Comparing Family Sharing Behaviors in BRCA Carriers with PALB2 Carriers

Joy E. Kechik
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Comparing Family Sharing Behaviors in BRCA Carriers with PALB2 Carriers

by

Joy E. Kechik

A thesis submitted in partial fulfillment of the requirements for the degree of Master of Science in Public Health with a concentration in Genetic Counseling Department of Global and Planetary Health College of Public Health University of South Florida

Major Professor: Deborah Cragun, M.S., Ph.D. Tuya Pal, M.D. Marleah Dean Kruzel, Ph.D.

Date of Approval: March 18, 2019

Keywords: hereditary breast cancer, family communication, familial disclosure, genetic counseling

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Dedication

I would like to take this opportunity to thank the individuals who have supported me throughout the thesis process. To my fiancé, Adam, I truly could not have completed this project without your love, support, and encouragement over the past two years. To my parents, thank you for your unconditional support and willingness to help me plan a wedding in the midst of completing this thesis. Finally, to my classmates, Deanna, Lindsey, and Réka, thank you for all of your support, understanding, and encouragement. It was not easy at times, but there is no other group I would rather have at my side during this whirlwind experience.
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Abstract

Identifying individuals with hereditary cancer predisposition can improve health outcomes for patients and their family members through early cancer detection and prevention strategies. Prior research about family sharing of genetic test results among those with hereditary breast cancer has overwhelmingly been limited to the *BRCA1* and *BRCA2* genes. The present study sought to compare family sharing behaviors in women with pathogenic *BRCA* variants to women with pathogenic variants in the more recently identified and characterized *PALB2* gene. A total of 18 *BRCA* carriers and 13 *PALB2* carriers were interviewed about family sharing practices using a semi-structured guide based on the Integrated Behavioral Model. Barriers and facilitators to family sharing were similar for both *BRCA* and *PALB2* carriers, with logistical difficulties and emotional struggles related to anticipated negative reactions from relatives being the most salient barriers. The most important facilitators were: attitude that sharing enables health protection, provider recommendation, strong family relationships, confidence in sharing basic information, knowledge of what to share and how to share, and belief that sharing is highly important. Given similar attitudes, norms, and control beliefs related to family sharing, similar, but tailored interventions may be effective at increasing family disclosures among both groups. Such interventions should involve a discussion of patients’ attitudes towards sharing with healthcare providers to strengthen motivations and address barriers and provision of informational resources to increase confidence and knowledge. Family sharing resources should clearly specify which relatives need to be informed, why sharing is important, and how at-risk relatives may benefit.
Introduction

Breast cancer is the second most prevalent cancer in women with over 260,000 estimated new cases in the United States in 2018 (Surveillance, Epidemiology, and End Results Program, National Cancer Institute, 2018). Roughly 5-10% of female breast cancer patients have an inherited predisposition, most commonly due to BRCA1 or BRCA2 (American Cancer Society, 2017). The lifetime risk to develop breast cancer for women with pathogenic BRCA variants is 60-70% (Kuchenbaecker et al., 2017), compared to a 12.4% lifetime risk for average women (Surveillance, Epidemiology, and End Results Program, National Cancer Institute, 2018). In addition to BRCA1 and BRCA2, there are other highly penetrant genes that also confer increased risks for breast cancer. The gene PALB2 (partner and localizer of BRCA2) is estimated to account for 1-3% of hereditary breast cancers (Antoniou et al., 2014; Casadei et al., 2011; Couch et al., 2015; Cybulski et al., 2015; Thompson et al., 2016), with lifetime breast cancer risks ranging 33-58%, modified by family history of breast cancer (Antoniou et al., 2014; Couch et al., 2017).

Next-generation sequencing and use of multi-gene panels has reduced costs and increased efficiency of clinical genetic testing for hereditary breast cancer, thereby increasing identification of high-risk individuals – particularly those with pathogenic variants in breast cancer genes besides BRCA (Antoniou et al., 2014; Ricker et al., 2018). Identifying hereditary predisposition to breast cancer is an important step for enabling early detection, prevention, and risk management strategies and for guiding cancer treatment (Black, McClellan, Avard, & Knoppers, 2013; Katapodi, Northouse, Milliron, Liu, & Merajver, 2013; Ricker et al., 2018). Given the higher risk and earlier onset of disease, women with pathogenic variants in BRCA1, BRCA2,
PALB2, and other breast cancer genes are eligible for increased surveillance and other preventive measures starting at younger ages (Couch et al., 2017; Ricker et al., 2018). According to national guidelines, high-risk screening and/or consideration of risk-reducing options may begin as early as age 25 (sometimes younger) for BRCA carriers and age 30 (sometimes younger) for PALB2 carriers (National Comprehensive Cancer Network, 2018). High-risk screening can diagnose breast cancer at an earlier, more treatable stage, thus prolonging survival, whereas prophylactic mastectomy and salpingo-oophorectomy (when appropriate) can effectively reduce breast cancer risks (Domchek et al., 2010; Lauby-Secretan et al., 2015; Nelson et al., 2014). For mutation carriers who have already developed cancer, the benefit of identifying hereditary predisposition is focused on preventing a second primary cancer and informing treatment decisions (Ricker et al., 2018).

Identification of women with a cancer-predisposing variant confers health implications for their family members, as well (McCarthy & Armstrong, 2014; Nelson et al., 2014). Relatives of a BRCA or PALB2 carrier may have up to a 50% chance to harbor the same gene mutation and associated cancer risks (Antoniou et al., 2014; Cheung, Olson, Yu, Han, & Beattie, 2010). For this reason, women found to carry a pathogenic variant in one of these cancer-predisposing genes are encouraged to notify their relatives of the result and the availability of genetic testing and risk management (Dancyger, Smith, Jacobs, Wallace, & Michie, 2010). Relatives who choose to pursue genetic testing for themselves may be able to clarify their own cancer risks and determine optimal risk management strategies (Daly, Montgomery, Bingler, & Ruth, 2016; Fehniger, Lin, Beattie, Joseph, & Kaplan, 2013; Katapodi et al., 2017). If relatives are determined to have inherited cancer predisposition, they can then execute health protective behaviors that may reduce breast cancer morbidity and mortality.
Family sharing (also called family communication or intra-familial communication or disclosure in the literature) is a complex yet critical step within the cancer control continuum (Daly et al., 2016; Derbez, 2018; Division of Cancer Control and Population Sciences, National Cancer Institute, 2017; Peters et al., 2011). Currently, it is the responsibility of the individual tested to notify their relatives of any potential risks (Daly, 2015; Kardash, Fehniger, Creasman, Cheung, & Beattie, 2012). Studies have shown that rates of family sharing among BRCA carriers are relatively high, ranging from approximately 73% to 96% (Daly et al., 2016; Fehniger et al., 2013; Finlay et al., 2008; Hughes et al., 2002; Ricker et al., 2018). The most important reasons cited for sharing genetic results include making relatives aware of risk, suggesting they undergo genetic testing, and fulfilling a perceived responsibility to inform (Hughes et al., 2002; McGivern et al., 2004). Seeking emotional support and advice about management decisions have also been reported as motivators for sharing (Hamilton, Bowers, & Williams, 2005; Hughes et al., 2002). Despite the importance of sharing, rates of disclosure previously reported indicate that some at-risk relatives remain uninformed and unaware of potential cancer risks (Black et al., 2013; Daly et al., 2016). Furthermore, testing rates among family members remain low, ranging from roughly 15-50%, even when results are shared (Blandy, Chabal, Stoppa-Lyonnet, & Julian-Reynier, 2003; Lieberman et al., 2018).

The relationship between family sharing and various individual, familial, and sociocultural factors has been documented regarding disclosure of BRCA results (Nycum, Avard, & Knoppers, 2009). Personal feelings and perceptions of risk, relatives’ attitudes, knowledge, and finding “the right time” may impact the decision to share genetic results with family members (Blandy et al., 2003; Cheung et al., 2010; Daly et al., 2016; Dean & Rauscher, 2018; Derbez, 2018; Hamilton et al., 2005; Lafrenière, Bouchard, Godard, Simard, & Dorval, 2013;
Lapointe et al., 2013; Nycum et al., 2009). Prior studies have shown that first-degree family members are most likely to receive genetic risk information, suggesting that more distant family members who may also benefit are often excluded (Blandy et al., 2003; Elrick et al., 2017; Kardashian et al., 2012; Katapodi et al., 2013; MacDonald et al., 2007; McGivern et al., 2004). Family communication styles, traditions, religious beliefs, and norms have also been shown to influence the decision to share (Etchegary, Potter, Perrier, & Wilson, 2013; Katapodi et al., 2013; Koehly et al., 2009; Lafrenière et al., 2013; Peters et al., 2011). Minimal contact and/or emotionally distant relationships with relatives have also been implicated as barriers to disclosure of results (Daly et al., 2016; Elrick et al., 2017; Etchegary et al., 2013; Hughes et al., 2002; Kardashian et al., 2012; MacDonald et al., 2007; McGivern et al., 2004). Those with a strong family history of BRCA-related cancers are more likely to share compared to families with a less striking history of cancer (Dean & Rauscher, 2018; Kardashian et al., 2012). Women are more likely to communicate genetic information than men, and information is more often communicated to female relatives and younger generations (Cheung et al., 2010; Elrick et al., 2017; Etchegary et al., 2013; Finlay et al., 2008; Kardashian et al., 2012; MacDonald et al., 2007; Patenaude et al., 2006; Vadaparampil, Malo, de la Cruz, & Christie, 2012).

Previous research about family sharing related to hereditary breast cancer has focused almost exclusively on disclosure of BRCA1 and BRCA2 results (D’ Audiffret Van Haecke & de Montgolfier, 2016; Ricker et al., 2018). Ricker et al. (2018) is the only published study to explore family sharing among those with a gene mutation in other hereditary breast cancer genes (though not exclusively hereditary breast cancer genes); however, they did not assess for barriers and facilitators related to family sharing. Rather, a survey containing a combination of “yes/no” and open-ended questions was utilized to measure rates of communication of genetic test results.
and family follow-up and a single Likert scale question was used to measure attitude about the benefit of family sharing. *PALB2* carriers were included in the Ricker et al. (2018) study, though the number of *PALB2* participants was not specified.

Given the limited data on family sharing and hereditary breast cancer beyond *BRCA*, the present study sought to further our understanding of family sharing among women with pathogenic *PALB2* variants compared to women with pathogenic *BRCA* variants. It is unclear whether different gene carriers experience unique barriers and facilitators with family sharing and require different approaches to improve rates and quality of family sharing. Eliciting and comparing disclosure behaviors in these two groups is therefore a critical first step in identifying potentially modifiable factors that may serve as effective targets for interventions for *PALB2* carriers, as well as assessing the applicability of *BRCA*–related interventions (Cheung et al., 2010; Elrick et al., 2017). Addressing the most salient barriers and facilitators will be necessary to increase rates of family sharing, enable more at-risk individuals to be proactive in cancer risk management, and ensure that all have the opportunity to benefit from genetic testing. The current study utilized qualitative methods to capture more in-depth and comprehensive data underlying the motivators and barriers to family sharing, as this was not captured as part of the survey conducted by Ricker et al. (2018) (Bradley, Curry, & Devers, 2007).
Methods

Participants

Participants were recruited by a research team at Vanderbilt University from a group consented to the GeneCARE study. GeneCARE participants were English-speaking females, 18 years or older, and living in the United States with a documented pathogenic/likely pathogenic variant or variant of uncertain significance (VUS) in a gene associated with hereditary cancer. The current study was limited to women enrolled in GeneCARE with a BRCA1, BRCA2, or PALB2 pathogenic/likely pathogenic variant who indicated willingness to take part in an in-depth telephone interview. All PALB2 carriers and a subset of BRCA carriers who met this criteria were purposively selected for interviews in order to maximize diversity in family sharing and medical management practices. We aimed to conduct 10 interviews for each carrier group according to recommendations for achieving theoretical saturation, or the point at which no new themes are emerging. Prior studies have found that small sample sizes ranging from 10 to 12 participants can be sufficient for collecting most of the salient ideas and reaching saturation (Guest, Bunce, & Johnson, 2006; Saunders et al., 2018; Weller et al., 2018). The study was approved by Institutional Review Boards at Vanderbilt University and the University of South Florida.

Instrumentation

The study team developed a semi-structured interview guide (Appendix A) based on the Integrated Behavioral Model (IBM) (Figure 1), which proposes that five main constructs directly influence behavior and intention is the most important determinant (Montano & Kasprzyk, 1992). The IBM framework is an extension of the Theory of Planned Behavior (TPB), which has
been utilized in previous studies to understand family communication of genetic risk (Montgomery et al., 2013; Wiens, Wilson, Honeywell, & Etchegary, 2013). Both theories state that behavioral intention is the product of attitudinal, normative, and control beliefs; however, the IBM incorporates knowledge and skills, salience, and environmental constraints as behavioral modifiers. The IBM was chosen as the framework for this study as these additional constructs may play an important role in the family sharing process.

**Figure 1.** The Integrated Behavioral Model.

An essential step in applying the IBM is conducting interviews with the population of interest to elicit information about their beliefs (Montano & Kasprzyk, 1992). The interview guide was designed to elicit seven IBM-related domains we thought would reveal underlying differences and similarities in the family sharing behaviors of **BRCA** carriers and **PALB2** carriers (Table 1). These domains included: 1) attitudes, 2) normative influences, 3) perceived control
and environmental constraints, 4) self-efficacy, 5) knowledge and skills, 6) salience, and 7) intention or decision.

**Table 1. Targeted IBM-Related Constructs**

<table>
<thead>
<tr>
<th>Construct</th>
<th>Definition</th>
<th>Example Questions to Elicit Construct</th>
</tr>
</thead>
</table>
| Attitudes                        | Emotional response to the idea of sharing, beliefs about the anticipated or actual outcomes of sharing | • How did you feel about the idea of sharing your genetic test result with family members?  
• Were there any benefits of sharing?  
• Were there any negative effects of sharing? |
| Normative Influences             | Social pressures to share or not share results with family                | • Did a healthcare provider encourage you to share your result with family?  
• Who would support you sharing your result?  
• Did some relatives not want to hear about your result? |
| Perceived Control & Environmental Constraints | How easy or difficult it is to share test results with family and environmental conditions that might prevent sharing | • What made it easy for you to share your genetic test result?  
• What made it hard for you to share your genetic test result? |
| Self-Efficacy                    | Confidence and effectiveness in sharing                                   | • On a scale of 1-10, how confident were you sharing your result with family?  
• Which family members did you feel most confident sharing with?  
• What types of resources do you think could be helpful? |
| Knowledge & Skills               | Possessing the knowledge and skills to communicate results to family and convey the value of genetic testing | • Describe for me how you shared your result with family?  
• What information did you tell your family about your result? |
Table 1 (continued)

<table>
<thead>
<tr>
<th>Construct</th>
<th>Definition</th>
<th>Example Questions to Elicit Construct</th>
</tr>
</thead>
<tbody>
<tr>
<td>Salience</td>
<td>Beliefs about how important it is to share results</td>
<td>• When someone tests positive for a cancer gene mutation, on a scale of 1-10 how important is sharing that result with family?</td>
</tr>
</tbody>
</table>
| Intention or Decision| Indication of readiness or decision to share or not share results with family | • Which family members did you talk to about your genetic test result?  
• Do you intend to share your result with this family member in the future?  
• Did you tell any non-relatives about your result? |

 Procedures

Baseline demographic and clinical data were available on all participants through completion of the GeneCARE survey. Participants provided informed consent to the interview at the time of enrollment in the survey portion of GeneCARE and consent was confirmed verbally prior to audio-recording each respective interview. The semi-structured interview guide was used to assess their initial reaction to their genetic test result, information about medical management decisions (results of which are not within the scope of the current study), and what they perceived to be facilitators and barriers to sharing their result with various family members. The discussion focused on the at-risk side of the family, if that could be determined based on the family history. Otherwise, both sides were considered at-risk and data for both sides of the family were obtained. Each interview lasted approximately 30-60 minutes.

Interviews were conducted by 2 investigators trained in human subjects’ protection. Audio recordings were transcribed verbatim and memos were created by the interviewer after each interview to document important themes, memorable quotes, or striking observations.
Memos and transcripts of the first several interviews were analyzed to assess the need for additional questions, revisions to the guide, and additional codes.

Data Analysis

A codebook was developed by three of the researchers based on the interview guide and a single coder analyzed each transcript using RQDA qualitative data analysis software. Data analysis utilized a thematic approach, with steps related to data immersion, generating codes, and identifying, reviewing, and defining themes (Nowell, Norris, White, & Moules, 2017). Prior to coding, transcripts from the first several interviews were reviewed in-depth in order to become familiar with the data (Bradley et al., 2007). Transcripts were then coded line-by-line using theory driven a priori codes and inductive, data-driven thematic codes developed through an iterative process (Tracy, 2012; Tracy & Hinrichs, 2017).

The following codes were added during initial analysis of the interview transcripts: 

\textit{ATT\_fam positive; ATT\_fam negative, ATT\_fam other; KNOW\_information; and DEC\_not shared non-family}. Furthermore, the following codes were anticipated but subsequently deleted from the codebook after initial analysis: \textit{ATT\_ignore; KNOW\_risks to family; and KNOW\_risks and benefits}. All transcripts were then re-analyzed to ensure that a priori and data-driven codes were utilized appropriately. Interviews were classified using a total of 31 codes within seven theoretical constructs. The final codebook can be found in Appendix B.

Through coding, sorting, and review of the data, the most salient themes regarding family sharing were identified and interpreted in the context of the IBM framework. Particular attention was paid to items mentioned in one carrier group, but not the other. Illustrative quotes were selected to accompany each theme related to factors that facilitate or inhibit sharing of genetic
test results with family members. Demographic and clinical characteristics of the study participants were summarized using descriptive statistics.
Results

Participant Characteristics

A total of 168 BRCA carriers and 22 PALB2 carriers who completed the GeneCARE survey expressed interest in participating in the in-depth interviews. Eighteen BRCA carriers and thirteen PALB2 carriers were ultimately interviewed for this study. Additional participants were recruited beyond the original target sample size to ensure that at least ten interviews for each group were completed. These additional participants were recruited using the same methods discussed previously.

Participant demographic and clinical characteristics are shown in Table 2. BRCA carriers and PALB2 carriers had a mean age of 53.67 and 55.62 years, respectively. The majority of carriers in both groups self-identified as Non-Hispanic White. Most of the BRCA participants and all of the PALB2 participants reported themselves as college graduates. Approximately 72% of the BRCA carriers and 85% of the PALB2 carriers reported having private insurance. 13 BRCA carriers and nearly all PALB2 carriers had a personal history of cancer. While almost all PALB2 participants were the first member of their family to be genetically tested, the majority of BRCA carriers were uncertain if other relatives had tested first.

Themes Related to Family Sharing

In-depth interviews with BRCA carriers and PALB2 carriers revealed twelve major themes related to family sharing. Themes were organized into seven IBM-related theoretical constructs and are described according to construct in detail below. The following themes emerged within the ‘attitudes’ construct: health protection, anticipated negative emotions from
Table 2. Participant Demographics

<table>
<thead>
<tr>
<th></th>
<th>BRCA1/2 n = 18</th>
<th>PALB2 n = 13</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years Mean (Range)</td>
<td>53.67 (30 – 71)</td>
<td>55.62 (39 – 69)</td>
</tr>
<tr>
<td>Race/Ethnicity, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NHW</td>
<td>8 (44.4)</td>
<td>12 (92.3)</td>
</tr>
<tr>
<td>Black</td>
<td>4 (22.2)</td>
<td>1 (7.7)</td>
</tr>
<tr>
<td>Hispanic</td>
<td>6 (33.3)</td>
<td>0</td>
</tr>
<tr>
<td>Highest Completed Education, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤ 12th grade/GED</td>
<td>2 (11.1)</td>
<td>0</td>
</tr>
<tr>
<td>Vocational School/Some College</td>
<td>3 (16.7)</td>
<td>0</td>
</tr>
<tr>
<td>College Graduate</td>
<td>13 (72.2)</td>
<td>13 (100)</td>
</tr>
<tr>
<td>Other</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Insurance, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Private</td>
<td>13 (72.2)</td>
<td>11 (84.6)</td>
</tr>
<tr>
<td>Military/Veteran</td>
<td>2 (11.1)</td>
<td>1 (7.7)</td>
</tr>
<tr>
<td>Medicare</td>
<td>2 (11.1)</td>
<td>1 (7.7)</td>
</tr>
<tr>
<td>Medicaid</td>
<td>1 (5.6)</td>
<td>0</td>
</tr>
<tr>
<td>Personal History of Cancer, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>5 (27.8)</td>
<td>1 (7.7)</td>
</tr>
<tr>
<td>Breast</td>
<td>12 (66.7)</td>
<td>12 (92.3)</td>
</tr>
<tr>
<td>Breast and Ovarian</td>
<td>1 (5.6)</td>
<td>0</td>
</tr>
<tr>
<td>First Family Member Tested, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>1 (5.6)</td>
<td>1 (7.7)</td>
</tr>
<tr>
<td>Yes</td>
<td>4 (22.2)</td>
<td>12 (92.3)</td>
</tr>
<tr>
<td>Unknown</td>
<td>13 (72.2)</td>
<td>0</td>
</tr>
</tbody>
</table>

family members, and family reactions range from supportive to not supportive. The ‘perceived norms’ construct revealed normative influence from providers and family. Themes within the ‘perceived control and environmental constraints’ construct included strong family relationships, lack of contact and communication barriers, and impact of public knowledge and awareness of BRCA. Themes related to the ‘self-efficacy’ construct were confidence in sharing basics and informational resources boost self-efficacy. In terms of knowledge and skills, participants knew what to share and how to share. The ‘salience’ construct revealed the theme that sharing is important when risks are high, actionable and the relative is prepared. Finally, the ‘intention and decision’ construct showed high rates of sharing and intention to share.
Attitudes

Participant attitudes towards family sharing were divided into positive and negative attitudes. Both \textit{BRCA} and \textit{PALB2} carriers felt strongly that sharing their positive genetic test result would protect the health of their family members via follow-up genetic testing and/or increased cancer surveillance. Both groups frequently quoted the saying “knowledge is power” to succinctly describe why they felt positively about sharing. It was apparent that participants viewed sharing as a way to protect not only their living relatives, but also future generations.

\textbf{Table 3. Theme: Health Protection}

<table>
<thead>
<tr>
<th>Brief description</th>
<th>Illustrative quotes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Participants felt that sharing would allow relatives to be proactive in their own cancer risk management</td>
<td>“I think information is power, because once you have the information you can make better decisions. So I wanted them to have the necessary information for them to make decisions for themselves and their families.” (\textit{PALB2} carrier, age 63)</td>
</tr>
<tr>
<td></td>
<td>“I wanted to make sure if anybody out there has the gene, they needed to know about it so they could take whatever precautions were necessary so that they didn’t get breast cancer. I felt sort of empowered to get this information to them and make sure that they protected their health.” (\textit{PALB2} carrier, age 60)</td>
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<td></td>
<td>“I feel like that if you know your chances are better to get cancer, then you can do something about it before it happens.” (\textit{BRCA} carrier, age 69)</td>
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<td>“I wanted them to know so that they have the option of testing. That they would know it is available and make the decision… if you just don’t know that you have it, things can happen in the future, and if you do know then you can do stuff to prevent it.” (\textit{BRCA} carrier, age 71)</td>
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Women in both the \textit{BRCA} and \textit{PALB2} groups were concerned about how their family members might respond when learning about their positive genetic test result. The two groups
acknowledged that sharing may cause family members to experience a variety of negative emotions, including fear, worry, distress, and guilt for having passed down the mutation. A few participants were uncertain if their family members would have access to knowledgeable providers or recommended follow-up care after learning about their risk. Interestingly, only a single participant in each carrier group was hesitant to share their result with family due to concerns for privacy.

Table 4. Theme: Anticipated Negative Emotions from Family Members

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<tr>
<th>Brief description</th>
<th>Illustrative quotes</th>
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<tbody>
<tr>
<td>Participants felt that sharing their result could cause family members to feel scared, worried, and overwhelmed</td>
<td>“I was concerned because, like I said, I know it’s going to be stressful for them. They’re going to have to make their decision as to what they want to do with this information.” (PALB2 carrier, age 57)</td>
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<td>“I was sad, and then obviously people I told are gonna be sad…it’s a scary thing to learn, to know you could carry this gene.” (PALB2 carrier, age 49)</td>
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<td>“Fearful of putting an element of fear about that person’s health in their head. You know, possibly making them fearful of dying from ovarian cancer more so than breast cancer.” (BRCA carrier, age 52)</td>
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<td></td>
<td>“If my mother were still alive I may have been more hesitant for her to know because I would think, knowing her personality, she would feel guilty for having passed this along to us.” (BRCA carrier, age 59)</td>
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</table>

Despite participants’ concerns about negative emotional reactions, participants found that many family members reacted positively when learning about the positive genetic test result. Relatives were reported as being supportive, grateful, receptive, and not surprised by the information. Nonetheless, some family members did not show interest in learning about the test result and, as anticipated by participants, certain relatives became worried or scared. Several
family members reportedly ignored the information. Multiple *BRCA* carriers stated their family members were in denial, confused, or did not fully understand the result.

**Table 5. Theme: Family Reactions Range from Supportive to Not Supportive**

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<th>Brief description</th>
<th>Illustrative quotes</th>
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<tr>
<td>The reactions of family members ranged from positive/supportive to negative/not supportive</td>
<td>“I had one uncle who said, “You are very brave.” I didn’t get any negative. I only got positive, “Yeah thanks for letting us know” kind of thing.” (<em>PALB2</em> carrier, age 63). “I don’t think they were that surprised, because like I said, the breast cancer has been running in the family, and my sister had the ovarian cancer, so it wasn’t like totally out of the blue.” (<em>PALB2</em> carrier, age 57) “One of my sisters told me to mind my own business. Her health is her prerogative, and I should mind my own business. That was very unexpected.” (<em>PALB2</em> carrier, age 59) “Two out of three [siblings] were glad. One wasn’t…she was more like, “I wish I didn’t know.” (<em>PALB2</em> carrier, age 60) “I think my sisters were more supportive, because they have daughters too, and the breast cancer runs in women more so my sisters were probably the most supportive and the most interested in it.” (<em>BRCA</em> carrier, age 64) “A lot of them were happy that they were given the information, but it was one of those things, “thanks for giving me the information” but they didn’t really follow up on it.” (<em>BRCA</em> carrier, age 49) “Well, with my sister she just said…” I’m not doing this, I’m not dealing with this, if I’m meant to die from breast cancer or ovarian cancer then I will.” (<em>BRCA</em> carrier, age 52) “His attitude is kinda like, it doesn’t affect me right now, I don’t really care. But he’s also, he’s very much one to be in denial and that’s his personality. He’d rather not know the “I don’t have to think about it” kind of thing.” (<em>BRCA</em> carrier, age 59)</td>
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Normative Influence

Healthcare providers had the most significant normative influence for participants with regards to family sharing. The majority of these providers were genetic counselors, but other genetics professionals (e.g. geneticist, genetics nurse), oncologists, and surgeons were also mentioned as encouraging family sharing as part of recommended follow-up. All but a few participants recalled a specific conversation when their provider encouraged them to share their result with close and extended relatives on the at-risk side of the family, if that could be determined. In terms of familial influence, most participants expected their family members would want to know about their positive genetic test result. However, participants in both groups expressed concerns that certain family members would not be receptive to this information or they would not understand the significance. Only one PALB2 participant (age 65) mentioned her religious upbringing and “Catholic guilt” as a source of pressure to share.

Table 6. Theme: Normative Influence from Providers and Family

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<tr>
<th>Brief description</th>
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<tr>
<td>Most participants were encouraged by a healthcare provider to share their positive genetic test result with at-risk relatives.</td>
<td>[Were there any recommendations the genetic counselor gave you that you hadn’t done at this point?] “Yeah, there was nothing else for me to do outside of just talk with your family, just to let them know, to share what my diagnosis [test result] was.” (PALB2 carrier, age 49)</td>
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<td>[What were some of the things that your breast surgeon told you to do because you have this BRCA result?] “First thing was to get the other breast removed…second thing was to get my ovaries removed…and then tell like my family, so that they can also get tested.” (BRCA carrier, age 60)</td>
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<td>Many participants felt their families would be supportive of sharing, though some expected their families would not be supportive.</td>
<td>“I pretty much knew my cousins that I shared it with, that they would appreciate it, so I didn’t feel like I was telling them anything they would not appreciate knowing.” (PALB2 carrier, age 69)</td>
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<td>Brief description</td>
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<tr>
<td>Many participants felt their families would be supportive of sharing, though some</td>
<td>“I knew they were gonna be supportive. I knew nobody was gonna question my decision. I didn’t feel anybody was gonna not believe me. They’re a very rational, reasonable, supportive bunch of people. So I just knew I could share it with them.” (<em>PALB2</em> carrier, age 60)</td>
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<td>expected their families would not be supportive.</td>
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<td>“I’m afraid though, because I feel like they might be the type to say, “What is that? Mind your own business.”” (<em>PALB2</em> carrier, age 59)</td>
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<td>“[My sister-in-law] had asked me to do genetic testing. They were waiting for results to see if my brother should get tested.” (<em>BRCA</em> carrier, age 64)</td>
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<td>“I would like to sit down with her [niece] and talk to her about it but other family members say, “No, don’t.” There’s a divide in the family…because she’s getting married next year and it might make her feel less of…that she might feel like damage goods.” (<em>BRCA</em> carrier, 59)</td>
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<td>“I didn’t expect much a reaction from them. They didn’t have much of a reaction…when it comes to cancer we all kind of share anyway.” (<em>BRCA</em> carrier, age 38)</td>
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*Perceived Control and Environmental Constraints*

When asked specifically about what made it easier to share genetic results with family, participants in both the *BRCA* and *PALB2* groups endorsed strong familial relationships. Open family communication styles and frequent contact made the task of sharing less daunting and more convenient. Additionally, it was helpful if relatives had prior knowledge of a participant’s personal cancer diagnosis and/or the family history of cancer. Help from other family members by communicating to other relatives, sharing contact information, or even initiating the sharing process made it easier for many participants.
Table 7. Theme: Strong Family Relationships

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<th>Brief description</th>
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<tr>
<td>Participants with strong family ties found it easier to share their result with at-risk relatives</td>
<td>“I was very open with my family about everything, my treatments and everything, so they were already aware of what I was going through and what I was having done. So, I guess that made it easier because it wasn’t like I was calling them out of the blue and telling them that I have this. They already knew.” (PALB2 carrier, age 51)</td>
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<td>“We’re a pretty close bunch, so I had full access to them… there’s definitely open lines of communication.” (BRCA carrier, age 49)</td>
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<td>“My dad has some nieces that we don’t talk to directly but we know how to get ahold of them indirectly through mutual family members and friends.” (BRCA carrier, age 52)</td>
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</table>

Conversely, participants in both groups felt that distant relationships with relatives and difficulty contacting family members made it harder to share. A BRCA carrier mentioned it was difficult for her to share with her family members in a different country due to lack of resources in their native language. Only a single participant in the PALB2 group cited relatives’ education level as a source of hardship in sharing.

Table 8. Theme: Lack of Contact and Communication Barriers

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<th>Brief description</th>
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<tr>
<td>Participants had to overcome estranged relationships and communication barriers to share with certain at-risk relatives.</td>
<td>“Everything was difficult. I had to find them… because you lose touch with people.” (PALB2 carrier, age 65)</td>
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<td>“I don’t communicate with them very often, so it’s not like it was purposely done. It just didn’t happen.” (PALB2 carrier, age 48)</td>
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<td>“I’m just not that close with them… we just don’t see each other that often and we don’t really share information that personal.” (BRCA carrier, age 30)</td>
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<td>“The problem is that a lot of the information is English and not all of them speak English, so that made it a little bit harder.” (BRCA carrier, age 46)</td>
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Of note, publicity and awareness of the *BRCA* genes was mentioned by participants in each group as impacting family sharing, but for different reasons. One *BRCA* carrier felt the publicity from celebrity disclosures, specifically Angelina Jolie, made sharing with family easier. Similarly, a *PALB2* participant (age 48) used the *BRCA* gene as an example when describing *PALB2* to family members. She stated, “I told them the type of genetic mutation it was and what I understood, [and] how it related to *BRCA.*” A different *PALB2* carrier (age 59) felt that awareness of *BRCA* actually made non-relatives that she shared with less sympathetic: “They’re like, “It’s not *BRCA.*” I mean they believe me, but it’s just not known. They probably just think, “Oh, you don’t have the real gene, cause you don’t have *BRCA.*” Fortunately, this participant said that her family members felt differently about *PALB2,* and “figured whatever it was, it was bad and important.”

**Table 9.** Theme: Impact of Public Knowledge and Awareness of *BRCA*

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<tr>
<th>Brief description</th>
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<tr>
<td>Participants felt that awareness of <em>BRCA</em> among the public impacted the sharing process.</td>
<td>“Having it be <em>PALB2</em> makes me feel like lesser than, like it’s not a real risk…Even in my own mind, it’s not <em>BRCA,</em> it’s a smaller risk, even though I have evidence that it’s very active in my family. Then how I feel others just discount me so much, because it’s not <em>BRCA.</em> Even people who know, but not my family, but people who know. Even doctors, I feel like just really discount the risk, cause it’s not <em>BRCA.</em>” (<em>PALB2</em> carrier, age 59)</td>
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“Because that [Angelina Jolie *BRCA* disclosure] was in the news, they understood, there was no explaining or anything. They got it.” (*BRCA* carrier, age 60)

**Self-Efficacy**

Overall, participants in the *BRCA* group and the *PALB2* group felt confident in their ability to effectively share with family members. Participants felt most confident communicating
with their close female relatives, such as sisters, mothers, and cousins. Some participants felt less confident because they “didn’t know everything” or were unable to answer all of their family members’ questions. On the other hand, one BRCA carrier (age 37) with a background in genetics felt especially confident talking to her family about her result, saying, “I think just having a background in genetics made it easier for me, both in that I had a better understanding of it and also because people trusted me more.”

Table 10. Theme: Confident in Sharing Basics

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<tr>
<th>Brief description</th>
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| Participants felt very confident sharing their test result with at-risk relatives, but less confident answering subsequent questions. | “I wasn’t worried about it, I wasn’t insecure about it, I wasn’t not confident that I understood it. I felt I knew enough to share it intelligently.” (PALB2 carrier, age 54)  
“‘There’s a lot of questions that I didn’t know the answer to and even my doctor didn’t. Because again, five years ago they really didn’t have a lot of information about the PALB2 gene.” (PALB2 carrier, age 49)  
“I felt confident about it because I had it done after my cancer diagnosis and my sister had already had it done. I kind of had an inkling that I would be positive with that, so we talked about it among ourselves, my sisters and I.” (BRCA carrier, age 60)  
“Well I don’t have all the answers, you know. There’s a lot of questions… there’s a lot of things I didn’t know.” (BRCA carrier, age 64) |

Confidence was bolstered by written information about their gene mutation and the associated risks from a provider or even the genetic testing laboratory. While the majority of women in both groups were offered resources to aid disclosures, roughly 1/3 of participants did not report receiving materials. Several PALB2 carriers found that the family letter from their provider (most often a genetic counselor) made sharing accurate information much easier. One
**BRCA** participant watched videos prior to genetic counseling, and thought that alternatives to printed handouts could be beneficial for sharing, too. When asked what other resources may be helpful with family sharing, both the **BRCA** and **PALB2** groups suggested a handout containing information on why sharing is important and a short script of what to say and additional online resources for gathering more information. When asked if having a healthcare provider disclose results would help participants feel more efficacious about sharing, there were mixed feelings in both groups for fear of bombarding relatives without notice or the disclosure being too impersonal. Though, one **BRCA** carrier (age 52) mentioned her sister would “take it more seriously” coming from a healthcare provider.

**Table 11.** Theme: Informational Resources Boost Self-Efficacy

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<th>Brief description</th>
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<tr>
<td>Participants feel more confident when given resources about their gene mutation and the associated risks to use for sharing.</td>
<td>“I would say perhaps when you receive the information from the geneticist, maybe a little script from the geneticist on, “Here’s why it’s important to share with your family members. Here’s some talking points. Here’s some nice ways to deliver it.” Maybe that would’ve been a nice thing to have in your back pocket when you’re going out to share this information.” (PALB2 carrier, age 60)</td>
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<td>“Well, I think having that letter, and even recently my younger brother said, “I need to get that stuff done.” So I scanned my letter and resent it to him. I think having that written information is very, very helpful.” (PALB2 carrier, age 63)</td>
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<td>“With the letter, more confident, because here’s what I got, here’s the results, here’s a copy. It helped versus just telling someone because I think people believe, whether it’s right or wrong, if they have something in print and shows research and shows the lab and shows whatever, I think they’re more likely to believe it.” (PALB2 carrier, age 60)</td>
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<td>“Maybe some more links of like websites to visit, that would have given me more information to look on my own. You know, like reputable ones.” (PALB2 carrier, age 39)</td>
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</table>
Participants were asked to offer advice or suggestions to other patients considering sharing a test result with family. Both groups recommended sharing simple information with at-risk relatives. Collectively, they would encourage others to research and prepare before sharing and send resources to family members afterwards. Both groups stressed focusing on facts rather than emotions, and if conflicted about sharing, considering which family members need to know and why.

**Knowledge and Skills**

Participants were well-informed about which family members were at-risk and utilized a variety of methods to disclose their positive result. Many participants shared in-person, either in an individual or group setting, or via phone, text, email, or social media. Both groups frequently
enlisted the help of other family members to ensure that all at-risk relatives were contacted.

Many participants provided or at least offered their family members resources to supplement the initial conversation. Interestingly, more PALB2 carriers compared to BRCA carriers utilized a family sharing letter from their provider to disseminate the information. The information communicated to relatives was fairly consistent between the two groups, focusing on the cancer gene involved, associated risks, heritability, and availability of genetic testing and follow-up care options. PALB2 carriers consistently mentioned breast and pancreatic cancer risks when recalling their conversations with family members, however there was variability in reporting ovarian cancer risk.

Table 12. Theme: Knowing What to Share and How to Share

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<tr>
<th>Brief description</th>
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<tr>
<td>Participants demonstrated strong knowledge of methods for sharing and relevant information to provide when sharing their test result.</td>
<td>“So what I decided to do on my own was make a list of paternal cousins and send out letter letting them know what had happened with our family, and then sent them a little information on PALB2 – not a lot to overwhelm.” (PALB2 carrier, age 65)</td>
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<td>“I doubt I told any in person, initially…I probably sent out a group text or something.” (PALB2 carrier, age 39)</td>
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<td>“I said, “I had the genetic testing. I do carry the PALB2 gene. After mom was tested, it confirmed which side of the family the PALB2 gene comes from, what the result is, it is higher probability of beast and pancreatic cancer and just you should be aware of that. You should get tested if you’re interested.” And that’s how I put it.” (PALB2 carrier, age 60)</td>
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<td>“I mean because some people have said they sent letters to their family members and stuff like that. I mean I would have never dreamed of doing that. You know, I called everybody.” (BRCA carrier, age 64)</td>
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Table 12 (continued)

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<tr>
<td>Participants demonstrated strong knowledge of methods for sharing and relevant information to provide when sharing their test result.</td>
<td>“We had a big, not a big, but my dad, his 80th birthday was a few weeks ago, and yeah, everybody now in my family, which most of them I hadn’t seen for several years, but they all know now.” (BRCA carrier, age 52)</td>
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<td>“I talked to them about it and told them basically passed on all of the information and the chances that they might have it… I told them about their increased chances of the certain types of cancer. I told them I had the documentation if they’d like to see it.” (BRCA carrier, age 59)</td>
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Salience

Both the BRCA and PALB2 groups felt that family sharing was highly important because it enabled family members to take appropriate actions. Many admitted they would want this information from another family member who tested positive. Multiple participants in each group cautioned that there are circumstances in which sharing may be less important, for example if the recipient is not prepared to learn of the risk or is expected to react poorly based on their personality or past behaviors. Nonetheless, participants who anticipated or experienced a negative reaction from a family member stated they would still share despite the perceived or actual negative outcome. One PALB2 participant (age 69) shared, “I felt like if I had angered her or made her upset, then she wasn’t thinking in her best interest, and that wasn’t going to stop me [from sharing].”

Surprisingly, participants in each group explained that the importance of sharing with family was somewhat dependent on our understanding of the gene’s penetrance and associated risks. Specifically for PALB2, one participant explained that as the gene became more understood and the management recommendations changed, sharing became more important. Participants in both groups admitted having perceptions that female relatives were at greater risk
given the associated cancer risks compared to male relatives, but acknowledged that both women and men could be carriers of the familial variant.

**Table 13.** Theme: Important When Risks Are High, Actionable and Relative is Prepared

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<td>Participants felt that sharing a positive genetic test result is important in most situations.</td>
<td>“It’s important. People need to know what they’re up against. If you don’t know what your history is, your medical history is, how can you counteract it? How can you start making changes as early as you possibly can to thwart off any possible disease inflicting you.” (<em>PALB2</em> carrier, age 49)</td>
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<td>“I felt like it was information that I didn’t have before that was very important to share.” (<em>PALB2</em> carrier, age 69)</td>
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<td>“I think it’s very important because then I at least have the knowledge and then I can do with it what I want… I might have been really upset if a couple of my cousins hadn’t shared this and then all of a sudden I got breast cancer.” (<em>BRCA</em> carrier, age 64)</td>
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<td>“I think it’s probably most important if it affects their health perspective, but if it’s just mostly about you sharing information about your own health, I don’t think it’s important. I mean, if we’re talking about you find out that you have a mutation that they might have too, then I guess I’d say it’s more [important].” (<em>BRCA</em> carrier, age 30)</td>
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<tr>
<td>Participants felt that sharing a positive genetic test result is less important if family members cannot handle knowing.</td>
<td>“You have to know the people that you’re going to be telling and come up with an idea of, “Should I do this or not?”… You have to weigh the pluses and the minuses of telling them or not telling them.” (<em>PALB2</em> carrier, age 57)</td>
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<td>“It’s important to share it…it’s important to share it with the ones you want to share it with, if there was a reason why. Let’s say it was not going to be a good idea to tell someone because of their particular state of mind or health or something, then of course it’s not going to be necessary.” (<em>PALB2</em> carrier, age 48)</td>
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<tr>
<td>Participants felt that sharing a positive genetic test result is less important if family members cannot handle knowing.</td>
<td>“It depends on how close you are with them and just how much information they really need to know. Like I said, some people can’t handle it for the fact that they may not understand everything that you are talking about.” <em>(BRCA carrier, age 60)</em></td>
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<tr>
<td>Participants felt that sharing a positive genetic test result is more important when there are high risks and relatives can take action, especially females.</td>
<td>[On a scale of 1 to 10, how important is sharing your result with family?] “When I first got diagnosed and they said, “Oh we don’t know much about <em>PALB2</em>,” I would have said maybe like a 3 or 4. Now that I think the standard of care is if you have the <em>PALB2</em> you do get a mastectomy right away and you’re put on high alert, that’s a lot different than what we talked about in 2015.” <em>(PALB2 carrier, age 54)</em></td>
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<td>“I think maybe if they would have been female, I don’t know why, but I would have been more praying to maybe tell them, because of the breast and ovarian aspect.” <em>(PALB2 carrier, age 57)</em></td>
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<td></td>
<td>“I think it’s mostly just how it affects their health, and I guess how severe your mutation is, whether it’s something that carries a higher risk of having a disease or if it’s like, “No, you’re definitely gonna get it.” <em>(BRCA carrier, age 30)</em></td>
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<td>“In my mind, she’s the only one [at risk], it’s not true that it only affects her but it affects her more because she’s female.” <em>(BRCA carrier, age 55)</em></td>
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**Intention and Decision**

Participants reported sharing their result among various first-, second-, and third-degree relatives on the at-risk side of their family (if known), otherwise both sides of their family. Immediate family members, including children, siblings, and parents, were consistently informed, whereas nieces, nephews, aunts, uncles, and cousins were not always contacted. For both the *BRCA* and *PALB2* groups, family members that were not directly contacted by the participant were often informed by a different family member. Young children were usually not
informed of the positive genetic test result, though participants expressed intention to share with them in the future. Participants did not want to burden their children with this information and felt it would be better to wait until the information could be fully understood and used for medical decision-making.

Overall, participants were very satisfied with their decision to share their result with family members. Several participants expressed frustration, though, due to lack of follow-up among their family members. While reflecting on her decision to share, one BRCA carrier (age 52) felt “completely satisfied with [my decision], completely unsatisfied with their reactions. All of them.” Participants in both groups said that financial issues, competing life demands, perceived lack of relevance, and preference towards not knowing their carrier status were frequent barriers that family members faced related to genetic testing. Some participants expressed that sharing may need to be an on-going conversation to ensure appropriate family follow-up.

Results were frequently shared with non-family members, such as friends, support groups, co-workers, and spouses. Similar to their attitudes with family members, participants reported sharing with non-relatives to increase awareness of genetic testing and the importance of screenings, like mammograms, provide life updates, and receive support. Many participants were prompted to share their result with non-relatives when the topic came up in conversation. A PALB2 carrier (age 51) said, “I didn’t bring it up unless it was something that somebody asked me about or whatever. But I’m not the kind of person to hide things, so if somebody asked me something I’d tell them.” When asked about disclosing to co-workers, a few participants preferred to keep their private and professional lives separate, thus chose not to share in work settings.
Table 14. Theme: High Rates of Sharing and Intention to Share

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<tr>
<th>Brief description</th>
<th>Illustrative quotes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Participants reported sharing (directly or indirectly) or intending to share with</td>
<td>“I knew that my mom had talked to her brother about it and then he talked to his</td>
</tr>
<tr>
<td>the majority of their at-risk relatives.</td>
<td>sons. So that took care of that family. My mom had another sister that she wasn’t</td>
</tr>
<tr>
<td></td>
<td>really in touch with, but I think her brother ended up talking to the sister. I</td>
</tr>
<tr>
<td></td>
<td>didn’t really feel the need to share the news with anyone.” (BRCA carrier, age 30)</td>
</tr>
<tr>
<td></td>
<td>“I think that when he’s a little bit older I’m going to suggest that, you remember</td>
</tr>
<tr>
<td></td>
<td>how I had cancer, and that you might wanna ask your doctor about getting tested for</td>
</tr>
<tr>
<td></td>
<td>this just to see if you have it.” (BRCA carrier, age 52)</td>
</tr>
<tr>
<td></td>
<td>“I would say 18, but I would probably push it out. So maybe out of college or</td>
</tr>
<tr>
<td></td>
<td>something when he’s starting to actually get a life and get things settled for</td>
</tr>
<tr>
<td></td>
<td>himself.” (PALB2 carrier, age 39)</td>
</tr>
<tr>
<td>Participants reported sharing with non-family members, such as friends, coworkers,</td>
<td>“I’ve told most of my friends about it. and because I think it’s very important</td>
</tr>
<tr>
<td>and support groups.</td>
<td>for people to know even if they’re not facing it, that maybe they know somebody</td>
</tr>
<tr>
<td></td>
<td>else who should be tested or whatever and every time I hear about somebody whose</td>
</tr>
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<td></td>
<td>parent had pancreatic cancer or whose had ovarian cancer, my first question is</td>
</tr>
<tr>
<td></td>
<td>have they ever been tested? Have you ever been genetically tested?” (BRCA carrier,</td>
</tr>
<tr>
<td></td>
<td>age 59)</td>
</tr>
<tr>
<td></td>
<td>“They’re friends, people who I care about and who care about me and wanted to</td>
</tr>
<tr>
<td></td>
<td>know what was happening with my diagnosis and all the things that went along with</td>
</tr>
<tr>
<td></td>
<td>it like this…people wanted to be informed and involved and so I informed them</td>
</tr>
<tr>
<td></td>
<td>and I involved them” (PALB2 carrier, age 48)</td>
</tr>
</tbody>
</table>

Barriers and Facilitators to Family Sharing

The major themes identified through in-depth interviewing with BRCA and PALB2 carriers served as barriers and facilitators to family sharing. Facilitators, or factors that promoted family sharing, included the following themes: health protection; normative influence from providers; strong family relationships; and high confidence, knowledge, and salience. Barriers, or factors that inhibited family sharing, included the themes anticipated negative emotions from
family members and lack of contact and communication barriers. The remaining themes were endorsed as both promoting and inhibiting sharing, thus could not be discretely assigned as a facilitator or barrier to sharing.
**Discussion**

Our findings suggest that women with a pathogenic *BRCA* variant or *PALB2* variant experience similar barriers and facilitators when disclosing a positive genetic test result to at-risk relatives and may benefit from similar interventions to improve rates and quality of family sharing. To our knowledge, this is among the first studies to qualitatively examine barriers and facilitators outside the realm of *BRCA*-related test results, thus adding to the literature on family sharing in other hereditary breast cancer genes. According to the Integrated Behavioral Model (IBM), participants' attitudes, normative influences, and personal control beliefs served as barriers and facilitators that influenced their motivation to share and, in combination with other factors, their ultimate decision to share. These findings applied to the IBM framework are shown in Figure 2. It seems that facilitating factors outweighed barriers to sharing, which enabled the high rates of disclosures reported by this sample.

**Figure 2.** Family Sharing for *BRCA* and *PALB2* Carriers Using IBM Framework.
**Theme: Health Protection**

Participants in both the *BRCA* and *PALB2* carrier groups reported similar facilitators to family sharing, most importantly the attitude that disclosing to at-risk relatives enables health protective behaviors. This theme is consistent with previous studies that have found the most salient motivators for sharing were to make relatives aware of possible risks and enable appropriate follow-up care (Hughes et al., 2002; McGivern et al., 2004). A more recent study by Ricker et al. (2018) similarly found that both high- and moderate-penetration gene carriers agreed that family sharing is important for facilitating early detection and prevention strategies among at-risk relatives. Although previously reported in the literature, sharing for the purpose of receiving emotional support and advice was not a primary motivator among this sample (Hamilton et al., 2005; Hughes et al., 2002). Many participants already felt supported and informed, so they were not motivated to share for these reasons.

**Theme: Anticipated Negative Emotions from Family Members**

Women with *BRCA* variants or *PALB2* variants had similar concerns about family sharing, particularly related to how family members would respond. Although this did not keep participants in this study from sharing, the majority of women in both groups felt that disclosing their positive genetic result might cause certain family members to feel fear, worry, distress, and even guilt. Other studies have similarly found that individuals are less likely to share if they anticipate family members reacting poorly (Derbez, 2018; Forrest K et al., 2003; Hamilton et al., 2005; Lafrenière et al., 2013). It appears that this barrier can be overcome, as observed in this sample, when individuals are sufficiently motivated by other factors, such perceived benefits, importance, confidence, and ease of sharing.
Theme: Family Reactions Range from Supportive to Not Supportive

Family reactions have been reported as ranging from interest to disinterest (Gaff, Collins, Symes, & Halliday, 2005). For the most part, family members in this study were reported as responding positively during family sharing (e.g. supportive, grateful, receptive, not surprised) or indifferent to the news. Individuals in the position to disclose a positive genetic test result to family may find relief in knowing that family members are often receptive during family sharing, even if they do not act upon the information provided; however, individuals should be prepared for any relatives that may react negatively.

Theme: Normative Influence from Providers and Family

Encouragement from healthcare providers to share genetic test results was the most consistent source of normative influence among both BRCA and PALB2 carriers, as expected support from family members was variable. As discussed in Black et al. (2013), healthcare professionals have an important role in initiating the family sharing process and identifying all at-risk relatives. Providers are especially important for helping patients understand the significance of sharing with their more extended relatives. The pre-test counseling session has been viewed as an advantageous opportunity to introduce the idea of family sharing, though ongoing support after the pre-test meeting is important for patient follow-through (D’ Audiffret Van Haecke & de Montgolfier, 2016). Although a few participants could not recall a specific conversation, they all reported that their provider(s) presumably encouraged them to notify family.

Theme: Strong Family Relationships

Women in both carrier groups felt that strong relationships with their families made it easier to share their positive genetic test result. Participants who communicated with relatives
frequently and openly found it easier to disclose this information, even more so if the family members had known about the participant’s cancer diagnosis and/or the family history. Family communication styles, norms, and awareness have been shown to influence willingness to share (Dean & Rauscher, 2018; Etchegary et al., 2013; Kardashian et al., 2012; Katapodi et al., 2013; Koehly et al., 2009; Lafrenière et al., 2013; Peters et al., 2011). Strong family relationships were also exhibited via relatives’ willingness to help with the disclosure process. The significance of involving other family members in the sharing process has been described (Koehly et al., 2009).

**Theme: Lack of Contact and Communication Barriers**

*BRCA* and *PALB2* participants both cited distant relationships and logistical struggles as factors that made sharing their positive test result with at-risk relatives more difficult. Minimal contact due to emotionally distant relationships with relatives has been reported as a barrier to family sharing frequently in the literature (Daly et al., 2016; Elrick et al., 2017; Etchegary et al., 2013; Hughes et al., 2002; Kardashian et al., 2012; MacDonald et al., 2007; McGivern et al., 2004). While many participants were able to overcome logistical hurdles, like trouble obtaining contact information or actually making contact, some *BRCA* and *PALB2* carriers did not and ended up not disclosing to all at-risk relatives. As reported in other studies, these communication barriers frequently inhibit family sharing, even if non-communication is unintentional (Nycum et al., 2009).

**Theme: Impact of Public Knowledge and Awareness of BRCA**

Participants in both carrier groups mentioned the publicity of the *BRCA* genes as impacting the family sharing process. On one end, family members’ prior knowledge and awareness of *BRCA* made disclosing a *BRCA* or even a *PALB2* result somewhat easier since the concept was familiar. Celebrity *BRCA* disclosures, such as Angelina Jolie, and the influx of
direct-to-consumer genetic tests have been shown to increase awareness and even uptake of genetic testing (Roberts & Dusetzina, 2017). However, one PALB2 carrier was frustrated that PALB2 was viewed by others as a “less serious” hereditary cancer gene compared to BRCA. This participant’s experience is alarming, especially the misconceptions from healthcare providers, given that PALB2, like BRCA, is considered a highly penetrant cancer gene.

On-going educational efforts are needed to raise awareness about hereditary cancer beyond BRCA among providers and the public so that lack of understanding does not inhibit family sharing and medical management (Dean & Rauscher, 2018).

*Theme: Confident in Sharing Basics*

BRCA and PALB2 participants both reported high confidence in their ability to share their positive genetic test result with at-risk relatives, which is likely due in part to this sample’s high educational background. These women were most confident disclosing to their close, female relatives, which is consistent with previous reports that information is more often communicated to female relatives (Cheung et al., 2010; Elrick et al., 2017; Etchegary et al., 2013; Kardashian et al., 2012; MacDonald et al., 2007; Patenaude et al., 2006; Vadaparampil et al., 2012). Difficulty or uncertainty when responding to relatives’ questions diminished participants’ perceived ability to share effectively. This finding suggests that highly educated BRCA and PALB2 carriers feel confident disclosing basic information about their result to relatives, but may benefit from having resources and contact information for genetics professionals on-hand when sharing. Individuals need to feel prepared in order for familial disclosures to occur and those that have more knowledge may feel more comfortable (Cheung et al., 2010; Dean & Rauscher, 2018).
Theme: Informational Resources Boost Self-efficacy

Most participants were at least provided some written information about their specific gene and the associated cancer risks from their provider (frequently a genetic counselor), but not all received resources related to or to assist with the family sharing process. Several women in the PALB2 carrier group found that the family sharing letter from their provider was especially helpful in disseminating information to at-risk relatives. The use of family sharing letters as a patient resource has become standard practice when heritable genetic risks are identified (Dheensa, Lucassen, & Fenwick, 2018). Providers did not consistently offer participants in either group family sharing letters, so it is difficult to determine whether or not the utility of the letter was specific to the PALB2 group. It is possible that PALB2 carriers found the family sharing letter more helpful given that there is less information and awareness regarding the PALB2 gene compared to BRCA1 and BRCA2.

BRCA and PALB2 carriers suggested that a handout explaining the significance of family sharing, tips for how to share, and even a short script of what to say would be helpful when disclosing to relatives. Kardashian et al. (2012) designed an educational sharing risk information tool (ShaRIT), consisting of genetic information along with family resources (including a letter to family members, FAQ sheet, contact information for providers, and support websites and brochures) that was well-received by participants. A similar web-based educational aid developed by Katapodi et al. (2018), called the Family Gene Toolkit, was well-received during focus groups. Based on participants’ responses, interventions like these could be effective at increasing confidence with sharing and the likelihood of disclosures. None of these included a script of what to say to relatives, so that may be a valuable addition. An example family sharing script can be found in Appendix C.
**Theme: Knowing What to Share and How to Share**

The participants in both the BRCA and PALB2 carrier groups demonstrated a clear understanding of which family members were ‘at-risk,’ what risk information was important to share, and how they might go about sharing, though this is not always the case (Blandy et al., 2003; Daly et al., 2016). This finding is likely related to higher education levels among our sample and consequently greater understanding of relevant information to share. Conversations with family members focused on the cancer gene involved, associated cancer risks, heritability, and availability of genetic testing and risk management. The associated cancer risks reported by the PALB2 carriers varied slightly in terms of ovarian cancer, likely due to changes in the scientific community’s understanding of PALB2-associated risks over time (Metcalf, Akbari, Narod, & Lerner-Ellis, 2017). This highlights the importance of on-going communication with patients or finding ways for patients to receive updated information related to their gene mutation.

**Theme: Important When Risks Are High, Actionable and Relative is Prepared**

The belief that family sharing is highly important was a facilitator for both BRCA and PALB2 carriers. Multiple participants in each group felt that family sharing was less important in certain situations, for instance if they expected that family members would react poorly to the news. This observation relates back to anticipated negative emotional reactions from relatives and concerns that certain family members may not be prepared to learn about possible risks. The Disclosure Decision-Making Model explores how individuals assess recipients when making disclosures, and in the context of BRCA has demonstrated an association between perceived readiness of relatives and likelihood of family sharing (Dean & Rauscher, 2018; Greene, 2009). Participants who experienced a negative reaction from a relative after sharing said they would
still have shared despite the outcome, which suggests that participants feel sharing is more important than the perceived duty to protect relatives from emotionally troublesome information.

The importance of sharing was also modified by the gene penetrance, associated risks, and availability of follow-up care. Participants expressed that sharing was more important when the cancer risks were high and more certain, and if relative’s had the ability to consider risk-management strategies. Uncertainty regarding VUS test results has been shown to negatively impact family sharing due to the complexity of the result and lower perceived utility of this information for relatives (Hughes et al., 2002; Patenaude et al., 2006; Vadaparampil et al., 2012). Participants in this study were all gene positive, but may similarly see genetic test results as less relevant to family members when there is limited or evolving knowledge of gene penetrance, cancer risks, and recommended follow-up care. In some cases, this led participants to feel sharing was more important for at-risk female relatives rather than male relatives, given the breast and ovarian (when applicable) cancer risks. Participants admitted feeling that sharing was less important for older relatives, given the lower likelihood of pursuing genetic testing or follow-up care. These gender and age tendencies with sharing have been reported in the literature before (Dean & Rauscher, 2018; Finlay et al., 2008; Patenaude et al., 2006).

**Theme: High Rates of Family Sharing and Intention to Share**

Consistent with the literature on BRCA carriers, this sample of women with BRCA variants and even women with PALB2 variants showed high rates of family sharing, frequently disclosing their result to immediate family members and variably notifying more extended relatives (Blandy et al., 2003; Daly et al., 2016; Elrick et al., 2017; Fehniger et al., 2013; Finlay et al., 2008; Hughes et al., 2002; Kardashian et al., 2012; Katapodi et al., 2013; MacDonald et al., 2007; McGivern et al., 2004; Ricker et al., 2018). Participants managed to inform the
majority of first-, second-, and third-degree relatives at least indirectly through other family members. Both groups were highly satisfied with their decision to share their positive genetic test result, but were less impressed with their family members’ follow-up. It has been well-documented that rates of genetic testing among at-risk relatives are low and interventions are urgently needed to improve family follow-up (Blandy et al., 2003; Katapodi et al., 2017; Lieberman et al., 2018). Fortunately, participants were not deterred from sharing due to low rates of genetic testing among family members.

Participants in both groups usually did not discuss their result with young children because they anticipated a lack of understanding and utility of the information. This finding is appropriate given that genetic testing for adult-onset hereditary cancer syndromes is not recommended for minors and medical management would likely not change until around age 25-30 (Caga-anan, Smith, Sharp, & Lantos, 2012; Kesserwan, Friedman Ross, Bradbury, & Nichols, 2016; National Comprehensive Cancer Network, 2018). These women intended to wait until their child reached a certain age, point of maturity, or readiness, which is a common approach taken by other women in this type of situation (Hamilton et al., 2005; Patenaude et al., 2006).

Study Limitations

There are several strengths of this study to acknowledge. To start, this study is one of the first to compare family sharing behaviors among BRCA and PALB2 carriers. Participants were required to provide documentation of a BRCA1, BRCA2, or PALB2 pathogenic variant, so we did not need to rely on a self-reported carrier status. Additionally, the sample was diverse with regard to gene status, which enabled greater variety and comparison of interview responses. Although participants were primarily white, highly educated, and privately insured, this sample was representative of the population traditionally accessing genetic services and, thus, most
likely to face the decision to share (Armstrong, Micco, Carney, Stopfer, & Putt, 2005; Cragun et al., 2017). Extra interviews for each carrier group were scheduled to ensure the target sample size would be reached, which ultimately allowed us to include a greater number of participants in this study. After coding the initial ten interviews for each carrier group and identifying themes, the additional eight BRCA and three PALB2 interviews were completed and analyzed to ensure that major barriers and facilitators related to family sharing had been captured.

Despite these strengths, this study does have several limitations. Participants were selected from a highly motivated population of women who are part of a cancer registry and willing to participate in research, which may have introduced sampling bias despite attempts to purposively select those who did not share with all relatives and those from underserved ethnic/racial groups. In terms of generalizability of these findings, it should be noted that perceived barriers and facilitators may differ among those who indicated willingness to participate and those who did not, especially given the high rates of sharing reported in this sample. Furthermore, there may be barriers and facilitators unique to younger generations, as well as minority populations and lower socioeconomic status groups with historically lower rates of family sharing, that could not be captured with this sample (Cheung et al., 2010; Etchegary et al., 2013; Fehniger et al., 2013).

The current study relied solely on self-reported family sharing behaviors, so true rates of sharing may differ from the self-reported rates. Because the outcome or quality of participants’ communication was beyond the scope of this study, we did not confirm family members’ reactions or what information they were told. Nevertheless, we were able to infer some participant misconceptions about PALB2-associated cancer risks that may have been communicated from the interviews. The time elapsed between genetic testing and disclosure was
not assessed, though this may be an important factor to consider in future studies related to family sharing.

**Practice Implications**

Current findings indicate that health care professionals play an important role in facilitating the family sharing process across both carrier groups (Black et al., 2013). Studies have found, though, that variability among providers and clinical sites makes it difficult to create a standardized protocol for addressing family sharing (D’ Audiffret Van Haecke & de Montgolfier, 2016). It has been suggested that more time should be devoted to this topic during the post-test counseling visit and even afterwards via follow-up correspondence (D’ Audiffret Van Haecke & de Montgolfier, 2016). During these conversations, it would be beneficial to clarify at-risk relatives and discuss patients’ beliefs about family sharing in order to identify motivations and address any barriers (Gallo, Angst, & Knafl, 2009). Based on the current findings, we would expect similar, but tailored interventions to be successful at improving rates of family sharing for both BRCA and PALB2 carriers.

Being well-supported and -informed throughout the family sharing process has been shown to positively impact the experience of disclosing genetic test results (Lafrenière et al., 2013). Providers should offer patients resources that explain why sharing is important and contain key talking points, tips for how to share, and contact information for genetics professionals to reduce uncertainty and build confidence (Mendes, Paneque, Sousa, Clarke, & Sequeiros, 2016). Family sharing letters and other types of educational aids are acceptable, effective reminders to share and even remind family members to follow-up (Mendes et al., 2016). Given PALB2 carriers’ high endorsement of family sharing letters, it may be particularly
helpful to offer these resources to carriers of less common gene mutations. Figure 3 depicts how these practice implications can be incorporated into the family sharing process.

Figure 3. Practice Implications for Providers Flowchart.

Research Recommendations

Additional research is needed regarding family sharing outside the setting of high-risk hereditary cancer syndromes, such as Hereditary Breast and Ovarian Cancer syndrome and Lynch syndrome, to include other highly and moderately penetrant cancer genes. Research efforts should further examine disclosure behaviors in understudied, minority groups who may experience unique barriers and facilitators that require tailored interventions. Future studies should assess the role of providers, the utility of resources, and patients’ efficacy in communicating genetic risk information to relatives in order to develop effective interventions to
improve rates and quality of family sharing, overcome age and gender discrepancies with sharing, and increase follow-up among at-risk relatives.
Conclusions

The Integrated Behavioral Model (IBM) provides a highly relevant framework for identifying issues related to family sharing of genetic risk information and developing appropriate and effective interventions. Current findings suggest that women with pathogenic \textit{BRCA} variants and women with pathogenic \textit{PALB2} variants experience similar attitudes, normative influences, and personal control beliefs when disclosing positive genetic test results to at-risk relatives, thus may benefit from similar, but tailored interventions to improve rates of sharing. Based on participant responses, future interventions should involve a discussion of patients’ beliefs about sharing with healthcare providers to strengthen motivations and address other barriers and provision of informational resources to increase confidence and knowledge. It is crucial that these family sharing resources clearly specify which relatives should be informed, why sharing is important, and how at-risk relatives may benefit.
References


Appendix A:

Interview Guide Questions by Integrated Behavioral Model Construct

Experiential attitude

- How did/do you feel about the idea of sharing your genetic test result with family members?
- What would be good about sharing this information?
- What would be bad about sharing this information?
- Did you struggle emotionally to tell them?

Instrumental attitude

- Were there any negative effects of sharing?
- Were there any benefits of sharing?
- Do you think there are benefits of sharing your result?
- What would be the negative effects of sharing your result?
- How likely do you think sharing your result would lead to these positive or negative outcomes?

Normative influence

- Please give me examples of how family members reacted when you told them your genetic test result.
- What did these individuals say to you after they heard your result?
- Who supported you sharing your result?
- Was anyone against you sharing your result?
- Did you fear their reaction?
- Do you feel they would be against you sharing?
- Who would support you sharing your result?
- Who might be against you sharing your result?
- Did some relatives not want to hear about your result?

Perceived control and environmental constraints

- What made it easy for you to share your genetic test result?
- Are you not close with any of your family members?
- Explain for me if you feel there is anything that could make it easier for you to share your genetic test result with family members.
- Were you not able to get a hold of certain relatives?
• Did you simply not have the time to share your result?
• Was anything going on in your life or your family members’ lives that influenced your decision?

Self-efficacy

• On a scale of 1-10, how confident were you in talking to your family members?
• Why not a ___ [lower value]?
• Which family members did you feel most confident sharing this information with?
• How certain are you that you can share your result with family members if you wanted?
• Which family members do you feel most confident sharing your result with?
• Would a brief family sharing letter provided to you be helpful in sharing this information?
• Would any other assistance by a professional be helpful?
• If available, would you prefer for a healthcare professional to share your genetic test result with family members, with your permission?
• Do you have any suggestions for how other patients can share their genetic test result with their family members?
• What type of resources do you think could be helpful?

Knowledge and skills to perform behavior

• Describe for me how and what information you gave these family members when letting them know about your genetic test result.
• What did you say when telling them your result/did you tell certain family members differently versus others?
• How did you inform them of your result?
• Were you not given enough information?
• Are you not sure how to talk to your family members?
• If you have not shared with family but plan to, what information would you share with them?
• How might you go about sharing your result?

Salience of behavior

• When someone tests positive for a gene mutation associated with hereditary cancer [or has a VUS], on a scale of 1-10 how important is sharing those genetic test results with family members?
• Please describe why you feel this way?
• What would make it a ___ [insert higher value]?
• Was it because you wanted them to consider having genetic testing themselves?
• Is it important for family members to have genetic testing? Why or why not?
• Were you not encouraged to share your result with family members?

Intention or decision to perform behavior
• Apart from healthcare professional(s), did you talk to anyone else about your genetic test result, meaning did you tell anyone else that you had genetic testing and/or tell them about your genetic test result?
• Did you tell friends, family members, coworkers, etc.?
• [If you told family members]: Which family members did you talk to about your genetic test result; for example, your mother, sister, or uncle?
• How satisfied are you with your decision to share your result?
• Do you intend to share your result with family members in the future? Why or why not?
## Appendix B:

### Final Codebook

<table>
<thead>
<tr>
<th>Description</th>
<th>Code</th>
<th>Code Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Attitudes</strong></td>
<td>ATT_negative</td>
<td>participant's negative attitude about sharing</td>
</tr>
<tr>
<td></td>
<td>ATT_positive</td>
<td>participant's positive attitude about sharing</td>
</tr>
<tr>
<td></td>
<td>ATT_mixed</td>
<td>participant's mixed positive and negative attitude about sharing</td>
</tr>
<tr>
<td></td>
<td>ATT_indifferent</td>
<td>participant's indifferent attitude about sharing</td>
</tr>
<tr>
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<td>ATT_expected</td>
<td>family member attitude was expected</td>
</tr>
<tr>
<td></td>
<td>ATT_not expected</td>
<td>family member attitude was not expected</td>
</tr>
<tr>
<td></td>
<td>ATT_fam positive</td>
<td>family reacted positively to sharing</td>
</tr>
<tr>
<td></td>
<td>ATT_fam negative</td>
<td>family reacted negatively to sharing</td>
</tr>
<tr>
<td></td>
<td>ATT_fam other</td>
<td>family reacted neither positively or negatively to sharing</td>
</tr>
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<td><strong>Normative Influence</strong></td>
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</tr>
<tr>
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<td>NORM_not supportive</td>
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<tr>
<td></td>
<td>NORM_mixed</td>
<td>mixed about sharing</td>
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<td><strong>Perceived Control/Environmental Constraints</strong></td>
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<tr>
<td></td>
<td>PC_difficult</td>
<td>things making it difficult to share</td>
</tr>
<tr>
<td>Description</td>
<td>Code</td>
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<td>-------------</td>
<td>---------------</td>
<td>-------------------------------------------------------</td>
</tr>
<tr>
<td>Self-Efficacy</td>
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<td>confident can share with family</td>
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<td></td>
<td>SE_mixed</td>
<td>confident can share with certain family members</td>
</tr>
<tr>
<td></td>
<td>SE_not confident</td>
<td>not confident can share with family</td>
</tr>
<tr>
<td></td>
<td>SE_resources</td>
<td>things that would help with family sharing</td>
</tr>
<tr>
<td></td>
<td>SE_advice</td>
<td>advice for others in family sharing</td>
</tr>
<tr>
<td>Knowledge/Skills</td>
<td>KNOW怎么办</td>
<td>knowledge of how to communicate risk information</td>
</tr>
<tr>
<td></td>
<td>KNOW_information</td>
<td>knowledge of information to communicate to others</td>
</tr>
<tr>
<td>Salience</td>
<td>SAL_high</td>
<td>it is important to share with family</td>
</tr>
<tr>
<td></td>
<td>SAL_low</td>
<td>it is not important to share with family</td>
</tr>
<tr>
<td></td>
<td>SAL_mixed</td>
<td>it may be important to share with some family members but not others</td>
</tr>
<tr>
<td>Decision/Intention</td>
<td>DEC_shared family</td>
<td>shared with family</td>
</tr>
<tr>
<td></td>
<td>DEC_not shared</td>
<td>have not shared with family</td>
</tr>
<tr>
<td></td>
<td>DEC_shared conditionally</td>
<td>shared with family under certain conditions/circumstances</td>
</tr>
<tr>
<td></td>
<td>DEC_intend to share</td>
<td>intend to share with family in the future</td>
</tr>
<tr>
<td></td>
<td>DEC_satisfaction</td>
<td>satisfaction regarding decision to share</td>
</tr>
<tr>
<td></td>
<td>DEC_shared non-family</td>
<td>shared with non-family members, such as friends or co-workers</td>
</tr>
<tr>
<td></td>
<td>DEC_not shared non-family</td>
<td>not shared with non-family members</td>
</tr>
</tbody>
</table>
Appendix C:

Family Sharing Sample Script

Hi [relative’s name]. Thank you for taking time to talk with me today. I have some news to share with you that is hard for me to say and might be hard for you to hear. You are someone that I love and care about, so I think this is important information for you to know. I did a blood test that found I have a change in my DNA that increases my chance to get certain cancers. This change is in the part of my DNA called [gene], which increases the chance for [associated cancer types] cancers. This result helps explain why I got my [cancer type] cancer. This change does not mean I will for sure get cancer/another cancer. But, now that I know I have a higher chance, I have decided to do more screenings/surgery to catch a future cancer early/reduce my chance of cancer as much as possible.

This DNA change is something that can run in families, meaning that you and other relatives might have it, too. Both guys and girls in the family could have it and have a higher chance for the cancers I mentioned. We think it’s coming from mom/dad’s side of the family, which could explain the cancers on that side. I know this might be scary to hear, but thankfully there is something you can do. You should talk to a genetic counselor about genetic testing. Genetic testing can tell if you have the same DNA change as me and if you need to worry about higher cancer risks. If you have the change, your doctors will follow you more closely. If you don’t have the change, then you won’t have to worry or do anything extra. I really hope you will consider genetic testing. I don’t want you to get cancer like I did, especially when there is
something we can do to stop it. Just know that I want to help you do whatever you can to protect your health.

I have some information for you that I got from my genetic counselor/provider. It has everything I just told you and some contact information for professionals if you have more questions. I know that was a lot to hear, but I thought it was important for you to know. What are you thinking?
Appendix D:

Informed Consent Form

Institutional Review Board
Informed Consent Document for Research

Principal Investigator: Tuya Pal, M.D.  Revision Date: 11/15/18
Study Title: GeneCARE: A Follow-Up Package for Gene-Based Care for Women At-Risk for Inherited Cancer
Institution/Hospital: Vanderbilt University Medical Center

This informed consent applies to adult women living in the United States who are at-risk for hereditary cancer with a documented pathogenic mutation or variant of uncertain significance (VUS) in a gene associated with hereditary cancer.

Name of participant: __________________________ Age: __________

The following is provided to you to tell you about this research study. Please read this form with care and ask any questions you may have about this study. Your questions will be answered. Also, you are given the opportunity to download a copy of this informed consent form for your records.

You do not have to be in this research study. You can stop being in this study at any time. If we learn something new that may affect the risks or benefits of this study, you will be told so that you can decide whether or not you still want to be in this study. If you are a Vanderbilt patient, your medical record may contain a note saying you are in a research study. Anyone you authorize to receive your medical record will also get this note.

1. What is the purpose of this study?

You are being asked to take part in this new research study (conducted through Vanderbilt University Medical Center and in partnership with collaborators from the University of South Florida) that is enrolling adult women who are at-risk for hereditary cancer and have a known pathogenic mutation or VUS in a gene associated with hereditary cancer. The purpose of this study is to better understand access to follow-up care recommended by a healthcare professional after genetic testing and how patients go about sharing their genetic test results with family members. About 500 people will take part in this study.

2. What will happen and how long will you be in the study?
If you agree to be in this study, we will ask you to take an online survey. This will take about 10-15 minutes of your time. At the end of the survey, we will ask if you would be willing to take part at a later time in an in-depth phone interview that will be recorded.

If you agree to take part in the phone interview and are selected for this second part of the study, we will schedule a later time and date for your interview. At that time, a member of the study team from Vanderbilt or the University of South Florida will call you and ask you more questions over the phone. This phone interview will be recorded and will take about 30-60 minutes of your time.

After the phone interview, the study team from Vanderbilt may contact you to ask you to contact up to five of your blood-related adult family members (18 years of age or older) to ask their permission to share their contact information with the study team so they may receive information about inherited cancer. You will need to contact these family members and ask for permission to share their contact information with the study team. Once we receive this information and permission to contact, we will mail or phone them to provide general information about hereditary cancer services and where they can get more information about inherited cancer. We will also provide them with contact information of the study team if they want more information.

3. Costs to you if you take part in this study:

There is no cost to you for taking part in this study.

4. Side effects and risks that you can expect if you take part in this study:

Questionnaire and Interview:
This study only involves a brief online survey (all participants), and a phone interview and follow-up contact (up to 100 selected participants), therefore the risk of injury or personal harm due to this study is very low. There is always the chance that some of your private information may be accidentally released. The study team will do everything possible to reduce these risks. All study staff have received required training on how to keep information private.

Family Contact Information:
If you are one of the 100 participants selected for the second part of this study, we will ask you to identify up to five blood-related adult family members and share their contact information with us after getting their permission. Strong steps will be taken to keep this information private, and it will not be used for any purpose outside of this study. You have the right to not provide information about your family for this research. We understand that family members may react differently towards sharing this type of information for the purposes of research.

5. Risks that are not known:
There may be risks that we do not know about at this time. If we find any other risks we will let participants know.

6. Payment in case you are injured because of this research study:

If it is determined by Vanderbilt and the Investigator that an injury occurred as a direct result of the tests or treatments that are done for research, then you and/or your insurance will not have to pay for the cost of immediate medical care provided at Vanderbilt to treat the injury. There are no plans for Vanderbilt to pay for any injury caused by the usual care you would normally receive for treating any illness or the costs of any additional care. There are no plans for Vanderbilt to give you money for the injury.

7. Good effects that might result from this study:

a) The benefits to science and humankind that might result from this study: This study may help to increase our overall knowledge of access to follow-up care recommended by healthcare professionals after genetic testing and how patients share genetic test results with family members. This knowledge can help to develop strategies to improve follow-up care and family sharing among those at risk for inherited cancer.

b) The benefits you might get from being in this study: None.

8. Other treatments you could get if you decide not to be in this study:

This is not a treatment study. You may decide not to be in the study and nothing about your healthcare will change.

9. Payments for your time spent taking part in this study:

If you enroll online and complete the online survey, you will receive a $10 gift card. If you are selected for and complete the in-depth phone interview, you will receive a $50 gift card to reimburse you for your time.

10. Reasons why the study doctor may take you out of this study:

You may be taken out of the study if you request it. If you are taken out of the study for any other reason, you will be told why.

11. What will happen if you decide to stop being in this study?

Being in this study is your choice. You can choose to stop being in this study at any time. Any routine care you receive will not change if you choose to participate or if you choose not to participate in this study. If we learn something new that may affect the risks or benefits of this study, you will be told so that you can decide whether or not you still want to be in this study. If you decide to stop being part of the study, you should contact
the study team. At that time, we will stop gathering information about you, however the data that is already part of the study will be kept.

12. Who to call for any questions or in case you are injured:

If you should have any questions about this research study or if you feel you have been hurt by being a part of this study, please feel free to contact Tuya Pal, M.D. C/O the GENECARE Study Team at [redacted].

For additional information about giving consent or your rights as a person in this study, to discuss problems, concerns, and questions, or to offer input, please feel free to call the Vanderbilt University Institutional Review Board Office at [redacted] or toll free at [redacted].

13. Confidentiality:

If you agree to take part in this study, all information collected by Vanderbilt University Medical Center and the University of South Florida during the study will be kept strictly confidential. In accordance with federal law, we will keep the study records private by storing them in a locked area or on a password-protected computer. Your identifying information, such as your name and contact details, will be kept separately in a secure location, so that only the study team can access it. When we use data collected in the study, the information that identifies you will not be used. Instead, we will give you a study identification number that no one else can use to identify you. Your name or other information that would allow someone outside the study to identify you will never be used in study publications or reports. Your study record will be kept separately from your regular medical record and insurers will not have access to your study records. If insurance companies, employers, or others obtain genetic information about you from this research, it has the potential to affect your insurability or employability. This is why we will do our best to ensure that privacy of all identifiable study records will be protected to the full extent provided by law.

Vanderbilt may share your information, without identifiers, to others or use it for other research projects not listed in this form. Vanderbilt, Dr. Pal, and her staff will comply with any and all laws regarding the privacy of such information. There are no plans to pay you for the use or transfer of this de-identified information.

Because this study is funded by the National Institutes of Health (NIH), it is conducted under a Certificate of Confidentiality. This Certificate keeps us from sharing your identifiable sensitive information (which is information gathered during the course of research that might identify you) gathered for research purposes unless you allow us to do so. It also keeps us from being forced to release your study information as part of a court, legislative, administrative or other proceeding.

There are times when the Certificate cannot be used. For example, we cannot refuse to give information to government agencies that oversee or fund research, such as the NIH.
Department of Health and Human Services (DHHS) or Food and Drug Administration (FDA). The Certificate also does not stop us from giving information to local government agencies, law enforcement personnel or others if we suspect you or someone else is in danger or if we are required to do so by law.

The Certificate does not keep you from giving out information about yourself and your treatment in this study. We will allow the release of some study information, such as lab test results, if you wish us to do so and you give us permission in writing. If you have any questions, please ask the study doctor or study staff.

14. Authorization to Use/Disclose Protected Health Information:

All efforts, within reason, will be made to keep your protected health information (PHI) private. PHI is your health information that is, or has been gathered or kept by Vanderbilt as a result of your healthcare. This includes data gathered for research studies by Vanderbilt and research collaborators at the University of South Florida that can be traced back to you. Using or sharing (“disclosure”) such data must follow federal privacy rules. By signing the consent for this study, you are agreeing (“authorization”) to the uses and likely sharing of your PHI. If you decide to be in this research study, you are also agreeing to let the study team use and share your PHI as described below.

As part of the study, Vanderbilt University Medical Center may share questionnaire data, the results of your study and/or non-study linked genetic results, as well as parts of your medical record, to the groups named below. These groups may include our research partners at the University of South Florida, the Federal Government Office for Human Research Protections and the Vanderbilt University Institutional Review Board. Federal privacy rules may not apply to these groups; they have their own rules and codes to assure that all efforts, within reason, will be made to keep your PHI private.

The study results will be kept in your research record for at least six years after the study is finished. At that time, the research data that has not been put in your medical record will be destroyed. Any research data that has been put into your medical record will be kept for an unknown length of time.

Unless told otherwise, your consent to use or share your PHI does not expire. If you change your mind, we ask that you contact the study team in writing and let them know that you withdraw your consent. The mailing address is:

GeneCARE Study Team 1500 21st Ave. So., Suite 2810 Vanderbilt University Medical Center Nashville, TN 37212

At that time, we will stop getting any more data about you. But, the health data we stored before you withdrew your consent may still be used for reporting and research quality.
If you decide not to take part in this research study, it will not affect your treatment, payment, or enrollment in any health plans or affect your ability to get benefits. You will be given the opportunity to download a copy of this informed consent form for your records.

STATEMENT BY PERSON AGREEING TO BE IN THIS STUDY
I have read this consent form and the research study has been explained to me. All my questions have been answered, and I freely and voluntarily choose to take part in this study.

_________________________  __________________________
Date  Signature of patient/volunteer

Consent obtained by:

_________________________  __________________________
Date  Signature

_________________________  __________________________
Printed Name and Title  Time
Appendix E:

University of South Florida IRB Approval Letter

11/26/2018

Deborah Cragun, PhD

RE:  Expedited Approval for Initial Review
IRB#: Pro00037381
Title: GeneCARE: A Follow-Up Package for Gene-Based Care for Women At Risk for Inherited Cancer

Study Approval Period: 11/24/2018 to 11/24/2019

Dear Dr. Cragun:

On 11/24/2018, the Institutional Review Board (IRB) reviewed and APPROVED the above application and all documents contained within, including those outlined below.

Approved Item(s):
Protocol Document(s):
USF proposal

It was the determination of the IRB that your study qualified for expedited review which includes activities that (1) present no more than minimal risk to human subjects, and (2) involve only procedures listed in one or more of the categories outlined below. The IRB may review research through the expedited review procedure authorized by 45CFR46.110 and 21 CFR 56.110. The research proposed in this study is categorized under the following expedited review category:

(6) Collection of data from voice, video, digital, or image recordings made for research purposes.

(7) Research on individual or group characteristics or behavior (including, but not limited to, research on perception, cognition, motivation, identity, language, communication, cultural beliefs or practices, and social behavior) or research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies.

Your study qualifies for a waiver of the requirements for the informed consent process as
outlined in the federal regulations at 45CFR46.116 (d) which states that an IRB may approve a consent procedure which does not include, or which alters, some or all of the elements of informed consent, or waive the requirements to obtain informed consent provided the IRB finds and documents that (1) the research involves no more than minimal risk to the subjects; (2) the waiver or alteration will not adversely affect the rights and welfare of the subjects; (3) the research could not practicably be carried out without the waiver or alteration; and (4) whenever appropriate, the subjects will be provided with additional pertinent information after participation.

Your study qualifies for a waiver of the requirement for signed authorization as outlined in the HIPAA Privacy Rule regulations at 45CFR164.512(i) which states that an IRB may approve a waiver or alteration of the authorization requirement provided that the following criteria are met (1) the PHI use or disclosure involves no more than a minimal risk to the privacy of individuals; (2) the research could not practicably be conducted without the requested waiver or alteration; and (3) the research could not practicably be conducted without access to and use of the PHI. A waiver of HIPAA Authorization is granted for this study. Pursuant to this waiver, the USF study team is allowed to obtain PHI of subjects who provide their signed HIPAA Authorization during the informed consent process conducted by the lead site, Vanderbilt University.

As the principal investigator of this study, it is your responsibility to conduct this study in accordance with IRB policies and procedures and as approved by the IRB. Any changes to the approved research must be submitted to the IRB for review and approval via an amendment. Additionally, all unanticipated problems must be reported to the USF IRB within five (5) business days.

We appreciate your dedication to the ethical conduct of human subject research at the University of South Florida and your continued commitment to human research protections. If you have any questions regarding this matter, please call [redacted].

Sincerely,

[Signature]

Melissa Sloan, PhD, Vice Chairperson
USF Institutional Review Board
Appendix F:

Vanderbilt University IRB Approval Letter

RE: IRB #180420 “GeneCARE”

Dear Tuya Pal:

A sub-committee of the Institutional Review Board reviewed the research application identified above. The sub-committee determined the study poses minimal risk to participants, and the application is approved under 45 CFR 46.1010 (F)(7). Approval is extended for the Protocol # dated March 7, 2018 and the Grant entitled GeneCARE: A Follow-Up Package for Gene-Based Care for Breast Cancer Survivors with Inherited Disease for Principal Investigator Tuya Pal.

The Consent Form(s) have been stamped with the approval and expiration date and this copy should be used when obtaining the participant’s signature. Federal regulations require that the original copy of the participant’s consent be maintained in the principal investigator’s files and that a copy be given to the subject at the time of consent. An additional record (i.e., case report form, medical record, database, etc.) of the consent process should also be maintained in a separate location for documentation purposes.

As the Principal Investigator, you are responsible for the accurate documentation, investigation and follow-up of all possible study-related adverse events and unanticipated problems involving risks to participants or others. The IRB Adverse Event/Unanticipated Problem reporting policy IILL is located on the IRB website at http://www.mc.vanderbilt.edu/irb.

If this trial requires registration as a clinical trial, accrual cannot begin until this study has been registered at clinicaltrials.gov and a National Clinical Trial Number (NCT) provided. Please provide the NCT# to the IRB as soon as it is obtained. If an approval is required from an additional source other than the Vanderbilt IRB, this must be obtained prior to study initiation. These approvals may include, but are not limited to CRC, SRC, IND, IDE.

Please note that approval is for a 12-month period. Any changes to the research study must be presented to the IRB for approval prior to implementation.


Sincerely,

Vanderbilt University
Human Research Protections Program – HRPP
Supporting the work of the IRB and Providing HRPP Oversight

1313 21st Ave., South, Suite 504
Nashville, TN 37232
www.vanderbilt.edu/irb
Appendix G:

Vanderbilt University Amendment Approval Letter

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<td>Principal Investigator</td>
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Date of IRB Approval: 9/10/2018

Institutional Review Board

Electronic Signature: Joern-hendrik.Wetlikamp@VUMC/Vanderbilt: (e0c468dd9c0f75d27e4aad1db416f1d)
Signed On: 09/10/2018 9:25:52 PM CDT
Amendment

Please indicate what is being changed with this amendment:

[X] Study Title/Grant Title
   | Increase in total subject numbers/acrual
   | Investigator's Brochure (IB) with NO change in safety data or the currently approved consent document(s)
   | Data and Safety Monitoring Report
   | Investigator's Brochure (IB) WITH changes in safety
[X] Consent Form changes
[X] Protocol changes
[X] Changes to recruitment materials
[X] Submission of new documents
   | Other
   | ADD a participating site to this study (for single IRB)

Please indicate the version date of the protocol:
2018-09-28

Please indicate the version date of the consent documents:
2018-09-28

Please provide the new title:
GeneCARE: A Follow-Up Package for Gene-Based Care for Women At Risk for Inherited Cancer

Please provide the rationale for the amendment/changes:
Expanding eligibility criteria to include English-speaking females with a confirmed pathogenic/likely pathogenic mutation or variant of uncertain significance (VUS) in an inherited cancer gene.

Increasing the sample size for in-depth telephone interviews from 50 to up to 100 women.

Updating the initial online survey to better reflect questions suitable for the expanded eligibility criteria.

Adjusting the in-depth interview guide to be more suitable for the expanded eligibility criteria.

Updating the initial email template to better reflect the expanded eligibility criteria

Updating the follow-up email template to reflect two versions: (1) One version for the initial 50 participants who will be selected for and complete the in-depth interview from the initial recruitment wave, (2) A new version for the remaining 50 participants who will be selected for and complete the in-depth interview from the expanded recruitment wave.

Date of IRB Approval: 9/10/2018

Institutional Review Board

Electronic Signature: Joern-Hendrik Wettkamp/VUMC/Vanderbilt: (e0c48d6c0c275a57e4a6d1dd41611d)
Signed On: 09/10/2018 9:25:52 PM CDT
Please itemize all changes to the consent documents:
Pg 1 - Title and targeted subjects.
Item 1, pg 1 - amended targeted subjects
Item 4, pg 2 - increased follow-up group
Item 5, pg 2 - added communication of any discovered risks.
Item 14, pg 4 - added data to be shared and with whom it will be shared.

Indicate how the new information will be communicated to currently enrolled participants, if applicable:
If subjects are chosen for the 2nd wave, they will be notified via email.

Does this amendment involve ionizing radiation?
[ ] Yes
[ ] No
[ ] N/A

Does this amendment change the billing plan?
[ ] Yes
[ ] No
[ ] N/A

Does this amendment change the IBC Review for Live, Recombinant, and/or Attenuated Microorganisms for Vaccination, Therapy, or Gene Transfer?
[ ] Yes
[ ] No

Date of IRB Approval: 9/10/2018

Institutional Review Board

Electronic Signature: Joern-hendrik Weitkamp/VUMC/Vanderbilt: [e0c463dc9c0f73a57e4aaf1d1db4161fd]
Signed On: 09/10/2018 8:25:52 PM CDT
### Funding Questions

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<td>VICTR funding support or use of VICTR facilities?</td>
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<td>Internal funds?</td>
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<td>Has a grant?</td>
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<tr>
<td>Is there a grant application or proposal required for the external support?</td>
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<tr>
<td>Does the study involve the use of Vanderbilt hospital facilities or assays related to human samples/tissue?</td>
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<td>Does this study have an associated billing plan?</td>
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Date of IRB Approval: 9/10/2018

Institutional Review Board

Electronic Signature: Joern-hendrik.Welkamp@VUMC/Vanderbilt : (e0c488dc90f75a57e4aad1d0b41511d)
Signed On: 09/10/2018 9:26:52 PM CDT
About the Author

Joy E. Kechik is a second-year genetic counseling graduate student at the University of South Florida with a B.S. in genetics from Purdue University. She is one of four students in the inaugural class for the USF Genetic Counseling Graduate Program. During her time at USF, Ms. Kechik worked as a graduate research assistant for a study looking at management decisions and family sharing behaviors among hereditary cancer gene carriers. She also had the opportunity to collaborate on two journal publications related to the complexities of genetic testing for hereditary colorectal cancer and barriers to genetic testing for hereditary breast cancer. Ms. Kechik will be graduating in May 2019 with a Master of Science in Public Health and is set to begin her career as a cancer genetic counselor in Vero Beach, Florida. She is looking forward to finishing her degree and having more free time to spend with her fiancé and her puppy, Lexi.