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Unaffected Women's Decisions to Have Prophylactic Risk-Reducing Mastectomies

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Unaffected Women's Decisions to Have Prophylactic Risk-Reducing Mastectomies

by

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Abstract

When a woman is at an increased risk of developing breast cancer due to a pathogenic mutation or a significant family history of the disease, she will be faced with choosing from among multiple management options, including risk-reducing mastectomy (RRM). The relative rate of RRM for both diagnosed and unaffected high-risk women has increased in recent years. Previous research has investigated the factors that influence women diagnosed with the disease to undergo RRM, but has not fully addressed how unaffected women make their decisions to choose RRM as an option when they are still healthy. This study was designed to specifically focus on decision-making factors of unaffected women at high risk for breast cancer due to a known pathogenic mutation or family history, and who had completed prophylactic RRM. Women participated in a mixed-mode survey that was guided by review of published literature. Factors such as perceived risk; anxiety about personal cancer risk; family implications; “closeness” to cancer; information from healthcare providers; and body image were studied for possible influence on the participants’ decision-making process. Twenty-five women participated by completing demographic information; answering multiple Likert scale questions; and reporting genetic mutation results and visits with various healthcare specialists. They answered four open-ended questions to extrapolate on influencing factors and the reasons they made their RRM decisions. Results showed that personal health and family implications were two of the most important influencers, and that association between concern for their sexuality and body image was significant. All 25 participants reported

satisfaction with their decisions, and level of education or age of children were not significant. This study allows the voices of women to speak to genetic counselors and other healthcare specialists about the various important factors that influence healthy high-risk women to make life-changing decisions for themselves and their family members.

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Chapter 1: Background

1.1 Breast Cancer Diagnosis and Treatment Review

Genetic testing for breast cancer susceptibility genes has been available clinically since 1996 (Hubbard & Lewotin, 1996). Since testing has been available for about 20 years, it is not uncommon for an unaffected individual to seek genetic counseling when a known mutation has been found in the family. Due to higher public awareness, unaffected individuals may recognize their family history as being significant and request a genetic counseling referral from their physician for information about genetic testing for risk-reducing purposes.

Women affected with breast cancer are offered several options of managing their cancer, including increased surveillance with MRI, ultrasound and frequent clinical breast exams, or with risk-reducing surgeries (RRS) such as bilateral mastectomies. Unaffected women with a significant family history or a known predisposing mutation have similar options; however, their intentions for undergoing prophylactic risk-reducing mastectomies (PRRM) has not been fully explored in the research arena.

Women who are faced with an increased risk for developing breast cancer have a daunting task before them. They are provided several options to manage their risk with each option having its own benefits and limitations. (RRS) in women who carry a *BRCA1* or *BRCA2* mutation decrease their risk for breast cancer by about 90% (Rebbeck et al., 2004). However, making the decision and choosing risk-reducing procedures is an intense process, and some women may struggle with their sense of sexuality, femininity,

and body image (Howard, Balneaves, Bottorff, & Rodney, 2011). Whereas surveillance is not invasive, it offers early detection of breast cancer but does not reduce cancer risk. Many women begin the decision process by evaluating how their medical management will affect their physical health, identity, relationships, and psychological health (Howard et al., 2011).

1.2 Breast Cancer Susceptibility

Public health data show that one in eight women will develop breast cancer in her lifetime (Howlader et al., 2015). However, this 12% risk of developing cancer can be affected by several factors with one of these factors being genetic predisposition. Most breast cancer cases, 70-80%, occur sporadically and randomly, often developing due to age factors, environmental influences and other unknown causes. Another 10-15% of breast cancer cases are considered to be familial —where a pattern is seen within a small family cluster, but there is no apparent genetic explanation of the cause. Of all breast cancer cases, only about 5-10% can be attributed to a single-gene hereditary cause. Because of the known heritability of breast cancer and identification of the major genes which cause hereditary breast cancer, women who have a significant family history often pursue genetic testing. National Comprehensive Cancer Network (NCCN) guidelines state that if a woman is found to be at a 20% or higher lifetime risk of developing breast cancer based on specific risk assessment tools, she is considered high-risk and should be offered genetic counseling and testing (NCCN, 2015). In addition to the risk model prediction, an unaffected individual is considered for further genetic risk evaluation when one or more of the following criteria are present in their close relatives (NCCN, 2015):

- a known mutation in a cancer susceptibility gene within the family,

- ≥ 2 breast cancer primaries in a single individual (first, second, or third degree relative),
- ≥ 2 individuals with breast cancer primaries on the same side of the family,
- ≥ 1 invasive ovarian cancer primary,
- First or second-degree relative was with breast cancer ≤ 45 y,
 - Personal and/or family history includes three or more of the following (especially if early onset): pancreatic cancer, prostate cancer (Gleason score ≥ 7), sarcoma, adrenocortical carcinoma, brain tumors, endometrial cancer, thyroid cancer, kidney cancer, dermatologic manifestations and/or macrocephaly, hamartomatous polyps of GI tract; diffuse gastric cancer
- Male breast cancer. (p.BR/OV-1)

BRCA1 and *BRCA2* are the most familiar genes relating to breast cancer; however, they are not the only breast cancer predisposing genes. Other genes that when mutated highly increase an individual's susceptibility to breast cancer are *TP53*, *CDH1*, *PTEN*, and *STK11*. More recently, *ATM*, *PALB2*, and *CHEK2* have been found to carry an empirical risk for breast cancer that can be 50% or greater, depending on family history. Some of these genes, when mutated, are also known to carry an increased risk for other specific cancers; however for this study we are concerned with the increased risk of breast cancer imparted by each of them.

Often, a dominant pattern of cancer is seen in the family, and the predisposition to cancer is passed through the family. Every individual is born with two copies of these

genes. One copy is inherited from the mother, and the other copy inherited from the father. There is an increased risk for developing breast cancer when just one copy of those genes has a DNA change (or mutation), which causes the protein to not work properly. The mutated gene can be inherited from either parent, and one copy of a mutation is enough to increase a person's chance to develop cancer. The individual who inherits or has one mutated gene is called a mutation carrier or heterozygote. Like most genes that increase an individual's risk for developing cancer, the genes related to breast cancer are usually involved in DNA repair and cell-cycle regulation.

1.3 Susceptibility Genes

BRCA1 and *BRCA2* are the most common genes associated with a hereditary risk for breast cancer, otherwise referred to as Hereditary Breast and Ovarian Cancer Syndrome (HBOC). Because *BRCA* mutation carriers are at a significantly increased risk for developing breast cancer throughout their lifetimes compared with the general population, medical management guidelines have been developed to help detect a new occurrence or recurrence of breast cancer (NCCN, 2015). Carriers of *BRCA* mutations have at least a 40%-75% lifetime risk of developing breast cancer (Antoniou et al., 2003; Chen & Parmigiani, 2007; Mavaddat et al., 2013). Economopoulou, Dimitriadis, and Psyrris (2015) estimated that 30% of hereditary breast cancer cases are due to mutations in *BRCA1* and *BRCA2*. These mutations in *BRCA1* and *BRCA2* are believed to be found in 1 in 300 or 1 in 500 women (0.2%-0.3%) of Northern European or African American ancestry (Ponder et al., 2000). *BRCA1*-associated breast cancer can present as triple-negative breast cancer, meaning that there are no estrogen or progesterone receptors in the tumor tissue and that HER-2 expression is not amplified (Foulkes, 2003). Of women

diagnosed with triple-negative breast cancer under the age of 40, about 11% of those are due to *BRCA* mutations (Young et al., 2009). However, we know that *BRCA1* and *BRCA2* are not the only high-risk breast cancer genes.

Li-Fraumeni Syndrome (LFS) is another hereditary cancer syndrome that predisposes women to develop breast cancer and is caused by a mutation in the *TP53* gene. Between 1 in 5,000 to 20,000 individuals in the world have LFS. Carriers of a mutation in this gene have a 90% lifetime risk to develop certain cancers such as leukemia, brain cancer, osteosarcomas and breast cancer. Breast cancer is the most commonly seen cancer in Li-Fraumeni patients, making up about one-third of cancers that affects individuals. Of women with breast cancer diagnosed before the age of 40, only 1% will have LFS (Sidransky et al., 1992), and of women diagnosed with breast cancer under the age of 30, 4% will be found to have a *TP53* mutation (Evans et al., 2010). While LFS does not affect many women, it does include a substantially increased predisposition to developing breast cancer. Women with LFS have a 56% risk of developing breast cancer by the age of 45, and 90% by the age of 60 (Economopoulou et al., 2015).

Hereditary diffuse gastric cancer (HDGC) is another cancer syndrome that increases an individual's risk for developing breast cancer and affects about 1 in 10,000 to 1 in 40,000 individuals. HDGC, as the name implies, carries an 83% lifetime risk for diffuse stomach cancer. A mutation in the *CDH1* gene causes HDGC and can increase a woman's risk for lobular breast cancer to 39% by the time she is 80 years old if she is from a family with HDGC (Pharoah, Guilford, & Caldas, 2001). Another study of *CDH1* predisposition to breast cancer estimates a woman's risk for developing breast cancer by

the age of 75 as around 52% (Gilpin, Nikkel, Connolly-Wilson, Stroop, & Yim, 2007). Individuals with mutations in *CDH1* are more likely to develop gastric cancer than other cancers associated with HDGC; however, *CDH1* mutations have been found in families with only a history of breast cancer (Masciari et al., 2007).

In addition to *TP53* and *CDH1*, a mutation in the gene *PTEN* carries a risk for breast cancer development and is responsible for Cowden syndrome (CS). Cowden syndrome has a population frequency of about 1 in 200,000. CS increases susceptibility for breast cancer up to 50% (Tan et al., 2012). Like other cancer susceptibility syndromes, CS carries risk for other cancers, as well. The commonly seen cancers in Cowden syndrome are breast cancer, thyroid cancer, and endometrial cancer (Tan et al., 2012), but individuals with *PTEN* mutations have also developed kidney and colorectal cancer. Breast cancer is the most common malignancy in affected individuals. CS can be clinically characterized by hamartomas found on mucinous tissues and trichilemmomas on the face that develop as the individual ages.

Mutations in *STK11* cause a syndrome called Peutz-Jeghers syndrome (PJS), which is characterized by gastrointestinal hamartomas and distinct freckling of the face. Carriers of a mutation in one copy of the *STK11* gene live with an increased risk for developing colon, pancreatic, ovarian, stomach, and breast cancer. Women with PJS have about a 50% risk of developing breast cancer throughout their lifetime (Economopoulou et al., 2015; Giardiello et al., 2000). PJS is less frequent in the population than the previous mentioned conditions, as it affects between 1 in 25,000 to 1 in 280,000 individuals in the world.

A woman may be at an increased risk for developing breast cancer due to additional genes besides the previously described high-risk genes. Three other genes including *ATM*, *PALB2*, and *CHEK2* genes have been previously described to carry a moderate risk for developing breast cancer. For example, a woman under the age of 50 who carries a mutation in *ATM* is at a 5-fold increased risk of developing breast cancer compared with the general population (60% risk compared to 12%). However, *ATM* is a low-penetrant gene, and only about 15% of women with a pathogenic variant will develop breast cancer (Ahmed & Rahman, 2006).

A mutation in a single copy of the *PALB2* gene can increase an individual's lifetime risk for breast cancer to about 35% (Economopoulou et al., 2015). If there is a family history of two or more first degree relatives with breast cancer diagnosed before 50 years old, the risk for developing breast cancer with a *PALB2* mutation could be as high as 58% (Antoniou et al., 2014).

Carrying a mutation in one copy of the *CHEK2* gene can increase breast cancer susceptibility to 37% across a woman's lifetime, specifically in North European descendants. Having two mutations, or being homozygous, can carry a lifetime risk of about 72% for breast cancer to develop in a woman. Homozygous individuals are at an increased risk of having bilateral breast cancer and generally will have poor outcomes. Mutations in *CHEK2* account for about 5% of breast cancer cases not caused by *BRCA1* or *BRCA2* (Economopoulou et al., 2015).

1.4 NCCN Guidelines for Medical Management

For high-risk unaffected women with known mutations in *BRCA1* or *BRCA2*, NCCN guidelines recommend that 18-year-olds should begin performing self-breast

exams. Starting at the age of 25, clinical breast exams should be done once or twice yearly. In addition to the clinical exam, women between the ages of 25 and 29 who are at a high risk (>20%) of developing breast cancer are recommended to have an annual MRI and an annual mammogram. Healthcare providers, including breast surgeons and genetic counselors, typically discuss RRS, such as prophylactic mastectomies who are at high-risk for developing breast cancer (NCCN, 2015, p.ADDIT2).

Prophylactic risk-reducing mastectomy (PRRM) is a surgical umbrella term which encompasses two types of breast surgeries that reduce an individual's risk of developing breast cancer, either for a first time or for a recurrence. One of these surgeries is contralateral prophylactic mastectomy (CPM). This surgery can be utilized in a woman who has decided with her surgeon that mastectomy is the most appropriate surgical treatment for her diagnosis of unilateral breast cancer. She may decide at the time of surgery, or years later, to have the other unaffected breast removed to reduce her risk for a second breast cancer, which is defined as CPM. Women who are considered high-risk for developing breast cancer but have not had a previous diagnosis of breast cancer can choose prophylactic bilateral mastectomies (PBM) which removes both breasts at the same time and reduces their overall breast cancer risk by about 90% (Rebbeck et al., 2004).

Metcalf et al. (2008) reported that uptake of RRM was highest in the United States compared to other countries, with 36% of their 706 *BRCA* mutation carriers undergoing RRM surgery. Only 22% of the 766 Canadian *BRCA* mutation carriers and 2.7% of Poland's 660 *BRCA* mutation carriers surveyed chose RRM. Many women, affected and unaffected, are choosing surgery over increased surveillance, and the rate of

uptake is rising. This is evident with the increasing uptake of CPM among women who have previously been diagnosed with cancer, as the National Cancer Data Base reported an increase from 2003 to 2010 of 9.3% to 26.4% in patients entered in the database (Pesce, Liederbach, Czechura, Winchester, & Yao, 2014). Several individual institutions in the U.S. have reported increasing trends in CPMs. The Division of Surgical Oncology at Ohio State University reported an increasing trend from 6.5% uptake of CPM in 1999 to 16.1% in 2007 (Jones et al., 2009). The Moffit Cancer Center experienced an increasing trend from 1994 to 2007 of women diagnosed with breast cancer who chose mastectomies instead of lumpectomies as their initial cancer treatment. In 1994, 38.8% of their breast surgeries were mastectomies, but by 2007, 59.8% of their surgeries were mastectomies (McGuire et al., 2009). While this does not compare CPM and PBM, it does show an increasing trend of uptake of more involved surgical procedures in women newly diagnosed with breast cancer.

1.5 Research into Influencing Factors

Previous research has investigated factors that influence women's decisions to undergo mastectomies. Two studies showed that women who came into a genetic counseling session already inclined to undergo surgery were very likely to follow through with their intentions after the session (O'Neill et al., 2010; Tong et al., 2015). Patients who have a high level of anxiety and worry about developing breast cancer have been reported to be more inclined to consider prophylactic surgeries over breast conservation and surveillance (van Dijk et al., 2003). Women who have experienced the battle against breast cancer through a family member are also more likely to choose RRS based on research by Howard et al. (2011).

van Dijk et al. (2003) studied how women's intentions for mastectomies changed when they were provided their objective risk value and noted that their amount of worry and anxiety changed, as well. The objective risk provided to women was calculated by the geneticist based on the woman's family history. Unaffected and affected women were included, and all were considered to be at high risk. Women who were quoted a low objective risk left with a lower perceived risk. This often also lowered their intention for prophylactic mastectomies. However, when women presented with high breast cancer worry and high perceived risk, they seemed more inclined to undergo prophylactic mastectomies (van Dijk et al., 2003). This viewpoint was also echoed by the results of a cohort of 696 women, which included both previously affected and unaffected individuals (Tong et al., 2015). The authors also noted that women who were not inclined to choose RRS prior to genetic testing were likely to change their minds if they were found to be a *BRCA1* or *BRCA2* mutation carrier (Tong et al., 2015). Another study specifically showed that patients looked more favorably upon risk-reducing procedures when a positive *BRCA1* or *BRCA2* result was given (O'Neill et al., 2010).

Along with higher levels of worry, some authors have found correlations with specific sociodemographics and uptake of RRS. Younger women with higher education and a greater understanding of breast cancer were more likely to have intentions to undergo RRM (Tong et al., 2015). Another study stated that age was the greatest predictor of their patients undergoing CPM (Pesce et al., 2014). Nineteen percent of affected women between the ages of 41 and 45 underwent CPM compared to 5.1% of affected women between the ages of 66 and 70. Also, rates of CPM from 2003 to 2010

increased the most in individuals under 45 years old: 9.3% to 26.4%. This study also noted surgical trends varied in different regions of the U.S. (Pesce et al., 2014).

Howard et al. (2011) discussed the importance of an individual's family history on a woman's decision to undergo RRM. Women who describe cancer as "close" have known a family member who had breast cancer and possibly saw the disease beginning at a young age. Women who have provided care to a relative battling cancer also described their cancer experience as being "close." When deciding between screening and surgery, women's "perceived proximity to cancer" factored in. For example, those who felt close often had a higher perceived risk and were more likely to undergo surgery (Howard et al., 2011). Another study found statistically significant differences in women who chose RRM versus surveillance and how family history impacted their choices. Twenty-five percent of women who chose to have RRM had lost their mother to breast cancer, while only 9% of women who chose surveillance lost their mothers. Furthermore, 18% of women who chose mastectomy over screening had lost both a first and second degree relative to breast cancer, while only 3% in the screening group had that experience. These results point to the impact which family medical history has on an individual's decision (Singh et al., 2013).

Deciding to proceed with RRM is not an easy decision and many women feel that their femininity and sexuality is threatened by both a diagnosis of breast cancer and the option of surgery. When women discuss their situation with close friends and family members, many of those conversations center around their sexuality, femininity, beauty, and self-image (Howard et al., 2011). American society generally emphasizes that a woman's femininity and sexuality are directly tied to her breasts, so losing one or both

breasts can be psychologically traumatic to some women (Jamison, Wellisch, & Pasnau, 1978). To maintain or re-establish their self-esteem and sense of sexuality, many women consider reconstruction after RRM. Al-Ghazal, Fallowfield, and Blamey (2000) compared women's perceptions of sexuality; self-esteem; depression and anxiety; and body image among women who had simple mastectomies, mastectomy with reconstruction, and lumpectomies. Overall, women who had lumpectomies were the most satisfied and expressed the least amount of morbidities related to their surgery, while women treated with mastectomy but who did not have reconstruction had statistically significantly higher morbidity related to the surgery. Sixty-eight percent of women who had a mastectomy expressed they were "feeling less sexually attractive as a result of [their] surgery" compared to 18% of those who had a lumpectomy and 25% of those who proceeded with reconstruction and expressed the same sentiment. These women who were treated with only mastectomy reported lower self-esteem and body image, with higher anxiety and depression in regards to their surgical choice. These authors argue for all women considering mastectomies to be offered and consider reconstruction to improve their psychological outcomes.

When counseling women who are considering PRRM, it is important to recognize all of the different influencing factors that may play into a woman's individual decision. NCCN guidelines (2015) emphasize the importance of multidisciplinary consultations as well as the weight of psychosocial aspects. It is also pertinent that these women meet with a multidisciplinary team of physicians including their breast surgeon and a plastic surgeon so these experts can more clearly discuss the options, risks, limitations, and benefits of various choices.

Many factors influence an affected woman's medical management. Others not specifically explored in previous research, but that could indirectly affect their findings could include the impact of media. As prominent figures share their health stories and decisions, they have the potential to spark a public response, increasing public awareness of a condition or procedure (Borzekowski, Guan, Smith, Erby, & Roter, 2014). Katie Couric televised her colonoscopy, resulting in noticeable increases in colonoscopy screening afterwards (Cram et al., 2003). Angelina Jolie Pitt publically announced that she underwent breast surgery to reduce her risk of developing breast cancer from 86% to 5% in May 2013. She shared her family's story of battling breast and ovarian cancer through several media sources (Borzekowski et al., 2014), and because of her publicity, her story created a surge in genetic counseling appointments and PRRM.

Evans et al. (2014) reported dramatic increases in referrals for genetic counseling and breast surgery consultations in 21 breast centers in the United Kingdom due to Angelina's public announcements. Their referral rates rose from May to October, and they saw a 2.5 fold increase in referrals in June and July of 2013 over the same period in 2012 (1,981 in 2012 to 4,837 in 2013). Media, as mentioned earlier, helps define a woman's sexuality but it can also influence medical management and be beneficial to women with similar medical circumstances.

1.6 Rationale and Need for Study

Multiple studies have investigated women's intentions to undergo prophylactic risk-reducing surgeries (Howard et al., 2011; Singh et al., 2013; Tong et al., 2015; van Dijk et al., 2003). However, the majority of participants in these studies have previously been diagnosed with breast cancer. Individuals without a personal history of breast

cancer choosing to have PRRM have not been the main focus of current research studies in the U.S. Prior research by Tong et al. (2015) provided a more comprehensive study investigating women's intentions for RRS. Even though they did include unaffected *BRCA* mutation carriers, these women made up only about one-third of all of the participants. These researchers recommended further research to "evaluate surgical decision making in...unaffected women" (Tong et al., 2015).

This study is specifically tailored to research the motivations of unaffected women who had been informed that they have a high-risk of developing breast cancer. The goal of our study was to understand what influences these individuals to choose PRRM. We were guided by previous research when selecting variables to measure, such as perceived risk, "closeness to cancer;" anxiety and worry related to cancer risk; family influences; family medical history; and women's demographics. Even though the majority of participants in previous studies had personal diagnoses of breast cancer, when unaffected individuals were included in the studies, they expressed similar themes in their rationale for choosing RRM as affected women. Therefore, we believe it is appropriate to measure these variables in a population of unaffected individuals who are at a high-risk to develop breast cancer.

To measure these factors in this specific population, we have targeted women who have not had a previous diagnosis of breast cancer, who have undergone genetic testing, and who have completed their PRRM. We hypothesize that these factors will be important influences on surgical management decisions regardless of a cancer genetic test result. We aimed to study women's responses about these multiple factors and ascertain which factors were most influential in their decision making process.

Chapter 2: Unaffected Women’s Decisions to have Prophylactic Risk-Reducing Mastectomies¹

2.1 Abstract

When a woman is at an increased risk of developing breast cancer due to a pathogenic mutation or a significant family history of the disease, she will be faced with choosing from among multiple management options, including risk-reducing mastectomy (RRM). The relative rate of RRM for both diagnosed and unaffected high-risk women has increased in recent years. Previous research has investigated the factors that influence women diagnosed with the disease to undergo RRM, but has not fully addressed how unaffected women make their decisions to choose RRM as an option when they are still healthy. This study was designed to specifically focus on decision-making factors of unaffected women at high risk for breast cancer due to a known pathogenic mutation or family history, and who had completed prophylactic RRM. Women participated in a mixed-mode survey that was guided by review of published literature. Factors such as perceived risk; anxiety about personal cancer risk; family implications; “closeness” to cancer; information from healthcare providers; and body image were studied for possible influence on the participants’ decision-making process. Twenty-five women participated by completing demographic information; answering multiple Likert scale questions; and reporting genetic mutation results and visits with various healthcare specialists. They answered four open-ended questions to extrapolate on influencing factors and the reasons

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they made their RRM decisions. Results showed that personal health and family implications were two of the most important influencers, and that association between concern for their sexuality and body image was significant. All 25 participants reported satisfaction with their decisions, and level of education or age of children were not significant. This study allows the voices of women to speak to genetic counselors and other healthcare specialists about the various important factors that influence healthy high-risk women to make life-changing decisions for themselves and their family members.

2.2 Introduction

Genetic testing for breast cancer susceptibility genes has been available clinically since 1996 (Hubbard & Lewotin, 1996). Since testing has been available for about 20 years, it is not uncommon for an unaffected individual to seek genetic counseling when a known mutation has been found in the family. Due to higher public awareness, individuals may recognize their family history as being significant and request genetic counseling for information about genetic testing for risk-reducing purposes.

Unaffected women with a significant family history or a known predisposing mutation are offered several options for managing their cancer risk, including increased screening with mammogram, MRI, ultrasound and frequent clinical breast exams, or RRS. However, their intentions for undergoing prophylactic bilateral mastectomies (PBM) has not been fully explored in the research arena.

Women who are faced with an increased risk for developing breast cancer have a daunting task before them, as each option has its own benefits and limitations. PRRM in women who carry a *BRCA1* or *BRCA2* mutation decrease the risk for breast cancer by

about 90% (Rebbeck et al., 2004). However, making the decision and choosing risk-reducing procedures is an intense process, and some women may struggle with their sense of sexuality, femininity, and body image (Howard et al., 2011). While surveillance is not invasive and offers early detection of breast cancer, it does not reduce cancer risk. Many women begin the decision process by evaluating how their medical management will affect their physical health, identity, relationships, and psychological health (Howard et al., 2011).

Multiple studies have investigated women's intentions to undergo prophylactic risk-reducing surgeries (Howard et al., 2011; Singh et al., 2013; Tong et al., 2015; van Dijk et al., 2003). However, the majority of participants in these studies have previously been diagnosed with breast cancer. Unaffected individuals choosing to have prophylactic bilateral mastectomies have not been the main focus of current research studies in the U.S. Recent research reported by Tong et al. (2015) provided a more comprehensive study investigating women's intentions for RRS. Even though they did include unaffected *BRCA* mutation carriers, unaffected women made up only about one-third of all of the 696 participants. These researchers recommended further research to "evaluate surgical decision making in...unaffected women" (Tong et al., 2015).

Our study seeks to understand what the important factors are that influence women's decisions to undergo PRRM when they are at an increased risk of developing breast cancer due to either a significant family history or if they have discovered that they carry a hereditary predisposing genetic factor that has significantly increased their risk to develop breast cancer.

2.3 Materials and Methods

2.3.1 Participants and design. We conducted an online survey of women who are at high risk of developing breast cancer. Participants were included in this research if they had not had a personal history of breast cancer, had cancer genetic testing, and had already completed prophylactic bilateral mastectomies at the time of taking the questionnaire. Also, participants had to be English literate to participate in the survey. Therefore, women were excluded if they had been previously diagnosed with breast cancer, had not undergone cancer genetic testing, or had not had prophylactic bilateral mastectomies by the time the survey was made available to them. These women were invited to participate in the research largely through support groups, either on Facebook (“Young Previvors”) or online through national breast cancer organizations, including BrightPink and FORCE (Facing Our Risk of Cancer Empowered).

We received permission to share our questionnaire through the high-risk support groups online. The primary investigator provided each group and/or society with the link to the survey and a brief description of the study to post online and distribute to their members and followers who are women at high risk of developing breast cancer but have not had a personal diagnosis of breast cancer.

2.3.2 Instrument. The survey contained 48 quantitative questions comprising categorical questions about demographics, type of insurance, and level of education. Likert-scale questions aimed to assess participants’ levels of anxiety, stress, and comfort related to their cancer risk and their surgical decisions. The survey also included five open-ended questions to allow patients to elaborate on their experience. The survey was reviewed and edited by all members of the committee. The study protocol was approved

by the University of South Carolina Institutional Review Board in August, 2015 and was open from September, 2015 until February, 2016.

2.3.3 Data analysis. Quantitative analysis was performed using SPSS Software Version 23. Spearman's correlation was used to identify significant relationships between variables within the survey group. Frequencies and percentages were calculated for all close-ended questions. An original questionnaire measuring anxiety consisted of twenty-one questions gauging the respondents' anxiety during the surgical decision making process. The scale showed a moderate level of internal consistency, as determined by a Cronbach's alpha of 0.74. The sum of this scale provided an anxiety score.

One-way ANOVA was performed to identify significant differences among the mean anxiety scores between completed education levels. Data was presented as mean \pm standard deviation. An independent-samples t-test was run to determine if there were differences in anxiety scores between varying groups among participants. Significance levels of $p \leq .05$ were used for all analyses. Qualitative data was analyzed by the primary investigator using content analysis to identify recurring themes. These themes were then compared among high and low levels of anxiety related to the decision making process.

2.4 Results

2.4.1 Demographics. A total of 46 individuals responded to the survey. Nineteen were excluded because they did not meet eligibility criteria: two had a personal history of breast cancer; one had not had genetic testing; and fifteen had not undergone PBM at the time the survey was conducted. Two other questionnaires were excluded because only demographic questions were answered. Data analysis was run on the

remaining twenty-five completed questionnaires. Sociodemographics for these participants are shown in Table 2.1.

Table 2.1 Participants' Demographics

	Frequency (<i>N</i> = 25)	Percentage (%)
Age		
20-29	8	32
30-39	12	48
40-49	4	16
≥50	1	4
Education Level		
Less than high school	0	0
High school graduate	1	4
Some college	1	4
Associate's degree	4	16
Bachelor's degree	8	32
Graduate degree	11	44
Medical Insurance		
None	2	8
Private	20	80
Medicaid	2	8
Medicare	0	0
Prefer not to answer	1	4
Number of Children		
0	10	40
1	4	16
2	9	36
3	2	8
≥4	0	0
Residency		
United States	21	
Northeastern states	6	
Southern states	8	
Midwestern states	5	
Western states	2	
Canada	2	
United Kingdom	1	
Prefer not to answer	1	

Fifteen of the 25 women had one or more children. A total of 28 children were reported from these 15 women. The average age of the children was 9 years. The ages of the children are shown in Table 2.2.

Table 2.2 Children’s Ages

Ages	Frequency
	<i>N</i> = 28
≤ 5	8
6 – 10	10
11 – 15	8
16 – 20	1
21 – 25	1

Of the 24 individuals who provided their cancer genetic results, 22 had a mutation in either the *BRCA1* or *BRCA2* gene. Sixteen respondents had a *BRCA1* mutation, and six had a *BRCA2* mutation. Two participants had received negative cancer genetic test results, and proceeded with PRRM based on family history concerns.

2.4.2 Risk perception. Participants were asked two questions regarding how high they perceived their risk to develop breast cancer was prior to choosing surgery: a) What was your risk of developing breast cancer in a percentage? and b) What was your perceived level of risk to develop breast cancer?. About half of the respondents (*n* = 13) stated they believed they had between a 75% risk to a 90% risk of developing breast cancer in their lifetime see Figure 2.1. When asked to qualitatively describe their perceived risk of developing breast cancer, twelve described their risk as being “high,” another twelve described their risk as being “very high,” and one respondent reported her risk to be “moderate or in the middle.”

Twenty-one participants answered the question asking who provided them with a cancer risk (Figure 2.2). The responses do not add up to 21, as participants were allowed to select multiple healthcare providers if more than one provided them with a risk

estimation. The healthcare providers who most consistently provided a cancer risk to the participants were genetic counselors, as 19 women received a personal cancer risk

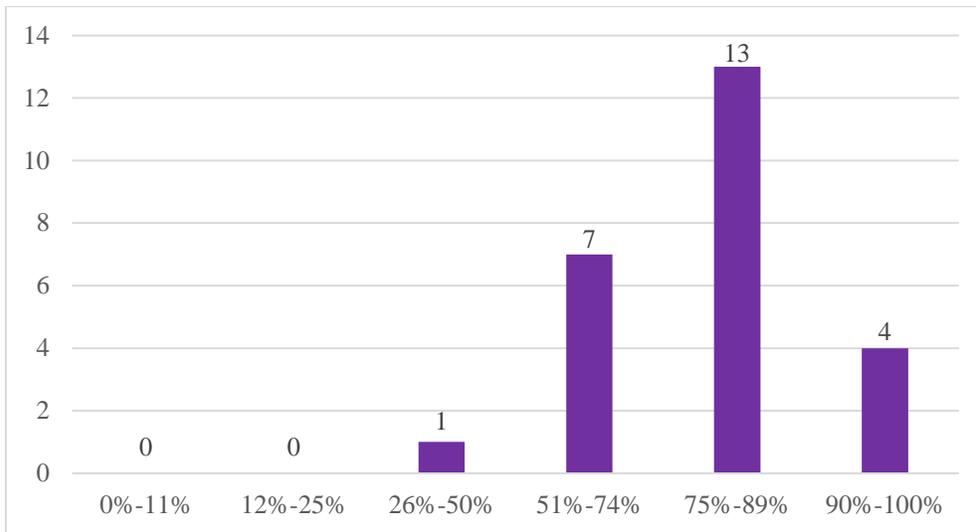


Figure 2.1 Estimated Risk of Developing Breast Cancer Prior to Surgical Decision

from them. The second most frequently selected providers were breast surgeons ($n = 14$), followed by oncologists ($n = 7$). Other healthcare providers who presented cancer risks included internists, OB/Gyns, and general practitioners.

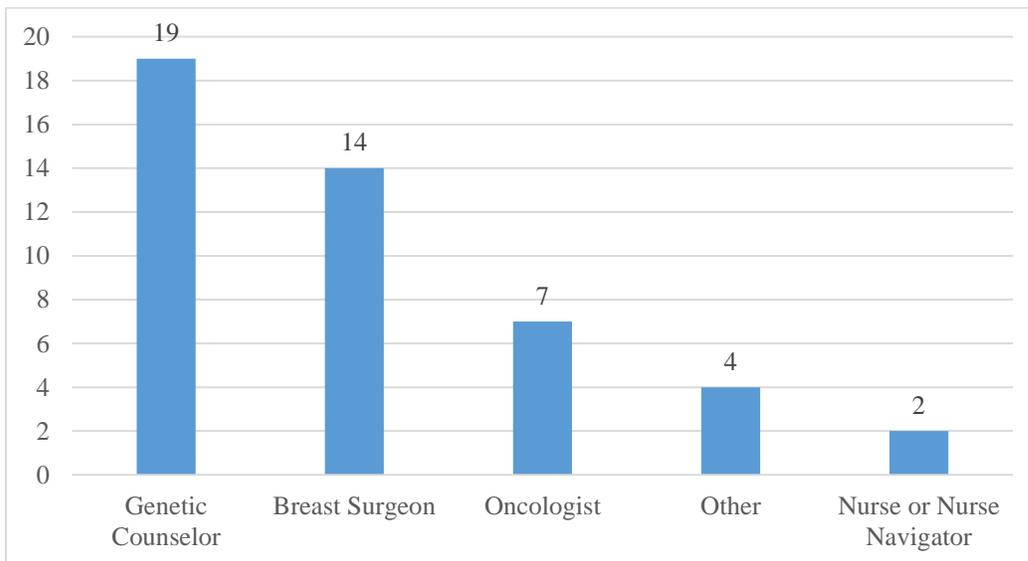


Figure 2.2 Healthcare Providers who Presented Personal Cancer Risk

Of the sixteen women with *BRCA1* mutations, eight stated in an open-ended question that they were quoted between a 60% and 90% chance of developing breast cancer, and six of these women specifically stated they were told they had “up to an 87% chance.”

Twenty-two participants responded to the statement “I believe my surgery has completely eliminated my risk of developing breast cancer.” Almost half of the respondents disagreed with that statement; five agreed with it; and five strongly agreed with the statement. When asked what they thought their risk was numerically after having PRRM, all twenty-two respondents selected their risk as being below 11% to develop breast cancer after their prophylactic surgery.

2.4.3 Anxiety throughout decision-making process. The average anxiety score of all 25 participants from the questionnaire was 47. Scores below the twenty-fifth percentile (scores less than 41) were considered to describe participants with relatively low anxiety, and scores above the seventy-fifth percentile (scores higher than 52) were considered to describe participants with relatively high anxiety when distributed on a box-plot. Six participants scored below 41 (relatively low anxiety); six participants had scores higher than 52 (relatively high anxiety); and thirteen participants scored between 41 and 52, representing relatively moderate anxiety during the surgical decision making process.

Participants were asked how their anxiety level changed after talking with healthcare providers and receiving their personal cancer risk assessment (Figure 2.3). Twenty-three women answered the question, and after receiving their personalized cancer

risk, two said their anxiety decreased, nine stated their level of anxiety was not affected, and twelve reported that their anxiety level increased.

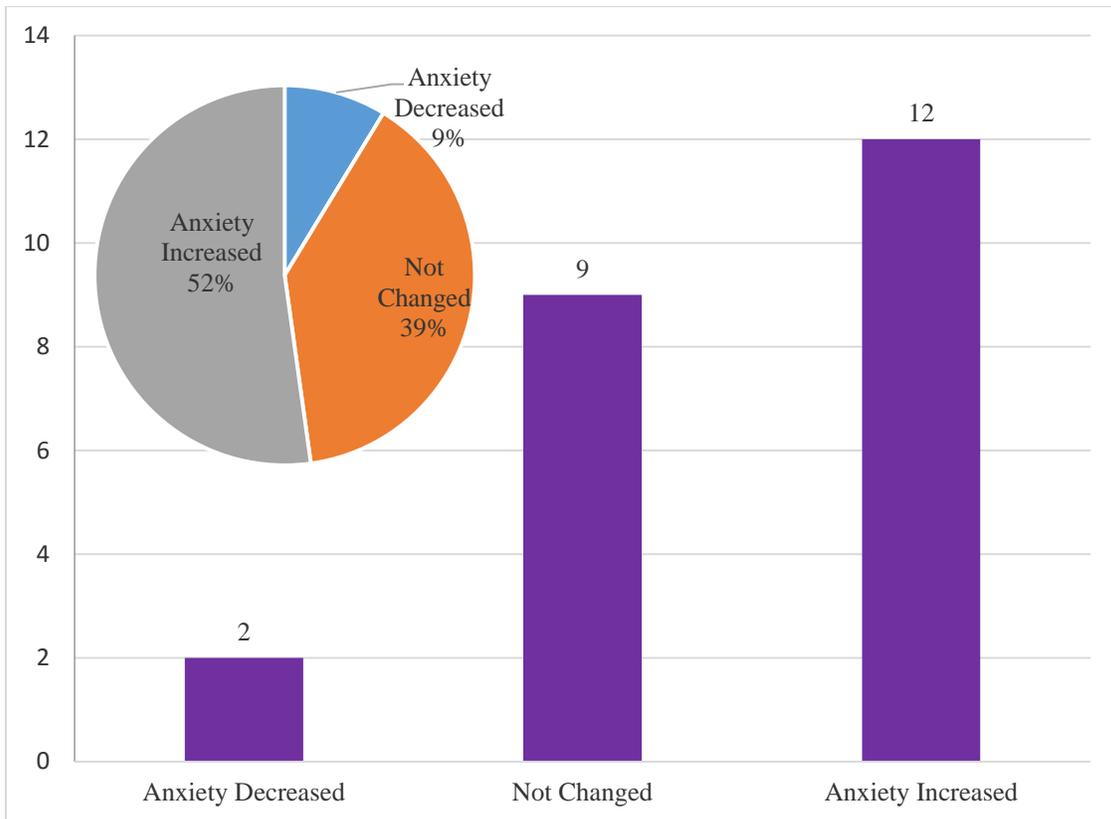


Figure 2.3 How Personal Cancer Risk Affected Anxiety Level

When asked to self-report their level of anxiety when they decided to have surgery as their treatment, four women described their anxiety level as “low”; seven described their level as “somewhat high”; ten described their anxiety level as “high”; and four described their anxiety level as “very high” (Figure 2.4). Throughout their decision making process, twenty-four of the twenty-five participants have been comfortable with the decision to have surgery. Since their surgeries had been completed, all twenty-five participants have been comfortable with the decision to undergo surgery.

A one-way ANOVA was conducted to determine if the mean anxiety levels (CWWS score) was different for groups with different levels of education completed.

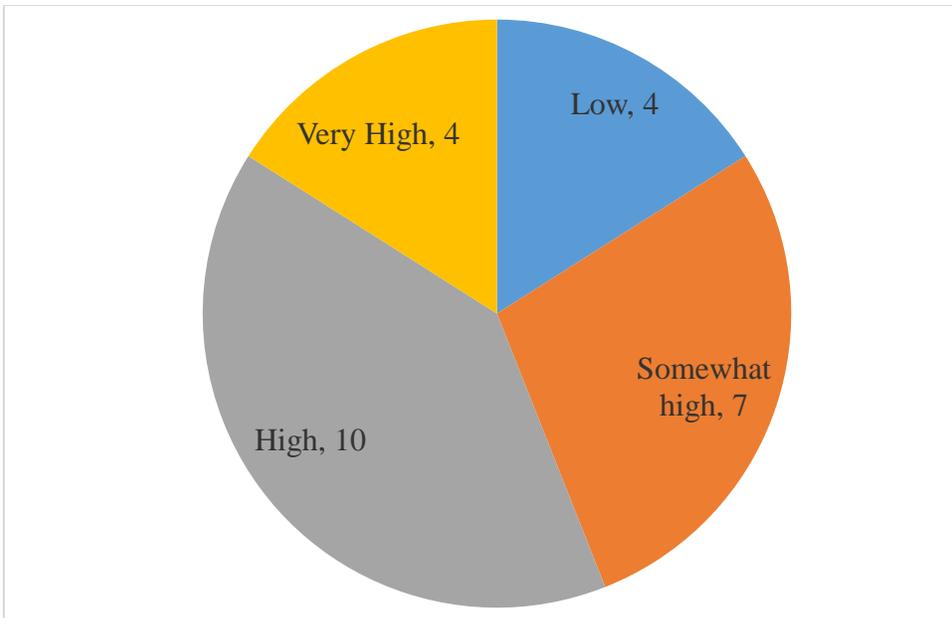


Figure 2.4 Anxiety Level when Deciding to Have Surgery

Participants who completed some college and an associate’s degree were not included in analysis because the population size was not greater than two. There were no outliers, as assessed by boxplot; data was normally distributed for each group, as assessed by Shapiro-Wilk test ($p > .05$); and there was homogeneity of variances, as assessed by Levene's test of homogeneity of variances ($p = 0.173$). CWWS scores increased from the some college group ($n = 4$, $M = 43 \pm 10$), to graduate degree group ($n = 11$, $M = 47 \pm 10$), to the Bachelor’s degree group ($n = 8$, $M = 48 \pm 7$) education levels groups, in that order, but the differences between the anxiety scores of the completed levels of education was not statistically significant, $F(2, 20) = 8.14$, $p = 0.66$ using a one-way ANOVA test.

2.4.4 Sexuality and Body Image. Utilization of Spearman’s correlation revealed a statistically significant positive correlation between women worrying about their sexuality and what their husband’s opinion was during the decision making process, $r_s = 0.410$, $p = .046$. Eleven of the twenty-four respondents disagreed with the statement “I was concerned with what my spouse or partner would think [during the decision making

process],” while thirteen agreed with that statement. Eighteen participants agreed with the statement “I was confident in my sexuality during the decision making process,” while seven disagreed with that statement. There was also a positive correlation between women feeling comfortable with their sexuality and their body image, $rs = 0.403, p = .03$. Of the 25 participants, eight women stated they were not worried about how the surgery would affect their body image, while seventeen women did express concern for their body image.

2.4.5 Genetics and family influences. Twenty-four women answered how old they were when they had genetic testing. The average age of participants when they had genetic testing was 30 years of age, with a range from 19 to 51 years of age.

Participants were asked if they were the first to have genetic testing in their families and if other family members had the same mutation. In response to the question asking if they were the first to have genetic testing in their family, fourteen reported that they were not and ten reported that they were the first. Of the twenty-two women who reported a mutation from their genetic results, fourteen reported that other family members had the same mutation and eight women were the first to have this mutation in their family.

There was one participant who had no one in her family including mother’s and father’s side who had been diagnosed with breast cancer. There were fourteen women who had immediate family diagnosed with breast cancer. Thirteen respondents reported there was a family history of breast cancer on their mother’s side, and eight women reported breast cancer on their father’s side. Two participants reported family history of breast cancer from both their mother’s and father’s side. Eight participants were involved

with caring for a family member diagnosed with breast cancer, and fifteen reported not being involved in the care. Several participants expressed that the desire to undergo surgery was influenced by watching family members struggle with cancer treatments. When asked to provide the three most important factors they considered when deciding to have surgery, family was listed by 14 of the 20 who responded to that question (70%).

When asked if any family member had passed away from breast cancer or cancer that had metastasized from breast cancer, twenty-three responded. Thirteen reported a family member dying from breast cancer or metastasis, and ten reported not having a family member die from breast cancer. Of the family members who passed away, four were first degree relatives, seven were second degree relatives, and two were third or fourth degree relatives. An independent-samples t-test was run to determine if there were differences in anxiety between participants who reported a family death related to breast cancer or those who did not. The average anxiety score was compared between women who reported family deaths due to cancer and those who have not had that experience using an independent t-test. Anxiety scores were only slightly higher in individuals who had not had family members pass away ($n = 10$, $M = 47. \pm 8$) than those who reported family deaths due to breast cancer ($n = 13$, $M = 46 \pm 9$). There was no statistically significant difference between the two groups' anxiety scores.

An independent-samples t-test was run to determine if there were differences between the mean anxiety scores of women who did and did not have children ($n = 10$, $M = 47 \pm 10$; $n = 15$, $M = 47 \pm 8$, respectively). No statistically significant differences was found. An independent-samples t-test was again employed to determine if there were differences in anxiety scores between participants who had children 9 years old and

younger ($n = 8$, $M = 49 \pm 7$) versus participants who had children ages 10 and older ($n = 7$, $M = 44 \pm 8$). There was no statistically significant difference between the two groups' anxiety scores.

In response to questions about participants' surgery decision making process, twenty-two of twenty-five respondents said their family gave them the support they needed during this time. Qualitative responses collected from open-ended questions helped with explaining the quantitative data. One participant expressed how much her family supported her decision: *"I did not have a SINGLE person in my family or friends try to convince me otherwise or even present the option of not having surgery."* In addition to this, the majority of participants reported that they were not concerned with what their family thought of their decision to have surgery ($n = 19$).

Participants were also asked how undergoing surgery made them feel about family planning. About half of the participants who responded to this agreed with the statement "Going through with surgery did not make me nervous about planning a family." ($n = 13$ of 24). Responses were consistent when participants responded to "I was anxious about how my surgery could affect my family plans or family planning." One woman explained how planning a family made the decision to have surgery more difficult:

I did not want to wait until after having kids, but that was a tough choice for me. I feel guilty that I will never be able to breast feed, but I ultimately decided it was more important for my future children to have a healthy, living mom.

A common theme of how important family was emerged from free response questions trying to gauge what were important factors that played into participants' decision making process. Qualitative data from participants who had negative genetic testing were analyzed with participants who had a hereditary genetic predisposing mutation. Responses from the women with negative genetic testing aligned with the themes expressed by the women with positive genetic tests. There were twenty responses relating to the importance of family, with common phrases of wanting to "[be] there for my children and husband," "wanting to see my kids grow up," and not wanting to put family members through the trauma of fighting cancer.

2.4.6 Personal surgical decision. The most commonly selected avenues of hearing that prophylactic surgery was a management option were from breast surgeons ($n = 15$), genetic counselors ($n = 14$), and the media featuring Angelina Jolie Pitt's personal experience ($n = 10$). Breast surgeons ($n = 21$) and plastic surgeons ($n = 22$) were the healthcare providers with whom most participants discussed the option of preventive breast surgery. Other healthcare providers selected included genetic counselors ($n = 15$), gynecologists ($n = 15$), family practitioners ($n = 12$), and oncologists ($n = 11$). However, the participant's spouse or partner was selected more frequently when asked "Who did you talk with the most about your medical management?" ($n = 7$). Alternative responses included breast surgeon ($n = 4$), other (aunt, support group, gynecologist, and genetic counselor, $n = 4$), friend ($n = 3$), and mother ($n = 3$).

Having a medical procedure that was affordable and of high quality was another theme expressed by the women in this survey. Several respondents emphasized how important it was to them to be able to have skilled doctors in charge of their surgery.

When asked in a free-response question what the key factors were when deciding to proceed with surgery, this theme was expressed by the following statements: “*Finding good doctors;*” “*Trust in the medical team;*” and “*[it] is VERY important that you select a skilled medical team.*” Having the option of reconstruction was also very important to our participants, as they expressed in the open-ended question about important aspects of their surgical decision making process. Also, when asked if they agreed with the statement “Having the option of reconstruction made me more comfortable with undergoing bilateral preventive breast surgery.”, only one respondent of the twenty-four respondents who answered it disagreed with that statement. Four participants emphasized that patient cost was an influencing part, as all four stated that surgery was more affordable surveillance by mammogram and MRIs.

Another theme that emerged was preserving themselves. Responses such as: “*not wanting to die;*” “*Do the surgeries and have a chance [at life];*” “*not having to fight to live,*” and “*maintaining my personal health*” fully expressed these women’s desires to live prosperous lives. Under this “preserving self” theme, many women expressed that being in control and proactive was very crucial. One woman’s response summed up the rest: “*I wanted the surgery to be on 'my terms' rather than losing more control if I did get cancer.*” Another woman’s sentiment was: “*I felt like there was a really strong chance I would get breast cancer and I didn't want to just wait for it to show up.*” These same women mentioned that if they were to be diagnosed with breast cancer, they would have chosen a double mastectomy as their surgical treatment of choice.

Participants were also questioned about their experiences with breast cancer screening. Table 2.3 displays what procedures, exams, or results our participants

encountered before having surgery. One woman explained that she chose surgery over screening because *“The emotional roller coaster [of screening] was ridiculous...And none of those [screening options] are fool proof. Best option was to remove the tissue of concern.”* Other women expressed similar sentiment with wanting *“peace of mind,”* and *“not wanting to worry anymore.”*

Table 2.3 Screening Procedures Prior to Preventive Surgery

Procedure/Exam/ or Results	Number of Women <i>n</i> = 22	Percentage (%)
Lump or other finding on self-breast exam that made you call your doctor	8	36
Clinical breast exam that required a mammogram	6	27
Call-back for repeat mammogram	6	27
Mammogram result that concerned your doctor	8	36
Ultrasound after mammogram	12	55
Positive breast MRI	4	18
Breast biopsy	4	18

Avoiding getting cancer and cancer treatment was another common theme expressed as critical factors that played into the surgery decision. *“Because once you have cancer you don’t know if you will survive it. I would rather just not get it”* was one woman’s response. Of the twenty women who explained what the three most important factors were when deciding to have preventive breast surgery, fourteen mentioned they were fearful of receiving a cancer diagnosis or having to undergo chemotherapy and radiation. One brutally honest answer was having the *“desire to avoid chemo and entering early menopause, losing hair, [and] feeling like hell.”*

2.5 Discussion

This study helped further investigate factors that influence women to undergo prophylactic risk-reducing surgery when they are at a high risk to develop breast cancer

and have not had a previous personal diagnosis of breast cancer. Even though this study had a small sample size, some of the results complimented data and conclusions previously reported in literature. However, some findings in this study contradict other publications, and explanations for this discrepancy could not be fully explored in this short term study. Data gathered through this original questionnaire highlights several areas of interest involved in the participants' decision making process.

2.5.1 Sociodemographics. The women who completed this questionnaire were of similar sociodemographics as other women considering RRS in previously reported studies. Tong et al. (2015) found from their population of 71 unaffected individuals who expressed intentions for undergoing PRRM, that women of a younger age and who had at least a college education were most likely to consider PRRM. When assessing education and intentions to undergo PRRM, women with a college education had a 76% greater odds of considering PRRM. Three-fourths of the participants in this study had at least college education and 20 of the 25 participants were under the age of 40. When investigating whether mastectomies have increased in prevalence, McGuire et al. (2009) from the Moffit Cancer Center also reported that women of younger ages, specifically younger than 40, were more frequently choosing risk-reducing surgeries. Women involved in Moffit's study had been diagnosed with breast cancer; however, their findings supported that younger women often find RRS more favorable for treatment. Our study of participants across an age range of 24 to 54 years agrees with their results.

2.5.2 Risk perception. All the participants who had a positive genetic test result had mutations in *BRCA1* and *BRCA2* genes and the majority of them had relatively good awareness of the risk associated with breast cancer. Participants were not asked what

they thought their risk was prior to genetic testing but were asked how they perceived their risk prior to making the decision to have surgery as treatment. Regardless, the participants had been given appropriate risk assessments to help them make this life-changing decision. Based on the participants' education background, it is not surprising to see them report such specific risks and to have such good recall from their medical appointments. Also of note, about half of respondents understood that this RRM did not fully eliminate their risk to develop breast cancer in the future. While they reduced their risk by about 90%, there is still a residual risk that they could develop breast cancer in the future. This level of understanding could also be attributed to their education and possibly greater attention to detail.

2.5.3 Anxiety throughout decision-making process. With the original questionnaire that assessed participants' anxiety, relative anxiety level was compared within the study population. Previous research reports that women who have higher anxiety associated with cancer risk are more likely to undergo RRS (Tong et al., 2015; van Dijk et al., 2003). Unfortunately, there was not a control group to which we could compare participants' anxiety scores measured by our instrument to gauge whether our participants had higher levels of anxiety. The questionnaire utilized within this study was specifically designed for women who had undergone PRRM, thus making it difficult to compare scores to women who had not undergone surgery for treatment. However, anxiety scores were compared within the study participants.

Because we designed original questions for an anxiety score, we could only compare our anxiety scores within the participants of this study. Thus, we cannot predict if their true anxiety scores would have shown a more sensitive picture of their anxiety.

Perhaps, for instance, all of the participants' baseline anxiety scores may have been judged as "high" on another scale due to this specific topic and to their life-changing decision to undergo PRRM. Then the spread of these scores on our scale may not be a sensitive measure of their true anxiety, whereas the differences between the individuals in our study may have shown significance on a different anxiety scale.

One hypothesis investigated whether women with children had higher relative levels of anxiety throughout their decision making process compared to women without children. There was not a statistically significant difference between the two mean scores. Further evaluation was done to assess whether women with younger children (9 years or younger) had higher anxiety levels than the women with older children. Again, no statistically significant difference was found between the mean anxiety scores of the two groups. This study was retrospective and thus participants may not have fully accurately remembered how they felt during the decision making process. Also, participants were asked what their children's ages were at the time they filled out the questionnaire, not the ages of their children when they were considering surgery. Some participants who had children by the time they completed the survey did not have children when they were considering surgery, and thus may not have been as worried. There may not be a statistically significant difference of the two groups because women may still be concerned with family planning before they have children. This is evident in a few participants who expressed a desire to avoid cancer *so that* they could one day have a family: "*scared to die young before I can marry my boyfriend and raise kids with him*" and "*living long enough to start and raise a family*" were reasons these two participants chose to have PRRM. Singh et al. (2013) described in their study of 136 unaffected

BRCA1 and *BRCA2* mutation carriers that having children was associated with women having prophylactic mastectomies to reduce their risk of developing breast cancer. Our study could possibly be limited in this finding due to the number of our participants, but within the study population, there were about equal number of participants who did ($n = 15$) and who did not ($n = 10$) have children.

We also hypothesized that anxiety scores would differ significantly depending on the highest level of education completed. There was no statistically significant difference noted through analysis; however, of the three groups compared (associate's degree, Bachelor's degree, and graduate degree), the mean anxiety score was highest among those who had a Bachelor's degree. It is possible that since they are college educated, they have a moderate awareness and knowledge of cancer but they may not fully understand all the intricacies and nuances of hereditary breast cancer. Thus, their limited knowledge could be a source of their somewhat higher anxiety score. Participants were not asked as to which field they studied in college or graduate school, so their college major or specialty could also affect their level of understanding and concern. Previous research found that women who had a college education or higher were more likely to choose PRRM than women with less education. Our study may support that finding because all but two of our participants did have education beyond high school. However, it is possible there is sample bias in our study, as the support groups who distributed our survey may have consisted largely of women with higher education.

2.5.4 Sexuality and body image. Women's femininity is often depicted in art and in the media emphasizing their breasts. A woman's breasts can help define her sexuality in her mind. Being able to breastfeed can also be tantamount to defining

womanhood. Therefore, a woman deciding to remove her breasts to protect herself from disease can be a psychological battle. Several studies have reported women feel that their femininity is attacked by the threat of breast cancer (Howard et al., 2011). Our study found a significant association between participants' concern for their body image and sexuality. Some women find reassurance in the fact that breast reconstruction is available after their mastectomies (Howard et al., 2011; Tong et al., 2015; van Dijk et al., 2003). This can be said about the participants in our study, also, as 23 of 24 respondents agreed that having reconstruction as an option made choosing PRRM more comfortable.

Another component that affects women's perceived sexuality is how their significant other views them (Howard et al., 2011; Jamison et al., 1978). The significant association for concern of how their spouse or partner views them and how they view their own sexuality expresses this influence. The majority of our participants also agreed that while making the decision to have surgery, they were concerned with how their significant other felt, as spouses and partners were selected most frequently when asked who they included in their decision making process.

2.5.5 Personal surgical decision. Several women expressed that this journey and the decision to have PRRM was a personal one. One of the most frequently listed factors that participants considered important when making their decision was to maintain and keep themselves healthy. These women, as with the many other women who have been in similar situations, have a strong desire for life. Common statements, such as "*not wanting to have to fight to live*" and "*living a full life*" express these women's desire to protect themselves. Many women wanted to be able to make medical management decisions on their own terms rather than have a diagnosis of breast cancer and face losing

control of their health. One woman's expression, "*I feel empowered to be proactive,*" captures what all the participants expressed about encompassing their desire to maintain their health.

Participants also explained that they had surgery to alleviate the worry associated with heightened surveillance. Having to be screened, waiting for something to be found, and then making medical decisions was a looming cloud of stress, and many women chose to have surgery to avoid "*close calls*" and the endless anguish. All of the participants expressed that they were completely satisfied with their decisions to have PRRM. They each gave great consideration to the benefits and limitations, and made the decision that was best for their health and well-being.

2.5.6 Limitations and future research. Common limitations of Internet-based research, such as self-reported data, unknown response rates, and the inability to control who accessed the survey are all possible limitations of this study. Finding support groups for this target population was more difficult than expected, and it was even more difficult to include women who chose to have PRRM with negative genetic results. Another limitation was the small sample size for this study. The women who did participate were self-selected and were more motivated individuals to share their medical testimony. Also, the women surveyed were largely younger and highly educated which may not truly represent the larger population of unaffected women at a high-risk to develop breast cancer. Another study limitation was that there was not a control group or another group of women with whom we could compare anxiety scores.

Future research should strive to include and investigate unaffected women at high-risk to develop breast cancer but who have a negative cancer genetic test result.

Even though in our study, women with a negative genetic test expressed similar sentiments as women with a positive genetic test, this cannot be generalized to other women who have a significant family history and a negative genetic test because we only had two women who fell into that category. Also, our study, along with others in the published literature, show that many other factors other than the pure risk associated with genetic predisposition have a strong influence on the decision to undergo surgery to prevent breast cancer.

2.5.6 Implications for genetic counselors. Understanding the influencing factors that affect a woman's decision can help genetic counselors provide targeted counseling, support referrals, and include education to better foster informed decisions. Genetic counselors are also equipped to facilitate a multi-disciplinary conversation to advocate for what is best for the patient. While the majority of our participants were carriers of *BRCA1* and *BRCA2* mutations and had clear cancer risks, more and more women are receiving hereditary cancer gene panel testing which reveals pathogenic mutations in other high-risk cancer-associated genes. Being able to comprehend what is important to the patient can help in facilitating the decision making process.

Additionally, genetic counselors should be clued into their patient's concerns and desires because genetic counselors are involved in several key positions throughout a woman's decision making process. The vast majority of our participants answered that genetic counselors provided their personal cancer risk. Genetic counselors are vital to providing accurate risk-assessment to allow women to make the best informed decision they can. Furthermore, when counselors are connected with their patients, they assist in all major aspects of the decision making process, including anticipatory guidance about

future issues such as what type of reconstruction can be done, risk to family members and patient's children, and coping with the psychological effects of the decisions the women make.

2.6 Conclusions

This study was conducted to further explore what influenced unaffected women who were at a high-risk of developing breast cancer to pursue prophylactic risk-reducing mastectomies. Participants were asked how known influencing factors affected their decision making, such as the impact their decision would have on family, their sexuality, and their perceived risk to develop cancer.

Women were motivated to have PRRM to maintain their health and well-being. Staying healthy so that they could be around and experience the joys of life were strong influences. The majority of participants reported they had a "high" or "very high" risk of developing cancer. They underwent surgery to prevent an unwanted diagnosis of cancer, to avoid harsh cancer treatments, and to alleviate the apprehension and worry associated with their annual mammograms and MRIs. Almost all of the participants reported having had a family history of breast cancer, which was also a key motivator to avoid cancer.

Participants expressed varying degrees of anxiety. Some of the same factors that influenced their decision to have PRRM also were associated with their level of anxiety. Most women expressed their anxiety as being moderately high to very high throughout their decision making process. They expressed being concerned about their appearance and how surgery might compromise their sexuality. They felt that having the surgery on their own terms was the wisest medical decision for themselves.

Health care providers, especially genetic counselors, can more appropriately support women through this medical management odyssey when they better understand what factors are important and motivating to the women they counsel.

Chapter 3: Conclusions

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Appendix A: Survey Welcome Letter

Thank you for participating in our survey. Your feedback is important.

This survey was designed to understand factors that influence women who are at a high risk of developing breast cancer but have not been diagnosed themselves and their decision to undergo preventive breast surgery.

Preventive breast surgery is the term used throughout the survey to describe the risk-reducing surgery. Other terms you may be familiar with are prophylactic bilateral mastectomy or risk-reducing mastectomy. This surgery involves the removal of breast tissue of both breasts in a woman who has NOT had previous diagnosis of breast cancer. In this survey a diagnosis of ductal carcinoma in situ (DCIS) is considered a diagnosis of breast cancer.

This survey was NOT designed to include women who have had a previous diagnosis of breast cancer, or who have undergone contralateral prophylactic mastectomies. Contralateral prophylactic mastectomy is a surgical procedure in which women remove the breast that has not had breast cancer in it. For example, if a woman had cancer diagnosed in her right breast, removing her healthy left breast to prevent another cancer would be a contralateral prophylactic mastectomy.

Sharing your experience can help genetic counselors and other healthcare professionals provide better psycho-social and clinical care for women facing an increased risk of breast cancer and the complex medical management decision making process.

All responses gathered from the survey will be kept anonymous and confidential. The results of this study might be published or presented at academic meetings; however, participants will not be identified.

Your participation in this research is voluntary. By completing the survey, you are consenting that you have read and understand this information. You may withdraw from the study at any time by not completing the survey. The survey should take you about 20-30 minutes to complete.

Thank you for your time!

If you have any questions or concerns, please feel free to contact us. If you have any questions about your rights as a research participant, you may contact the Office of Research Compliance at the University of South Carolina at (803)777-7095.

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Appendix B: Online Survey

SECTION A: CRITERIA INFORMATION: The following section has questions to see if participants qualify to take part in this survey.

1. Do you have a personal history of breast cancer now or in the past?*
 - a) Yes
 - b) No
2. Have you had genetic testing for Breast Cancer genes?*
 - a) Yes
 - b) No
3. Have you had bilateral preventive breast surgery?*
 - a) Yes
 - b) No

SECTION B: ABOUT YOU! In this brief section we want to collect some general information about you. Everything collected will be protected and will not be shared.

4. What is your current age?*
5. What is the highest level of education you have completed?
 - a) Did not finish high school
 - b) High school graduate
 - c) Some college
 - d) Associate degree
 - e) Bachelor degree
 - f) Graduate degree (Master's, PhD, MD, etc.)
6. What type of medical insurance do you have as your primary insurance?
 - a) None
 - b) Private
 - c) Medicaid
 - d) Medicare

7. How many children do you have?

- a) 0
- b) 1
- c) 2
- d) 3
- e) 4 or more

8) What are the current ages of your children?

First child	
Second child	
Third child	
Fourth child	
Fifth child	

9. Do you live in the United States? (Including Puerto Rico)*

- a) Yes
- b) No

10. If yes to the previous question, in what state or territory do you live?

11. If you do not live in the US, in which country do you live?

SECTION C: REMEMBERING YOUR FEELINGS ABOUT YOUR DECISION: This section asks questions to help us understand how you felt during your decision making process.

12. When I was making my decision for bilateral preventive breast surgery, my anxiety level was:

- a) Very low
- b) Low
- c) Somewhat high
- d) High
- e) Very High

13. Please indicate the level of agreement you felt with following statements during your decision making process.

	Strongly Disagree	Disagree	Agree	Strongly Agree
Other people's opinions did not influence my decision making process				
I felt anxious about the breast surgery				
I was worried about reconstructive surgery.				
Going through with the surgery did not make me nervous about planning a family				
I was confident in my sexuality during this decision making process				
Thinking about the recovery process made me nervous				
I was comfortable with my sexuality throughout the decision making process				
I was concerned with what my family would think				
I was concerned with what my spouse/partner would think				
I was worried about my body image				
Reconstructive surgery did not make me nervous				
At first, I felt uncomfortable about my decision				
At the time of my surgery, I felt comfortable knowing I was doing the right thing for me				
I felt anxious about my sexuality				
I was worried about my insurance coverage for the surgery				
I was concerned about having to miss work in order to recovery from my surgery				
I felt comfortable about my decision to have surgery from the beginning of my decision making process				
I was anxious about how my surgery could affect my family plans and/or family planning.				
My family gave me the support I needed when I was making my decision.				
Since surgery, I have been comfortable with my decision				
Having the option of reconstruction made me more comfortable with undergoing bilateral preventive breast surgery				

SECTION D: RISK PERCEPTION

14. Before I made my decision for bilateral preventive surgery, I felt my risk for developing breast cancer was best described by the following numbers:

- a) 0%-11%
- b) 12%-25%
- c) 26%-50%
- d) 51%-75%
- e) 75%-90%
- f) 90%-100%

15. Before I made my decision for bilateral preventive surgery, I felt my risk for developing breast cancer was best described by the following level:

- a) Very low
- b) Low
- c) Moderate or in the middle
- d) High
- e) Very High

16. Has any healthcare provider told you what your risk was for developing breast cancer?*

- a) Yes
- b) No

SECTION E: RISK OF DEVELOPING BREAST CANCER: The following three questions are looking to see which health care provider gave you your risk and how that affected your feelings at the time.

17. Who provided you with your personal risk for developing breast cancer? You may mark more than one.

- a) Breast Surgeon
- b) Oncologist
- c) Nurse or Nurse Navigator
- d) Genetic Counselor
- e) Breast Surgeon
- f) Oncologist
- g) Nurse or Nurse Navigator
- h) Genetic Counselor
- i) Other

18. Of the healthcare providers who gave you your risk, how did he/she describe your risk to you?

19. After hearing the risk given from the above health care professional(s), how did it affect your anxiety level?

- a) The risk lowered my level of anxiety and worry
- b) My level of anxiety and worry was not changed by this risk
- c) The risk raised my level of anxiety and worry

SECTION F: GENETIC TESTING: During your decision making process, your genetic test may have influenced your choices. These next few questions ask about this specific part of your decision process

20. What was your age when you had Genetic Testing for Breast Cancer Genes?

21. Were you the first one in your family to have genetic testing for Breast Cancer genes?

- a) Yes
- b) No

22. Receiving my genetic test results greatly increased my anxiety about developing Breast Cancer.

- a) Strongly disagree
- b) Disagree
- c) Agree
- d) Strongly agree

23. Did your genetic test report a "mutation" or "change" in a breast cancer gene?*

- a) Yes
- b) No

24. In what gene was a "mutation" or "change" found?*

- a) BRCA1
- b) BRCA2
- c) TP53
- d) STK11
- e) CDH1
- f) ATM
- g) PALB2
- h) CHEK2
- i) Other gene OR if your test reported more than one mutation in different genes (PLEASE SPECIFY THE GENE(S) IN THE BOX BELOW)

25. Was/were the DNA change(s) reported in the cancer-related gene classified as a mutation or a variant of unknown significance (VUS, VOUS)?

26. Did someone else in your family have this "mutation" or "change" before you were tested?

- a) Yes
- b) No

27. What prompted your thoughts about bilateral preventive breast surgery, since your genetic testing results were negative?

SECTION G: FAMILY HISTORY WITH BREAST CANCER: In genetics, Family is defined by biological members, or those to whom you are related by blood: mother, father, brothers, sisters, halfsiblings, grandmothers, grandfathers, aunts, uncles, cousins, nieces, and nephews. The following questions ask about those in your Family who have received a diagnosis of breast cancer. Male family members are included in these questions because breast cancer does not affect women only; men can also develop breast cancer.

28. How many members of your immediate family (mother, father, sisters, brothers) have been diagnosed with breast cancer?

29. How many family members on your mother's side of the family have had a diagnosis of breast cancer? (Do not include your mother if she has been diagnosed with breast cancer.)

30. Of the individuals diagnosed with breast cancer on your mother's side, who would you consider yourself to be the closest with?

31. How many family members on your father's side of the family have had a diagnosis of breast cancer? (Do not include your father if he has been diagnosed with breast cancer.)

32. Of the individuals diagnosed with breast cancer on your father's side, who would you consider yourself to be the closest with?

33. Has anyone in your family passed away from breast cancer or other cancers caused by breast cancer (metastasis)?

33a. How were you related to the individual(s) who passed away from breast cancer?

34. Were you a caregiver to any of your family members diagnosed with breast cancer?

- a) Yes
- b) No
- c) I helped out sometimes.

35. If you were a caregiver to family members diagnosed with breast cancer, how old were you when they were diagnosed with breast cancer?

SECTION H: SOCIAL HISTORY WITH BREAST CANCER:

37. Have you had a personal experience of a close friend being diagnosed with Breast Cancer?

38. Were you a caregiver for your friend diagnosed with breast cancer?

- a) Yes
- b) No
- c) I helped out occasionally.

39. If you have had a close friend diagnosed with breast cancer, please explain how your friend's diagnosis of breast cancer affected your decision making process.

40. If you were a caregiver to your friend(s), how old were you when they were diagnosed with breast cancer?

SECTION I: PERSONAL SURGICAL HISTORY: Section I contains questions about how you gathered information regarding preventive surgery, who you discussed your medical management options with, and your personal breast health history.

41. How did you hear about the option to have surgery? (Check all that apply.)

- a) Family Physician or Internist
- b) OB/Gyn
- c) Breast Surgeon
- d) Oncologist
- e) Genetic Counselor
- f) Family Member
- g) Friend
- h) Support Group
- i) Facebook or other online resource
- j) Angelina Jolie's experience
- k) Other (please specify)

42. What healthcare providers did you talk with about having preventive breast surgery? (Check all that apply.)

- a) Family Doctor
- b) Gynecologist
- c) Breast Surgeon
- d) Oncologist
- e) Genetic Counselor
- f) Plastic Surgeon
- g) Other (please specify)

43. Who did you talk with the most about your medical management?

- a) Spouse/Partner
- b) Family Physician
- c) OB/Gyn
- d) Breast Surgeon

- e) Oncologist
- f) Genetic Counselor
- g) Mother
- h) Sister
- i) Friend
- j) Another woman who went through a similar experience
- k) Other (please specify)

44. What were the three most important factors influencing your decision to have surgery?

45. Please share any additional comments about the important factors influencing your decision that you would like us to share with other patients who are considering prophylactic bilateral mastectomies.

46. I believe my surgery has completely eliminated my risk of developing breast cancer.

- a) Strongly disagree
- b) Disagree
- c) Agree
- d) Strongly Agree

47. I felt I had adequate information about the risks and benefits of preventive breast surgery to make my decision

- a) Strongly disagree
- b) Disagree
- c) Agree
- d) Strongly Agree

48. After my preventive breast surgery, I believe my risk of developing Breast Cancer is:

- a) 0%-11%
- b) 12%-25%
- c) 26%-50%
- d) 51%-75%
- e) 76%-90%
- f) 91%-100%

49. Please select other medical management options you were considering as strongly as preventive breast surgery.

- a) Mammograms (annual)
- b) MRI scans (annual)
- c) Clinical exams (done by OB/Gyn or Family Doctor)
- d) Self-Exams
- e) Risk-reducing medication (Tamoxifen or other)
- f) Removal of ovaries to reduce my risk of breast cancer
- g) Removal of ovaries and Fallopian tubes to reduce my risk of breast cancer

- h) Reconstructive surgery after preventive breast surgery
- i) Other (please specify)

50. Please check the box if you have had any of the following breast exams, procedures, or results.

- a) Lump or other finding on self-breast exam that made you call your doctor
- b) Clinical breast exam that required a mammogram
- c) Call-back for repeat mammogram
- d) Mammogram result that concerned your doctor
- e) Ultrasound after mammogram
- f) Breast biopsy (usually done with ultrasound)
- g) Positive breast MRI
- h) Breast implants BEFORE your decision about preventive breast surgery
- i) Breast reduction BEFORE your decision about preventive breast surgery

51. Please explain why you chose to undergo preventive breast surgery rather than have increased surveillance.