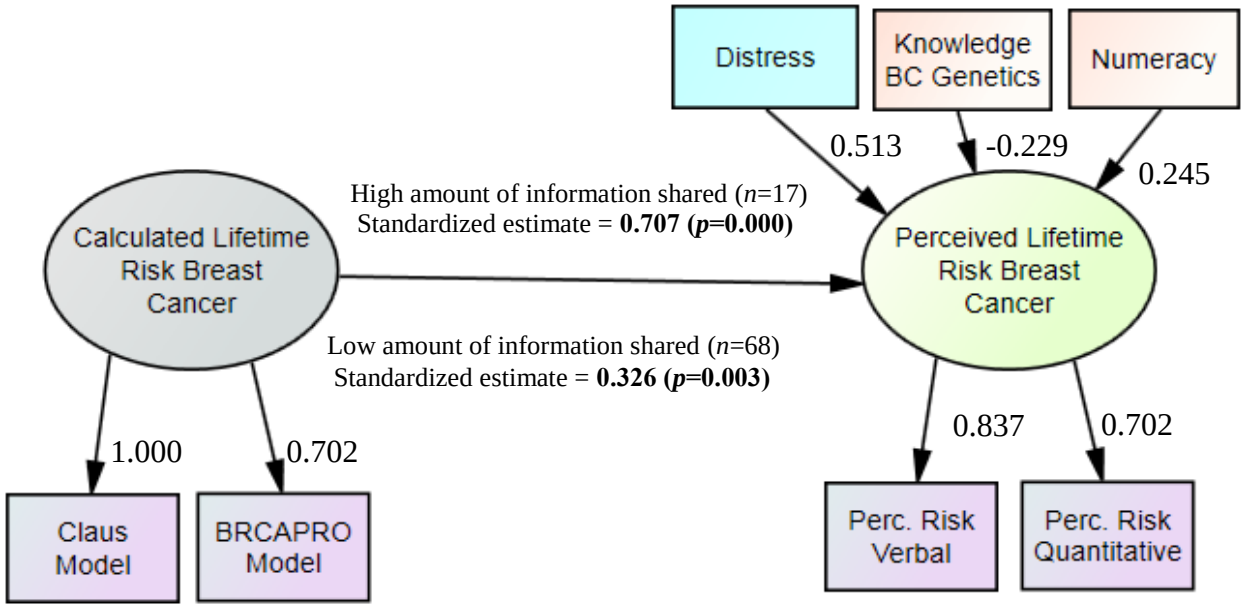


Figure 5.1

Final moderation model allowing regression of Perceived Risk on Calculated Risk to vary with information shared.*

* Chi-Square Test of Model Fit 22.550, *df* = 28 (*p* = 0.755); Difference in chi-square compared with model constraining equal regressions of Perceived Risk on Calculated Risk = 4.79, *df*=1, (*p* =0.0287)

Note: All analyses and were conducted with respect to the unstandardized solution. Standardized coefficients are presented here for interpretability. All included covariates and indicator variables were significant ($p < 0.05$). Beta weights for explanatory covariates and indicator variables have been weighted based on group size and combined so that information in the model can be presented with one diagram. Thus, coefficients for all parameters should be considered to reflect the whole sample except for the arrow between the latent variables *Calculated* and *Perceived* lifetime risk for breast cancer. This arrow represents the accuracy of risk perception in women who reported that low or high amounts of information were shared with them by their relative who received genetic counseling and testing. As can be seen in the bolded numbers, women reporting high amounts of information shared were found to be more than twice as accurate in their risk perceptions based on our measure.

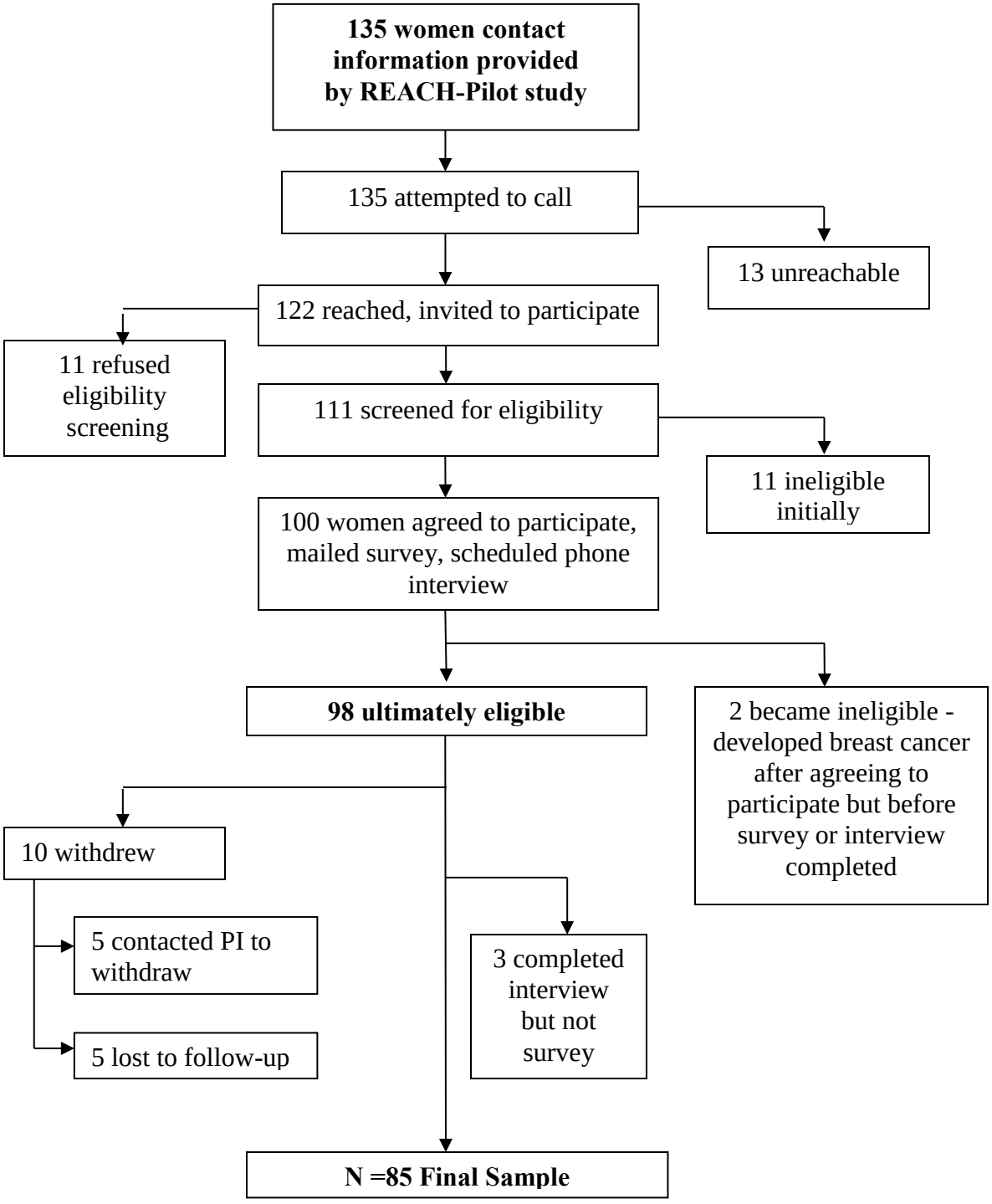


Figure 5.2
Flow of participants

Table 5.1

Demographics of participants and nonparticipants

	Participants $n = 85$				Nonparticipants $n = 11$			
Category	*n*	(%)	*M*	*(SD)*	*n*	(%)	*M*	*(SD)*
Age			52.2	(8.9)			55.4	*9.8*
Race/ ethnicity								
Non-Hispanic White	84	(98.8)			11	(100.0)		
Asian	1	(1.2)			0	(0.0)		
Education								
High school/ GED	13	(15.3)			0	(0.0)		
Some college/ vocational	32	(37.6)			6	(54.5)		
4 -year degree	28	(32.9)			2	(1.8)		
Graduate degree	12	(14.1)			3	(2.7)		

[a] Nonparticipant data were provided by 11 of 23 women who did not participate because they, refused screening, withdrew, were lost to follow-up, or became ineligible. Other nonparticipants refused to provide demographic data. Percentages are based on nonparticipants who provided data.

Table 5.2

Calculated risk

Model		[Range %]	*M*	(*SD*)	Lifetime ≥15%risk *n*	(%)	Lifetime ≥20% risk *n*	(%)
Gail								
	5-year	[0.6-12.0]	3.14	(2.3)				
	Lifetime	[8.3-38.8]	20.07	(6.6)	72	(84.5)	29	(34.1)
Claus								
	5-year	[0.2-5.7]	2.15	(1.2)				
	Lifetime	[2.0-38.3]	11.84	(6.7)	14	(16.5)	9	(10.6)
BRCAPRO								
	5-year	[0.8-2.2]	1.24	(0.5)				
	Lifetime	[4.0-14.7]	9.53	(2.0)	0	(0.0)	0	(0.0)

Table 5.3

Descriptive data for responses to psychological and cognitive measures

Variable	[range]	*mean*	(*SD*)	Cronbach's Alpha
Distress (Impact of Events Scale)	[1-46]	8.20	(11.1)	0.890
Health Literacy (Set of Brief Questions)	[6-12]	10.91	(1.3)	NA
Knowledge about Breast Cancer Genetics (BGKQ)	[1-24]	10.26	(5.5)	0.854
Numeracy (Rausch Based Numeracy Scale)	[2-8]	4.48	(1.5)	0.530

Note: *n*=85 for Cronbach's alpha calculations for health literacy and knowledge. One participant refused to answer all numeracy questions and was excluded from analysis of that instrument and one participant did not answer one question on the Impact of Event Scale; therefore, on these measures, Cronbach's alpha is calculated for *n*=84.

Table 5.4

Sharing/ understanding of information from family member's genetic counseling session

Question	Response		*n*	(%)	*M*	*SD*
Please rate on a scale of 0-5 how much information your sister/ mother shared with you about what she learned in her genetic counseling session, with zero being she shared nothing about the session to five being she shared a great deal.	Shared nothing	0	16	(18.8)	2.04	1.53
		1	20	(23.5)		
		2	17	(20.0)		
		3	15	(17.6)		
		4	11	(12.9)		
	Shared a great deal	5	6	(7.1)		
	Total		85	(99.9)		
Please rate how well you understand the information she shared on a scale of 0-5 with zero being that you don't understand it at all to five being that you understand a great deal.	Don't understand at all	0	0	(0.0)	3.57	1.49
		1	4	(4.7)		
		2	5	(5.9)		
		3	15	(17.6)		
		4	20	(23.5)		
	Understand a great deal	5	25	(29.4)		
	Total Valid		69	(81.2)		
	Nothing was shared		16	(18.8)		
	Total		85	(100.0)		

CHAPTER 6

DETAILED RESULTS

Chapter 6 includes detailed analysis and results that were beyond the scope of the prepared manuscripts.

IRB Approval

IRB approval was received by the University of Utah on September 4, 2013.

Recruitment

Contact information was provided by the REACH Pilot research team (PI Anita Kinney) for 135 women who had indicated willingness to be contacted again for future cancer-related research. Information was transmitted via encrypted email. Initial recruitment letters were mailed. Women were recruited from September through November 2013. The script for the recruiting telephone call, including eligibility questions are found in Appendix A.

Of the 135 potential participants, we were able to reach 122 by telephone to assess for interest in participation and eligibility. Eleven refused screening with 8 stating that time was the primary reason they did not want to participate and three cited lack of interest – 1 of those specifically noting that she does not believe the cancer in her family is hereditary.

When asking the screening questions to potential participants, we stopped asking questions when we received an answer that would disqualify the participant from participation. Participants may have been deemed ineligible based on more than one criterion; however, we can only report on the first criterion that disqualified them. Of the 11 ineligible women at the initial screening, 2 women were outside the range of 40-74, 2 women had a cancer besides nonmelanoma skin cancer, 2 women were of Ashkenazi Jewish descent, 3 women received genetic counseling for breast or ovarian cancer themselves (2 of which also mentioned that they had genetic testing for the *BRCA1/2* mutation), and 2 women who had prophylactic oophorectomies. Overall, 100 women were initially eligible and consented to participate. These women were mailed survey packets including consent cover letters.

Of the 100 women who were mailed surveys, 2 became ineligible, contacting the PI to report that they had been diagnosed with breast cancer before they were able to complete the survey and had their scheduled interviews. Ten women withdrew from the study. Of those, 5 contacted the PI and 5 became unreachable. Those contacting the PI gave cited time constraints as a reason with 2 mentioning that filling out the family history portion of the survey would take too much time because of their large families. The other 5 were lost to follow-up. These women became unreachable after the survey had been mailed and appointments had been set for telephone interviews. Some rescheduled their telephone interviews one or more times because they stated they needed more time to collect the family history. After up to five unsuccessful attempts were made to reschedule, no further calls were attempted. These women never returned a completed survey and were therefore presumed to withdraw. Additionally, 3 women completed

telephone interviews but did not return the survey packet. After four voicemail reminders and no response back from the participants, we determined that we would not be able to include these women in our final analysis. Therefore, the final sample includes 85 women belonging to 62 family clusters who completed both the telephone interview and the written survey. Of the 122 women contacted, 69.7 were eligible, and agreed to participate and completed the study. Of the 98 women who were screened, and determined to be eligible, 86.7% completed the study (Figure 5.2). Interviews were completed between September and November 2013.

Data Cleaning

Once all data were entered into IBM SPSS software version 21; several iterative processes were undertaken for data cleaning. All dates were sorted high to low and scanned for outliers. Frequency tables were created for categorical variables and histograms were created for continuous variables including instrument sums and means. Outliers and missing data were investigated by going back to the data collection instruments and comparing them against data that were entered. In several cases, the data file was updated to reflect the accurate information.

Family Member Who Received *BRCA1/2* Test

Contact information was sent to us for women who completed the REACH-Pilot study. These women were identified as having a sister or mother who received genetic counseling and testing with indeterminate negative *BRCA1/2* test results. We did not know which relative had received counseling and testing and so we asked women which relative had received genetic testing and counseling. Sixty-five women (76.5%) reported

that their sister was the member of their family who had genetic testing and counseling, 18 women reported it was their mother, and 2 women did not know who in their family had genetic testing or counseling.

Measures

Demographics

Women's ages ranged from 40-71 with a mean of 52.2 (*SD* 8.9). Nearly all women (98.8%) reported their race as non-Hispanic White with 1 woman reporting her race as Asian. Women in the sample were highly educated. All women had completed high school or the equivalent, 43.5% had a 2- or 4-year college degree, and 14.1% had a postgraduate degree (see Table 4.2). Age, race, and education were similar between nonparticipants who shared demographic information and study participants. Further demographic factors were not collected for nonparticipants. Nearly 80% of participating women described themselves as married and most described themselves as Latter-day Saints (Mormon) when asked about religious affiliation.

Risk Perception

Women were asked via written survey to report what they thought their chances were of getting breast cancer with comparative verbal and quantitative responses. Comparative verbal risk perception was assessed by asking the question, "In your opinion, compared to other women your age, what are your chances of getting breast cancer?" About a third of women thought their chances were "the same" as other women. Over 50% thought their chances were "higher" or "much higher," and about 13% thought their chances were "lower" or "much lower" (see Table 4.4).

Comparative, quantitative risk perception was measured by first presenting women with the following information, "On average 12 women out of 100 will get breast cancer in their lifetime." Women were given an illustration of 100 women with 12 out of 100 women shaded to illustrate the concept. Women were then instructed,

> Picture yourself in a room with 100 women exactly like you (same risk-factors.) How many of you will get breast cancer in your lifetime? Please pick a number between 0 and 100. You can pick any number between 0 and 100.

Women gave responses ranging from 1% to 95% perceived lifetime risk with an average of 25.62%, *SD* = 19.94. More women wrote "12" % than any other number (16 women of 85, or 19.0%). The next most frequently written number written was "20" (13 women) and "25" was written by 10 women. Most women described their risk as lying between 5 and 30%; however, some selected very high numbers. One woman described her lifetime risk as being 95%, and 2 women selected 90% (see Figure 6.1).

Cancer-related Distress

Cancer-related distress was measured using the Impact of Events Scale (Horowitz et al., 1979). Women were given a list of 15 comments that have been made by people after stressful life events. The stressor for this study was defined as a family history of cancer. Women were asked to indicate how frequently the comments were true for them during the past 7 days. The scale is scored as, not at all = 0, rarely = 1, sometimes = 3, and often = 5. Therefore, it is possible to score 0 to 75 points on the 15-item scale with higher scores indicating higher levels of distress. Most women in this study reported a low amount of distress related to their family history of breast cancer. Scores ranged from 0 – 46 points with an average of 8.20 (*SD* = 11.10) (see Table 5.3). One participant skipped one item on this scale. To compensate for this missing data point, the mean of

each item was calculated and multiplied by the number of items in the scale. The Cronbach's Alpha was 0.890 for the Impact of Event's scale in this sample, calculated using the 84 participants who completed every item.

Health Literacy

Self-assessed health literacy was measured using the Set of Brief Questions developed by Chew, Bradley, and Boyko (2004). Three questions asked about participants' abilities to read hospital/medical materials and fill out medical forms. Items are scored on a five-point scale (range 0 to 4 points) with higher scores indicating higher self-reported levels of health literacy. There were no missing data for these three questions. Participants rated themselves highly on self-literacy questions with averages above 3.5 on each question (see Table 6.1). Chew, Bradley, and Boyko (2004) do not promote using the three items as scale, however we did run a Cronbach's Alpha on the three questions and found it to be 0.511 (see Table 5.3).

Knowledge about Breast Cancer Genetics

In this study, breast cancer genetic knowledge was measured using the 27-item Breast Cancer Genetic Counseling Knowledge Questionnaire (BGKQ) (Erblich et al., 2005). Twenty-three items are answered as either "true," "false," or "don't know," four items are multiple choice items with five to six options (see Appendix B). Items were scored as correct if the correct answer was chosen. Items were scored as incorrect if an incorrect answer or "don't know" was chosen. The questionnaire has a total possible sore of 27. Participants in this study scored between 1 and 24 with a mean of 10.26

(*SD*=5.50). There were no missing data on this scale. The Cronbach's Alpha was calculated at 0.854 (see Table 5.3).

Numeracy

Numeracy was measured using the Rausch-based numeracy scale recently developed by Weller, Dieckmann, Tusler, Mertz, Burns, and Peters (2012). The scale includes 8 questions that test the ability to understand and use mathematic concepts such as probability and percent; it also tests the ability to interpret numbers presented in a table (see Appendix B). This measure was completed by 84 of 85 participants. One participant wrote that she refused to answer those questions. All other participants attempted to answer every question or wrote "don't know" in the answer field. Scores in this study ranged from 2 to 8 with a mean of 4.48 (*SD*=1.54). The maximum score for this instrument is 8, representing a high level of numeracy. Cronbach's Alpha for this scale was 0.537 in this sample (see Table 5.3). In initial testing of this instrument, Weller et al. (2012) obtained a Cronbach's alpha of 0.71 – however, they suggested that for measuring a broad, higher-order construct, mean interitem correlation is a better measure of internal consistency.

Information from Family Member's

Genetic Counseling Session

Women in this study had either a sister or a mother diagnosed with breast cancer, attended genetic counseling, and received a blood test that did not identify a *BRCA1/2* mutation. Women were asked in the interview to rate how much information their sister or mother shared with them. Surprisingly, 18.8% of women said their family member

shared nothing about her genetic counseling (see Table 5.4). Given that these women were referred into the initial REAH Pilot study (P.I. Anita Kinney) by family members who participated in the REACH noninferiority trial, we expected that they would know about the genetic counseling visit. When women reported that their family member "shared nothing," it created a challenge in our interview flow. The next question in the interview asked women to rate how well they understood the information that was shared. Initially, we entered zero as if they gave this response, figuring that our participants had zero understanding if zero information was shared. However, as more data came in we found that some women reported a very high level of understanding when very little information was given. They would say something like, "all she told me is that she doesn't have the gene, so yeah, I understood that very well." We then changed our interview format so that if women reported no information was shared, we skipped the item about level of understanding. Thus, we have 16 women who reported that their family member shared nothing. For 5 of these women, we rated them as zero understanding and for 11 we rated them as "missing" (see Table 5.4). Generally, as less information was shared, women rated their understanding of the information higher (see Figure 6.2). This could be interpreted as smaller amounts of information were easier to understand. It seems that it was easier for women to understand small amounts of information. On average, women rated the amount of information shared as a 2.04(*SD*=1.53) on a 0-5 scale and their understanding as a 3.57(*SD*=1.49) on the 0-5 scale.

Sharing Information with Primary Care Providers

Women were asked whether they had shared information with their primary health care providers about (1) their family history of cancer, (2) their sister or mother's genetic counseling, or (3) their sister or mother's test results. Two women indicated that they "didn't know" the answer to one or more of those questions. Nearly 90% of women had shared information about their family history of cancer with their primary care providers, but very few indicated that they shared information about their family member's genetic counseling or genetic test results (see Table 6.2).

Summary Letter/ Informational Pamphlet

Women were asked whether they were aware that their sister or mother received a summary letter about their genetic counseling session. Only 12 women (14.1%) reported that they were aware of such a letter. Of those who were aware of a letter, 7 women saw the letter and 2 were given a copy to keep. Three women report that they shared information about the letter with their primary care provider. Two women report that their primary care provider received a copy of the letter. Of the 12 women who were aware of the letter, 3 (25%) indicated that some of the information in the letter applies strongly to them (see Table 6.3). Four women reported that they were aware of an informational pamphlet that their sister or mother received as a part of the genetic counseling session. Two women reported that they saw the pamphlet and 1 reported that she read it. On a zero to five scale, these 3 women rated the pamphlet as applying to them at levels three, four, and five, with five representing "some information in the pamphlet applies strongly to me. None of the women shared the pamphlet with their primary care provider.

Mammography

During the telephone interview, women were asked questions related to their understanding and use of mammography. After a definition was read, all women in the sample reported that they had previously heard of a mammogram. Most women reported that a doctor or a family member recommended that they receive a mammogram.

We asked how often mammography was recommended. Response options included (1) just one time (2) every year (annually), (3) every 2 years, and (4) other. Most women (86.8%) reported received recommendations from their primary care providers for annual mammography. In the interview, we allowed for the option of free response answers to the question of how often mammography was recommended in addition to the options we provided. The intent of this free response option was to allow for clarification of the "other" response. However, some women chose to clarify their answers even though they selected one of our other options. Free response answers to the question of how often mammography was recommended were summarized by the interviewers as follows:

- told to start having them, no specific time fame,
- starting at an earlier age than normal,
- every 3 months for a while
- now and every 6 months
- every 2-3 years,
- every 3 years,
- every 5 years,
- 1st annual, then every three, now annual again,

- one doctor - one time only because of a lump, second doctor “periodic”
- just heard that it was important in the last 5 years

Occasionally a woman noted that she “didn’t know” whether a certain type of person (e.g., doctor) recommended a mammogram or not. For the purposes of this study, we counted these women as not receiving the recommendation because in our perception, a recommendation not recalled is as good as a recommendation not received. One woman in the sample had a mammogram but states it was never recommended by anyone that she have it. This woman didn’t give a response for how often mammography was recommended because it did not apply. This particular participant with a lifetime risk of 16.2 according to the Claus model receives mammograms annually and plans to continue to receive them annually despite them not being recommended. She did state that her doctor looks at her mammograms each year at her physical exam.

All but 1 woman in the sample had previously received a mammogram. Of the 85 participants, 76 (89.4%) received their most recent mammogram as a screening test. Of those 76, 68 (89.5%) received their most recent screening mammogram within the past 2 years (see Table 4.7). The number of months since most recent mammogram ranged from zero to 103 with an average of 12.74 (*SD*=19.31). More than 90% of women received their most recent mammogram as part of a routine screening (see Table 6.4). The one woman in the sample who had never had a mammogram reported that she had received a recommendation for a mammogram from her doctor.

To assess a pattern of mammography, we also asked about the mammogram before the most recent. Nearly 80% of the sample had received a mammogram within 2

years of the most recent (see Table 6.5) and the vast majority of those were also part of routine screening (see Table 6.6).

Nearly all women in the sample plan to receive annual mammography in the future (see Table 6.7). Women were also given the option of a free response related to the frequency of their mammography plans. Free responses were summarized by the research team as follows:

- Annual to 18 months
- Every 1-2 years
- Every 3-4 years
- Every 4-5 years
- Every 5 years
- Every 7 years
- Unless directed otherwise

Magnetic Resonance Imaging (MRI)

Women were also asked about their familiarity with and use of MRI. In this sample, only 52.9% of participants had ever heard of breast MRI before the test was described in the telephone interview. Thirteen women reported receiving a recommendation for breast MRI and 7 reported that they had received a breast MRI (see Table 6.8). These 7 women estimated that their MRI took place between 5 and 65 months ago with a mean of 37.3 months (over 3 years) ago. Two women reported that they had their MRI for screening purposes and the other 5 reported that it was because of a symptom or a follow up from a previous abnormal test (see Table 6.9). Only 2 women reported receiving more than one MRI, with 1 reporting that the MRI prior to the most

recent was for screening and the other reporting that it was a follow-up from an earlier abnormal test.

The question, "do you plan to receive breast MRIs in the future?" did not perform as well as we had hoped. Many women reported that they had never heard of an MRI, had never been recommended to have an MRI, and had never had an MRI. According to our survey, these women were still supposed to be asked whether they planned to receive breast MRI in the future or not. Sometimes the question was skipped by the interviewer. Often women answered "if it is recommended I will." One woman said, "It sounds like a good idea." The intent of this question was to determine whether or not women had plans to screen in the future with MRI; however, most women did not know and struggled to answer this question with a simple "yes," "no," or "don't know." After several interviews, the interviewers began to code responses of "if it is recommended" as a "don't know" since women could not know whether or not it would be recommended in the future. Because the answers to this question were coded inconsistently the results are not presented here.

Health Care

The vast majority of women reported that they had health insurance had a physician as their primary care provider. A few women had a Nurse Practitioner or a Physician Assistant as their primary care provider (see Table 6.10).

Subject Burden

Most women (72.9%) reported that it took 30 minutes or less to complete the survey, 22.4% took between 30 and 60 minutes, and 4.7% took more than 1 hour to

complete the survey. Most women (74.1%) completed the survey in one sitting. Instructions encouraged participants to complete the survey independently. Most women (96.5%) reported that they completed the survey independently; however, 3 women reported they did have help.

There was space at the end of the survey for additional comments. One participant noted that she had her husband help with the math portion. Another simply claimed, "I hate math!" Several participants felt like they did not know many of the answers on the knowledge questions. One noted that the study made her feel less worried about developing breast cancer.

We asked participants twice if we could contact them in the future for research, on the survey and during the telephone interview. On the survey, 81 women (95.3%) marked yes, 2 women marked no, and 2 women did not answer the question. At the conclusion of the interview, women were asked verbally if they would allow us to contact them again; 78 (91.8%) agreed to future contact while 7 (8.2%) did not.

The number of telephone interviews conducted by members of the research team include Deborah O. Himes 39(45.9%) and two research assistants: Amy Hullinger 26(30.6%), and Ali Hatch 20 (23.5%). Both research assistants were undergraduate students in a baccalaureate nursing program. Both completed privacy (HIPPA) and human subjects research training (CITI).

Specific Aims 1 and 2

The results related to the first two specific aims are covered thoroughly in the proposed manuscripts and so are not repeated here. The first two specific aims were:

Specific Aim 1

Specific aim 1 was to calculate an estimate of women's lifetime risk for breast cancer and compare this estimate to women's perceived risk about developing future breast cancer. This aim included three research questions:

1. What is the average calculated risk for breast cancer using the Claus model, the BRCAPRO model, and the Gail model for women (with sisters or mothers who received genetic counseling and indeterminate negative *BRCA1/2* results)?
2. What percent of women (with sisters or mothers who received genetic counseling and indeterminate negative *BRCA1/2* results) qualify for annual MRI breast screenings based on NCCN guidelines (a lifetime risk for breast cancer $\geq$ 20%) based on the Claus or the BRCAPRO risk calculators?
3. What percent of women (with sisters, mothers, or daughters who have received genetic counseling and had indeterminate negative *BRCA1/2* results) over-estimate vs. underestimate their risk as compared to their calculated risk for breast cancer?

Specific Aim 2

Specific aim 2 was to determine whether self-reported screening plans and self-described screening practices are in alignment with risk-based guidelines in women whose first-degree female relatives have received genetic counseling and indeterminate negative *BRCA1/2* test results. This aim includes two research questions:

1. What percent of women whose first-degree female relatives have received indeterminate negative test results **report that they are screening for breast**

cancer according to risk-based guidelines, i.e., are women who have ≥20% lifetime risk of developing breast cancer, receiving both annual mammogram and MRI (as recommended by the National Comprehensive Cancer Network (NCCN) and the American Cancer Society (ACS))?

2. What percent of women whose first-degree female relatives have received indeterminate negative test results **report receiving recommendations for breast cancer screening** from their primary care physicians or from another source that are consistent with the National Comprehensive Cancer Network (NCCN) and American Cancer Society (ACS) guidelines based on the level of risk (i.e., annual mammography if < 20% lifetime risk and ≥ 40 years of age; mammography with MRI if ≥ 20% and ≥ 30 years of age)?

Specific Aim 3

The third study aim involved statistical analysis using latent variables. This specific aim changed from proposal defense to study implementation because it became evident that the variable *"understanding of information shared"* was not a reliable variable and because the third research question became irrelevant after the second question was answered in the affirmative. Below is the initial specific aim with accompanying research questions followed by an explanation about how the questions changed and how they were answered.

Specific Aim 3

Specific aim 3 was to determine the contribution of a woman's self-rated understanding of genetic health information, shared by her first-degree female relative

about genetic counseling sessions, to her risk perception and to the accuracy of her perception of individual lifetime risk for breast cancer while controlling for confounding influences of factors known to contribute to risk perception, including age, education, health literacy, numeracy, knowledge about breast cancer genetics, and self-reported distress related to family history of breast cancer and perceived personal risk for breast cancer. This aim includes the following research questions:

1. What is the magnitude of the relationship between calculated lifetime risk for breast cancer and perceived lifetime risk for breast cancer?
2. Does a woman's self-rated understanding of genetic health information shared by her first-degree relative moderate the accuracy of risk perception?
3. Does a woman's self-rated understanding of genetic health information shared by her first-degree relative predict risk perception?

A model with latent variables was developed to test relationships between calculated risk and perceived risk, a relationship we are referring to as accuracy of risk perception. Additionally, we wanted to assess whether a woman's *self-rated understanding* of genetic health information shared by her sister or mother might predict her risk perception or moderate the accuracy of her risk perception (see Figure 3.2). Covariates that may influence risk perception were selected for the initial model based on Tilburt's Model of Risk Perception in High Risk Populations (2011).

As we began to collect data, we realized that a woman's self-rated understanding of information shared may not be the best indicator to use. Many women reported that their sisters or mothers shared very little information. On a 0 to 5 scale, the mean response was 2.04 (*SD*=1.53). Nearly 19% reported that their sister/mother shared

nothing about the genetic counseling session. We were unable to assess how well women understood information when they reported that "nothing" was shared. Our initial thought was to mark these as having zero understanding. However, as the data came in, we noticed that quite often, women who said very little was shared reported high levels of understanding for that little bit of information (see Figure 6.2). We determined that a rating of *amount of information shared* would be a better variable to include (see redrawn Latent Variable Model in Figure 6.3).

Statistical Analysis with Latent Variables

Data were assessed for missing items and outliers using descriptive statistics and appropriate figures as described in the section on missing data.

Dependent variables for the latent variable model (quantitative and verbal perceived risk and calculated risk by Claus and BRCAPRO) were evaluated for non-normality as normality is an assumption of SEM. MPlus has a sophisticated model in that the assumption of normality is not required for the observed explanatory covariates (distress, numeracy, and knowledge in our model). They can be of arbitrary distribution and everything is conditioned on them regardless of their values (Muthén & Muthén, 1998-2010).

Multivariate normality is, however, a requirement for the indicators of latent variables (verbal and quantitative perceived risk and calculated risk by Claus and BRCAPRO). These indicator variables were analyzed for normality by looking at histograms and by looking at the absolute value of skewness over the standard error of the skewness. Transformations for variables with absolute values greater than 2 were attempted to see if greater normality could be achieved. To achieve greater distribution

normality, Clause Lifetime Risk was transformed by taking the log (y+1, to avoid zeros) and the quantitative estimate of perceived risk was transformed by adding one and taking the log (y+1 to avoid zeros).

Evaluating the Moderating Effect of Information Shared on Agreement Between Perceived and Calculated Risk

An attempt was made to estimate the model as originally conceptualized, including all covariates to evaluate the moderating effect of the amount of information shared on the relationship between calculated risk and perceived lifetime risk. This model failed to converge, indicating that the model did not fit the data. Therefore, a simplified model consisting of the two latent variables, their dependent (indicator) variables and the amount of information shared stratified by two levels, was created. This simplified model also failed to converge. An additional transformation was conducted to bring the variances between the quantitative and qualitative indicators of perceived risk into similar ranges. The quantitative was multiplied by 10. This linear transformation has no effect on the statistics but makes the iterative process more stable.

A model including all covariates also failed to converge, perhaps due to small sample size. Covariates were removed and then added back in a stepwise fashion, retaining only those that were found to be statistically significant ($p<0.05$). Ultimately, covariates retained in the model included numeracy, knowledge about breast cancer genetics, and distress (see Figure 6.3). Age, education, and health literacy were found not to be significant and were not included in the final model.

We had considered including a family grouping variable. However, the intraclass correlation of the average of the four dependent variables was .022, indicating the

observations were essentially independent of family grouping. Therefore, we did not include the family grouping variable. Most women belonged to a unique family. The final sample included 85 women belonging to 62 family clusters. Considering family group as a cluster is important in theory, but in this case, the contribution was negligible.

Moderation

It was hypothesized that the amount of information shared moderates the relationship between risk perception and calculated risk. The effect of moderation was evaluated by comparing two models, one with moderation (allowing different slopes and intercepts for the regression of perceived risk on calculated risk) and one with no moderation (with slopes and intercepts equal in the two strata).

The variable "information shared" was stratified into high and low groups based on the amount of information women reported their family member had shared with them about the genetic counseling session. The low group (n=68) included women who responded between 0 and 3 and the high group (n=17) included women who responded 4-5 on the Likert scale. Stratifying on the basis of all six options (0-5) that women could have chosen was not feasible due to small sample size. We evaluated splitting the group into low and high based on different breaking points ($\leq$1, $\leq$2, and $\leq$3) and all yielded a similar pattern. We also attempted a three-group solution with a low group (0,1) a medium group (2) and a high group (3-5). This split showed a proper low, medium, high "dose" effect with a p-value of (0.15), indicating that with the current sample size, we did not achieve significance with a three-level split for the variable *amount of information shared*. Splitting the sample into two groups reflecting high and low amounts of shared

information (0-3, 4-5 responses) seemed to be the best split and demonstrated a significant moderation effect with our sample size.

Model Fit

A chi square test was conducted to assess significance of the difference of deviance between the models. A difference in chi-square between the model with moderation and the model where the groups were constrained to be equal was 4.79 (*df*=1) (p = 0.287). This indicates significant improvement in model fit when groups are not constrained to be equal. Fit indices for the alternative model assessing moderation effect of amount of information shared were: Chi-Square Test of Model Fit 22.550 (*df*=28, p=.7552), RMSEA = 0.0000, 90% CI [0.000-0.086]. A nonsignificant chi-square indicates that the model–implied covariance matrix is consistent with the population covariance matrix and supports the model; in other words, the model and the data are not significantly different (Kline, 2010). RMSEA is below 0.05, indicating good model fit .

Covariates numeracy, knowledge, and distress were all significant (p< 0.05). Of the three, distress had the greatest impact on perceived risk (0.513), slightly more than double the impact of numeracy (0.245), and knowledge (-0.229). Where higher levels of numeracy and distress were associated with higher levels of perceived risk, however, higher levels of knowledge about breast cancer genetics were associated with lower perceived risk (see Figure 5.1).

Individual parameter estimates for this model are presented in Table 6.11 (for the Low information group) and Table 6.12 (for the high information group). It can be noted that regression relationships with observed explanatory covariates were equal across strata, but that the regression of perceived risk on calculated risk and intercept for

perceived risk differed based on amount of information shared. Note that the group with a low amount of information shared had a lower accuracy of risk perception (0.326) or agreement between perceived and calculated risk. The group with a higher amount of information shared had over double the level of accuracy of risk perception (0.707) (see shaded areas on Table 6.11 and Table 6.12).

Thus, we have the answer to the first and second research questions of specific aim 3: The magnitude of the relationship between calculated and perceived lifetime risk for breast cancer **is** moderated by the amount of information a woman has received by her sister or mother who attended genetic counseling. Women who reported higher amounts of information shared had over twice the agreement as those with low amounts of information shared (**0.707 vs. 0.326** – standardized estimates)

Because the moderating effect was found, answering the third research question of specific aim 3, "Does a woman's self-rated understanding of genetic health information shared by her first-degree relative predict risk perception?" becomes irrelevant. This question assumes a single relationship of *amount of information shared* on risk perception. There is not a single relationship between the latent variables for all individuals. To ignore the moderating relationship and run a model assessing direct effect would be to purposely choose a model that fits the data more poorly and analyze it.

Discussion

A woman's rating of amount of information shared was found to moderate the agreement between the latent variables "calculated lifetime risk for breast cancer" and "perceived lifetime risk for breast cancer." Higher levels of information shared resulted

in higher parameter estimates (see Table 6.11 and Table 6.12). See the results and discussion in Chapter 5 for further explanation.

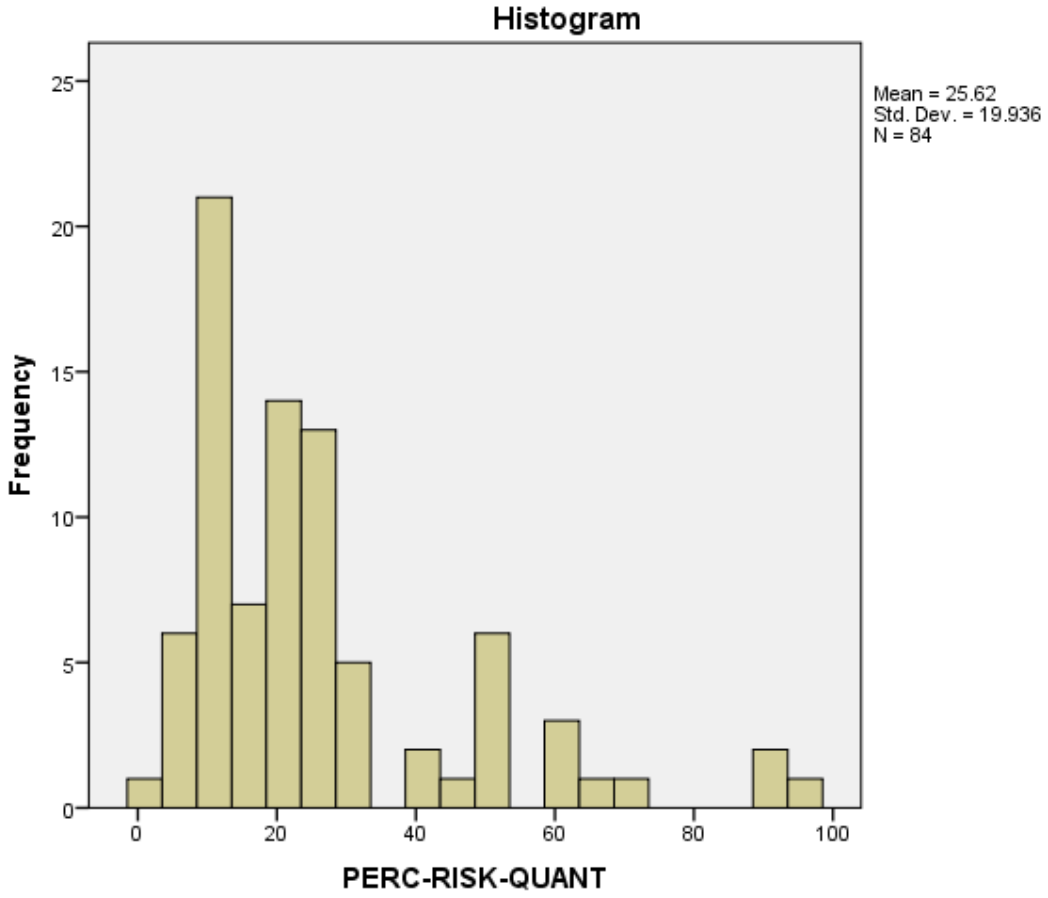


Figure 6.1
Perceived risk – comparative quantitative

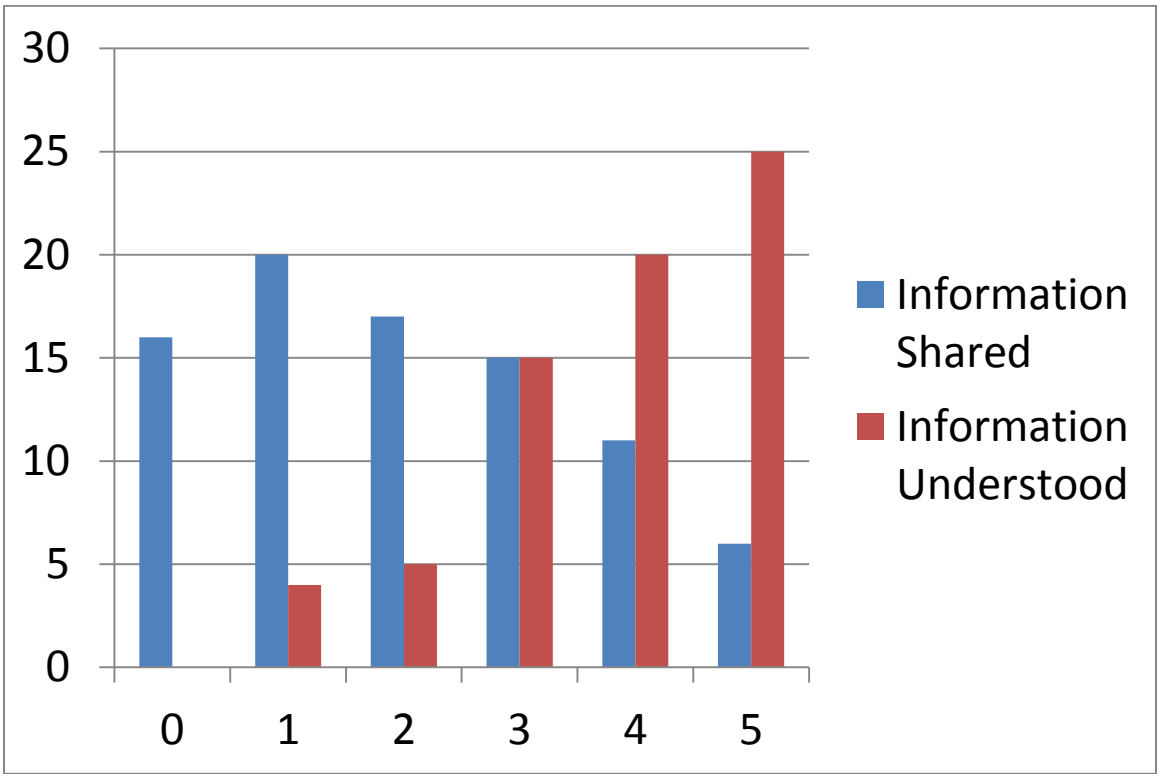


Figure 6.2
Information from family member's genetic counseling session

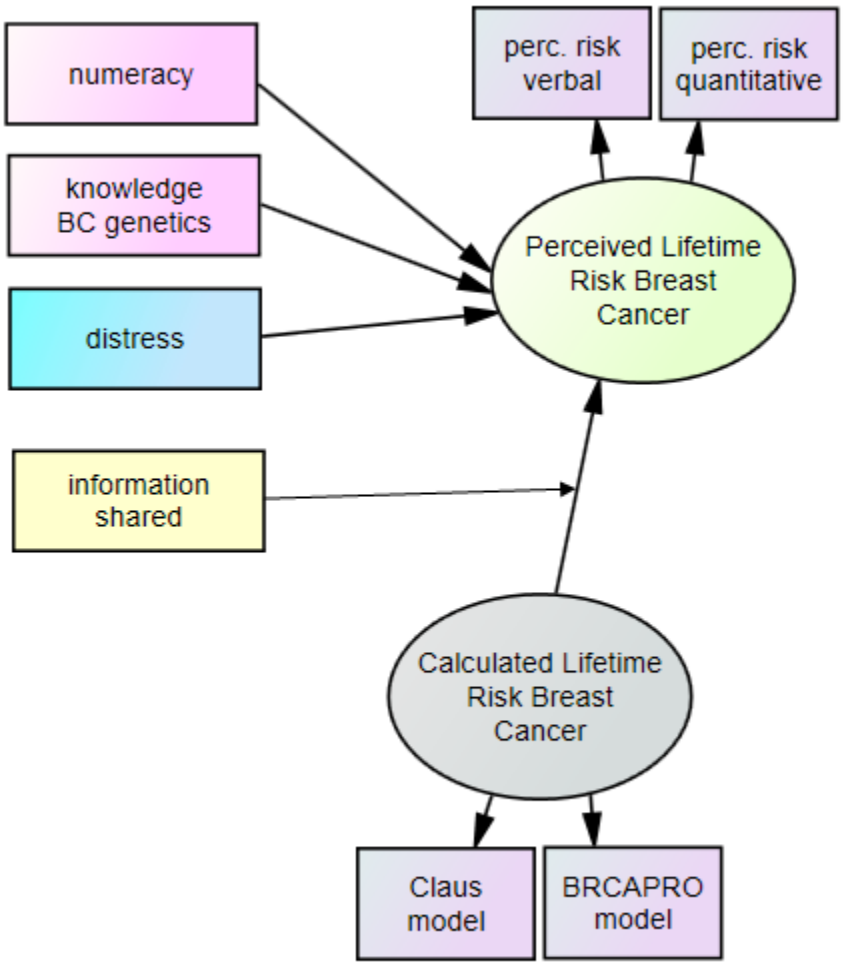


Figure 6.3
Revised latent variable model

Table 6.1
Self-reported health literacy

Question	Response	*n*	(%)	Points	*M*	*SD*
How often do you have someone help you read hospital materials?					3.81	0.45
	Never	71	(83.5)	4		
	Occasionally	12	(14.1)	3		
	Sometimes	2	(2.4)	2		
	Often	0	(0.0)	1		
	Always	0	(0.0)	0		
	Total	85	(100.0)			
How confident are you filling out medical forms by yourself?					3.52	0.75
	Extremely	54	(63.5)	4		
	Quite a bit	25	(29.4)	3		
	Somewhat	4	(4.7)	2		
	A little bit	1	(1.2)	1		
	Not at all	1	(1.2)	0		
	Total	85	(100.0)			
How often do you have problems learning about your medical condition because of difficulty understanding written information?					3.56	0.63
	Never	52	(61.9)	4		
	Occasionally	28	(33.3)	3		
	Sometimes	3	(3.6)	2		
	Often	1	(1.2)	1		
	Always	0	(0.0)	0		
	Total	85	(100.0)			

Table 6.2
Information shared with PCP

	n	(%)
Family History of Cancer		
Yes	76	(89.4)
No	9	(10.6)
Don't Know	0	(0.0)
Total	85	(100.0)
Sister/ Mother's Genetic Counseling		
Yes	21	(24.7)
No	62	(72.9)
Don't Know	2	(2.4)
Total	85	(100.0)
Sister/ Mother's Test Results		
Yes	19	(22.4)
No	65	(76.5)
Don't Know	1	(1.2)
Total	85	(100.0)

Table 6.3
Genetic counseling summary letter

	n	(%)
Aware of the letter		
Yes	12	(14.1)
No	70	(82.4)
Don't Know	3	(3.5)
Total	85	(100.0)
Sister/ Mother told me about it		
Yes	8	(9.4)
No	4	(4.7)
Total	12	(100.0)
I saw it but didn't keep a copy		
Yes	5	(41.7)
No	7	(58.3)
Total	12	(100.0)
I received a copy to keep		
Yes	2	(16.7)
No	8	(66.6)
Don't Know	2	(16.7)
Total	12	(100.0)
I read the letter		
All	2	(28.6)
Part	3	(42.8)
None	2	(28.6)
Total	7	(100.0)
I understand the letter		
not at all = 0	0	(0.0)
1	0	(0.0)
2	1	(8.3)
3	5	(41.8)
4	4	(33.3)
very well = 5	1	(8.3)
Missing	1	(8.3)
Total	12	(100.0)
Some information in the letter applies to me		
none =0	0	(0.0)
1	0	(0.0)
2	2	(16.7)
3	2	(16.7)
4	4	(33.3)
some strongly = 5	3	(25.0)
Missing	1	(8.3)
Total	12	(100.0)

Table 6.4
Reason for most recent mammogram

Reason	*n*	(%)
Part of routine exam of checkup	76	(89.4)
Because of a symptom or health problem	3	(3.5)
Follow-up from earlier abnormal test	5	(5.9)
Have not had a mammogram	1	(1.2)
Total:	85	(100.0)

Table 6.5
When was the mammogram before the most recent?

	n	(%)
Most recent was the first (no prior)	*5*	(5.9)
A year ago or less before most recent	49	(57.6)
More than 1 but not more than 2 years before the most recent	19	(22.4)
More than 2 but not more than 3 years before the most recent	3	(3.5)
More than 3 but not more than 5 years before the most recent	4	(4.7)
More than 5 years before the most recent	4	(4.7)
Has not had a mammogram	1	(1.2)
Total:	85	(100.0)

Table 6.6
Reason for mammogram before the most recent

Reason	*n*	(%)
Part of routine exam of checkup	73	(85.9)
Because of a symptom or health problem	4	(4.7)
Follow-up from earlier abnormal test	2	(2.4)
Never had mammogram, or most recent was first	6	(7.1)
Total:	85	(100.0)

Table 6.7
Mammography future intentions

Question	*n*	(%)
Plan to receive future mammography?		
Yes	83	(97.6)
No	1	(1.2)
Missing	1	(1.2)
Total	85	(100.0)
How often mammography future?		
Annually	72	(84.7)
Every 2 years	4	(4.7)
Less often than every 2 years	1	(1.2)
Other	6	(7.1)
Missing	2	(2.4)
Total	85	(100.1)

Table 6.8
Breast MRI recommendations

Question		*n*	(%)
Ever heard of breast MRI			
Yes		45	(52.9)
No		40	(47.1)
Ever had breast MRI			
Yes		7	(8.2)
No		74	(87.1)
Anyone recommend breast MRI?			
Yes		13	(15.5)
No		72	(84.7)
	Total	85	(100.0)
Who recommended a breast MRI?			
Family member?		2	(2.4)
Doctor?		8	(9.5)
Nurse Practitioner?		1	(1.2)
Physician's Assistant?		0	(0.0)
Other kind of person?		4	(4.8)
How often recommended?			
Just once		7	(8.3)
Annually		2	(2.4)
Other		4	(4.8)
	Total	13	(100.0)

Table 6.9
Reason for most recent breast MRI

Reason	*n*	(%)
Part of routine exam of checkup	2	(2.4)
Because of a symptom or health problem	3	(3.6)
Follow-up from earlier abnormal test	2	(2.4)
Total:	7	(100.0)

Table 6.10
Health insurance and type of PCP

Category	*n*	(%)
Health Insurance		
Yes	78	(91.8)
No	1	(1.2)
PCP Type		
Doctor	69	(81.2)
Nurse Practitioner	5	(5.9)
Physician Assistant	4	(4.7)
None	7	(8.2)

Table 6.11
Parameter estimates for latent variable model: Low amount of information shared*

Parameter	Estimate	Standard Error	Est/SE	*p* value	Standardized Estimate
Measurement Relationships					
Calculated Risk by					
BRCAPRO	2.960	0.326	9.090	0.000	0.702
Claus	1.000	0.000	999.000	999.000	1.000
Perceived Risk by					
Verbal	0.121	0.018	6.842	0.000	0.827
Quantitative	1.000	0.000	999.000	999.000	0.846
Claus					
Intercept	2.433	0.056	43.142	0.000	5.232
Residual Variance	0.000	0.000	999.000	999.000	0.000
BRCAPRO					
Intercept	9.506	0.225	42.159	0.000	4.847
Residual Variance	1.952	0.299	6.519	0.000	0.507
Perceived Risk Verbal					
Intercept	2.953	0.244	12.109	0.000	3.550
Residual Variance	0.219	0.069	3.185	0.001	0.316
Perceived Risk Quantitative					
Intercept	26.442	2.077	12.734	0.000	3.931
Residual Variance	12.857	4.524	2.842	0.004	0.284
Structural Relationships					
Perceived risk on Calculated (Accuracy)	3.992	1.354	2.949	0.003	0.326
Perceived risk on Numeracy	7.620	3.106	2.454	0.014	0.258
Perceived risk on Knowledge	-7.187	2.930	-2.453	0.014	-0.225
Perceived risk on Distress	4.328	0.877	4.936	0.000	0.491
Perceived risk Intercept	0.000	0.000	999.000	999.000	0.000

*Perceived level of information shared = 0-3 (*n*=68)

Table 6.12
Parameter estimates for latent variable model: High amount of information shared*

Parameter	Estimate	Standard Error	Est/SE	P value	Standardized Estimate
Measurement Relationships					
Calculated Risk by					
BRCAPRO	2.960	0.326	9.090	0.000	0.702
Claus	1.000	0.000	999.000	999.000	1.000
Perceived Risk by					
Verbal	0.121	0.018	6.842	0.000	0.877
Quantitative	1.000	0.000	999.000	999.000	0.892
Claus					
Intercept	2.433	0.056	43.142	0.000	5.232
Residual Variance	0.000	0.000	999.000	999.000	0.000
BRCAPRO					
Intercept	9.506	0.225	42.159	0.000	4.847
Residual Variance	1.952	0.299	6.519	0.000	0.507
Perceived Risk Verbal					
Intercept	2.953	0.244	12.109	0.000	3.031
Residual Variance	0.291	0.069	3.185	0.001	0.230
Perceived Risk Quantitative					
Intercept	26.442	2.077	12.734	0.000	3.336
Residual Variance	12.857	4.524	2.842	0.004	0.205
Structural Relationships					
Perceived risk on Calculated (Accuracy)	10.744	2.899	3.706	0.000	0.707
Perceived risk on Numeracy	7.620	3.106	2.454	0.014	0.195
Perceived risk on Knowledge	-7.187	2.930	-2.453	0.014	-0.246
Perceived risk on Distress	4.328	0.877	4.936	0.000	0.599
Perceived risk Intercept	0.923	1.558	0.592	0.554	0.131

* Perceived level of information shared = 4 -5 (*n*=17)

CHAPTER 7

SUMMARY

Sisters and daughters of women who have received genetic counseling and testing for breast cancer have the potential to receive personal genetic information about their own risk for breast cancer. This is important because women often make decisions about screening and prevention based in part on their perceptions and women in these families may be at higher risk than the average population. The American Cancer Society (ACS) and other organizations have recommended annual breast MRI in addition to annual mammography for women at elevated-risk for breast cancer, defined as having a lifetime risk of $\geq$20% based on estimation models that take extensive family history into account. Genetic testing and counseling provides information important to family members beyond the person receiving the testing.

If the pattern of cancer in a family is suspicious for familial or hereditary cancer, a woman who has had cancer may undertake genetic testing for a *BRCA1/2* mutation. Women and their families go into genetic counseling hopeful that they will walk away with some amount of certainty. Women who receive testing want to know, "will I get cancer again or not?" and "are my sisters and daughters going to get cancer or not?" Unfortunately risk assessment is not a process that ends in certainty (Bylund et al., 2012). It is a process that ends in odds ratios and percent chance over a specified number of years.

The majority of women who have breast cancer and are the first person in their family to receive *BRCA1/2* testing receive an *indeterminate negative* test result, meaning that no harmful mutation was identified. However, women in these families may remain at risk-based on the familial pattern of cancer in the family. In families with an *indeterminate negative* test result, uncertainty persists (S. C. O'Neill et al., 2006). Unaffected sisters, mothers, and daughters of these women do not have the option to be tested for a *BRCA1/2*. It is not standard practice to test unaffected women because (1) if a mutation is **not** found, they are no further along in their understanding of risk than they were before because it is not possible for them to get a *true negative* result and (2) chances of finding a mutation in an unaffected woman from a family where the most likely candidate for *BRCA1/2* testing has already tested indeterminate are extremely small.

Recommendations for those identified with a dangerous *BRCA1/2* mutation are clearer. Women with mutations know they are at high risk and have specified prevention and surveillance methods open to them. Their family members not diagnosed with cancer can be tested if they choose and they will receive either a *positive* or a *true negative* test result. Then women in the family who test positive will also know they are at high risk. Women who test negative are *truly negative* having no greater risk than the general population. Neither women with positive or negative results know for certain that they will or will not get breast cancer, but at least they know that they do or do not carry the dangerous gene mutation and that is one level of certainty.

It is difficult for women with a sister or mother with indeterminate *BRCA1/2* test results to know what to think or what they should do about their own risk for breast

cancer. Women may talk about risk in their family, but information shared by the genetic counselor about family risk analysis is often not shared accurately with the other women who do not have cancer and did not attend genetic counseling (Vos, Menko, et al., 2011).

Primary care providers are responsible to help women navigate muddy waters of understanding their risk for breast cancer and screening according to risk-based guidelines. Advising women about risk is complex. Cancer in women from families with breast cancer predisposing mutations only account for 5% of all breast cancers. A much larger portion comes from women in families that are at elevated-risk where no autosomal dominant gene mutation has been identified (P. D. P. Pharoah, Antoniou, Easton, & Ponder, 2008). It is important to stratify women based on their risk because more intensive screening is advised for women at high risk. In the absence of an identified mutation, risk in the family must be assessed based on the family pedigree and personal risk factors. Calculating risk can be confusing as there are several different risk calculators and each provides different calculations for the same woman. Further complicating matters, professional organizations provide conflicting recommendations regarding risk-based screening.

Women who receive genetic counseling and testing are typically provided with a genetic counseling summary letter that among other things identifies other members in the family who may be at elevated-risk for breast cancer and encourages women to alert these family members that they may be at risk and require additional screening or be a candidate for chemoprevention. A typical excerpt from a summary letter might include:

> As we mentioned earlier, your female relatives are still considered at increased risk for developing breast cancer. We recommend that they have annual clinical breast exams starting by age 25 and begin having annual mammograms at age [10 years prior to dx OR 35, whichever comes first]. The American Cancer Society

> currently recommends MRI be added to the screening plan for women with a 20% or greater lifetime risk for breast cancer. Your relatives may not meet this criterion based on your history alone, but this additional screening may be appropriate if they have other risk factors or dense breast tissue. Medications have been found to help reduce breast cancer risk. Women who take medications such as tamoxifen for 5 years can reduce their risk of breast cancer by as much as 50%. (W. Kohlmann, personal communication, July 29, 2011)

Genetic counselors typically do not contact relatives of their patients directly because of privacy concerns. However, research has shown that even in families where a positive *BRCA1/2* mutation has been found, all family members do not receive the information that was shared in genetic counseling. In families where an indeterminate test result was received, the amount of information shared is even lower. Often, information that is shared is inaccurate.

It should be noted that it is not necessary for information to be shared by the woman who received genetic counseling with her sister or daughter for risk-based care to be provided. A woman's risk for breast cancer should be assessed based on the family history whether an indeterminate *BRCA1/2* test has been received or if no *BRCA* testing has been undertaken in the family. We hypothesized that having a family member go through the process of counseling and testing might spark interest in women, prompting them to ask questions of their sisters and mothers, and also of their primary care providers about their own risk for breast cancer.

Purpose

The purpose of this cross-sectional descriptive study was to assess risk perception and calculated risk in sisters and daughters of women who had received indeterminate *BRCA1/2* test results. Additionally we sought to determine whether women were receiving breast cancer screening recommendations and participating in breast cancer

screenings that are in accordance with risk-based guidelines. We wanted to understand the impact of information shared about genetic counseling sessions by close relatives on the accuracy of risk perception for women potentially at increased familial risk of breast cancer.

The first specific aim of this study related to assessing women's risk for breast cancer. The aim had three parts: (1) to calculate women's risk for breast cancer, (2) determine how many women would be considered to be at increased or high risk (thus qualifying for more intensive screening according to certain guidelines), and (3) determine how many women over-estimate vs. underestimate their risk. The second specific aim for this study involved (1) determining whether women were receiving mammography and breast MRI screenings according to risk-based guidelines and (2) whether their health care providers were recommending that they do so. The third specific aim asked (1) how accurate women were in their risk perceptions and (2) whether the amount of information shared by their sisters and mothers who attended genetic counseling influenced their accuracy of perceptions about risk for future breast cancer.

Methods

Following IRB approval, we sent potential participants an introductory letter followed up by a telephone call to screen women for eligibility and invite them to participate. These women had previously completed a study titled REACH-pilot. Women had been referred to the REACH-pilot study by their sisters or mothers who had received genetic counseling and testing with indeterminate negative *BRCA1/2* results.

Women who agreed to participate completed a written survey and provided a three-generation pedigree as part of a mailed packet. They also participated in a telephone interview. Data were collected about risk perception for future breast cancer using verbal and quantitative estimates. We assessed factors that are known to influence risk perception, including distress, knowledge, health literacy, and numeracy. We calculated women's objective risk for breast cancer using three software-based statistical models (Gail, Clause, and BRCAPRO). We asked women how much information their sisters or mothers had shared with them related to the sister's/mother's genetic counselling session and how well they understood that information. Further, we asked about whether they were aware if their sister/mother received a genetic counseling summary letter or an informational pamphlet about breast cancer genetics. Finally we collected information about what recommendations women had received about breast cancer screening and about their recent breast cancer screenings.

Analysis

We completed a statistical analysis using latent variables to test the influence of *amount of information shared* by sisters and mothers about genetic counseling on a woman's accuracy of risk perception. The model was based broadly on the Common Sense Model of Self-regulation by Leventhal et al. (2003) and informed by Tilburt et al. (2011). We operationalized accuracy of risk perception as the level of agreement between perceived and calculated risk.

Results

Specific Aim 1

The average lifetime risks for women in this study varied by model used and were found to be: Gail 20.07 (*SD*=6.6), Claus11.84 (*SD*=6.7) and BRCAPRO 9.53 (*SD* = 2.0). Our results were consistent with previous findings that the Gail model estimates tend to be higher than the Claus model for most participants (McTiernan et al., 2001). Nine women, 10.7% of the sample, had a lifetime risk as calculated by the Claus model that was 20% or higher and are therefore considered to be at elevated-risk for breast cancer.

We considered women to "over-estimate" their risk according to a given calculator if they estimated more than 3% higher than that calculator. Conversely, if women's estimates were more than 3% below a given model calculation, they were considered to have underestimated according to that model. It was rare for all three risk calculators to provide lifetime risk estimates within 6% of one another. Therefore, it would be nearly impossible for most women to be considered "accurate" by all three risk calculators; in fact, some women were counted as overestimating by one model and underestimating by another. Women tended to over-estimate their risk compared to calculations obtained using the Claus and BRCAPRO models (73.8% and 78.6%, respectively). On the other hand, 57.1% of women either underestimated or gave similar estimates compared to the Gail model results.

Specific Aim 2

We found that 88.2% of the women in our study had lifetime risk calculations by the Claus model that were lower than 20%. According to the American Cancer Society, these women should be screening annually with mammograms since all were over 40

years old. Most were doing very well, with 68.1% receiving a screening mammogram within the past year and 86.9% within the past 2 years. All but 10 women in our sample received recommendations for annual mammograms. The American Cancer Society recommends that high-risk women receive annual breast MRI screening in addition to annual mammography. All of the women in our sample who were at elevated-risk had received a mammogram within the past year, but none had received a breast MRI at any time; similarly, none had received a recommendation for screening breast MRI. Therefore, none of the women in our sample who were at elevated-risk are counted as screening by risk-based guidelines or receiving appropriate risk-based screening recommendations.

Specific Aim 3

Statistical analysis using latent variables demonstrated that the amount of information shared by close relatives about their genetic counseling session moderates the accuracy of risk perceptions in their family members who did not receive genetic counseling. Difference in chi-square compared with model-constraining equal regressions of Perceived Risk on Calculated Risk = 4.79, df=1, (p =0.0287). In the final model, the Chi-Square Test of Model Fit 22.550, df = 28 (p = 0.755) indicated that the model fit the data well. The correlation between calculated and perceived risk was 0.326 (p=0.003) in the *low amount of information shared* group and 0.707 (p=0.000) in the *high amount of information shared* group (standardized values). This indicates that the amount of information shared by sisters and mothers who received genetic counseling significantly improves the accuracy of risk perception while controlling for cognitive and emotional factors known to influence risk perception. In fact, women who reported that their sisters

and mothers shared more with them had nearly twice the accuracy of risk perception as those who reported low amounts of information shared. Unfortunately, only about 20% of the women reported a high amount of information was shared with them.

Limitations

This study is limited in the fact that our sample only included women 40 and older. If we had the resources to include women down to age 30, we would have likely found a greater percent of women in the high-risk category. Lifetime risk decreases as women age because less of their "lifetime" exists. We would have liked to include women between the ages of 30-39 because the ACS recommends MRI screening begin at age 30 for women at elevated-risk. Generalizability of this study may also be limited by sample size and homogeneity of our population.

It should also be noted that the perceived amount of information shared is not an objective measure of either the amount of information shared or the accuracy of information shared. A variety of other factors could influence the perception of amount of information shared. For example, in families that generally communicate a lot, a certain amount of information may be perceived as sparse, where the same amount of information shared in a family that generally communicates rarely would be seen as a great deal of information. It was beyond the scope of this study to evaluate the actual amount or content of information shared.

Another potential limitation in this study is that we do not have information about their relationships between our participants and their PCPs. An important finding was that none of the women at elevated-risk received breast MRI screening recommendations. Because there were only 9 women in the elevated-risk group, it would have been difficult

to draw generalizable conclusions about these relationships had we gathered that data. However, if this study were to be repeated in the future with a larger sample, it would be helpful to obtain information about the patient/ PCP relationship, including how long the woman has been following with her PCP and whether or not she receives regular check-ups. Annual exams are often the time when family history is updated and screening and prevention options are discussed.

As noted elsewhere in this dissertation, we do not have enough data to report on over-screening. PCPs may recommend screening tests based on factors besides age and calculated risk level. Clinical findings such as breast density or heightened anxiety in the patient could prompt a PCP to begin mammograms earlier or order them annually rather than biennially. Thus, all we were able to report is whether women were meeting minimum guideline standards.

Discussion

The discovery that family members have improved accuracy of risk perception when counselees share more information about their genetic counseling sessions with them is a novel finding. Encouraging counseled women to share information with their family members is the most common method used by genetic counselors to disseminate information within a family.

Unfortunately, most women did not fall in the category of receiving high amounts of information. This study supports the idea that counselors may need to play a greater role in either helping women share information with family members or sharing information directly. Privacy concerns typically prevent counselors from sharing information without consent; however, several genetic counseling practices have piloted

projects to obtain consent from their counselees and then send postcounseling letters directly to family members. This has been piloted in families with known *BRCA1/2* mutations (Suthers et al., 2006), but we have not found evidence that it has been tried in families with indeterminate results where the pedigree is concerning.

Primary care providers face the challenge of helping women understand their risk and recommending risk-based screenings for breast cancer. This task is made difficult by the fact that models using extensive family history are needed to determine if women meet the 20% lifetime risk threshold for screening breast MRI recommendations. These models take a great deal of time both to collect the required family history and to enter the data. There seems to be a need for increased collaboration between genetic counselors and primary care providers. Given that 10% of women were at ≥ 20% lifetime risk and none had received recommendations for breast MRI screening suggests that these women had not been identified as being at high risk by primary care. These women had sisters or mothers who had received genetic counseling and risk assessment, meaning that risk in the family had been evaluated by a professional, but the message about more intensive breast screenings does not seem to be getting through. To illustrate this point, we share a couple details about 2 women at elevated-risk.

One woman who was 43 years old was not sure if it was her mother or sister who had genetic counseling. She thought it was probably her mother, but neither of them had told her that they received counseling. Her mother had breast cancer at age 48 and she has two sisters with breast cancer; one at 44 and one at 48. She said that no information was shared about her family member's genetic counseling session. This woman estimated

her own lifetime risk to be 12%. The Claus model showed that she had a 29% lifetime risk for breast cancer. She had never heard of breast MRI screening before.

Another woman was 42 years old. Her sister had breast cancer at age 37 and her mom at age 39. She mentioned during the telephone interview that she does not believe what she was told, that the cancer in their family is "not genetic," which is how she understood the interpretation of her sister's *BRCA1/2* test. Her physician told her that her risk is "about double" for breast cancer because of the family history. She said that she has heard of breast MRI, but no one has recommended it for her. She estimated her own risk to be 30%. By the Claus model she had a risk of 38%.

These stories demonstrate a lack of information being shared and a lack of understanding in relatives of women who received genetic counseling and testing. The first woman had no idea that genetic counseling had taken place. The second woman knew that it had taken place, but did not understand the implications for her – she thought the results meant that the cancer in her family was "not genetic." She was not aware that screening with MRI was an option. The first woman did not have an accurate perception of risk; she thought her risk was average at 12% and marked "average" for the verbal response – however, her risk was close to 30%. The second woman was fairly accurate in her risk perception. However, neither was receiving risk-based screenings.

Future Research

Further research is needed to establish effective ways of disseminating information within families that may result in women at risk for breast cancer being offered risk-appropriate screenings for breast cancer. Further research is needed to assess

methods that will help PCPs identify women at risk and provide recommendations for risk-based screenings for breast cancer.

Practice Implications

Our findings have implications for both genetic counselors and primary care physicians. Counselors should not assume that women will share messages clearly with family members at risk. Genetic counselors may want to consider writing letters, specifically for family members in cases where model estimations indicate close relatives may qualify for breast MRI screening. These letters could be given to the counselee to hand deliver or mailed directly to family members if the counselee gives permission. Once the pedigree has been entered for the patient being counseled, it only takes one click in CancerGene software to change the proband and calculate lifetime risk for a sister or a daughter. This type of communication may improve risk perception in the counselee's close relatives and is important because perception of risk plays a role in decisions people make about how to care for their health (Collins & Street, 2009). Tilburt et al. (2011) note, "misperception of risk has been shown to both increase and decrease use of preventive health services and therefore can have significant implications for the health of those at greater than average-risk of developing cancer" (p. 2).

Primary care providers, in addition to genetic counselors, may be trained in performing breast cancer risk assessments (Moyer, 2013). Our findings suggest that some women at elevated-risk may not have been identified as such by their primary care providers. It can be a challenge in a busy practice to find the time to complete such assessments. It may be possible to train office staff to collect and input information that is

needed for family history intensive models or to have patients enter their own data on a web-based instrument. This is another avenue for future research.

The US Preventive Services Taskforce recently updated guidelines for primary care providers to screen women in order to identify those who would benefit from an in-depth risk assessment. They identified five brief screening instruments that can be used for this purpose (Moyer, 2013). Women identified as potentially at elevated-risk by these instruments can then be further assessed, either by the provider (if trained) or be referred to genetic counselors for assessment.

Based on our findings, primary care providers should not assume that women will tell them if a family member has received genetic counseling and testing. Likewise, if a woman tells her primary care provider that her sister was tested and found that the cancer is "not genetic," the PCP should not assume that the woman does not have elevated-risk based on the family pedigree. Therefore, even in families where genetic counseling has been provided to a member, PCPs still need to screen and may need to perform a full risk assessment.

APPENDIX A

RECRUITING LETTER AND SCRIPTS

This appendix includes materials used in the recruiting process. First is a recruiting letter that served as our first contact with potential participants. This letter was mailed to 135 women. Next is the script used for our recruiting telephone call. This internal document was used to screen participants and invite eligible women to participate. This instrument was also use to collect demographic information from women who declined participation.

Recruiting Letter for Potential Participants

Dear [First Name, Last Name]

We hope this letter finds you and your family well. We are writing to invite you to participate in a research study. The purpose of our study is to learn about women who have a sister or mother who has received genetic counseling. We are doing this study to find out what family members of women who have received genetic counseling know about their risk for cancer and what they should do to screen for cancer.

We were given your name because you participated recently in another study called the "*Breast Cancer Prevention Pilot Study*." In the questionnaire for that study you indicated that you would be willing to be contacted again for cancer-related research studies. We hope that you will consider participating in this new important study. Participation involves completing a questionnaire and a telephone interview.

We will telephone you in a few days to ask you if you would like to participate. Participation in the study is completely voluntary. You can choose not to take part. You can choose not to finish.

If you chose to participate we will mail you a packet of questions and set up a good time for the telephone interview. The packet of questions will takes approximately 15 minutes to answer. We will ask that you mail it back to us in a postage-paid envelope that we will provide. We will also ask you to participate in a telephone interview that will take about 40 to 60 minutes to complete. During this phone call we will ask you for information about your family history of cancer and about things that you are doing to screen for cancer. From the information we collect during this interview we will be able to calculate your lifetime risk for breast cancer. If you would like to have that information yourself we can send it to you following the interview in a letter that you can share with your primary health care provider if you would like.

As a thank-you for your participation we will mail you a $25.00 Visa gift card once we have received the completed packet and completed the interview.

The questionnaires and information from the telephone interview will be kept confidential. The questionnaires are kept in locked cabinets and entered into a secure

database. Only staff that needs to use the information provided in the questionnaires will have access to them.

The principal investigator for this study is Deborah O. Himes MSN, APRN. If you have any questions, complaints, or if you feel you have been harmed as a result of participation, you can call her at (801) 422-6066. Contact the Institutional Review Board (IRB) if you have questions regarding your rights as a research participant. Also, contact the IRB if you have questions, complaints or concerns which you do not feel you can discuss with the investigator. The University of Utah IRB may be reached by phone at (801) 581-3655 or by e-mail at irb@has.utah.edu .

Our research assistants will be calling you in a couple of days to see if you would be willing to help us with this study. They can answer questions about the study. If you agree to participate, they will mail you the question packet and schedule a time for the interview. **By completing the questionnaire and answering the telephone interview questions you are giving your consent to participate.** If you have any questions or concerns, if you don't hear from our research assistants in a couple of days or if you would prefer NOT to participate or be contacted please call Deborah Himes at (801) 422-6066 or by email at deborah-himes@byu.edu.

We will be in touch soon,

Thank you,

Deborah O. Himes

Participant ID:

Time Zone:

+/- hours

Hello Ms. [participant name],

This is _____ with the Family Risk Assessment Research Project.

We sent you a letter about our study last week… is this a good time for me to ask you a couple of questions?

no – set call-back time

yes- proceed

That's great. As we mentioned in the letter, we are interested in learning about family members of women who have received genetic counseling. We are doing this study because we want to know what family members understand about their own risk for cancer and what they should do to screen for cancer. Did you receive the letter?

[if no, read through letter. If yes, go on]

May I ask 7 quick questions to see if you are the kind of person we are looking for to participate in our study?

1. Are you between at least 40 years old and not older than 74? [no = disqualified]	SCRN1	0 = no (disqualified) 1 = yes age is ok
2. Have you ever had cancer yourself? (anything but non-melanoma skin cancer) = [yes disqualified]	SCRN2	0 = had cancer (besides melanoma)– (disqualified) 1 = no cancer
3. Are you of Ashkenazi Jewish descent [yes= disqualifies]	SCRN3	0 = "Ashkenazi Jewish Descent (disqualified)" 1= "Not Ashkenazi"
4. Have you ever had genetic counseling yourself? [yes = disqualified]	SCRN4	0 = had genetic counseling (disqualified) 1 = no genetic counseling
5. Have you ever had genetic testing (a blood test) for breast cancer genes yourself? [yes = disqualified]	SCRN5	0 = had genetic testing (disqualified) 1 = no genetic testing of self
6. Have you had a bilateral mastectomy (surgery to remove both breasts?) [yes = disqualified]	SCRN6	0 = had bilateral mastectomy (disqualified) 1 = no bilateral mastectomy
7. Have you had your ovaries removed? [yes = disqualified]	SCRN7	0 = had prophylactic oopherectomy (disqualified) 1 = ovaries intact 2 = ovaries out other reason (cysts)

[If DISQUALIFIED at any question – thank for time and end call]

[If QUALIFIED –proceed to next page]

[Qualified]

It sounds like you would be a perfect person for us to include in our study. There are two parts to this study, a survey that we would mail to you and an interview that we would conduct over the telephone at a later time. The questionnaire takes about 20 minutes to complete and the telephone interview takes about 60 minutes. If you complete both, we will send you a $25.00 Visa gift card as a thank you.

Would you be willing to let us mail you the survey?
mailOK

0 = NO, not willing to participate 1= YES, ok to mail survey

[if NO skip to end "NO – Refuse Participation] [if YES, go on]

[YES - Agree to Participate]

That's great. We would like to send you a questionnaire in the mail. It will take approximately 20 minutes to answer the questions. We would then like you to mail it back to us – we will include an addressed and stamped envelope for you.

After you have completed the questionnaire we would like to have an interview over the telephone to ask some questions about your family health history and your own health that will help us calculate an estimate of your personal risk for breast cancer. We will also ask some questions about your healthcare. Can we schedule a time for that telephone call now?

There is one more thing we will include along with the survey it is a family history questionnaire. If you are able to fill it out and send it back it will help us during our telephone interview. The amount of time it takes to complete this questionnaire will vary depending on the size of your family and whether you know your family's medical history of the top of your head or if you need to do some research. This may be something that you would like to keep a copy of for yourself.

[Schedule telephone call for a time approximately 12 – 15 days in the future to allow enough time for the packet to be mailed, completed, returned and reviewed prior to the telephone call. However, if packets are not received back before the telephone call the telephone interview will still take place.]

Date scheduled –

That's great. Do you have any questions for me at this time? Let me give you a phone number that you can call if you have any further questions or if you need to get in touch with us – Deborah Himes (801) 422-6066.

The packet should be arriving in 2-3 days. Please complete it and put it back in the mail as quickly as you can. We would like to receive it back before the telephone call.

Thank you so much for your time. I look forward to talking with you again.

[NO – refuse participation]

I'm sorry you won't be able to help us. Before you go I have five quick questions. Answering will take less than a minute and will help us know if there are differences between those who participate in this study and those who don't. We want to be sure that there isn't a certain group of people who aren't getting their voices heard in this research. Are you willing to answer these questions?

NOptpDATA

0 = NO, won't answer demographics for non-participators
1=YES WILL ANSWER QUICK QUESTIONS

[If YES proceed] [if no, thank and end call]

What is the main reason that you would prefer not to participate?
NOptpREASON

_____
50 characters – free text

What is your Age?
NOptpAGE

Enter age _____
-99 Refuse

Are you Spanish, Hispanic, or Latino/a? (For example, Mexican or Mexican American, Cuban or Cuban American, Puerto Rican, Dominican, Central or South American)
NOptpHISP

0 = no
1 = yes
-77 = not sure
-99 = Refuse

What Race do you consider yourself to be?
NOptpRACE

1= White
2 = Black or African American
3 = American Indian or Alaska Native
4 = Asian
5 = Native Hawaiian or other Pacific Islander
6= Other
-77 = Not sure
-99 = Refuse

NOptpOTHrac

If states "other above" write how interviewee would describe race:

(25 characters)

Finally,
What is the highest level of education you have completed?

NOptpED

1= Less than high school
2 = High School/ GED
3 = Some College
4 = 2 Year College Degree (Associates)
5 = 4 Year College Degree (Bachelors – BA, BS)
6= Master's Degree
7 = Doctoral Degree
8 = Professional Degree (MD, JD)
-77 = Not sure
-99 = Refuse

Thank you for your time.

APPENDIX B

PACKET QUESTIONS AND INSTRUMENTS

The following pages include images of documents mailed to potential participants who had agreed over the telephone to participate. The first images are of the IRB approved consent covered letter followed by images of the survey and the family history questionnaire. In the survey instrument, names used by researchers such as "Impact of Events Scale" are not presented to the participants. For example, the first question includes our two measures of risk perception; 1a is our verbal measure and 1b is our quantitative measure. The question section is titled "Thoughts about Your Risk" for the participants. The following list provides the concept being measured and the name of the instrument used to measure it (if applicable) by question number:

1. Risk perception/ Comparative Verbal and Comparative Quantitative
2. Distress/ Impact of Events Scale
3. Health Literacy/ Brief Set of Screening Questions
4. Numeracy/ Rausch-Based Numeracy Scale
5. Knowledge/ Breast Cancer Genetic Counseling Knowledge Questionnaire
6. Media Sources of Breast Cancer Information and How Much Women Talk with Selected Family Members about the Family History of Breast Cancer
7. Demographics

Consent Cover Letter

Family Risk Assessment Study

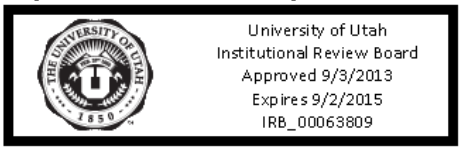
Dear Ms. [participant name],

Thank you for agreeing to let us mail you this packet of questions as part of our study. As mentioned in our previous letter, the purpose of the study is to learn about family members of women who have received genetic counseling. We are doing this study because we want to know what family members of women who have received genetic counseling understand about their risk for cancer and what they are doing to screen for cancer.

We would like you to complete the enclosed questionnaire and return it in the enclosed self-addressed, stamped envelope. The questionnaire should take about 20 minutes to complete. We ask that you return it to us as soon as you can. We would like to receive it before our telephone interview that is scheduled for [date]. The telephone interview should take about 60 minutes to complete.

There are no direct benefits to you for participating in the study. If you would like, we will provide you with a letter at the end of the study describing your personal risk for breast cancer based on your health history and the family medical history information you share with us over the telephone. This could be a benefit to you and your primary healthcare provider as you make decisions about your health care together. It is not anticipated that this study will cause you any harm, however it is possible that answering some questions could make you feel uncomfortable or nervous. Another potential harm could occur if the information you share with us is not kept private.

We have extensive steps that we will take to protect your privacy as a participant in this study. We will keep your completed questionnaire locked in a file cabinet in a locked office. Any information you provide over the telephone will be entered into a password



protected computer. A number will be used to identify your information instead of your name on both the paper questionnaire as well as the computer files. Only research team members may view the information you provided. Only the lead investigator will have a list that matches participant names with their ID numbers.

If you have any questions, complaints or feel that you have been harmed by this research please contact Deborah O. Himes MSN, APRN at (801) 422-6066 or by email at deborah-himes@byu.edu .

Contact the Institutional Review Board (IRB) if you have questions regarding your rights as a research participant. Also, contact the IRB if you have questions, complaints or concerns which you do not feel you can discuss with the investigator. The University of Utah IRB may be reached by phone at (801) 581-3655 or by e-mail at irb@hsc.utah.edu.

It should take a total of about one and a half hours to be in this study including the survey as well as the telephone interview. Participation in this study is voluntary. You can choose not to take part. You can choose not to finish the questionnaire or omit any question you prefer not to answer without penalty or loss of benefits. By returning this questionnaire, you are giving your consent and authorization to participate.

After we have received this questionnaire back and completed the telephone interview we will send a Visa gift-card in the amount of $25.00 as a thank you. We truly appreciate your willingness to help us move this important research forward. We are excited to learn about family members of women who have received genetic counseling so that we can help improve their healthcare.

Thank you,

Deborah O. Himes

FOOTER FOR IRB USE ONLY
Version: 112011

Family Risk Assessment Project

Start Here

Please note: Special instructions to help you fill out this questionnaire will always be found in these yellow shaded boxes. Some of the questions in the questionnaire look alike, but they ask about slightly different things that are important to you so please answer all of the questions.

Thoughts about Your Risk

-1 These questions ask what you think about your BREAST CANCER RISK

1a In your opinion, compared to other women your age, what are your chances of getting breast cancer?

- ☐ Much lower
- ☐ Lower
- ☐ The Same
- ☐ Higher
- ☐ Much Higher
- ☐ Don't Know

1b Read First

On average 12 women out of 100 will get breast cancer in their lifetime.

Below is a picture with
12 women out of 100 shaded dark.

Average risk is
12 out of 100

Picture yourself in a room with 100 women **exactly like you** (same risk-factors).

How many of you will get breast cancer in your **lifetime**?

Please pick a number between 0 and 100.
For Example:
0 = no women out of 100
100 = 100 women out of 100

You can pick any number between 0 and 100

Write answer here:

I think my risk is
_____ out of 100

Your Thoughts & Feelings

-2 Below is a list of comments made by people after stressful life events. Please mark each item indicating how frequently these comments were true for you DURING THE PAST SEVEN DAYS. If they did not occur during that time please mark "not at all."

Thinking about your family history of cancer, how often would you say:

		Not at all	Rarely	Sometimes	Often
2a	I thought about it when I didn't mean to.	☐	☐	☐	☐
2b	I avoided letting myself get upset when I thought about it or was reminded of it.	☐	☐	☐	☐
2c	I tried to remove it from memory.	☐	☐	☐	☐
2d	I had trouble falling asleep, because of pictures or thoughts about it that came to my mind.	☐	☐	☐	☐
2e	I had waves of strong feelings about it.	☐	☐	☐	☐
2f	I had dreams about it.	☐	☐	☐	☐
2g	I stayed away from reminders of it.	☐	☐	☐	☐
2h	I felt as if it hadn't happened or wasn't real.	☐	☐	☐	☐
2i	I tried not to talk about it.	☐	☐	☐	☐
2j	Other things kept making me think about it.	☐	☐	☐	☐
2k	Pictures about it popped into my mind.	☐	☐	☐	☐
2l	I was aware that I still had a lot of feelings about it, but I didn't deal with them.	☐	☐	☐	☐
2m	I tried not to think about it.	☐	☐	☐	☐
2n	Any reminder brought back feelings about it.	☐	☐	☐	☐
2o	My feelings about it were kind of numb.	☐	☐	☐	☐

How You Work with Written Healthcare Information

- 3 The following questions ask about how you work with written healthcare information.

3a How often do you have someone help you read hospital materials?

- ☐ Never
- ☐ Occasionally
- ☐ Sometimes
- ☐ Often
- ☐ Always

3b How confident are you filling out medical forms by yourself?

- ☐ Extremely
- ☐ Quite a bit
- ☐ Somewhat
- ☐ A little bit
- ☐ Not at all

3c How often do you have problems learning about your medical condition because of difficulty understanding written information?

- ☐ Never
- ☐ Occasionally
- ☐ Sometimes
- ☐ Often
- ☐ Always

How You Work with Numbers

- 4 The following questions will help us understand how you work with numbers. We realize that you may not know all the answers. Please answer these questions by yourself, as best as you can.

4a

Imagine that we roll a fair, six-sided die 1,000 times. Out of 1,000 rolls, how many times do you think the die would come up as an even number?

Answer:_____ Print Clearly

4b

In the BIG BUCKS LOTTERY, the chances of winning a $10.00 prize are 1%.

What is your best guess about how many people would win a $10.00 prize if 1,000 people each buy a single ticket from BIG BUCKS?

Answer: _____ people Print Clearly

4c

In the ACME PUBLISHING SWEEPSTAKES, the chance of winning a car is 1 in 1,000.

What percent of tickets of ACME PUBLISHING SWEEPSTAKES win a car?

Answer:_____% Print Clearly

4d

If the chance of getting a disease is 10%, how many people would be expected to get the disease out of 1000?

Answer:_____ people Print Clearly

4e

If the chance of getting a disease is 20 out of 100, this would be the same as having a _____% chance of getting the disease.

Answer:_____% Print Clearly

4f

Suppose you have a close friend who has a lump in her breast and must have a mammogram. Of 100 women like her, 10 of them actually have a malignant tumor and 90 of them do not. Of the 10 women who actually have a tumor, the mammogram indicates correctly that 9 of them have a tumor and indicates incorrectly that 1 of them does not have a tumor. Of the 90 women who do not have a tumor, the mammogram indicates correctly that 81 of them do not have a tumor and indicates incorrectly that 9 of them do have a tumor. The table below summarizes all of this information. Imagine that your friend tests positive (as if she had a tumor), what is the likelihood that she actually has a tumor?

	Tested Positive	Tested Negative	Totals
Actually has a tumor	9	1	10
Does not have a tumor	9	81	90
Totals	18	82	100

Answer: The likelihood is _____out of _____ Print Clearly

4g

A bat and a ball cost $1.10 in total.
The bat costs $1.00 more than the ball.

How much does the ball cost?

Answer:_____ Print Clearly

4h

In a lake, there is a patch of lily pads. Every day, the patch doubles in size.

If it takes 48 days for the patch to cover the entire lake, how long would it take for the patch to cover half of the lake?

Answer: _____ days Print Clearly

What You Understand about Breast Cancer Genetics

-5 The following questions will help us understand what you know about breast cancer genetics.

Make a mark to indicate if the statement is true or false or if you don't know. Please answer the questions by yourself, to the best of your ability.

		True	False	Don't Know
5a	50% of inherited genetic information (about breast cancer risk) is passed down from a person's mother.	☐	☐	☐
5b	25% of inherited genetic information (about breast cancer risk) is passed down from a person's father.	☐	☐	☐
5c	There is more than one gene that can increase the risk for breast cancer.	☐	☐	☐
5d	A woman who has a sister with a breast cancer gene mutation has a 1 in 4 chance of having a gene mutation herself.	☐	☐	☐
5e	A father can pass down a breast cancer gene mutation to his daughters.	☐	☐	☐
5f	One in 10 women has a breast cancer gene mutation.	☐	☐	☐
5g	All women who have a breast cancer gene mutation will get cancer.	☐	☐	☐

If the currently available genetic tests were to indicate that a woman has a breast cancer gene mutation she is at increased risk for:

		True	False	Don't Know
5h	Breast Cancer	☐	☐	☐
5i	Ovarian Cancer	☐	☐	☐
5j	Lung Cancer	☐	☐	☐
5k	Bladder Cancer	☐	☐	☐

If a woman who <u>already had</u> breast cancer was found to have a breast cancer gene mutation, she is at increased risk for developing:

		True	False	Don't Know
5l	Another Breast Cancer	☐	☐	☐
5m	Ovarian Cancer	☐	☐	☐
5n	Lung Cancer	☐	☐	☐
5o	Bladder Cancer	☐	☐	☐

		True	False	Don't Know
5p	Women who test positive for breast cancer gene mutations are generally more likely to develop breast cancer at a young age.	☐	☐	☐
5q	A **man** who carries a breast cancer gene mutation has an increased risk of developing breast cancer himself.	☐	☐	☐
5r	If a woman tests positive for a breast cancer gene mutation, her male relatives' risk for developing prostate cancer are lowered.	☐	☐	☐
5s	A woman may be at greater risk for developing ovarian cancer if she has several close relatives with ovarian cancer.	☐	☐	☐
5t	A woman may be at greater risk for developing ovarian cancer if she has several close relatives with breast cancer.	☐	☐	☐
5u	A woman who has her healthy ovaries removed will definitely not get ovarian cancer.	☐	☐	☐
5v	A woman who has her breasts removed will definitely not get breast cancer.	☐	☐	☐
5w	Screening for ovarian cancer often does not detect a tumor until it is more advanced.	☐	☐	☐

5x How many copies of a non-working breast cancer gene must one inherit to be at inherited risk for breast cancer?

- ☐ 0
- ☐ 1
- ☐ 2
- ☐ 3
- ☐ Don't know

5y What is the approximate risk that the average woman in the United States will develop breast cancer in her lifetime?

- ☐ 12%
- ☐ 24%
- ☐ 58%
- ☐ 72%
- ☐ Don't Know

5z If a genetic test were to indicate that a woman inherited a breast cancer gene mutation, then how likely is she to develop breast cancer in her lifetime?

- ☐ Up to 15% chance
- ☐ Up to 25% chance
- ☐ Up to 40% chance
- ☐ Up to 50% chance
- ☐ Up to 85% chance
- ☐ Don't know

5aa Select the procedure that is NOT appropriate for the detection of ovarian cancer.

- ☐ Ultrasound
- ☐ Pap smear
- ☐ CA-125 blood test
- ☐ Pelvic examination
- ☐ Don't know

Ways You Get Information about Cancer and Cancer Screening

-6 These questions will help us understand how you get and discuss information about breast cancer.

People get information about BREAST CANCER, including how to screen for it, how it may be inherited, and how to prevent it, from many sources. In the last 12 months, how much have you read or heard about BREAST CANCER from the following sources?

		Not at All	A Little	Some	A Lot	Does Not Apply
6a	Newspaper	☐	☐	☐	☐	☐
6b	Magazine	☐	☐	☐	☐	☐
6c	Radio	☐	☐	☐	☐	☐
6d	Television	☐	☐	☐	☐	☐
6e	Internet	☐	☐	☐	☐	☐
6f	Email	☐	☐	☐	☐	☐
6g	DVD or video	☐	☐	☐	☐	☐
6h	Brochures, pamphlets, etc.	☐	☐	☐	☐	☐
6i	Other, please explain	☐	☐	☐	☐	☐
6j						

Print Clearly

Please indicate how much you talk about BREAST CANCER with the following family members?

		Not at All	A Little	Some	A Lot	Does Not Apply
6k	Mother	☐	☐	☐	☐	☐
6l	Father	☐	☐	☐	☐	☐
6m	Spouse/ Significant Other	☐	☐	☐	☐	☐
6n	Children	☐	☐	☐	☐	☐
6o	Sister(s) who attended genetic counseling	☐	☐	☐	☐	☐
6p	Sister(s) who did NOT attend genetic counseling	☐	☐	☐	☐	☐
6q	Brother(s) who attended genetic counseling	☐	☐	☐	☐	☐
6r	Brother (s) who did NOT attend genetic counseling	☐	☐	☐	☐	☐
6s	Grandparent(s)	☐	☐	☐	☐	☐
6t	Grandchild(ren)	☐	☐	☐	☐	☐
6u	Aunt(s), great aunt(s)	☐	☐	☐	☐	☐
6v	Uncle(s), great uncle(s)	☐	☐	☐	☐	☐

-7 These questions will help us describe the people who participated in this project.

7a What is your age? _____ Print Clearly

7b What is the highest level of education you have completed?

- ☐ Less than high school
- ☐ High School graduate or GED
- ☐ Some College, but no degree
- ☐ Vocational/ technical school graduate/ certificate
- ☐ 2 Year College Degree (Associates degree – AA, AS)
- ☐ 4 Year College Degree (Bachelors – BA, BS)
- ☐ Master's Degree (MA, MS)
- ☐ Doctoral Degree (PhD)
- ☐ Professional Degree (MD, JD etc.)

7c What is your current marital status?

- ☐ Married
- ☐ A member of an unmarried couple
- ☐ Separated
- ☐ Divorced
- ☐ Widowed
- ☐ Never been married

7d What is your religious affiliation?

- ☐ Protestant Christian
- ☐ Roman Catholic
- ☐ Evangelical Christian
- ☐ Jewish
- ☐ Muslim
- ☐ Hindu
- ☐ Buddhist
- ☐ Latter-Day Saint (Mormon)
- ☐ None
- ☐ Other, please explain: _____

7e

7f Are you Spanish, Hispanic, or Latina? (for example, Mexican or Mexican American, Cuban or Cuban American, Puerto Rican, Dominican, Central or South American)

- ☐ Yes
- ☐ No
- ☐ Not Sure

7g What Race do you consider yourself to be?

- ☐ White
- ☐ Black or African American
- ☐ American Indian or Alaska Native
- ☐ Asian
- ☐ Native Hawaiian or other Pacific Islander
- ☐ Other, please explain: _____

7h

7i Are you currently covered by health insurance?
- ☐ Yes
- ☐ No

7j Who is your primary healthcare provider? (A primary health care provider is a person you go to for common problems and checkups).
- ☐ A doctor
- ☐ A nurse practitioner (NP)
- ☐ A physician's assistant (PA)
- ☐ Other _____

7k
- ☐ Don't have a primary care provider

-8 These last questions ask about completing this questionnaire.

8a What is today's date? _____ Print Clearly

8b About how long did it take to complete this questionnaire?
- ☐ 30 minutes or less
- ☐ More than 30 minutes but less than 1 hour
- ☐ More than one hour

8c Did you complete this questionnaire in one sitting, or did you do it in more than one sitting?
- ☐ I completed all of the questionnaire in one sitting
- ☐ I completed the questionnaire in more than one sitting

8d Did anyone help you complete this questionnaire?
- ☐ Yes
- ☐ No

8e May we contact you again to notify you of cancer-related research?
- ☐ Yes
- ☐ No

-END- Thank you for completing this questionnaire and participating in the Family Risk Assessment Project. If you have any questions please contact Deborah Himes at (801) 422-6066 or email at deborah-himes@byu.edu. If you have any additional comments please write them in the space below.

Additional Comments:

We would appreciate it very much if you would return your completed questionnaire within the week using the postage-paid envelope provided.

#

Family History Questionnaire

Participant ID (filled in by research team):_____

Please read these instructions before beginning the Family History Questionnaire.

1) Please list all your blood relatives, whether or not they have had cancer. Do not provide information about adopted, foster or step-relatives.
2) If exact age is not known, please estimate as best you can: (e.g. early 40's, late 60's)
3) You may need to speak with other relatives to increase the accuracy of the information on this questionnaire. We understand that sometimes information is just not available to you. Some of the questions that you can ask your relatives with cancer include:
   - *Specific type of cancer (e.g. breast, colon, ovarian, etc.)*
   - *Unilateral or bilateral (e.g. left breast or both breasts)*
   - *Second cancers – for relatives who developed a second cancer, did the second cancer result from spreading of the first cancer or was it considered a separate new cancer.*
   - *Age at diagnosis*
   - *Current age or age and cause of death*
4) There is a page at the end to list additional blood relatives. Please indicate how the relatives with cancer are related to you. If there is still not enough room, please list answers to questions on a separate piece of paper.
5) If you have any questions about completing the questionnaire, please contact the Deborah Himes at 801-422-6066 or via email at deborah-himes@byu.edu.
6) You can mail the questionnaire back with the enclosed envelope. We suggest making a copy of the paper for your own records before you mail it.

Additional comments (If you have additional comments after filling out this form please write them here):

_____

_____

_____

_____

You, Your Parents and Your Grandparents

	Date of Birth	Living or Deceased (check one)	Current age or age at death	Affected with cancer? (check one)	Type of cancer/s and age of diagnosis (ex. breast 56, colon 77)		Significant medical problems and/or cause of death
					Type	Age	
You		_X_ L __ D		__ Y __ N __ ?			
Your mother		__ L __ D		__ Y __ N __ ?			
Your father		__ L __ D		__ Y __ N __ ?			
Your mother's father		__ L __ D		__ Y __ N __ ?			
Your mother's mother		__ L __ D		__ Y __ N __ ?			
Your father's father		__ L __ D		__ Y __ N __ ?			
Your father's mother		__ L __ D		__ Y __ N __ ?			

Your Children:

If you do not have any children, check here ____.

First Name*	Date of Birth	**M**ale or **F**emale (check one)	**L**iving or **D**eceased (check one)	Current age or age at death	Affected with cancer? (check one)	Type of cancer/s and age of diagnosis (ex. breast 56, colon 77)		Significant medical problems and/or cause of death
						Type	Age	
		__M __F	__L __D		__Y __N __?			
		__M __F	__L __D		__Y __N __?			
		__M __F	__L __D		__Y __N __?			
		__M __F	__L __D		__Y __N __?			
		__M __F	__L __D		__Y __N __?			
		__M __F	__L __D		__Y __N __?			
		__M __F	__L __D		__Y __N __?			
		__M __F	__L __D		__Y __N __?			

***If your children have different parents, please write the parent's name in brackets**

Your Grandchildren:

If you do not have any grandchildren, check here ____.

List First Name [in brackets write, "son or daughter of ___"]*	Date of Birth	**M**ale or **F**emale (check one)	**L**iving or **D**eceased (check one)	Current age or age at death	Affected with cancer? (check one)	Type of cancer/s and age of diagnosis (ex. breast 56, colon 77)		Significant medical problems and/or cause of death
						Type	Age	
		__M __F	__L __D		__Y __N __?			
		__M __F	__L __D		__Y __N __?			
		__M __F	__L __D		__Y __N __?			
		__M __F	__L __D		__Y __N __?			
		__M __F	__L __D		__Y __N __?			
		__M __F	__L __D		__Y __N __?			
		__M __F	__L __D		__Y __N __?			
		__M __F	__L __D		__Y __N __?			

****Please write the parent's name in brackets***

Your Siblings:

If you do not have any siblings, check here ____.

First Name*	Date of Birth	**M**ale or **F**emale (check one)	**L**iving or **D**eceased (check one)	Current age or age at death	Affected with cancer? (check one)	Type of cancer/s and age of diagnosis (ex. breast 56, colon 77)		Significant medical problems and/or cause of death
						Type	Age	
		__M __F	__L __D		__Y __N __?			
		__M __F	__L __D		__Y __N __?			
		__M __F	__L __D		__Y __N __?			
		__M __F	__L __D		__Y __N __?			
		__M __F	__L __D		__Y __N __?			
		__M __F	__L __D		__Y __N __?			
		__M __F	__L __D		__Y __N __?			
		__M __F	__L __D		__Y __N __?			

****If half siblings, please indicate in brackets if shared parent is through mother or father***

Your Aunts and Uncles (Mother's side):
If you do not have any aunts or uncles on your mother's side, check here _____.

First Name	Date of Birth	**M**ale or **F**emale (check one)	**L**iving or **D**eceased (check one)	Current age or age at death	Affected with cancer? (check one)	Type of cancer/s and age of diagnosis (ex. breast 56, colon 77)		Significant medical problems and/or cause of death
						Type	Age	
		__M __F	__L __D		__Y __N __?			
		__M __F	__L __D		__Y __N __?			
		__M __F	__L __D		__Y __N __?			
		__M __F	__L __D		__Y __N __?			
		__M __F	__L __D		__Y __N __?			
		__M __F	__L __D		__Y __N __?			
		__M __F	__L __D		__Y __N __?			
		__M __F	__L __D		__Y __N __?			

Your Aunts and Uncles (Father's side):

If you do not have any aunts or uncles on your father's side, check here _____.

First Name	Date of Birth	**M**ale or **F**emale (check one)	**L**iving or **D**eceased (check one)	Current age or age at death	Affected with cancer? (check one)	Type of cancer/s and age of diagnosis (ex. breast 56, colon 77)		Significant medical problems and/or cause of death
						Type	Age	
		__M __F	__L __D		__Y __N __?			
		__M __F	__L __D		__Y __N __?			
		__M __F	__L __D		__Y __N __?			
		__M __F	__L __D		__Y __N __?			
		__M __F	__L __D		__Y __N __?			
		__M __F	__L __D		__Y __N __?			
		__M __F	__L __D		__Y __N __?			
		__M __F	__L __D		__Y __N __?			

Your Nieces & Nephews:

If you do not have any nieces or nephews, check here____.

First Name [in brackets write "son or daughter of ___"]*	Date of Birth	**M**ale or **F**emale (check one)	**L**iving or **D**eceased (check one)	Current age or age at death	Affected with cancer? (check one)	Type of cancer/s and age of diagnosis (ex. breast 56, colon 77)		Significant medical problems and/or cause of death
						Type	Age	
		__M __F	__L __D		__Y __N __?			
		__M __F	__L __D		__Y __N __?			
		__M __F	__L __D		__Y __N __?			
		__M __F	__L __D		__Y __N __?			
		__M __F	__L __D		__Y __N __?			
		__M __F	__L __D		__Y __N __?			
		__M __F	__L __D		__Y __N __?			
		__M __F	__L __D		__Y __N __?			

Please write the parent's name in brackets

Additional Relatives with cancer (please include cousins):

If you do not have additional relatives with cancer, check here ____.

First Name And Relationship to you [Ex. Maternal Aunt Mary's Daughter]	Date of Birth	**M**ale or **F**emale (check one)	**L**iving or **D**eceased (check one)	Current age or age at death	Affected with cancer? (check one)	Type of cancer/s and age of diagnosis (ex. breast 56, colon 77)		Significant medical problems and/or cause of death
						Type	Age	
		__M __F	__L __D		__Y __N __?			
		__M __F	__L __D		__Y __N __?			
		__M __F	__L __D		__Y __N __?			
		__M __F	__L __D		__Y __N __?			
		__M __F	__L __D		__Y __N __?			
		__M __F	__L __D		__Y __N __?			
		__M __F	__L __D		__Y __N __?			
		__M __F	__L __D		__Y __N __?			

APPENDIX C

TELEPHONE INTERVIEW QUESTIONS AND INSTRUMENTS

The following pages include images of the instrument used to collect data during the telephone interview. This instrument was for internal use only and includes the codes for data entry and variable labels.

Telephone Interview -- Data Collection Instrument
For internal use by Research Assistants

Participant Number: _____ Interviewer: _____
Scheduled Interview Date/ Time:_____

Scheduling Notes: call dates/ times/ voice mail. Date survey mailed/ received. Reminders etc.

Interview Script

	Script & Questions	Variable Code
	Hello, this is _____ with the Family Risk Assessment research project. I'm calling for our interview appointment. Is this still a good time for us to talk? ☐ Yes – Great – let's go ahead and begin. ☐ No – Reschedule – ideally call back shortly vs. different day – record scheduling notes in space above.	
	First of all I want to thank you again for your participation and remind you that participation in this study is voluntary and that all information you provide in this interview will be kept confidential.	
	IF SURVEY NOT RECEIVED OR IS INCOMPLETE - USE INCOMPLETE SURVEY DECISION TREE FOR PRELIMINARY INTRODUCTION - IF SURVEY IS COMPLETE SKIP THIS STEP AND BEGIN WITH THE INTRO THAT FOLLOWS	
	I anticipate that this interview will take ABOUT **35-45 minutes** to complete**. As a reminder, by answering the questions on the survey and in this interview you are consenting to participate in this study**. During this telephone interview I will be asking you questions about what your [SISTER/MOTHER] shared with you about her genetic counseling and how you might have shared or discussed breast cancer risk with your primary care provider. I will also be asking you about your family health history. Do you have a copy of the health history form we mailed? IF PARTICIPANT COMPLETED THE HEALTH HISTORY FORM AND HAS A COPY ASK THEM TO GET IT NOW IF THEY DON'T ALREADY HAVE IT.	
	Since many people have never been in an interview exactly like this, let me start by reading you a paragraph that tells a little bit about how it works: I am going to read you a set of questions exactly as they are worded so that every participant in the project is answering the same questions. Some of the questions may sound repetitive or very similar; however, I still need to read them as written. Please bear with me on some of the more detailed and tedious questions that I may ask. If you have any questions or need to have something repeated, just ask me.	

	Your [SISTER/MOTHER] who **would have** referred you to this study recently participated in genetic counseling. During her genetic counseling, she **would likely have** received information about breast cancer and had a DNA test to see if she has a change in her genes (mutation) that may have contributed to her breast cancer. **It's likely** she also received some information about her potential risk for future breast cancer and about possible risk to the family for breast cancer. I have a few questions for you related to your [SISTER's/MOTHER's] genetic counseling.	
	First, would you please rate on a scale of 0-5 **how much information** your [SISTER/MOTHER] shared with you about what she learned in her genetic counseling session. With zero being she shared **nothing** about the session to five being she shared a **great deal**: **IF 0 skip GC2** 0 1 2 3 4 5	GC1
	Please rate how well you understand the information she shared on a scale of 0-5 with zero being you **don't understand it at all** to five being you **understand a great deal.** 0 1 2 3 4 5	GC2
	A PRIMARY HEALTHCARE PROVIDER is someone like a doctor, nurse practitioner or physician's assistant who can diagnose, prescribe and order tests to help take care of your health.	
	Have you shared information about your **family history of cancer** with your primary healthcare provider? (1) YES (0) NO (-77) DON'T KNOW (-99) REFUSE	PCP1
	Have you shared information about your [SISTER's/MOTHER's] **genetic counseling session** with your primary healthcare provider? (1) YES (0) NO (-77) DON'T KNOW (-99) REFUSE	PCP2

	Have you shared information about your [SISTER's/MOTHER's] **DNA blood test** (the *BRCA* test) with your primary healthcare provider? (y/n) (1) YES (0) NO (-77) DON'T KNOW (-99) REFUSE	PCP3
	Upon completion of genetic counseling and testing your [SISTER/MOTHER], may have been given a **SUMMARY LETTER** about her session. Summary letters **usually** give women information about THEIR test results as well as potential impact on FAMILY MEMBERS' risk for breast cancer.	
	Were you **aware** if your [SISTER/MOTHER] received a Genetic Counseling Summery Letter? (1) YES (0) NO **(IF "NO" SKIP REST OF THE LTR QUESTIONS)** (-77) DON'T KNOW (-99) REFUSE	LTR1
	Approximately how long after she had her counseling did you find out about the SUMMARY LETTER? *[Could you please estimate in days AND/OR weeks about how long **AFTER** your [SISTER's/MOTHER's] genetic counseling that she told you about the SUMMARY LETTER?]* _____WEEKS _____DAYS, (-77) DON'T RECALL/ DON'T KNOW (-99) REFUSE **(convert answer to number of days – participants best guess)**	LTR2
	Now I'm going to read a list of statements about the **SUMMARY LETTER**. Please answer "yes" if a statement is true or "no" if it is not.	
	Did she tell you about it (summarize it)? (1) YES (0) NO (-77) DON'T KNOW (-99) REFUSE	LTR3
	Did she READ IT TO YOU word for word? (1) YES (0) NO (-77) DON'T KNOW (-99) REFUSE	LTR4

	Did she LET YOU SEE or READ IT? (1) YES (0) NO (-77) DON'T KNOW (-99) REFUSE	LTR5
	Did she GIVE YOU A COPY to **KEEP**? (1) YES (0) NO (-77) DON'T KNOW (-99) REFUSE	LTR6
	Did you (0) READ NONE OF IT (1) READ PART OF IT (2) READ ALL OF IT (-77) DON'T KNOW (-99) REFUSE	LTR7
	On a 0-5 scale please rate how well you feel that you **UNDERSTAND** the information in your [SISTER's/MOTHER's] **SUMMARY LETTER** from her genetic counseling with zero being that you **don't understand it at all** and 5 being that you **understand it very well**. 0 1 2 3 4 5	LTR8
	On a 0 – 5 scale please rate how strongly you feel that some of the information in the **SUMMARY LETTER <u>applies to you</u>**, with 0 being that **none of the information** applies to you and 5 being that **some of the information in the letter applies strongly** to you 0 1 2 3 4 5	LTR9
	Have you shared information from the **SUMMARY LETTER** with your HEALTHCARE PROVIDER? (1) YES (0) NO **(IF NO SKIP TO PAMPHLET QUESTIONS)** (-77) DON'T KNOW **(SKIP TO PAMPHLET QUESTIONS)** (-99) REFUSE **(SKIP TO PAMPHLET QUESTIONS)**	LTR10
	The next questions ask for information about how you shared the **SUMMARY LETTER** with your primary healthcare provider. Please answer YES or NO to each of the following questions:	
	Did you tell your HEALTHCARE PROVIDER about the SUMMARY LETTER at an **OFFICE VISIT**? (1) YES (0) NO (-77) DON'T KNOW (-99) REFUSE	LTR11

	Did you call your HEALTHCARE PROVIDER on the **TELEPHONE** to discuss the SUMMARY LETTER? (1) YES (0) NO (-77) DON'T KNOW (-99) REFUSE	LTR12
	Did you **GIVE** your HEALTHCARE PROVIDER a **COPY** of the SUMMARY LETTER? (1) YES (0) NO (-77) DON'T KNOW (-99) REFUSE	LTR13
	Is there some **OTHER WAY** you shared the information from the SUMMARY LETTER with your HEALTHCARE PROVIDER that I didn't mention? (1) YES (0) NO (-77) DON'T KNOW (-99) REFUSE If yes, INTERVIEWER writes the **OTHER WAY** of sharing below:	LTR14 LTR15
	Upon completion of genetic counseling and testing your [SISTER/MOTHER] **may have been** given an **INFORMATIONAL PAMPHLET** about BREAST CANCER GENETICS.	
	Were you **aware** if your [SISTER/MOTHER] received an INFORMATIONAL PAMPHLET? (1) YES (0) NO **(IF "NO" SKIP REST OF THE PMPLT QUESTIONS)** (-77) DON'T KNOW (-99) REFUSE	PMPLT1
	Did your [SISTER/MOTHER] share the pamphlet with you? (1) YES (0) NO (-77) DON'T KNOW (-99) REFUSE	PMPLT2

	When did you find out about the **INFORMATIONAL PAMPHLET**? Could you please estimate in days AND/OR weeks about how long AFTER your [SISTER's/MOTHER's] genetic counseling that she told you about the **INFORMATIONAL PAMPHLET**? _____WEEKS _____DAYS, (-77) DON'T RECALL/ DON'T KNOW (-99) REFUSE	PMPLT3
	Now I'm going to read a list of statements about the **INFORMATIONAL PAMPHLET**. Please answer "yes" if a statement is true or "no" if it is not.	
	Did she tell you about it (summarize it)? (1) YES (0) NO (-77) DON'T KNOW (-99) REFUSE	PMPLT4
	Did she READ IT TO YOU word for word? (1) YES (0) NO (-77) DON'T KNOW (-99) REFUSE	PMPLT5
	Did she LET YOU SEE or READ IT? (1) YES (0) NO (-77) DON'T KNOW (-99) REFUSE	PMPLT6
	Did she GIVE YOU A COPY to **KEEP**? (1) YES (0) NO (-77) DON'T KNOW (-99) REFUSE	PMPLT7
	Did you (0) READ NONE OF IT (1) READ PART OF IT (2) READ ALL OF IT (-77) DON'T KNOW (-99) REFUSE	PMPLT8
	On a 0-5 scale please rate how well you feel that you **UNDERSTAND** the information in your [SISTER/MOTHER] **INFORMATIONAL PAMPHLET** from her genetic counseling with zero being that you **don't understand it at all** and 5 being that you **understand it very well**. 0 1 2 3 4 5	PMPLT9

	On a 0 – 5 scale please rate how strongly you feel that some of the information in the **INFORMATIONAL PAMPHLET applies to you**, with 0 being that **none of the information** applies to you and 5 being that **some of the information in the letter applies strongly** to you 0 1 2 3 4 5	PMPLT10
	Have you shared information from the **INFORMATIONAL PAMPHLET** with your HEALTHCARE PROVIDER? (1) YES (0) NO **(SKIP PAMPHLET QUESTIONS)** (-77) DON'T KNOW **(SKIP PAMPHLET QUESTIONS)** (-99) REFUSE **(SKIP PAMPHLET QUESTIONS)**	PMPLT11
	The next questions ask for information about how you shared the **INFORMATIONAL PAMPHLET** with your primary healthcare provider. Please answer YES or NO to each of the following questions:	
	Did you tell your HEALTHCARE PROVIDER about the **INFORMATIONAL PAMPHLET** at an OFFICE VISIT? (1) YES (0) NO (-77) DON'T KNOW (-99) REFUSE	PMPLT12
	Did you call your HEALTHCARE PROVIDER on the TELEPHONE to discuss the **INFORMATIONAL PAMPHLET**? (1) YES (0) NO (-77) DON'T KNOW (-99) REFUSE	PMPLT13
	Did you **GIVE** your HEALTHCARE PROVIDER a **COPY** of the **INFORMATIONAL PAMPHLET**? (1) YES (0) NO (-77) DON'T KNOW (-99) REFUSE	PMPLT14

	Is there some **OTHER WAY** you shared the information from the **INFORMATIONAL PAMPHLET** with your HEALTHCARE PROVIDER that I didn't mention. (1) YES (0) NO (-77) DON'T KNOW (-99) REFUSE If yes, INTERVIEWER writes the **OTHER WAY** of sharing below: [ ]	PMPLT15 PMPLT16
	The following questions are about breast cancer screenings including mammogram and breast magnetic resonance imaging (also called MRI). Both mammograms and MRIs create images of the breast to screen for breast cancer. A mammogram is an x-ray of each breast. When a woman has a mammogram she usually stands and the breast is compressed between two pieces of plastic while the x-ray is taken.	
	Before the test was described, had you ever heard of a **MAMMOGRAM**? (1) YES (0) NO (-77) DON'T KNOW (-99) REFUSE	MMO-1
	Has anyone ever recommended that you receive a **MAMMOGRAM**? (1) YES (0) NO **(SKIP NEXT TWO QUESTIONS)** (-77) DON'T KNOW **(SKIP NEXT TWO QUESTIONS)** (-99) REFUSE **(SKIP NEXT TWO QUESTIONS)**	MMO-2

	**Will you tell me what kinds of people have recommended** that you receive a **MAMMOGRAM** (Please say yes or no as I read through types of people)?	
	Family Member	MMO-3-FM
	(1) YES	
	(0) NO	
	(-77) DON'T KNOW	
	(-99) REFUSE	MMO-3-MD
	Doctor	
	(1) YES	
	(0) NO	
	(-77) DON'T KNOW	
	(-99) REFUSE	MMO-3-RN
	Nurse	
	(1) YES	
	(0) NO	
	(-77) DON'T KNOW	
	(-99) REFUSE	MMO-3-NP
	Nurse Practitioner	
	(1) YES	
	(0) NO	
	(-77) DON'T KNOW	
	(-99) REFUSE	MMO-3-PA
	Physician Assistant	
	(1) YES	
	(0) NO	
	(-77) DON'T KNOW	
	(-99) REFUSE	
	HAS ANY OTHER TYPE OF PERSON RECOMMENDED THAT YOU HAVE A **MAMMOGRAM**? (IF YES, WRITE BELOW)	MMO-3-OTH
	(1) YES	
	(0) NO	
	(-77) DON'T KNOW	MMO-3-OTH-TXT
	(-99) REFUSE	
	How often was it recommended that you receive a **MAMMOGRAM**?	MMO-4
	(1) JUST ONE TIME	
	(2) EVERY YEAR (ANNUALLY)	
	(3) EVERY TWO YEARS	
	(4) OTHER _____	
	(-77) don't know	MMO-4-TXT
	(-99) refuse	

	Have you ever had a **MAMMOGRAM**? (1)YES (0) NO **(IF 'NO'SKIP TO MMO-11)** (-77) DON'T KNOW **(SKIP TO MMO-11)** (-99) REFUSE **(SKIP TO MMO-11)**	MMO-5
	When was your most recent **MAMMOGRAM**? (1) A year ago or less (2) More than 1 but not more than 2 years ago (3) More than 2 but not more than 3 years ago (4) More than 3 but not not more than 5 years ago (5) More than 5 years ago (-77) Not sure/ don't know (-99) refuse	MMO-6
	What was the month and year of your most recent **MAMMORGRAM** (best estimate)? Month: _____ Year_____ **Enter as: mon 20yy**	MMO-7
	Why did you have your most recent **MAMMOGRAM**? (1) Part of a routine examination or checkup (2) Because of a symptom or health problem. (3) Follow-up of an earlier abnormal test (-77) Not sure/ do not know (-99) refuse	MMO-8
	When did you have the **MAMMOGRAM** before your most recent one? (1) The most recent was the first mammogram/ so no prior **(skip to MMO11)** (2) A year ago or less before the most recent (3) More than 1 but not more than 2 years before the most recent (4) More than 2 but not more than 3 years before the most recent (5) More than 3 but not more than 5 years before the most recent (6) More than 5 years before the most recent (-77) Not sure/ don't know (-99) refuse	MMO-9
	Why did you have that **MAMMOGRAM**? (1) Part of a routine examination or checkup (2) Because of a symptom or health problem. (3) Follow-up of an earlier abnormal test (-77) Not sure/ do not know (-99) refuse	MMO-10

	Do you plan to receive **MAMMOGRAMS** in the future? (1) YES (0) NO **(if no, SKIP next question)** (-77) DON'T KNOW (-99) REFUSE	MMO-11
	How often do you plan to get **MAMMOGRAMS** IN THE FUTURE? (1) EVERY YEAR (ANNUALLY) (2) EVERY TWO YEARS/ EVERY OTHER YEAR (3) LESS OFTEN THAN EVERY TWO YEARS (4) Other _____ (-77) DON'T KNOW (-99) REFUSE	MMO-12 MMO-12-TXT
	A breast MRI takes pictures of the breast using a magnetic field rather than x-rays. When a breast MRI is performed a woman lies face down on a platform with openings for the breasts. The breasts are not compressed during the procedure. During the test the platform slides into a cylinder-shaped tube.	
	Before the test was described, had you ever heard of a **BREAST MRI**? (1) YES (0) NO (-77) DON'T KNOW (-99) REFUSE	MRI-1
	Has anyone ever recommended that you receive a **BREAST MRI**? (1) YES (0) NO **(SKIP NEXT TWO QUESTIONS)** (-77) DON'T KNOW **(SKIP NEXT TWO QUESTIONS)** (-99) REFUSE **(SKIP NEXT TWO QUESTIONS)**	MRI- 2

	If yes, who has recommended that you receive a **BREAST MRI** (say yes or no as I read each of these types of people)? Family Member (1) YES (0) NO (-77) DON'T KNOW (-99) REFUSE Doctor (1) YES (0) NO (-77) DON'T KNOW (-99) REFUSE Nurse (1) YES (0) NO (-77) DON'T KNOW (-99) REFUSE Nurse Practitioner (1) YES (0) NO (-77) DON'T KNOW (-99) REFUSE Physician Assistant (1) YES (0) NO (-77) DON'T KNOW (-99) REFUSE HAS ANY OTHER TYPE OF PERSON RECOMMENDED THAT YOU HAVE A **BREAST MRI**? (IF YES, WRITE BELOW) (1) YES (0) NO (-77) DON'T KNOW (-99) REFUSE [ ]	MRI-3-FM MRI-3-MD MRI-3-RN MRI-3-NP MRI-3-PA MRI-3-OTH MRI-3-OTH-txt
	How often was it recommended that you receive a **BREAST MRI**? (1) JUST ONE TIME (2) EVERY YEAR (ANNUALLY) (3) EVERY TWO YEARS (4) OTHER _____ (-77) don't know (-99) refuse	MRI-4

	Have you ever had a **BREAST MRI**? (1) YES (0) NO **(SKIP TO MRI-11)** (-77) DON'T KNOW **(SKIP TO MRI-11)** (-99) REFUSE **(SKIP TO MRI-11)**	MRI-5
	When was your most recent **BREAST MRI**? (1) A year ago or less (2) More than 1 but not more than 2 years ago (3) More than 2 but not more than 3 years ago (4) More than 3 but not more than 5 years ago (5) More than 5 years ago (-77) Not sure/ don't know (-99) refuse	MRI-6
	What was the month and year of your most recent **BREAST MRI** (best estimate)? Month: _____ Year_____ **Enter as: mon 20yy**	MRI-7
	Why did you have your most recent **BREAST MRI**? (1) Part of a routine examination or checkup (2) Because of a symptom or health problem. (3) Follow-up of an earlier abnormal test (-77) Not sure/ do not know (-99) refuse	MRI-8
	When did you have the **BREAST MRI** before your most recent one? (1) The most recent was the first mammogram/ so no prior **(SKIP to MRI 11)** (2) A year ago or less before the most recent (3) More than 1 but not more than 2 years before the most recent (3) More than 2 but now more than 3 years before the most recent (4) More than 3 but not more than 5 years before the most recent (5) More than 5 years before the most recent (-77) Not sure/ don't know (-99) refuse	MRI-9
	Why did you have that **BREAST MRI**? (1) Part of a routine examination or checkup (2) Because of a symptom or health problem. (3) Follow-up of an earlier abnormal test (-77) Not sure/ do not know (-99) refuse	MRI-10

	Do you plan to receive **BREAST MRIs** in the future? (1) YES (0) NO (if no, SKIP next question) (-77) DON'T KNOW (-99) REFUSE	MRI-11
	How often do you plan to get **BREAST MRIs** IN THE FUTURE? (1) EVERY YEAR (ANNUALLY) (2) EVERY TWO YEARS/ EVERY OTHER YEAR (3) LESS OFTEN THAN EVERY TWO YEARS (4) Other _____ (-77) DON'T KNOW (-99) REFUSE	MRI-12
	The answers to this next set of questions will be used to determine your risk for breast cancer. We will run the information through a risk calculator within the next **couple of weeks**. If you would like to have that information I'll be able to mail you the results when I mail your thank you letter. Some people want to know their risk because they believe it helps them and their healthcare providers take care of their health. Some don't want to know about it because they think they might worry about it too much. When I get to the end of our questions I'll be asking you if you would like to know what the calculators say about your risk.	
	Do you have a medical history of any breast cancer or breast changes including: Ductal Carcinoma in situ (DCIS) Lobular Carcinoma in situ (LCIS) Hyperplasia (without atypia) Atypical hyperplasia (1) YES (0) NO (-77) DON'T KNOW (-99) REFUSE IF YES CIRCLE THE SPECIFIC TYPE OF BREAST CHANGES	GRC-1
	What is your age? _____ years (-77) don't know (-99) refuse	GRC-2
	What was your age at the time of your first menstrual period? _____ years (-77) don't know (-99) refuse	GRC-3

	What was your age at the time of your first live birth of a child? _____years (0) no live births (-77) don't know (-99) refuse	GRC-4
	How many of your first-degree relatives (mother, sisters, daughters) have had breast cancer? _____first-degree relatives (-77) don't know (-99) refuse	GRC-5
	Have you ever had a breast biopsy? (1) YES (IF YES ANSWER NEXT 2 QUESTIONS) (0) NO - **(SKIP NEXT TWO QUESTIONS)** (-77) DON'T KNOW - **(SKIP NEXT TWO QUESTIONS)** (-99) refuse	GRC-6
	How many breast biopsies have you had? (include both positive or negative) _____ biopsies	GRC-6A
	Have you had at least one breast biopsy with atypical hyperplasia? (1) YES (0) NO (-77) don't know (-99) refuse	GRC-6B
	[may look at survey – if declared as white and marked with "no" under "Latina", just transfer over and state "you've indicated your race as white or Caucasian, correct?"] Please choose the term that best describes you. We recognize that these may not be the terms that people would choose for themselves.	
	What is your race/ ethnicity? (1) White (2) African American (3) Hispanic (4) Asian American (if Asian is selected answer next) (5) American Indian or Alaskan Native (-77) don't know (-99) refuse	GRC-7A

	What is your sub race/ ethnicity? **(Only ask if they answer Asian American above)** (1) Chinese (2) Japanese (3) Filipino (4) Hawaiian (5) Other Pacific Islander (6) Other Asian-American (0) no sub-race/ ethnicity (-77) don't know (-99) refuse	GRC-7B
	What is your height? _____feet _____inches (RA Convert to inches for data entry)	TC-1
	What is your Weight? _____lbs	TC-2
	Have you gone through menopause yet? (1) YES (0) NO (-77) don't know (-99) refuse If so, what age did you go through menopause? _____ years	TC-3A TC-3B
	Have you ever used Hormone Replacement Therapy? (0) never (1) current user (2) past user (more than 5 years ago) (3) past user (less than 5 years ago) (-77) don't know (-99) refuse If current or past user. How many years has HRT been used? _____ years	TC-4A TC-4B

	For this next part I'll review the family history information you sent. I've drawn up a pedigree based on those yellow pages you filled out. Will you listen as I read through what I've drawn and correct me if I've got something wrong? I may also ask some questions to clarify what I've written. AT THIS POINT THE INTERVIEWER WILL REVIEW THE FAMILY PEDIGREE OF ALL FIRST AND SECOND DEGREE RELATIVES, PLUS ANY AFFECTED THIRD DEGREE RELATIVES. INFORMATION COLLECTED FOR EACH FAMILY MEMBER WILL INCLUDE: • CURRENT AGE OR AGE OF DEATH • IF CANCER DX:TYPE, AGE, MARKERS • GENETIC TESTS.	PEDIGREE
	When we review the information you have shared with us we will calculate an estimate of your risk for breast cancer. If you would like to have a copy of that estimate we would be happy to mail it to you as soon as we have it. This would be something that you could share and discuss with your primary healthcare provider.	
	Would you like us to mail you a copy of the risk estimate when we have it? (1) YES (0) NO	DSCLOS
	Thank you so much for participating today. We have one final question for you. As we continue on with our research would you be willing for us to contact you again if we think that information from you would be helpful in a future study? (1) YES (0) NO	FTR-CNTCT
	**[If SURVEY packet already received]** We will be mailing out a $25.00 Visa gift card as a thank you right away. **[If SURVEY packet not received back]** As soon as we receive your packet of questions we will mail a $25.00 Visa gift card to you as a thank-you	

APPENDIX D

THANK YOU LETTERS

[Thank-you letter for participants not wishing risk information]

Dear Ms. [Name]

On behalf of our research team, we thank you for participating in our study titled the Family Risk Assessment Project. You have provided us with valuable information that will help us better understand what family members of women who have received genetic counseling know about their risk for cancer and what they are doing to screen for cancer.

Please accept the enclosed gift card as a thank you for your time and effort. Feel free to call if you have any questions about your participation in the study at (801) 422-6066 or email deborah-himes@byu.edu.

We appreciate your participation.

Sincerely,

Deborah O. Himes MSN, APRN
Principal Investigator

[Thank-you letter for participants wishing risk information]

Dear Ms. [Name]

On behalf of our research team, we thank you for participating in our study titled the Family Risk Assessment Project. You have provided us with valuable information that will help us better understand what family members of women who have received genetic counseling know about their risk for cancer and what they are doing to screen for cancer.

As part of our study we used risk calculators to estimate women's lifetime risk for breast cancer based on the family history information they provided. You indicated that you would like to receive your estimates. Given the personal and family history you provided we have calculated the following breast cancer risk estimates for you using three different models.

Claus Model	[XX%] 5 year risk,	[XX%] lifetime risk
BRCAPRO Model	[XX%] 5 year risk	[XX%] lifetime risk
Gail Model	[XX%] 5 year risk	[XX%] lifetime risk

We encourage you to discuss any questions you may have about your risk for breast cancer, as well as breast cancer screening and prevention measures with your primary healthcare provider. The American Cancer Society and other organizations have issued breast cancer screening and prevention guidelines that are based on risk level. Your primary healthcare provider should be able to help you navigate that information. If you would like to find a genetic counselor in your area, one good resource is the National Society of Genetic Counselors website: www.nsgc.org .

Again, we thank you for participating in our study. Please accept the enclosed gift card as a thank you for your time and effort. Feel free to call if you have any questions about your participation in the study at (801) 422-6066 or email deborah-himes@byu.edu.

We appreciate your valuable participation.

Sincerely,

Deborah O. Himes MSN, APRN
Principal Investigator

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