MANAGEMENT CHOICES AND REPRODUCTIVE CONCERNS IN YOUNG WOMEN WITH BRCA MUTATIONS: A QUALITATIVE THEMATIC ANALYSIS

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Women who are found to carry BRCA1 or BRCA2 mutations are given recommendations of management options ranging from surveillance, to chemoprevention, and surgery. Choices regarding management may be influenced by experiences with cancer in a family. Besides management options, young women with a BRCA mutation may be concerned about reproductive choices. This study investigates the reproductive concerns in young women with BRCA mutations and how their choices regarding management are influenced by their family history. A secondary analysis employing a thematic analysis method was performed using interview transcripts. In the initial study open-ended email and telephone interviews were guided by grounded theory methodology. The current study was comprised of 14 women, aged 18-30 who tested positive for a BRCA1 or BRCA2 mutation. Two main themes were identified: 1. Management choices are highly influenced by the cancer histories of family members, 2. Young women who have a BRCA mutation experience a sense of urgency about their reproductive choices. Perceived closeness to family members with cancer appeared to impact decisions for medical management. The results of this study suggest which the participants who elected for prophylactic surgeries had an eminent sense of cancer risks that was largely based on the family history of cancer. A sense of feeling rushed into starting a family and concerns of passing on the BRCA mutation to their children were the reproductive concerns in young women with a BRCA mutation. From these results, health professionals may gain insight into the

management choices and concerns of young BRCA mutation carriers. This work also has relevance to public health by being applicable to common diseases and how management choices can be influenced by experiences within a family.

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PREFACE

I would like to acknowledge all of the participants in this study and for discussing their experiences so openly. The sharing of their experiences has provided me with insight into the personal impact of their BRCA mutations. These individuals have enhanced my professional development and are truly an inspiration.

I would like to thank my thesis committee for their insight and guidance, as well as my classmates who were supportive of my many inquiries. I'd also like to thank the Department of Human Genetics at the University of Pittsburgh for providing me with QSR's Nudist Vivo program for my analysis.

Finally, I would like to thank Dr. Rebekah J. Hamilton for providing me with the opportunity to perform my thesis on the interviews she had collected and had already performed an initial analysis on.

1.0 INTRODUCTION

A family history of breast and/or ovarian cancer is one important risk factor for a woman to develop these cancers. Before the BRCA1 and BRCA2 genes were discovered in the early 1990's, it was evident that certain families had a significantly higher incidence of ovarian and early breast cancers than the general population (Iau et al, 2007). Genetic studies from these families led to the discovery of the BRCA genes and their link with significantly increased risks for breast and ovarian cancers (Iau et al, 2007).

The discovery of the BRCA genes and mutation detection allowed individuals and their families to undergo mutation testing. Individuals with a mutation knew that they are at an increased risk for cancer in the future, while those without are at population risk for cancer (Thull & Vogel, 2004; Barnes-Kedar & Plon, 2002; Berliner & Fay, 2007). Women identified with a mutation who did not have cancer had options ranging from heightened cancer screening to prophylactic surgery. Prophylactic surgical options include bilateral mastectomies and oophorectomies, and would greatly reduce their risk to develop cancer (Hartmann et al, 1999; Hartmann et al 2001; Rebbeck et al 2004; Rebbeck et al, 2002). There is chemoprevention such as tamoxifen to reduce the risk for breast cancer or oral contraceptives to reduce the risk for ovarian cancer. Frequent screening is used in an effort to detect cancer at an early stage. The women in which a family mutation is not identified are not at an increased risk for cancer and

can be screened as the general population (Thull & Vogel, 2004; Barnes-Kedar & Plon, 2002; Berliner & Fay, 2007).

Several studies have been conduted on the efficacy of the management options for women who carried a BRCA mutation (Finch et al, 2006; Fisher et al, 1998; Narod et al, 1998; Meijers-Heijboer et al, 2001). Studies have also been performed on the uptake of screening vs. prophylactic surgery and on the difference between clinical characteristics and management options these women have chosen (Wainberg & Husted, 2004; Uyei et al, 2006; Meijers-Heijboer et al, 2000). There has been some research on the impact of BRCA testing on families or on the individual being tested (Kenen et al, 2003a; Kenen et al, 2003b; Stroup & Smith, 2007; van Dooren et al, 2005). However, there has been limited investigation into the management choices made by unaffected BRCA carriers ages 35 and younger and how such choices may have been impacted by family cancer experiences (Friebel et al, 2007). Additionally, few studies have been performed looking into how these management choices have impacted family planning (Smith et al, 2004; Staton et al, 2008). Since many BRCA carriers have grown up with cancer in their families, it is important to evaluate how these experiences may impact their management choices. Additionally, while there has been research on the perceptions of women thirty and over regarding prophylactic oophorectomies (Friedman & Kramer, 2005; Staton et al, 2008), there has been limited information on how women under thirty are impacted by having the choice of premenopuasal oophorectomies looming in their future.

The purpose of this study was to determine how family histories of cancer can influence the management choices made by a woman who carries a BRCA mutation. A secondary goal of this study was to investigate how the recommendation for a premenopausal oophorectomy influences the reproductive choices in young BRCA mutation carriers. A qualitative thematic

analysis was performed on interviews of young women who tested positive for a BRCA mutation. The themes identified in the interviews will be presented and discussed in this paper.

2.0 BACKGROUND AND SIGNIFICANCE

2.1 HEREDITARY BREAST AND OVARIAN CANCER (HBOC) AND BRCA1/BRCA2 GENE MUTATIONS

About 5-10% of all breast cancers are due to a single gene mutation leading to a genetic predisposition for cancer. About 80-90% of hereditary breast and ovarian cancers are caused by mutations in the BRCA1 and BRCA2 genes (Nussbaum & Isaacs, 2007; Thull & Vogel, 2004). The BRCA1 and BRCA2 genes were discovered in 1990 and 1994, respectively. The BRCA1 gene is located on chromosome 17 while the BRCA2 gene is located on chromosome 13 (Hall et al, 1990; Wooster et al, 1994). The BRCA genes are believed to have multiple functions, but with a primary function in tumor suppression and a role in DNA repair (Nussbaum & Isaacs, 2007; Thull & Vogel, 2004). A mutation in either the BRCA1 or BRCA2 puts a woman at an increased risk for breast and ovarian cancers. Families with a BRCA mutation typically show a clustering of breast and ovarian cancers, with mostly premenopausal breast cancers across multiple generations. The BRCA mutations are inherited in an autosomal dominant manner, meaning that the children of an individual (male or female) with a mutation have a 50% chance of inheriting it, and thus at an increased risk for breast and ovarian cancer.

In the general population, one in eight women (12.5%) will develop breast cancer during their life time (Ries et al, 2007). The median age of onset of breast cancer in the general

population is 61 (Ries et al, 2007). A woman's risk for ovarian cancer in the general population is one in seventy-two (< 1.5%) (Ries et al, 2007). Women with a BRCA1 or BRCA2 mutation have a greatly increased risk for both breast and ovarian cancers. Women with BRCA1 or BRCA2 mutations have a 50-87% risk to develop breast cancer by the age of 70, with a majority of women diagnosed before the age of 50 (Ford et al, 1994; Berliner & Fay, 2007). Women with a BRCA1 mutation have a 29-44% risk for ovarian cancer and those with a BRCA2 mutation have up to a 27% risk (Ford et al, 1998; Berliner & Fay, 2007). Women with a BRCA mutation have a 48-64% risk to develop contralateral breast cancer, which averages to about 2-3% risk for each year (Ford et al, 1994; The Breast Cancer Linkage Consortium, 1999). There is also an increased risk for other cancers in association with the BRCA mutations. In men the BRCA1 and BRCA2 mutations are associated with an increased risk for breast and prostate cancer. In addition, the BRCA2 mutation is associated with increased risks for melanoma and pancreatic cancer (Ford et al, 1994; The Breast Cancer Linkage Consortium, 1999; Barnes-Kedar & Plon, 2002).

The prevalence of the BRCA mutations in the general population is relatively uncommon, with a frequency of 1 in 300 to 1 in 800 (Berliner & Fay, 2007). However, the rate varies greatly between ethnic populations. For example, the Ashkenazi Jewish population has a frequency of 1 in 40 individuals having a mutation at one of three BRCA1 and BRCA2 specific sites (Berliner & Fay, 2007; Iau et al, 2007).

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2.2 BRCA MANAGEMENT

2.2.1 Surveillance

The purpose of surveillance for breast cancer is to identify suspicious lesions and/or catch cancer at an early stage. The recommendations from the National Cancer Care Network (NCCN) include: 1) Women who are at risk for a BRCA mutation and those who test positive should begin self breast exams at the age of 18 and perform them monthly; 2) Clinical breast exams should be performed semiannually beginning at age 25; 3) Annual mammogram and breast MRI beginning at age 25, or 10 years before the first diagnosis of breast cancer (NCCN, 2007). Breast MRI screening is used in addition to breast mammography because it is more sensitive in younger women (Uyei et al, 2006). The draw-backs to using breast MRI are the costs and availability, as well as a high rate of false-positives due to the lack of specificity (Nusbaum & Isaacs, 2007; Uyei et al, 2006). Although surveillance is less invasive than surgical options, it can have negative consequences, such as unnecessary biopsies and increased worry about cancer (Uyei et al, 2006). Unfortunately, screening does not always identify breast cancer at an early stage. It has been estimated that 25% of young, high risk women who are undergoing close surveillance will develop breast cancer and eventually die of distant metastasis despite a comparatively early diagnosis (Meijers-Heijboer et al, 2001; Meijers-Heijboer et al, 2000).

Surveillance for ovarian cancer typically begins at age 35 or 5-10 years earlier than the first diagnosis of ovarian cancer. The screenings involve a transvaginal ultrasound and CA-125 that are performed concurrently every 6 months (NCCN, 2007). When compared to screening for breast cancer, the current methods of screening for ovarian cancer are less than ideal for detecting early stage ovarian cancers. The CA-125 is elevated in only about 50% of stage I

ovarian cancers and is elevated in 90% of women with stage II or higher stage ovarian cancers. It also lacks specificity in that elevated levels are associated with endometriosis, fibroids, pregnancy and liver disease (Cherry & Vacchiano, 2002). Transvaginal ultrasound limitations include an inability to detect cancer in normal sized ovaries, detecting primary peritoneal cancer, and a lack of specificity (Cherry & Vacchiano, 2002).

Screening for men includes monthly self breast exams and annual clinical breast exams. Mammography is considered in men with parenchymal/glandular breast density, gynecomastia or suspicious breast findings. Surveillance for prostate cancer include an annual digital rectal examination and prostate specific antigen (PSA) testing (NCCN, 2007; Berliner & Fay, 2007).

2.2.2 Chemoprevention

Tamoxifen has been used as chemoprevention in premenopausal women at high risk and has shown a 49-62% reduction of breast cancer risk in women who received it for 5 years (Fisher et al, 1998; King et al, 2001). The occurrence of estrogen receptor-positive breast cancers were found to be greatly reduced by tamoxifen, while there was no difference in the occurrence of estrogen receptor-negative breast cancers (Fisher et al, 1998). Tamoxifen has side effects that include increased risk for endometrial cancer, blood clots, stroke, cataracts, and menopause-like symptoms (Fisher et al, 1998). There is some debate over the effectiveness of the treatment in women with a BRCA1/2 mutation, mostly due to the receptor status of the tumors. The majority of BRCA1 tumors are estrogen receptor-negative, and it is expected that tamoxifen will have better risk reducing effects in women with a BRCA2 mutation (Nusbaum & Isaacs, 2007).

Oral contraceptives have been used to reduce the risk for ovarian cancer both in the general population and in individuals with a BRCA mutation. Taking oral contraceptives for

over 6 years has been shown to reduce the risk of ovarian cancer by 60% in individuals with a BRCA mutation (Narod et al, 1998). However, one indication of the complexity in managing breast cancer risk in women with BRCA mutation is the fact that use of oral contraceptives in woman with a BRCA1 mutation has shown a modest *increase* in the risk for breast cancer (Nusbaum & Isaacs, 2007).

2.2.3 Prophylactic Surgery

The most effective method to prevent breast cancer is to have a bilateral prophylactic mastectomy (PM). Two mastectomy options exist, a total mastectomy or a subcutaneous mastectomy. A total mastectomy removes about 95-99% of breast tissue and includes the nipple-areola complex. A subcutaneous mastectomy removes a majority of breast tissue but leaves the nipple-areola complex, which leaves 5-10% of breast tissue. A total mastectomy is recommended in women with a BRCA mutation because there is still a risk to develop cancer in the nipple region. A total mastectomy reduces the risk for breast cancer by about 90% (Hartmann et al, 1999; Hartmann et al, 2001; Rebbeck et al, 2004). Some of the issues associated with prophylactic mastectomies are psychological consequences, effects on body image, surgical complications, suboptimal results from reconstruction, difficulties with intimacy and loss of sensation (Wainberg & Husted, 2004).

Due to the increased risk for ovarian cancer and the poor screening methods, having a prophylactic bilateral salpingo-oophorectomy (BSO) is often strongly encouraged for women with a BRCA mutation by health professionals. Both the ovaries and fallopian tubes are removed in a BSO, and often a woman opts to have her uterus removed as well, resulting in a

total hysterectomy. The risk for ovarian cancer after a BSO is reduced between 80-96%, with a residual risk of 4% for peritoneal cancer (Rebbeck et al, 2002; Berliner & Fay, 2007; Nusbaum & Isaacs, 2007; Finch et al, 2006). It is recommended that a woman with a BRCA mutation have a BSO between ages 35 and 40, or after they are finished with child bearing (NCCN, 2007). A premenopausal BSO is recommended, especially for BRCA1, due to the risk for ovarian cancer before the age of 40. One benefit of a premenopausal BSO is a 50% reduction in risk to develop breast cancer (Rebbeck et al, 2002; Berliner & Fay, 2007; Nusbaum & Isaacs, 2007). A major impact of a BSO on premenopausal women is the immediate onset of menopause. This is associated with the typical vasomotor symptoms, as well as an increased risk for osteoporosis, cardiovascular disease and sexual dysfunction. Short-term use of hormone replacement for these symptoms has not been shown to negate the protective effect on the breasts from the BSO (Guillem et al, 2006; Nusbaum & Isaacs, 2007).

2.3 DECISIONS FOR MANAGEMENT

Individuals who develop a serious illness may not have prior experience with the disease, so feelings regarding their diagnosis as well as their management decisions may not be based on longstanding views or beliefs about the disease. This may not be the case with hereditary diseases, where a person is born into the disease experience if it has been present in earlier generations (Werner-Lin, 2007). The majority of women who have tested positive for a BRCA mutation have had a heightened awareness of cancer during their lives (Foster et al, 2002). This awareness can come from a personal diagnosis of cancer, or witnessing a family member diagnosed with cancer who underwent treatment and/or died from the cancer (Foster et al, 2002).

2.3.1 Risk perceptions

A number of studies have evaluated how cancer family histories affect perceived cancer risks. Women with a strong family history of cancer appear to have a longstanding knowledge of the cancer, or come to a gradual realization through multiple affected relatives, or a relative dying at a young age (Forrest et al, 2003). To evaluate their own family's situation, women sometimes compare their families with 'the norm'. Individuals who recognize that the affected number of relatives exceeds 'the norm' may feel this is an indication that the cancers are due to more than just coincidence (Foster et al, 2002).

Ravies and Pretter (2005) were interested in the influence of a mother's breast cancer diagnosis on her adult daughter. For some women, a mother's diagnosis was a confirmation of their family history of specific risk for breast cancer. This served to increase their risk perception, enhance their fears of personal vulnerability, and contribute to their sense of cancer inevitability which reaffirmed their perception that this was what their future held (Ravies & Pretter, 2005). Women who had personal experience with their mother's cancer may have amplified their sense of personal susceptibility and this contributed to a diminished sense of future options (Ravies & Pretter, 2005).

Kenen et al. (2003a) performed a qualitative analysis on how women from HBOC families are influenced by family stores and their use of heuristics (deduced shortcuts used to make sense of complicated information) in the application and interpretation of genetic information. It was found that family stories influenced a woman's use of heuristics in interpreting their own risk and their choices of controlling this risk. Women from families with many cancer cases, and where a mother or sister died young used more heuristics than those with a less severe family history. Representativeness, availability and illusion of control were the

three main heuristics these women used. Availability refers to the ease of recall of a recent or dramatic event, such as the memory of a relative that died of cancer, to help make a decision.

Representativeness usually refers to a stereotype, such as believing in a greater risk to develop cancer because they look like a relative who had cancer (Kenen et al, 2003a). For example, one woman in Warner-Lin's (2007) study stated that she believed she would test negative because she looked more like her father's side of the family than her mother's, which is where the mutation was coming from. In hereditary disease families, disease experiences accumulate over generations and become legacies that are passed down. These legacies include information about who in the family or what type of person gets sick, and about disease onsets and outcomes (Werner-Lin, 2007). The age of earliest diagnosis of cancer in a family is often when a BRCA mutation carrier believes she will develop cancer or when her risk sharply escalates, as opposed to medical information about when risks do increase (Werner-Lin, 2007).

Illusion of control refers to an individual's attempts to control outcomes that are unlikely to change, such as changing one's diet to prevent cancer (Kenen et al, 2003a). Kenen et al. (2003b) found that many women internalized healthy life style messages such as having a positive attitude, eating a healthy diet and reducing stress in the belief that it would reduce the risk for cancer, or were at least worth doing.

The saliency of risks were more acute in women with many relatives with cancer, or mothers or sisters currently suffering from or had died from cancer, than in women with fewer, less recent cases in the family, or those that recovered from cancer (Kenen et al, 2003b). Risk perceptions are impacted by personal experiences with cancer, where women with a personal or significant family history of cancer are more likely to undergo preventative surgeries than women with no experience of cancer (Werner-Lin, 2007). Risk perceptions are also influenced

by the amount of control individuals believe they have over an outcome and the amount of fear associated with possible outcomes (Kenen et al, 2003a).

2.3.2 Factors associated with management choices

When a healthy woman from a BRCA family is choosing management options, she is likely to rely more heavily on her personal feelings of risk, rather than on statistical probability (Kenen et al, 2003a). The use of heuristics to evaluate this statement suggests that individuals are more apt to trust memories of past events to help guide their future choices (Kenen et al, 2003a). Kenen et al. (2003a) discovered that women use their family history and family experiences with cancer as reference points, and used them to evaluate their own risk perceptions for developing cancer and on deciding what to do about this risk, which involved finding ways to control their risk.

Studies have shown that women who are more inclined to have prophylactic mastectomies are more likely to have children and are younger (<50) (Meijers-Heijboer et al, 2000; Wainberg & Husted, 2004). Women opting for PM were generally younger when confronted with familial cancer than women who choose surveillance, and had a greater number of first or second degree relatives with cancer diagnoses (Wainberg & Husted, 2004). Metcalfe et al. (2008) found that women with mothers diagnosed with ovarian cancer had a significantly lower utilization of PMs than women whose mothers did not have ovarian cancer.

Women with a sister diagnosed with breast cancer were almost twice as likely to have a PM than those who did not have a sister with breast cancer (Metcalfe et al, 2008). The diagnosis of breast cancer in a sister can have a profound effect because sisters may have close bonds (van Dooren et al, 2005). Cancer distress was found to be related to having at least one sister with

breast cancer, a sister's recent diagnosis (< 3 years), and being closely involved in a sister's breast cancer process (van Dooren et al, 2005).

Staton et al. (2008) is a unique study because it used women from a generally younger age group (25-40) and looked at surgical choices and factors influencing them. Not surprisingly, it was found that the major factor for choosing a PM was concern about breast cancer. After that, factors possibly hindering a PM in less than half the women were concerns about appearance and sexuality. About a quarter of the women stated other factors influencing PM related choices, including desire to breast-feed and bear children, as well as concern about their relationship status. Of the women in the study by Staton et al. (2008), about 44% had already had a PM at the time, about 22% were likely to have a PM, about 29% said a PM was possible, and few women were never going to have a PM.

Staton et al. (2008) also looked into factors influencing a BSO and the likelihood of choosing a BSO. Again, it was no surprise that the major factor behind a BSO was concern about ovarian cancer. Over 50% of women felt that a concern for breast cancer was a factor in choosing a BSO. Conversely, over 50% of women felt that concerns about libido and early menopause were factors in deciding to forego a BSO. Desired fertility and concerns about sexuality were factors hindering a BSO in less than half the women, and about a quarter were concerned about their relationship status. With regards to having a BSO, around 28% had already had one, and about 65% were likely to have one, with only 7% of women saying they would possibly or never have a BSO.

Prophylactic oophorectomies have been shown to be utilized more among women aged 40 and older as opposed to those at younger ages (Wainberg & Husted, 2004; Meijers-Heijboer et al, 2000). It has also been shown that a BSO is opted for more frequently than PM (Friebel et

al, 2007; Wainberg & Husted, 2004). Wainberg & Husted (2004) suggested factors associated with the increased use of BSO such as greater perceived benefit of surgery due to the poor prognosis of advanced ovarian cancer; the lack of efficacy in ovarian cancer screening for detecting cancer at early stages; and the perception that a BSO is less invasive than PM, less surgical complications in regard to construction, and less detrimental to body image and integrity. Women with family histories of ovarian cancer are more inclined to have BSO than women without. Metcalfe et al. (2008) found that women whose mothers had a diagnosis of ovarian cancer were more likely to have a BSO than a PM.

2.3.3 Concerns regarding reproduction

Women who carry a BRCA mutation face unique reproductive concerns because a BSO is recommended when women are still at a fertile age. The only study identified about this topic was related to how genetic testing for a BRCA mutation influenced fertility intentions. Smith et al. (2004) included male and female carriers and non-carriers in questionnaires which were initiated soon after receiving the test results and completed two years later. They found that males who were carriers were more likely to want additional children than those who were not carriers. In contrast, female non-carriers were more likely to want additional children than carriers. It was found that female carriers were 5.5 times more likely to have changed their family planning than non-carriers because of their positive test results.

As previously discussed, there is a 50% chance that carriers can pass on their BRCA mutation to their children. Staton et al. (2008) found that almost 88% of their participants were either frequently or extremely concerned about passing on the mutation to their children. Because of the 50% risk, some women may choose to not have children, while others may opt

for preimplantation genetic diagnosis (PGD) as a way to ensure their children will not have a BRCA mutation (Friedman & Kramer, 2005). Staton et al. (2008) found that about 13% of the women in the study were likely to use PGD, while the majority of women in the study said it was possible or not an option.

Another unique concern for these women is the possible association of breast cancer with pregnancy. Andrieu et al. (2006) found no significant difference in breast cancer risk for parous versus nulliparous BRCA mutation carriers, however among parous women each additional birth reduced breast cancer risk by 14%; although this risk reduction is restricted to women over 40 years old. Age at first-full term pregnancy was found to play a role in reduction of breast cancer risk. Women with a BRCA2 mutation were at a reduced risk if they had their first full-term pregnancy before the age of 20 years, while women with a BRCA1 mutation who had their first full-term pregnancy at a later age appeared to have a lower risk for breast cancer. Additionally, breast feeding for over a year is associated with a reduced risk for breast cancer.

2.4 METHODOLOGY OF THE STUDY

Much of the literature associated with BRCA mutations and management decisions are quantitative studies and constitute the majority of the studies previously outlined. Quantitative studies are performed by analyzing numerical data that measure particular elements from which trends are discerned via statistical analysis. These studies are valuable in identifying some components of individuals' experiences, but they typically do not enable researchers to recognize and characterize the essence of significant social aspects (Beeson, 1997). Incorporation of these

studies was important because a complete understanding of the relevant data is necessary in the methodology of qualitative analysis (to be described in 4.0).

Qualitative research can enable the identification and characterization of particular aspects of reality that are not necessarily anticipated, thus permitting analysis beyond limitations in one's own perceptions (Beeson, 1997). Qualitative research is often used to explore meaning, it attempts to understand the complexities behind what people do and why (Beeson, 1997). Qualitative work can be useful to health care professionals as a way to familiarize, or to become sensitized, to the experiences of patients they are encountering.

There is a limited amount of qualitative data regarding management choices and reproductive concerns in women with BRCA mutations. Of the qualitative studies incorporated in the Background and Significance, the majority focus on risk perceptions (Werner-Lin, 2007; Raveis & Pretter, 2005, Kenen et al, 2003b) and those regarding familial interactions in relation to testing (Forrest et al, 2003; Foster et al, 2002). Kenen et al. (2003a) focused on how family experiences or stories affect information processing and thus guiding decisions regarding management.

3.0 AIMS OF THE STUDY

The current study was a secondary data analysis of a previously conducted grounded theory inquiry that investigated the management choices of BRCA positive women and how their family histories influence these decisions. The two aims of the current study are:

1. Determine how family histories of cancer can influence the management choices made by young BRCA mutation carriers.
2. Investigate how a premenopausal oophorectomy influences the reproductive choices in young BRCA mutation carriers.

4.0 METHODS AND PROCEDURES

The initial study, including recruitment and interviews of participants, was conducted by Dr. Rebekah J. Hamilton and was approved by the Institutional Review Board (IRB) (0505039) at the University of Pittsburgh. The current study comprising of a secondary analysis of the interviews was approved by the University of Pittsburgh IRB (PRO08040303).

4.1 INTERVIEWS WITH RESEARCH PARTICIPANTS

Participants in Dr. Hamilton's original study were women between the ages of 18 and 39 who had genetic testing for a BRCA mutation. The original study was a grounded theory study employing theoretical sampling for participant recruitment and question development. In grounded theory, data collection and analysis occur simultaneously and theoretical sampling is employed to guide data collection to build upon the emerging theory. While a complete grounded theory analysis could have been performed on the interviews used in the current study, the secondary analysis involved a more limited method (See section 4.4).

The more traditional process of data collection in the form of interviews for qualitative studies are interviews via telephone or in-person. Recently, email interviews have been introduced as an alternative to prior methods. Hamilton and Bowers (2006) have outlined practicalities and benefits of email interviews, as well as possible issues such as validity and

ethical concerns. The initial study incorporated either telephone or email interviews, depending on the participants' preferences. All interviews from the original study were performed by Dr. Rebekah J. Hamilton. The participants in this secondary data analysis were chosen by age (those aged 30 and younger), those confirmed to carry a BRCA mutation, and those without an invasive breast cancer diagnosis.

4.2 PARTICIPANT RECRUITMENT

Participants in the initial study were recruited by posting information notices on a hereditary breast/ovarian cancer syndrome support websites (FORCE: Facing Our Risk of Cancer Empowered: www.facingourrisk.org; and www.youngsurvival.org). Informed consent was received from all participants prior to being interviewed.

4.3 TRANSCRIPTION

Telephone interviews were transcribed verbatim from audiotapes to Microsoft Word by a professional transcriptionist. In accordance with the IRB, personal identifiers were removed and participants were given study numbers. The participants' and interviewer's grammar, pauses, unfinished sentences, and placeholders were preserved during the transcription in the best possible manner. Email interviews did not require transcription and were copied to Microsoft Word without any identifiers. Interview segments that were used in this report were subject to minor revision if the alteration did not detract from any meaning of the passage, but would

enable the reader to comprehend the passage with greater ease. Some examples of revisions include spelling and grammar correction, placeholder removal, and excision of minor interviewer contributions during telephone interviews.

4.4 SECONDARY ANALYSIS VIA THEMATIC ANALYSIS

Secondary analysis is the use of existing data to address research questions that are different from the initial questions asked in the original or primary study (Hinds et al, 1997). This secondary analysis used the approach described by Hinds et al. (1997) of extracting a subset of cases for a similar but more focused analysis in regard to the primary study. The original researchers or a new set of researchers can perform a secondary analysis, although a benefit of different researchers is a distance from the data and thus no firm or fixed ideas about the trends in the data set (Hinds et al, 1997). The present study is classified as secondary analysis because it involves an extended study of previously collected interview transcripts and was performed by an individual not previously involved in the original study.

The method chosen for the secondary analysis of the data was thematic analysis. Thematic analysis was chosen because it is a relatively quick and easy method to learn for researchers with little experience in qualitative research, and it is a flexible technique that allows for a wide range of analytic options (Braun & Clarke, 2006). Thematic analysis is a method of ascertaining, describing, evaluating and reporting themes within qualitative data (Boyatzis, 1998). Although thematic analysis is widely used, there is no clear agreement about what it is and what exact approach of analysis should be used by the researcher. The implication from the lack of definition is that interpretation for a thematic analysis at higher levels can be difficult.

Due to the wide range of analytic options, it is difficult to develop specific guidelines for higher-level phase analysis and the researcher can become hindered on which aspects of the data to focus upon (Braun & Clarke, 2006).

Thematic analysis can be used in a broad sense to provide a rich thematic description of an entire data set (inductive analysis), or a thorough description of a particular theme within the data (theoretical analysis) (Braun & Clarke, 2006). An inductive analysis is thought of as a 'bottom-up' or data driven approach. In this analysis, the themes or patterns identified are strongly linked to the data and not solely driven by the researcher's prior preconceptions or theories (Braun & Clarke, 2006; Boyatzis, 1998). Theoretical analysis is thought of as a 'top-down' or theory driven approach. Researchers using this theory are interested in a specific idea derived from a review of literature, from their prior research or from their clinical experience. A theoretical analysis is typically driven from the researcher's own theories and leads to a detailed analysis of a particular aspect of the data (Braun & Clarke, 2006; Boyatzis, 1998). All thematic analyses include both a description and interpretation of the themes identified in the data, with the interpretation relating to previous reports in the literature (Braun & Clarke, 2006).

An inductive thematic analysis approach was chosen because few qualitative studies have focused on young women with a BRCA mutation and what influences lie behind their management choices. The thematic analysis allowed for a cross-section analysis of the interviews to explore possible influences of the management choices made by young BRCA positive women. An additional benefit of the inductive analysis was the identification of unexpected themes in the data (Braun & Clarke, 2006). While this study is a thematic analysis, the researcher drew upon some aspects of grounded theory to aid in the data analysis.

The main steps performed during the thematic analysis in the present study are outlined below.

4.4.1 Familiarization of interviews and background literature

The transcripts were read by the author three times before coding in order to gain insight into possible themes imbedded in the interviews. Some initial notes were made during readings of each transcript and potential themes were noted. A comprehensive literature compilation and review was performed prior to coding and have been summarized in the Background and Significance section. The review of literature was performed to sensitize the author to subtle concepts that may be present in the interviews but could be over-looked during coding if they had not been previously introduced to the author (Braun & Clarke, 2006). Corbin & Straus (2008) encourage sensitivity to the data through literature review and clinical experiences. Reviews of literature are used to extend understanding of the data beyond what has already been suggested or established (Marks & Yardley, 2004). Additionally, every researcher has preconceptions that influence the analysis and interpretation of data and an in-depth literature review can help establish an initial framework for coding and provide data to support the researcher's assertions (Charmaz, 2006).

4.4.2 Initial code generation

Coding is the process of defining what is happening in the data and contemplating what it means (Charmaz, 2006). A code is essentially a label, and should use the fewest words possible and be conceptually meaningful to the data (Boyatzis, 1998). Coding is the first analytic step in

thematic analysis which enables researchers to try to determine the meaning behind participants' statements and to look at the data in novel ways (Charmaz, 2006). After initial coding, the codes can be organized into categories or themes, to re-focus the analysis at a broader level, and analysis is then centered around the themes (Braun & Clarke, 2006).

Initial coding is commonly used in thematic analysis and is used to remain open to possible interpretations of the data (Charmaz, 2006). A form of initial coding was used in this study. Specifically, Marks and Yardley (2004) described a method which involved the use of coding under broad categories which were sub-divided and/or rearranged upon further coding. 'In-vivo' codes, codes that are derived from participants' words, were used occasionally in order to preserve the meanings of the participants (Charmaz, 2006). When coding data, a decision needs to be made regarding whether a particular code can be placed in multiple categories, or in just one category (Marks & Yardley, 2004). The former was chosen due to the complexity of participants' stories and because the generated codes often pertained to more than one category.

Several tips from Boyatzis (1998) and Charmaz (2006) were used to aid in the coding process and included remaining open, staying close to the data, and keeping the codes concise and simple. Additional tips from Boyatzis (1998) regarding personal concerns were also used, such as not being distracted by sensory overload, fatigue, frustration or confusion.

The process of coding can be performed using various techniques, a few of which are discussed here. Line-by-line coding involves giving a code to each line, sentence or phrase in an interview. Charmaz (2006) states that line-by-line coding works well with detailed data and allows for identification of ideas that can be overlooked during reading for a general thematic analysis. Line-by line coding enables the researcher to look at the data both critically and analytically, preventing the researcher from loosing themselves in the participant's worldviews

and accepting them without question. A different method of coding has been described by Rennie (2006). He describes the breaking down of data into units of meaning followed by an interpretation of the meanings of each 'meaning unit'. Unlike line-by-line coding, his technique has no distinction between codes and categories, and represents all conceptualizations of meaning as categories. Rennie states that persons being interviewed wish to make a point, and once that point has been made they move on to something else, and so in deciding what constitutes as a 'meaning unit' the researcher is alert to the main point of a passage.

The process of coding used in the current study was based on Rennie's method of meaning units. This method was chosen because the majority of interviews were via email and the written answers were generally concise and each topic was addressed individually. Another benefit to using this method was that the experiences or stories from each participant seemed more significant when read as a whole or in a 'meaning unit'. Coding was performed on all portions that pertained to family members with cancer, management, reproduction issues, and issues related to control and risk perceptions. Other portions of the interviews that were read but not coded included the testing process and disclosure of the results with family members.

Coding in this study was facilitated using QSR's Nudist Vivo (version 7.0.281.0 SP4), a software program that assists researchers in coding qualitative transcripts and organizing the codes into possible themes. The transcripts were imported into this program from Microsoft Word.

4.4.3 Memo writing

Memo writing in grounded theory is an important step between coding and the completed analysis (Charmaz, 2006). Writing memos enhances early analysis and exploration of the data

and codes (Charmaz, 2006). Corbin & Strauss (2008) recommend beginning memo writing at the first analytic session and continuing throughout the analytic process. Memo writing enables the researcher to express thoughts about particular codes, it allows comparisons and connections to be made between codes and about possible themes, and enables conceptualization of themes (Charmaz, 2006). Although the current study was not a grounded theory analysis, memo writing was used in this study to facilitate the thematic analysis.

Charmaz (2006) explains that there is no particular methodology to memo writing, that the importance is in writing down thoughts or ideas. In the current study, memo writing began from the initial reading of the interviews, throughout the coding process and during identification and crystallization of themes. Referencing back to earlier memos was helpful to recall participants' stories, particular aspects of their interviews and thought concepts during each stage of the process.

4.4.4 Identification and characterization of themes

A theme captures an important aspect of the data in relation to the research question (Braun & Clarke, 2006). The importance of a theme is not necessarily in prevalence in the data, but whether it captures an important element in regard to the research question (Braun & Clarke, 2006).

Identification and characterization of themes was a process in this study. Themes were noted early on, beginning from the first reading of the data set and throughout the coding process. Using the Nudist Vivo software, codes were placed into categories after the first few interviews were coded, and organized into potential themes depending on their content. Codes were often classified under several themes. The codes of each additional interview were also

organized into possible thematic categories. Codes were sometimes rearranged during the analysis to better illustrate the themes identified in the data.

Once all the interviews had been coded and the codes classified under particular themes, the themes were written in a memo. This enabled the development of a preliminary thematic map showing the connections between each theme. The two themes discussed in this paper were selected from the thematic map and will be described in the Results section.

5.0 RESULTS

5.1 SUBJECT SAMPLE CHARACTERISTICS

Subjects for this study were randomly assigned after the following criteria were met: women aged 30 years and younger who tested positive for a BRCA mutation and did not have a diagnosis of invasive breast cancer. Initially, a total of 12 women were assigned, followed by the addition of a pair of sisters, for a total of 14 women who all tested positive for a BRCA mutation. Their ages range from 18 to 30, with a mean age of 25. Six women were married and 8 were single or dating, and only one woman had children. One woman had a personal history of ductal carcinoma in situ (DCIS), whereas the others had no personal history of cancer. The majority of subjects were Caucasian, although there was one individual of African American descent and two women of Ashkenazi Jewish descent.

5.2 THE IDENTIFIED THEMES

The thematic analysis identified multiple themes in the interviews, but for this thesis two distinct and yet related themes will be discussed in detail. These two themes were chosen because they are essentially new topics that have not been addressed in the literature before. The first theme relates to how cancer family history influences management decisions and the second theme is

how family planning is affected by management choices. The connecting factor between the two themes is the management options presented to these young women.

5.2.1 Theme # 1: Management choices and the impact of cancer in the family

Family shapes our lives, from the mundane such as sharing food preferences to the more substantial such as shared values, coping mechanisms, and even ways of communicating. It is often familial experiences that impact the decisions one makes. All of the women in this study have made plans regarding their management, whether it's having prophylactic mastectomies, planning for oophorectomies in the not-too-distant future, undergoing heightened screening, or even waiting till a future point to make a committed decision.

5.2.1.1 Women who have had a prophylactic mastectomy

The majority of women discussed their thoughts in regard to prophylactic mastectomies. Four of the women in this study (Beth, Emily, Amber and Jane) had already undergone prophylactic mastectomies and Melissa was scheduled to undergo surgery within three months of the interview. Most of the other women were following the recommended increased breast cancer surveillance. Of the five women who have or will undergo mastectomies, three were from families where the BRCA mutation was maternally inherited. Jane, Amber and Emily grew up with strong family histories of cancer, where as Beth and Melissa were confronted with cancer after childhood.

Beth's sister had a diagnosis of breast cancer at 32, and there was also a maternal aunt who died from breast cancer. She had waited for a year and half to get tested so she could decide what she would do with the test results. Knowing what her sister had to endure, she chose to

have a prophylactic mastectomy, which she underwent soon after testing positive for the BRCA2 mutation.

> I made the decision to get the mastectomy prior to getting the test results. Initially I was obviously upset with the test result but my original decision stuck to have the surgery…Initially I felt completely out of control with this but now I've come to accept this as "normal" and am almost "relieved" that I have my own little crystal ball in regards to my future medical status and CAN DO SOMETHING ABOUT IT BEFORE IT HAPPENS!!!...I realized how lucky I was, respectively, to my sister that was blindsided with a diagnosis and had to go through surgery, chemo, radiation and will forever have to worry about a reoccurrence.

Although as a child Jane never had a first degree relative affected with cancer, she grew up being influenced by the diagnoses in her father's family, as did her sister Jessica who is also in this study. Jane's paternal grandmother died from breast cancer in her mid 30's, leaving behind 10 young children. Being that her father was the second oldest, Jane is closer in age to some of her aunts and uncles, especially the two from her paternal grandfather's second marriage, than to some of her first cousins. Of her father's four sisters, three were diagnosed with breast cancer at 28, 31 and 34, and two of them had it three times; the fourth sister tested negative for the BRCA mutation. Jane's immediate and extended family was both emotionally and geographically close. After testing positive for the BRCA mutation, Jane decided to have a mastectomy at 28 because she didn't want the anxiety of screening and she felt that she was next in line to develop cancer.

> I'm not against [screening] but I decided to have a prophylactic mastectomy because I know me, so that every 6 months waiting I would have physical health problems. I'd have stomach problems, I'd be not sleeping, I don't do well with long-term anxiety. I can do short term anxiety.

Jane got a lot of support for her mastectomy from her parents as well as her aunts. During her phone interview, she talked about a discussion that she and an aunt had.

> She's very encouraging, and she felt that I was very courageous and had said, she has four children and said, you know, it's painful and I'm not taking that from you but you'll never have to be bald from treatment. If I knew what you know at your age, she says, I would have traded going through that for anything. She said you're never going to have to be throwing up from driving to chemo, and you're never going to have to explain to a little kid, you know, why you don't have breasts and that you have no hair…and so she's very positive about it. So you know, it sucks but I don't have to do that and hopefully I won't have to.

At the time of her phone interview, Jane had been 6 weeks out of recovery from her PM. Although she had a difficult time with the recovery process, she did not regret her decision for the surgery and feels a sense of comfort and relief.

The BRCA mutation in Melissa's family came from her paternal side. She had a paternal aunt who was diagnosed with breast cancer and died in her 30's and a paternal first cousin diagnosed with breast cancer. Melissa decided to have a mastectomy due to a fear of developing cancer during a pregnancy, as had happened to her aunt. Her decision was reinforced after having an ambiguous mammogram finding and undergoing a series of imaging tests, only to get a less than satisfactory diagnosis.

> For me, surveillance was never really an option. I know that my first aunt to die from breast cancer developed the disease while pregnant (it was diagnosed in its early stages a couple of months after she gave birth), and due to the fast growing nature of the cancer she had, she passed within 9 months. Given that I want children, I did not want to risk the same situation happening to me. Then, in 2005, I underwent my first mammogram, something was spotted on the film and I had to return for a second mammogram. When that was inconclusive, I underwent a breast ultrasound. When that remained inconclusive, I had to go back for an MRI. The result I received in the mail was that it seemed to be benign. After two mammograms, an ultrasound, and an MRI

> "seemed to be" was not the response I was looking for to feel safe. This incident just strengthened my decision to go ahead with the prophylactic mastectomy.

Melissa put a lot of thought into the choice for surgery and upon choosing the most appropriate method for her reconstruction. The majority of her research was performed on the FORCE website and in talking with other women who had undergone surgery and reconstruction. She was scheduled for surgery three months after her interview.

Emily's mother was diagnosed with breast cancer twice. Her grandfather's three sisters all died from breast or ovarian cancer, as did two of her mother's first cousins. After testing positive for a BRCA mutation, Emily waited about 9 months before she decided to have a prophylactic mastectomy in order to have some time to adjust to the test results.

The case of Amber is a unique case because she had been diagnosed with DCIS at 23, while the other women in this study have had no diagnosis of cancer. Her mother and maternal grandmother each had diagnoses of invasive breast cancer. She had a bilateral prophylactic mastectomy to prevent another diagnosis of cancer.

Thus, all of these women have been influenced by their family histories of cancer and decided to do something to prevent breast cancer in themselves. Both Melissa and Amber had personal experiences with cancer scares, which impacted their decisions for mastectomies.

5.2.1.2 Contemplation on prophylactic mastectomies

A majority of the women who have not had mastectomies are considering them, but are mostly not ready to have them at this point. Some of the women feel that they are too young to be thinking about prophylactic surgeries and some are "waiting to act", which will be discussed in section 5.2.1.6.

Kylie is the youngest participant in this study at 18. Her mother died at 32 from breast cancer when Kylie was 2 and her brother was 3. Kylie's maternal grandmother had three separate diagnoses of cancer, starting in her 30's until her passing in her 70's. Of Kylie's four maternal aunts, two tested positive, and two tested negative. Kylie is quite close with the one aunt who had both a mastectomy and oophorectomy, and this aunt was very supportive of Kylie's decision to get tested. She feels that her mother's death has had a big influence on her life, and feels that having the BRCA mutation is a connection with her mother. She said "my mom passing away is an enormous part of life and it has shaped who I am. I guess I just felt that I would carry the gene mutation because it was something that linked the two of us together, even if it is a negative thing". While she thinks she may be too young right now, she plans on having a mastectomy when she is older.

> I think my mother would have done absolutely anything to have the information I have. She would have done anything to be able to prevent her from leaving her family. Obviously I was too young to really know what she would have done, but from what I hear she and I am very much alike and I can almost guarantee if she was told she could get surgeries to decrease her chances, she would have. I feel like my mutation connects us in the way that the emotions I have, because of the mutation, are linked to the emotions I have because of loosing my mother and not having her here with me today. It just feels like I have inherited this in some ways to make me a stronger woman because she is not here to help and show me how to be strong. Maybe I'm just trying to be positive about my situation, but it does help me get through the tough days knowing she is there with me through this.

The previous section explained Jane's choice for a prophylactic mastectomy, and now her sister's plan for mastectomies will be explained. Jessica, 25, and her sister are very close, they describe themselves as each others best friend. While each sister had independently decided to undergo mastectomies, Jessica is more wary and afraid of having the surgery than her sister was. Part of this is from watching her sister undergo the surgery and having a lot of pain during her

recovery, and she is also concerned about the psychological impact of the mastectomies. Jessica still intends to undergo prophylactic mastectomies, just not at this point, and continues to be screened regularly.

While these two women have surgery as a definite option, several of the other women undergoing screening are content with what they are doing at this point. These women feel that they will eventually have mastectomies, but it is not something at the forefront of their minds. Their decisions on screening will be discussed in section 5.2.1.5.

5.2.1.3 Absolute last option

Tara was the only participant who indicated that a mastectomy is her last option and she has a unique family history. Tara's maternal grandmother died at 39 from an 8 year battle with breast and ovarian cancer. Her mother was 16 at the time, the oldest of four daughters, and took over acting as a mother to her siblings. Tara's mother was diagnosed with breast cancer at 31, when Tara was 4, and within 6 weeks of her diagnosis her 27 year old sister was also diagnosed with breast cancer. With these devastating diagnoses, all four sisters had mastectomies and within 5 years, all had their ovaries removed. This all occurred before the BRCA gene was identified, and Tara's family was one of the families used to identify the genes. It turned out that three of the four sisters had the family BRCA mutation. Tara has said that she was too young to really remember her mother and aunt's diagnoses, but she grew up in a family where women had no breasts. Below, Tara describes how she began to realize that this was not the norm.

> I thought that after women had their children they had their breasts removed. That was normal for me and I actually didn't know until I was, oh gosh, maybe a preteen that that was abnormal. I remember this is many, many years later, but I remember being a teenager, I don't know, we were someplace where my aunts were together and my mom and they were trying on clothes. For some reason all of us were getting ready for

> something, we all had our shirts off and I was the only one with breasts in the whole room and I was like, this is weird. I mean, that was what was weird was that I was the only one who still had them…I always thought it was normal for women to have them removed. It wasn't until, you know, I was at a swimming pool when I was like a preteen and saw older women who still had breasts. I just thought that's what happens when you get older, not necessarily because of cancer, but that is just what you did. So I had a very skewed conception of that when I was younger.

Tara was 21 when she found out she had the family BRCA mutation. At the time of the initial interview, she was 24 and married. She has been receiving in-depth screening since she received her results. In regard to prophylactic surgeries, she plans on having her ovaries removed after she is finished with her family, but feels differently about a mastectomy. Tara has said "I DO NOT want to have a mastectomy. That is my absolute last option as far as treatments go". She feels that breasts are a matter of femininity and sexuality and you see them all the time, where as having an oophorectomy is something internal and she is less concerned about this. This is an example of the family history influencing a young women to make different choices than the previous generation had in the face of increased risk.

5.2.1.4 Prophylactic oophorectomy

Due to the young ages of the women in this study, Claire, 30, was the only woman who had a prophylactic oophorectomy. Claire was 29 and married at the time of her oophorectomy, and they had decided to not have children based not only on her BRCA mutation but also on her experiences with PCOS (polycystic ovarian syndrome). Claire's family history was significant for her mother dying at 46 from four diagnoses of breast cancer starting at 29, and a maternal grandmother dying from ovarian cancer at 49. She has two sisters, and both have tested negative for the family mutation. Here she describes her reasoning behind choosing an oophorectomy over a prophylactic mastectomy.

> Shortly after my 29th birthday I decided that it was time to do something to help prevent the onset of breast and/or ovarian cancer, annual screenings are great for diagnosing a problems, but I wanted prevention…Since ovarian cancer is so difficult to diagnose in a timely manner, it was apparent to me that having my ovaries removed would be the greatest thing that I could do to drop the chances of ovarian cancer to nearly nothing and drastically reduce my chances of breast cancer. I know that many women in my situation also have a double mastectomy. At this time, its too drastic of a decision for me. It is so much more physically/mentally disfiguring and a much more difficult surgery with time off from work.

Aside from Claire's action at a young age, the majority of women in this study are interested in having oophorectomies eventually. Many of the women stated specific ages or age ranges to have oophorectomies, and some said that once they are sure their families are finished they will have their ovaries removed. The majority of these women have discussed how their physicians have recommended they have oophorectomies at 35 years of age.

A few of the women have mothers that underwent oophorectomies. Rachel was the only woman who discussed the problems her mother had from a premenopausal oophorectomy.

> Thinking about the oophorectomy, it scares me even more because after my mom had that she said her hormones have been all over the place. She has been moodier and she's gained a lot of weight…so I am like, okay, are these the things I have to look forward to in 15 years? You know, like going through menopause 15 years earlier than I should be, its kind of scary.

Some of the women mentioned fears of experiencing early menopause, but the majority are at this point more concerned with starting their families. The next theme regards family planning and these issues will be discussed.

5.2.1.5 Screening

About half the women in this study are undergoing surveillance for breast cancer, some are actively thinking about having mastectomies, while others are content with the screening and mastectomies are not a decision at this point. These women have discussed mastectomies and may have them eventually.

Sarah, 27, was raised by a single mother who was diagnosed with breast cancer at 42, when Sarah was almost 20. She and her mother are very close and the cancer diagnosis was hard on them both. Her mother's three paternal aunts died in their early 40's or early 50's. While her mother was the first in her generation to have cancer, others soon followed. Three of her mother's first cousins got breast cancer, two at 35 and one at 40. Sarah's mother had bilateral mastectomies and had her ovaries removed and Sarah "couldn't be prouder of her decision". Sarah is actively getting screened at this time and is waiting till she's 30 to decide on a new plan of action.

> At the age of 30 I will re-evaluate if I should continue screening the way I have been (in a screening trial or local hospital), or have a preventive mastectomy. My mom got a preventive mastectomy more than a year after her cancer treatment, after learning of the gene. She is very happy with the results and I have considered doing the same. The age 30 gave me a chance to be pro-active, yet not agonize over the decision.

Sarah admits to being afraid each time she gets screening.

> There is a LOT of anxiety that goes along with this diagnosis. Each time I go in for screening, there is an overwhelming feeling of "I wonder if this time will be the time they find it". At the same time, I feel so grateful to know and be empowered by the fact that I am making INFORMED decisions about my health and screening, rather than blindly wondering if I'm doing the right thing.

Heather's mother also had a diagnosis of breast cancer, but she knew about her BRCA mutation before then and chose to pursue surveillance. The cancer was found early and Heather's mother opted to have a bilateral mastectomy and have her ovaries removed. Heather's mother had an identical twin sister who died from breast cancer in hear early 30's, which prompted genetic testing and lead to the identification of the family mutation. Heather's grandmother and two other aunts also developed breast cancer after her aunt's death. Heather has decided to pursue screening, because it's what her mother did, and at 19 she feels that she is too young to be considering a mastectomy.

> My mom chose increased surveillance, and it is the option I am leaning towards. It was not an easy route (there were many times she had to have biopsies and tests), but when the caught her cancer for the first time, it was in a very early stage and she had a double mastectomy. She didn't have to go through chemotherapy, and she is not cancer-free…My mom has been my biggest influence since she dealt with everything before me. The surveillance worked so well for her, and I agree with her choices and think it will be the best decision for me as well.

Rachel's maternal aunt was diagnosed with breast cancer at 47 and had died by 49. Her grandmother was subsequently diagnosed with breast cancer. Due to her sister's aggressive cancer, Rachel's mother had an oophorectomy at about 39, soon after she was found to carry a BRCA mutation and she had a mastectomy later that year. Rachel, 24, describes herself as being a nervous person, and she distanced herself from her mother's surgeries.

> In retrospect, looking back on it I really distanced myself from my mom a lot, not from her personally but from what she had been going through. She would show all of her friends her surgery and talk about it a lot and I did not like to talk about it very much and I didn't really want to ever look at her mastectomies and reconstruction because I didn't want to think about it that much. The more I thought about it, I do get nervous about it.

After her BRCA testing and adjusting to the results, Rachel has since come to terms with her mother's choices. Rachel is pursuing surveillance, and while she has been thinking about mastectomies, she feels that she will probably wait until 35 to have a mastectomy.

These three women seemed to be influenced by their mothers' decisions. While it appears that two will happily follow their mother's example, it seems that Rachel has had some conflicting emotions in regard to pursuing surgical options.

5.2.1.6 Waiting to Act

Of the women in this study, there are two that appear to be "waiting to act," i.e., deferring on a management decision. This is a possible coping measure that may allow women to avoid thinking about the implications of their test results at the present time. Some women may get their usual surveillance, but not spend a great deal of time thinking through possible options. Others may completely avoid any decisions regarding screening or surgery.

While it may seem like avoidance, Nancy appears to have become stalled regarding her management. She is 26, married, and has two children. Nancy's paternal grandmother had an ovarian cancer diagnosis at 43 and a breast cancer diagnosis at 65 in 2001. Her aunt was diagnosed 6 months later with breast cancer at the age of 31. There have been multiple paternal cousins with diagnoses of breast cancer. Nancy was tested about four years prior to the interview, she had a mammogram and breast exam soon after testing positive, but had not had one since. She explained that she moved four hours away from the city where she had her initial testing and has not looked for a doctor in her area. Nancy is waiting till 30 to decide what to do, although she feels that she is more apt to pursue screening.

> I do feel like I'm waiting. I'm waiting for something to happen to force me to make a decision. Even though I try not to worry, I still do. I worry that I will get cancer, I worry that I could have the recommended surgeries and have a difficult time living with the emotional and physical aftermath. I worry that I'll make the wrong decision and hurt myself and my family. To me it's like knowing you're going to have a car crash and you can see it coming, but the option is to crash into something else, so what do you do? I do feel when I hit the age of 30 I will have to take a long, hard look at what my options are and firmly make a decision…I find the recommended screening difficult because if I dig deep I am afraid. I am afraid of finding cancer and I am afraid of finding nothing – but waiting to one time find cancer.

Another reason Nancy is not having screenings is because her insurance has a high deductible, but feels that she would do screening if there were a research study she could participate in that would make the screening costs minimal. She says that her husband and family try to pressure her to go get screening but she feels that financially it would be a burden, which contributes to her feeling a loss of control.

> I do not feel like I have any control over my present health situation. I feel like I have a ticking time bomb inside of me that I don't know when will explode. I feel like my financial issues take part in my lack of control. I cannot put any more pressure of debt on my family, however, I am in the dark about my own health and the only control I have (screening) is just not possible.

Dana's BRCA mutation also stems from her paternal family. Her father's first cousin had been diagnosed with breast cancer and was found to have a BRCA mutation, as did her daughter. Her paternal grandfather died from cancer where the primary tumor could not be identified. Dana's father decided to get tested and after he was found to be a carrier, she was pressured to test as well. Dana stated that she really did not understand why her father had decided to get tested. She explained that her parents told her to get tested and she did, without carefully considering the implications, and wonders "why I so blindly submitted to it". Now she wishes she waited to pursue testing, but she explained why she did get tested.

> It didn't really occur to me to question [testing]. I guess if they had given me the choice, I still would have done it, because I wouldn't really have been able to think of a good reason why not to. Of course, now that I know, I wish I had waited till I was about 35, since it seems like there's nothing much I can do between now and then except be (most likely needlessly) probed and groped by doctors.

Dana was 28 at the time of her interview and was working on her PhD. Due to her busy schedule, she decided that she would wait until after her PhD was finished (2.5 years) before worrying about making a decision. She was continuing to have screening and was doing what her doctors told her to do, but was not actively making decisions regarding her long term medical management.

While each of these women has put off making decisions about surgeries, they have different motives for this. Nancy has financial problems and combining that with a fear of finding cancer, she has been avoiding screening. Dana feels that there is nothing she can do about testing positive at this point, so she has postponed making a decision.

5.2.2 Theme # 2: Family Planning

A second major theme identified in the interviews was the impact of planning pregnancies and how this has been influenced by testing positive for a BRCA mutation. Due to recommendations for an oophorectomy between the ages of 35-40, these women must first decide whether or not they want to start a family and when, followed by possibly feeling pressured to finish their families early. Similarly, some women felt pressure to begin a family before or at the earliest age of cancer diagnosis in their family.

5.2.2.1 The pressure to start a family at a younger than expected age

A majority of the women in this study discussed how the future need of a premenopausal oophorectomy has affected their reproductive plans. Many women felt the pressure to begin a family earlier than they had planned due to the need to finish their family by 35 and have an oophorectomy. During the interim of waiting for her BRCA result, Melissa had explained her concerns to her then boyfriend, now husband, regarding surgery and feeling the need to start a family earlier.

> I also told [my husband] about my fears and concerns about needing to start a family much sooner than I had originally planned. That I wanted to be pregnant with my first child before the age of thirty, so that I could have a second by 32/33 and then have my ovaries out before I was thirty-five.

Due to a family history of young breast cancer, a few women in the study felt pressure to begin a family early before an age where the threat of breast cancer became salient. Tara is 24 and married and feels that she has a small window for having children due to the young ages of cancer diagnoses in her family.

> Interviewer: If it were a perfect world and let's say you didn't have this mutation, when do you think you would want to have children?
> Tara: 27 or 28
> Interviewer: So this just sort of pushes up the timeline for you?
> Tara: Yeah and I really think, actually I mean I feel like I know enough about, I mean, I am not an expert by any means but I feel like I know enough about the gene mutation and I know enough about my body and about reproduction that I know that I could wait till then. It would be okay waiting till then, however my aunt was 27 when she found her lump so being 24 I feel really limited on the time span for having children.

In a subsequent email interview, Tara further describes the pressure she feels to start a family.

> Hearing all that makes me feel like I need to get pregnant now because I have this ticking time-bomb in my body and I don't know when it's going to go off. My doctor tells me every visit that I need to start a family now. Hearing her say that really makes me feel pressured. Plus, my mom was 31 and my aunt was 27 when they were diagnosed. That makes me feel REALLY pressured.

The BRCA testing has impacted the reproductive choices of these women, thus resulting in them feeling rushed into thinking about when to start a family.

5.2.2.2 Considering starting a family

Even before young women with a BRCA mutation contemplate about when to begin a family, they need to decide whether they want to have children. The majority of women in this study had already decided that they wanted children, but two women were not interested in having children. While Dana had said that she never thought about having children, Claire seems to have only started thinking about children after she tested positive. An especially poignant statement was made by Claire when she decided to not have children and have an oophorectomy at the age of 29, although her diagnosis of PCOS did play an important role in this decision as well.

> I always thought that I'd have children, probably 'cause that's what most people do is get married and begin a family of their own, and my mother absolutely loved babies and couldn't wait to be a grandmother. I can still remember her the day before she died laying in the hospital bed rocking her arms as if she were cradling a baby and pointing to me with a smile. After she died I began to feel that I didn't want kids after all and came to the decision that it was OK to not have children and at the same time felt that intuition deep inside that made me feel that not having children would be best for my health and the rest of my life. I also wanted this mutation to stop with me and not affect another generation.

Many women in the study did discuss their concerns about passing on the BRCA mutation to their children, and this could be related to the hesitation of starting a family or the decision to not start a family.

5.2.2.3 Possibilities of passing on the mutation

Some women discussed that although they may pass the mutation on to their children, they will be able to discuss this with their children and help guide and support them if they test positive. Others suggested that in thirty years when their children were grown there may be better treatments and better forms of prevention. Emily discussed both of these issues in her email.

> I would definitely like to have a child in the next 10 years. Testing positive for the BRCA2 gene has made me consider the possibility of not wanting a child, because if passing the gene along, but then I realized that there are so many options and in 10 years there will hopefully be more. Furthermore, if I do have a child, a daughter, when the time comes I will be able to sit her down and discuss the gene. Also, now knowing so much more about the gene and the surgery I went through, I will be able to educate my children about the possibility of having the gene and how my quality of life is better knowing I won't get cancer because of the mastectomy.

While the majority of women in the study were concerned about the risks to their future children, reproductive techniques to avoid having children with a BRCA mutation were brought up in three different interviews. The reproductive techniques involve in-vitro fertilization, genetic testing of the embryos (PGD) and embryo selection for those that do not have a mutation. Rachel appeared to strongly contemplate PGD, and she explains her reasoning as to why she would consider this technology.

> I have been talking about this with my mom a lot lately, whenever we do talk about it, about the future related to me and the gene and I told her that, you know some people say you definitely should consider doing in-vitro so then I can select which eggs don't have the gene…I think I am more likely to do the in-vitro and I think I am more likely to select an egg that doesn't have it (the gene mutation)…I feel like if you can prevent the disease , and its not a disease, but if you can prevent the mutation then I would do anything I could to prevent it because I would honestly feel really, really guilty. Like lets project 40-50 years from now and my daughter finds out she has the gene and she gets cancer at 35 and she is sick or dies, I would be like, okay, well she wouldn't be alive at all, but I could have never had a child with cancer.

Thus, in addition to confronting the prospect of having to plan families at a younger age, these women also appear to contemplate the implications of passing on the mutation to their children.

5.2.2.4 Cancer and pregnancy

A few of the young women in this study acknowledged a fear of developing cancer during a pregnancy and being unable to treat it until after the birth of their child. Another concern of these women was having a diagnosis of breast cancer before becoming pregnant and the possibility of being unable to conceive after the chemotherapy and radiation treatments.

In Beth's case, she felt that she was next in line to develop cancer and was very concerned about a diagnosis before she began her family or during a pregnancy. This was a major deciding factor for her opting to have a prophylactic mastectomy.

> The timing of this decision [to have children earlier] was based largely in part of wanting to preserve my fertility. I thought about it this way: my maternal aunt was diagnosed with breast cancer at 34, my sister was diagnosed at 32 and at the time I was 30. Knowing this information I assumed that my time was limited before I got the same diagnosis of breast cancer (if I had the gene mutation). I knew that if I were to get diagnosed with breast cancer chemotherapy would likely kill my ovaries and therefore wouldn't be able to conceive. I haven't had any children and do want them, about the absolute worst thing that could possibly happen was to get pregnant before I had the surgery and then find a lump during the pregnancy and then have to decide what to do at

> that point. And finally, if I was to get diagnosed with breast cancer my husband and I wouldn't be able to adopt (for something like 5 or 7 years) if all of our fertility treatments failed. So based on all of these scenarios the only logical thing to do was to get the surgery now and hopefully avoid all of the above!

A couple of the women who had or were considering mastectomies expressed concerns regarding the inability to breast feed once they had mastectomies. Jessica talked about the possibility of postponing a mastectomy until after she had a child so she could breast feed.

> Having a mastectomy means, at this age at least, means I may not be able to breast feed, which really, really upsets me. I think it upsets me more than it upsets my sister. That is the one thing that I'm kind of holding onto. I may try and push my surgery further because of that very reason.

Some of the women who shared their fears of developing cancer during pregnancy or before starting a family, had a family history of this type of situation. These women had aunts who were diagnosed during a pregnancy and subsequently died, or had aunts that were diagnosed after having started their families and were unable to have more children after the chemotherapy.

5.2.3 Other themes identified in the analysis

Aside from the two themes discussed in this paper, there were also other themes identified in the interviews. Many other studies about BRCA carriers focus on women older than 30, and these women tend to be married. Over half the women in this study were single or dating, and three had already undergone prophylactic mastectomies. Some interview questions focused on dating and disclosing their BRCA mutations, for instance when these women told a man about their cancer risks. Of the single women who have had mastectomies and reconstruction, some described how they feel about intimacy, in regard to their self esteem and

body image. One or two women discussed explaining to men, with whom they would be intimate, about their breasts.

Another theme that arose during the interviews was when it came time to telling their friends about their getting tested or deciding on surgery. Some women discussed friends that completely did not understand the situation, and have since stopped talking about anything related to the BRCA mutation. Some friends did not react in expected manners, and this caused frustration in these women.

Many of the women used their management choices to develop a sense of control. Because they didn't know when cancer would happen or even if it happened, they pursued screening to catch it early or surgery to prevent it from happening. Because there is no consensus on mastectomies in carriers, a majority of women received varied opinions from medical professionals regarding their breasts. This was found to be a frustrating circumstance and a few of the women lost faith in the medical community.

In addition to the screening or surgical forms of management, many women in this study discussed lifestyle changes that they have made to try and reduce their perceived risks to develop cancer. Such lifestyle modifications included exercising more, loosing weight, quitting smoking, eating more vegetables or less processed food, and even becoming a vegetarian. A possible explanation for these lifestyle changes could be applied to the participants' need to feel a sense of control over reducing their cancer risks.

6.0 DISCUSSION

This current study represents one of the few that investigate how management choices in young BRCA positive women are influenced by their family experiences. Additionally, this study investigates the topic of family planning and reproductive concerns, which has received little attention in the literature. A brief summary of the results is that management choices of these BRCA positive women are greatly impacted by their experience of cancer in close family members. These women are confronted with having to make reproductive decisions at an earlier age than they would if they did not have a BRCA mutation, and many feel rushed into having their families early. Among the many themes identified in the analysis, the two themes focused on in this study were identified in the majority of interviews. The first theme was related to how the cancer in these BRCA families influenced the management decisions of young BRCA carriers. The second theme identifies how reproductive choices have been influenced by having a BRCA mutation and their management choices. This study has also demonstrated how personal and family experiences with cancer influences management choices.

In the following section, the study's findings are compared to previous research. This is followed by what aspects of this study may be found useful by health professional. Finally the limitations of the study are discussed, ending with recommendations for future studies.

6.1 STUDY FINDINGS IN COMPARISON TO PREVIOUS WORKS

6.1.1 Theme # 1: Management Choices and the Impact of Cancer in the Family

Perceived closeness of cancer can influence a woman's management choices. Some of the women felt that their risks were higher at certain ages, typically associated with the age of the youngest diagnosis in the family. Kenen et al. (2003b) suggested that the closer in age a woman is to a cancer diagnosis in a loved one, the more salient that risk becomes. The current study showed that women who felt that cancer was imminent were more likely to have a prophylactic surgery. This has also been described by Statan et al. 2008, who found that women are more likely to have a prophylactic surgery because of their concern for cancer.

After her sister's battle with breast cancer, Beth got genetic testing and had a mastectomy. While Beth was the only participant that had a sister with breast cancer, insight into Tara's family through her interview provided a similar view of reactions to a sister's diagnosis. The diagnosis of breast cancer in Tara's mother and aunt within 6 weeks of each other prompted the other two unaffected sisters to have bilateral mastectomies, eventually followed by oophorectomies. Beth underwent a PM because she felt that she was next, and in learning about the actions Tara's aunts took, one could infer that the aunts may have felt they were next as well. Cancer related worries are significantly higher in women who have a sister with breast cancer, one that was diagnosed less than three years previously and in women who were involved in the cancer process with their sisters (van Dooren et al, 2005). Metcalfe et al. (2008) had found that women that had sisters with breast cancer were twice as likely to have a PM. Similarly, Metcalfe et al. (2008) found that women with either a sister or mother with

ovarian cancer were more likely to have a BSO, but having a sister or mother with a breast cancer diagnosis was not associated with a BSO.

Another aspect to how management choices are influenced by perceived closeness of cancer is how distantly removed (both genetically and personally) the cancer is from an individual. Genetic distance implies third or fourth degree relatives, while personally distant implies that the relationship is not associated with closeness. This is likely the case in the two women identified to be 'waiting to act'. In both cases, the BRCA mutation comes from the paternal side of the family. In the case of Dana, the mutation was identified in a first cousin, which is both genetically and possibly personally distant, resulting in her feeling annoyed and frustrated about carrying a BRCA mutation. Conversely, in the case with Nancy, she has two second-degree relatives who had cancer but she seemed to be avoiding any healthcare management decisions. Previous research has suggested that women who do not have close relatives with cancer are less likely to experience emotional distress and are less likely to feel vulnerable (Foster et al, 2002).

Just over half the women in this study were undergoing surveillance, whether they were contemplating surgery or not. Although ages were not specified, Uyei et al. (2006) found that over half of the unaffected BRCA positive women opted for surveillance as opposed to prophylactic surgery. Tara's family was discussed previously, and in contrast to the generation above hers, she states that a mastectomy is her last resort. While she clearly acknowledges how cancer has impacted her family, the cancer diagnoses in her mother and aunt occurred when she was very young and she may have been too young to remember the details of their illness and remembers them as healthy for the majority of her life. This may be why Tara's comments contrast the findings of Foster et al. (2002) who found that individuals felt more vulnerable when

a close relative had a diagnosis of cancer. In Tara's case, she may have been too young at the time, and so she feels less vulnerable. Foster et al. (2002) also found that feelings of vulnerability increase with the nearing of a 'target age', usually when a relative was initially diagnosed with cancer. Tara makes note of this during her interview, and while it was three years away, it could influence her feelings of vulnerability in the near future. In addition, every female relative that Tara knows has survived breast cancer and she has seen the physical effects of mastectomies in her mother and aunts. Foster et al (2002) suggested that women who felt that breast cancer could be treated successfully had relatives who were long time survivors or who felt that early detection and treatment had improved over time, which could explain Tara's feelings about having a mastectomy.

6.1.2 Theme # 2: Family Planning

Most of the women in this study stated that at some point in their future they would have a BSO. Having a BSO was appeared to be a more definite decision than having a PM in this study and has been documented in other studies (Friebel et al, 2007; Wainberg & Husted, 2004; Di Prospero et al, 2001; Staton et al, 2008). While many of the women in this study felt rushed into thinking about their fertility at a younger age, there is no additional data to support this. The majority of studies the author identified regarding prophylactic oophorectomy generally limited the ages of participants to those 30 and older (Friebel et al, 2007; Uyei et al, 2006), made no distinction between age groups (Wainberg & Husted, 2004; Di Prospero et al, 2001), or did not focus on the aspect of having children (Staton et al, 2008). Smith et al. (2004) did analyze the fertility intentions of male and female carriers and non-carriers of a BRCA mutation who were

still able to have children. Questionnaires were initially given a few weeks after the BRCA test results were received and additional questionnaires were distributed during the two subsequent years to determine the differences in fertility plans between those who were and were not carriers. They found that male carriers were more likely to want additional children than those who were not carriers. However, female non-carriers were much more likely to want additional children than carriers. Overall, it was found that BRCA mutation carriers were 5.5 times more likely to have changed their family plans after receiving their results than non-carriers.

Women in this study expressed concern about passing on the BRCA mutation to their children. While one of these women decided to not have children in part based on mutation status, the others were not deterred from wanting children. This was supported by Staton et al (2008) who found that the great majority of women were at least frequently concerned with passing on the BRCA mutation to their children.

Of additional importance, the concept of PGD or IVF was not introduced by the interviewer during the interviews, and three participants brought it up independently. The two studies (Staton et al, 2008; Menon et al, 2007) that focused on use of PGD for BRCA1/2 found that 13-14% of individuals would consider PGD for BRCA1/2 during their next pregnancy. Menon et al. (2007) found that the majority of their participants viewed PGD for BRCA1/2 to be acceptable.

Based on their family history, it is not surprising that some women expressed concern about developing breast cancer during or soon after pregnancy. Andrieu et al. (2006) found no significant difference in breast cancer risk for parous versus nulliparous BRCA mutation carriers, however among parous women each additional birth reduced breast cancer risk by 14%; although this risk reduction is restricted to women over 40 years old. Age at first-full term

pregnancy was found to play a role in reduction of breast cancer risk. Women with a BRCA2 mutation were at a reduced risk if they had their first full-term pregnancy before the age of 20 years, while women with a BRCA1 mutation that had their first full-term pregnancy at a later age appeared to have a lower risk for breast cancer. Additionally, breast feeding for over a year is associated with a reduced risk for breast cancer. The author was unable to identify previous studied that addressed similar findings in female carriers.

6.2 IMPLICATIONS FOR GENETICS PROFESSIONALS

The information gleamed this study may allow genetic counselors and other genetics professionals to have a broader understanding of the management choices made by BRCA mutation carriers. In addition, the results might give genetic counselors a better appreciation of possible motivations behind management decisions made by unaffected women who come for counseling because their mother had breast cancer. People who have had close interactions with someone diagnosed with cancer can have strong and seemingly unrealistic fears about personal vulnerability to that particular cancer. These feelings of vulnerability can lead to desire for drastic methods of prevention when the cancer risks may not be significantly increased, as in cases of sporadic breast cancer in a family. A genetic counselor would be useful in this situation to explain the actual risks and offer some management advice.

As was discussed in theme 2, young women with BRCA mutations may feel forced at an early age into planning their reproductive futures. Clinicians working with these women need to be aware of this, and should at some point address the relevant issues with each woman. Reviewing the risks of cancer during pregnancy can allay some concerns, or listing the pros and

cons of breastfeeding may help a woman make an important management decision. A reminder that the majority of women have their first babies before the age of 35 may diminish a woman's sense of urgency in making a particular reproductive decision.

While PGD has been used to select against embryos with devastating diseases, such as Duchenne muscular dystrophy or Tay-Sachs, using PGD for adult onset, incompletely-penetrant diseases is a newer and more controversial method that genetics professionals now encounter. Even though the technique is expensive, discussing PGD and its ethical considerations with a young BRCA mutation carrier may be helpful, especially if they are concerned about their future children.

6.3 STUDY LIMITATIONS

Two possible limitation of this study are participant recruitment and selection bias. Although this bias is generally unintentional, it can occur in how participants were recruited and may be biased towards individuals with personality traits that make them more likely to participate in this type of study. Firstly, it involved recruitment on the FORCE website which could potentially select for particular individuals who tend to be open or proactive about their cancer risks because they are either visiting the site for information regarding management options or to participate in the online support community. Secondly, because this study involved in-depth interviews, it may have attracted those individuals who are more willing to discuss their management choices and families. Also, since this study is voluntary, only individuals who are motivated to respond will, while in contrast those people who are unwilling to discuss their BRCA experiences will avoid this particular study method.

Another limitation of this study was the variation in the level of details. In keeping with grounded theory methodology, the interviews were guided by issues discussed by the participants. Variation in details depended on what each participant wanted to focus on, and not necessarily on what this researcher was studying.

6.4 RECOMMENDATIONS FOR FUTURE STUDIES

Future expansions on this data could include a follow-up interview, perhaps five years after the initial interview, to determine what these women have done with regard to their management and whether they have children or have changed their reproductive decisions.

A new qualitative study could also be conducted that is a prospective multi-interview study on young women who are getting BRCA testing. The initial interview would occur either before the testing or before the result disclosure, a second interview could be conducted a couple of months after receiving the results, another interview about a year after having the results and the last interview at least three years later. This research would enable the researcher to identify how risk perceptions change, especially in regard to nearing an age when they believe their risks greatly increase. This approach would also follow the management options these women chose and whether they differed from the previous interviews, and answering the question if something pushed those women who were waiting to act. Changes in family interactions from both before and after the testing could also be incorporated.

Future studies could also be performed on individuals who tested negative for a BRCA mutation to determine how their reproductive decisions might be influenced by a negative test result and how their decision making processes might differ from individuals with a BRCA

mutation. Men could also be included in future studies because their reproductive choices may be impacted by a positive result for a BRCA mutation.

APPENDIX A

Listed below are the names and ages of the study participants, their ages and their current management choices.

Table 1. Participants' Ages and Management Choices

NAME	AGE	MANAGEMENT
Claire	30	BSO
Beth	30	PM
Emily	24	PM
Melissa	26	PM scheduled
Dana	28	Screening
Sarah	27	Screening
Tara	24	Screening
Amber	24	PM
Heather	19	Screening
Rachel	24	Screening
Nancy	26	Screening
Kylie	18	Screening
Jessica	25	Screening
Jane	28	PM

APPENDIX B

INSTITUTIONAL REVIEW BOARD LETTER

University of Pittsburgh

Institutional Review Board

3500 Fifth Avenue
Ground Level
Pittsburgh, PA 15213
(412) 383-1480
(412) 383-1508 (fax)
http://www.irb.pitt.edu

Memorandum

TO: LAURA SCHNIPPER

FROM: CHRISTOPHER RYAN PHD, Vice Chair

DATE: 6/4/2008

IRB#: PRO08040303

SUBJECT: The influence of family history on prophylactic surgery in young women who are BRCA positive.

The above-referenced project has been reviewed by the Institutional Review Board. Based on the information provided, this project meets all the necessary criteria for an exemption, and is hereby designated as "exempt" under section 45 CFR 46.101(b)(4).

Please note the following information:

- If any modifications are made to this project, please contact the IRB Office to ensure it continues to meet the exempt category.
- Upon completion of your project, be sure to finalize the project by submitting a termination request.

Please be advised that your research study may be audited periodically by the University of Pittsburgh Research Conduct and Compliance Office.

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