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Re-contacting Cancer Genetic Counseling Patients: Expectations of Patients and Physicians

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by

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Abstract

The landscape of cancer genetic counseling and testing is rapidly evolving. Genetic testing technology is improving, management guidelines are evolving, and genetic testing options are expanding. These frequent updates to the components of cancer genetics have increased the complexity of managing patient care over time. In particular, this raises questions on the duty to re-contact patients as new information becomes available. This study explored healthcare providers' duty to re-contact through the interests and expectations of patients, including which circumstances warrant re-contacting, which healthcare provider is responsible for re-contacting the patient, and the preferred method of re-contacting. Physicians' opinions on whether or not patients should be updated as well as the person responsible for updating were also explored. To answer the questions set forth in this study, we surveyed patients undergoing genetic counseling for a hereditary cancer condition and physicians who work with cancer genetic counselors. The study was limited by low response rate from patients, so no statistically significant results could be confirmed. However, both groups indicated re-contacting patients with updates was desirable and assigned a high level of responsibility to providers for delivering these updates to patients. The majority of patient participants believed the duty to keep patients informed fell primarily on the genetic counselor and preferred the genetic counselor to initiate contact. In contrast, physician participants indicated genetic counselors, referring physician, and a shared responsibility between these two providers most frequently as the responsible parties.

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Chapter 1: Background

1.1 Hereditary Cancer Syndromes

After age, a positive family history of cancer is the most significant risk factor for developing the disease (Armstrong, Eisen, & Weber, 2000). It is estimated that up to 10% of all cancers are hereditary, meaning there is a germline mutation in a cancer susceptibility gene that confers an elevated cancer risk (van der Groep, van der Wall, & van Diest, 2011). Oftentimes germline mutations in these genes result in a predictable phenotype allowing clinicians to assess an individual's likelihood for developing specific cancers. Genetic testing can be performed to identify and diagnose individuals with hereditary cancer syndromes, and personalized management can be implemented to reduce the lifetime cancer risk and cancer-related mortality (Feliubadaló et al., 2013).

Since genetic testing for hereditary cancer syndromes first became commercially available, our understanding and knowledge of hereditary cancers has grown. As of 1996, around a dozen cancer predisposing genes had been identified (Nelson, 1996). To date, germline mutations in over 49 genes have been associated with an increased cancer risk (Hall, Forman, Pilarski, Wiesner, & Giri, 2014). Each of these genes predisposes individuals to particular malignancies when a pathogenic mutation is present. In each case, the likelihood for developing cancer varies, with some mutations conferring up to an 80% or higher lifetime risk for developing the disease.

The majority of genetic testing for hereditary cancer syndromes relates to breast and colon cancers. Hereditary breast cancer has been attributed to mutations in multiple

genes. The first major gene associated with the development of breast cancer was *BRCA1*, which was linked to a region on chromosome 17 through linkage analysis studies in 1990 and subsequently sequenced in 1994 (Hall et al., 1990). A second gene, named *BRCA2*, was linked to chromosome 13 in 1994 using the same technique, then later sequenced in 1995 (van der Groep et al., 2011). Mutations in either of the *BRCA* genes are responsible for a condition known as BRCA-Related Breast and Ovarian Cancer syndrome (NCCN, 2016), or formerly as Hereditary Breast and Ovarian Cancer syndrome (HBOC), which predisposes carriers to breast, ovarian, prostate, and pancreatic cancers. Inherited mutations in these genes confer up to a 50-85% lifetime risk of breast cancer in females and an 8% lifetime risk of breast cancer in males. The lifetime risk of developing ovarian cancer in females can be as high as 40%, while the likelihood of developing prostate cancer in males is also increased (Shiovitz & Korde, 2015). Additionally, the probability of developing pancreatic cancer is elevated in both sexes, especially with mutations in *BRCA2*.

Along with *BRCA1* and *BRCA2*, pathogenic mutations in four other genes (*TP53*, *PTEN*, *STK11*, and *CDH1*) confer a high risk for breast cancer (Shiovitz & Korde, 2015; Weischer, Bojesen, Tybjoerg-Hansen, Axelsson, & Nordestgaard, 2007). Similar to the *BRCA* genes, each of these is part of a distinct clinical syndrome.

Mutations in the *TP53* gene are causative for Li-Fraumeni syndrome (LFS). This condition predisposes individuals to breast cancer, soft-tissue sarcomas, bone cancer, brain tumors, leukemia, adrenocortical carcinomas, and other forms of cancer (Nelson, 1996). Childhood cancers are also a common feature and occur in around 44% of carriers by the age of 18 years. In adulthood, the lifetime risk of developing breast cancer for

females with this syndrome is around 80%, and the chance of developing a soft tissue sarcoma is around 30% in both sexes (Bougeard et al., 2015). There is also a 40% chance of multiple primary tumors in individuals with LFS, which has been partly attributed to the individual's sensitivity to chemotherapy and radiation used to treat the first tumor (Bougeard et al., 2015).

PTEN Hamartoma Tumor syndrome (PHTS), also known as Cowden syndrome, is a condition associated with a higher incidence of breast, follicular thyroid, endometrial, and renal cancers, with the lifetime risks being as high as 80%, 35%, 28%, and 33%, respectively. There is an additional risk for colorectal cancers (9%) and melanoma (6%), and the risk of gastrointestinal hamartomas is increased (Tan et al., 2012; Ngeow, Sesock, & Eng, 2015). Peutz-Jeghers syndrome (PJS) is caused by a germline mutation in the *STK11* gene. Individuals with this condition are at an increased risk for developing a variety of gastrointestinal tumors, and females have a 50% chance of developing breast cancer (Hearle et al., 2006; van der Groep et al., 2011). Mutations in the *CDH1* gene cause a condition called Hereditary Diffuse Gastric Cancer syndrome (HDGC). Women with this condition have up to a 50% chance of developing breast cancer while the risk of gastric cancer is as high as 70% in males and 56% in females (Hansford et al., 2015; Stuckey & Onstad, 2015).

In addition to these high-risk gene mutations, moderate risk genes have recently been introduced into clinical cancer genetic testing. These genes, *ATM*, *BRIP1*, *PALB2*, and *CHEK2*, each confer an estimated two-fold increase in female breast cancer risk and are considered to have moderate penetrance (Shiovitz & Korde, 2015). Together with the higher penetrance genes, mutations in these genes are responsible for the majority of

hereditary breast cancer cases in which a genetic cause can be identified (Shiovitz & Korde, 2015).

Lynch syndrome, formerly known as Hereditary Non-Polyposis Colorectal Cancer syndrome (HNPCC), is one of the more common hereditary colon cancer syndromes. Individuals with Lynch syndrome are more susceptible to colorectal, endometrial, ovarian, stomach, and other cancers. This condition is caused by mutations in *MLH1*, *MSH2*, *MSH6*, *PMS2*, or *EPCAM*. Depending upon the gene in which the mutation is found, individuals with Lynch syndrome have anywhere from a 10-80% lifetime risk of developing colon cancer, a 15-60% lifetime risk of endometrial cancer, a 1-13% lifetime risk of stomach cancer, a 1-25% lifetime risk of ovarian cancer, and an elevated risk for hepatobiliary tract, urinary tract, small bowel, brain, sebaceous neoplasms, and pancreatic cancers (Barrow et al., 2009; NCCN, 2015).

An elevated colon cancer risk is a feature of hereditary polyposis syndromes as well. Familial Adenomatous Polyposis syndrome (FAP) carries close to a 100% lifetime risk for colon cancer and an increased risk for duodenal, pancreatic, and papillary thyroid cancers. There is an additional risk for hepatoblastomas and medulloblastomas during childhood (Hampel, Bennett, Buchanan, Pearlman, & Wiesner, 2015). FAP is caused by mutations in the *APC* gene. Juvenile Polyposis syndrome (JPS) is another hereditary polyposis syndrome with a 40% to 50% lifetime risk for colon cancer. This condition, which is caused by mutations in the *SMAD4* and *BMPR1A* gene, also raises the risk for stomach cancer up to 21% and notably increases the risk for other gastrointestinal cancers (NCCN, 2015; Hampel et al., 2015).

Other genes, beyond those mentioned above, have been linked to hereditary cancer. The features and associated cancer risks for some of these conditions are well-defined, while the implications of other pathogenic mutations are less appreciated. However, research on the genetics of inherited cancer is ongoing, and clinical understanding of hereditary cancer is emergent. The future of hereditary cancer genetics will look different than the current landscape described.

1.2 Management

For many of the currently well-characterized hereditary cancer syndromes, guidelines are in place for mutation-based cancer screening and management purposes. These recommendations are often based on the consensus statements of the National Comprehensive Cancer Network (NCCN), which has established guidelines on many of the well-defined hereditary cancer syndromes such as BRCA-Related Breast and Ovarian Cancer syndrome, LFS, PHTS, PJS, HDGC, Lynch, FAP, and JPS (NCCN, 2015). In accordance with our expanding knowledge of cancer genetics, NCCN has also started to develop guidelines defining which moderate risk genes warrant further consideration regarding protocols for high-risk breast screening and/or risk-reducing surgeries (NCCN, 2016).

The results of genetic testing can significantly impact patient care. For example, in women with a mutation in either *BRCA1* or *BRCA2*, NCCN (2015) recommends beginning breast surveillance at an earlier age. In the general population within the United States, women are screened for breast cancer by annual mammograms beginning at 40 years of age. Comparatively, NCCN recommends women with a *BRCA1* or *BRCA2* mutation begin either annual breast MRIs or annual mammograms between the ages of

25-29 years (2015). Screening is further increased in female mutation carriers who are 30 years of age or older to include alternating between mammograms and breast MRIs every six months. NCCN also recognizes that for some women with a mutation, the more appropriate choice may be to opt for a prophylactic bilateral mastectomy.

Surveillance for ovarian cancer in women with a mutation in *BRCA1* or *BRCA2* can be performed by transvaginal ultrasounds or serum CA-125. However, these screening options are poor tools for the detection of ovarian cancer. The most recent NCCN guidelines recommend against screening for ovarian cancer in favor of a risk-reducing bilateral salpingo-oophorectomy (BSO), typically performed between 35 and 40 years of age or upon completion of child bearing (NCCN, 2016). An additional benefit of a BSO is that it reduces the risk of breast cancer by 50% in women with this condition if performed prior to menopause (NCCN, 2016).

Lynch syndrome is another example of a hereditary cancer syndrome in which well-established management guidelines have been developed. NCCN (2015) recommends individuals with this condition begin colonoscopy screenings at the age of 20-25 years. These should be repeated every one to two years to screen for colorectal cancer. Additionally, a prophylactic hysterectomy and BSO is a risk-reducing option that should be discussed with women with Lynch syndrome who have completed childbearing (NCCN, 2015).

NCCN guidelines have not established testing criteria and/or management recommendations for every cancer predisposing gene, and it is less clear how to manage pathogenic mutations in some of the moderate risk genes. This does not nullify or decrease the utility of testing for mutations in such genes since in many cases, the results

may still be clinically actionable (Desmond et al., 2015). One specific example of this includes the *BRIP1* gene. As recently as March 2016, NCCN has come out with new recommendations for the consideration of risk-reducing BSO in women who carry a mutation in this gene. However, there is currently no defined criteria for *BRIP1* testing (NCCN, 2016) which is currently offered as part of a multigene panel test. Evidence-based guidelines are an important aspect of genetic testing and are meant to characterize genes in which mutations are clinically actionable. Therefore, these guidelines can support the need for genetic testing, especially to health insurance companies (Domchek, 2015).

Additionally, family history can impact cancer risk assessment and recommendations for clinical care. When there is a known familial mutation, family history-based recommendations might not be appropriate or necessary for all family members. Similarly, it is important to recognize the significance of identifying individuals with negative testing results in whom recommendations may be impacted based on family history alone.

In conjunction with consensus statements from NCCN, guidelines from other professional societies, such as the American Cancer Society (ACS) and the American College of Obstetricians and Gynecologists (ACOG), can be used to determine a high-risk breast screening protocol or the frequency of colon screening for example (Smith et al., 2016; Printz, 2016; Smith et al., 2015). Some differences exist between the recommendations from different societies. For example, there are minor variations in the age at which to begin screening, the frequency of screening, and other aspects. Overall

however, recommendations are generally consistent. Most importantly, guidelines are updated on a regular basis to keep pace with the ever-changing clinical environment.

1.3 Evolution of Genetic Testing Technology

Genetic testing was first introduced into clinical practices in the mid-1990s. The earlier approaches involved sequence analysis (Lynch, Snyder, Shaw, Heinen, & Hitchins, 2015) by Sanger sequencing to detect deleterious point mutations, small deletions, and small insertions within one to two single genes. Sanger sequencing has long been considered the gold standard for genetic testing and has been the traditional technology used for the detection of DNA-based mutations. However, since genetic testing for hereditary cancer syndromes first became commercially available, there has been exponential growth in both the methodology with which we test for gene mutations and our knowledge about their implications.

Although Sanger sequencing still has a prominent role in the laboratory, other techniques have since been developed to detect a wider array of deleterious gene mutations. Two such techniques, called quantitative multiplex PCR of short fluorescent fragments (QMPSF) and multiplex ligation-dependent probe amplification (MLPA) have been applied to identify large genomic deletions and duplications within the *BRCA1* gene. Using QMPSF, Casilli et al. (2002) identified two previously unreported mutations. The first novel mutation was a large deletion of exons 1-22. This individual had a personal history of breast and ovarian cancer and two affected first-degree relatives: one with breast cancer, the other with ovarian cancer. The other novel mutation, a deletion of exons 15-16, was detected in an individual with a family history of breast and ovarian cancer. In addition to these large deletions, three genomic rearrangements were detected

in this study. Another study by Hogervorst et al. (2003) analyzed 805 families with a history of breast and/or ovarian cancers and found pathogenic *BRCA1* mutations in 144 families using Sanger sequencing. The remaining 661 families with no identified mutations were then analyzed for large deletions using MLPA, and mutations in five additional families were detected.

Genomic rearrangements were originally believed to comprise a small percentage of the total number of cancer-predisposing mutations. Studies such as the ones by Puget et al. (1999) and Montagna et al. (2003) aimed to address the mutational spectrum and frequencies of the *BRCA1* gene, and these studies had variable results. In the study by Montagna et al. (2003), large genomic rearrangements accounted for more than 30% of the *BRCA1* mutations in an Italian cohort, while the Puget et al. (1999) study observed the proportion of large genomic rearrangements accounted for 8% of *BRCA1* mutations in a cohort of American families. From these and other similar studies, it is concluded that the proportion of genomic rearrangements responsible for any given hereditary cancer syndrome is dependent upon the gene and population in question, and there can be significant genetic variation from one population to the next.

The strategies for the detection of pathogenic mutations have continued to evolve. The latest technology currently being integrated into commercial genetic testing is next generation sequencing (NGS). NGS has the ability to potentially detect variants missed by traditional methods (D'Argenio et al., 2015), is more cost effective, and has a quicker turn-around time. Unlike traditional molecular testing methods, NGS is capable of analyzing multiple genes at one time, which has enabled genetic testing to evolve into multigene panel tests. This is significant, as other genes beyond *BRCA1* and *BRCA2* are

implicated in hereditary cancer syndromes, and additional cancer susceptibility genes with overlapping phenotypes are emerging. In fact, breast cancer is an overlapping feature of multiple hereditary cancer syndromes as discussed earlier (Doherty, Bonadies, & Matloff, 2015).

Risk assessment and management may be significantly impacted when newer technology and additional genes are incorporated into genetic testing. For example, in a study by Walsh and colleagues (2006), breast cancer families with prior negative *BRCA1* and *BRCA2* test results were analyzed for large genomic arrangements in the *BRCA* genes, as well as for mutations in three other genes related to hereditary breast cancer: *CHEK2*, *TP53*, and *PTEN*. Researchers observed that 17% of participants with no previously detected mutations in either *BRCA1* or *BRCA2* actually had a pathogenic mutation in one of the analyzed genes, including 12% with large genomic rearrangements in a *BRCA* gene. The remaining 5% had a mutation in *CHEK2*, *TP53*, or *PTEN*.

The study by Walsh et al. (2006) demonstrates the limitation of single gene analysis by Sanger sequencing alone and supports including deletion and duplication testing with single gene analysis. It also provides evidence for the utility of a multigene panel during risk assessment and genetic counseling. This testing approach is consistent with the National Society of Genetic Counselors (NSGC) practice guidelines (Berliner, Fay, Cummings, Burnett, & Tillmanns, 2013), which recommend that risk assessment and genetic counseling for individuals with a personal and/or family history of breast cancer should include the consideration of other hereditary cancer syndromes and genes in which breast cancer is a component. In fact, multigene panel testing that includes around two dozen different genes "represent a substantial (>40%) increase diagnostic

yield of risk-associated mutations compared to *BRCA1*/*2* testing alone" when BRCA-Related Breast and Ovarian Cancer syndrome is suspected (Desmond et al., 2015, p. 949). Furthermore, multigene panel testing results are "likely to change clinical management" in a substantial amount of individuals, making the results of testing clinically actionable (Desmond et al., 2015, p. 943). Individuals with strong family histories of cancer who underwent genetic testing while it was in its early stages and found no causative genetic mutation may benefit from a multigene panel.

1.4 Clinical Genetic Testing Timeline

The availability of genetic testing for hereditary cancer syndromes over the years warrants further consideration when reviewing the changing landscape of cancer genetics in the clinical setting. The evolutionary trajectory of testing has been influenced by both the scientific achievements mentioned above and political disputes, with the latter proving to be a limiting factor on the advancement and accessibility of testing. This is mainly attributed to Supreme Court rulings in the early to mid-1990s, which granted a series of patents covering human genes to various companies. This most significantly relates to patents that were granted over the *BRCA1* and *BRCA2* genes to a company called Myriad Genetics Inc., which gave them exclusive rights over the *BRCA* genes, mutations in these genes, and the diagnostic tests in which these mutations could be identified (Gold & Carbone, 2010).

Historically, genetic testing for hereditary cancer syndromes focused heavily on breast cancer because of its high prevalence in the general population and availability of families for research protocols. Myriad's patents allowed them to become the first company to market and benefit from commercial genetic testing of *BRCA1* and *BRCA2*.

In late 1996, the company introduced three principal diagnostic tests: 1) Comprehensive BRACAnalysis, which sequenced the entire *BRCA1* and *BRCA2* genes, 2) Single Site BRACAnalysis, used for detecting a specific familial mutation, and 3) Multisite three BRACAnalysis, which was designed to detect three specific mutations which have been observed at a higher frequency in the Ashkenazi Jewish population (Gold & Carbone, 2010).

Myriad's initial tests were not able to identify all mutations in the *BRCA1* and *BRCA2* genes, specifically large genomic rearrangements (Gold & Carbone, 2010). To keep up with technological advancements, the company came out with a newer version of their Comprehensive BRACAnalysis test in 2002, which incorporated the five most common large rearrangements in the *BRCA1* gene (Myriad Genetics, 2002). This test was later replaced by Myriad's BRACAnalysis Large Rearrangement Test (BART) in 2006, which can detect large genomic rearrangements in both *BRCA1* and *BRCA2*.

As research and technology progressed, the implication of other genes beyond *BRCA1* and *BRCA2* in the development of hereditary cancer began to receive more attention. Testing approaches began to shift from single gene testing to the simultaneous analysis of multiple genes with the development of NGS. The first widely available multigene panel test for hereditary breast cancer was introduced in 2012 by Ambry Genetic Laboratories (Lundy, Forman, Valverde, & Kessler, 2014), enabling the possibility of analyzing multiple genes at once for the first time. However, at this time Myriad still held exclusive rights over *BRCA1* and *BRCA2* genetic testing and as a result, multigene panel tests offered by other laboratories could not include these genes on their panels.

Opinions surrounding the ethics of gene patenting had been circulating since the patents were first issued. Societies such as the American College of Medical Genetics (ACMG) expressed concerns that gene patents "limited the accessibility of competitively priced genetic testing services and hinder[ed] test-specific development of national programs for quality assurance" (ACMG, 1999, p. 237). These concerns were not unwarranted. One leading example of this relates to the availability of comprehensive testing for the *BRCA* genes. Deletion and duplication analysis was not routinely included in all *BRCA* testing until 2013 despite the introduction of BART in 2006 (Myriad Genetics, n.d.). BART had to be ordered separately and was not typically covered by insurance (Shannon et al., 2011). At this time other commercial laboratories were standardly offering deletion and duplication analysis for all genes that were sequenced. However, due to the gene patents, patients seeking *BRCA* testing did not have a choice in laboratory.

Following a few years of turmoil and controversy, the Supreme Court overturned its ruling on gene patents in 2013, stating that patents could not be obtained on DNA segments because they are a product of nature (Cook-Deegan & Niehaus, 2014). This has enabled other laboratories to perform *BRCA1* and *BRCA2* testing and to include these genes on their hereditary cancer panels. This, along with the advent of NGS, has led to a decrease in the cost of genetic testing. Furthermore, it is suspected that the cost of testing has an impact on guideline stringency. A decrease of cost could have a trickle down affect allowing more people to have access to genetic testing (Meldrum, Doyle, & Tothill, 2011). Therefore, someone who did not meet genetic testing criteria based on earlier guidelines may do so now or in the future.

1.5 Duty to Re-contact

The above scenarios illustrate the ever-changing landscape of what genetic testing can accomplish. However, in some situations these advancements in testing also raise ethical, legal, and practical concerns. In particular, this raises questions on the duty to re-contact patients as new information becomes available. The duty to re-contact is defined in the genetics arena as the "ethical and/or legal obligation to re-contact former patients about new genetic information" (Otten et al., 2015). In cancer genetics, situations in which the duty to re-contact patients may become a concern include but are not limited to 1) when a hereditary predisposition had been suspected, but no diagnosis had been made using previous testing techniques, and a new diagnostic test has become available (Fitzpatrick, Hahn, Costa, & Huggins, 1999); 2) when a change in cancer screening and management guidelines occurs; and 3) when insurance guidelines change to allow for additional genetic testing.

The only policy statement addressing the duty to re-contact genetics patients was issued by ACMG in 1999 (ACMG, 1999). According to the statement, the referring physician, primary care provider, and patient should receive a written summary of the appointment from the genetics provider, which should include the recommendation to inquire about updates in the future. Additionally, it states the primary care provider is responsible for encouraging the patient to inquire about updates and re-contact genetics when needed. Therefore, the patient needs to be aware of his or her duty to re-contact. No other policy statements on the matter have been made by the ACMG or any other professional society.

In many situations, it is not practical to re-contact all former patients. Barriers such as the amount of staff time required to re-contact every single patient ever seen at that particular clinic and tracking down patients who have changed address or telephone number are often cited as limitations. Furthermore, in the genetics arena the service provider often acts as a consultant, and the relationship between provider and patient is not intended to be longitudinal (Fitzpatrick et al., 1999).

Previous research on this topic has found that patients with colon cancer who underwent genetic counseling desired highly personalized updates (Griffin et al., 2007). The vast majority, 90% of those surveyed, indicated that it was the healthcare provider's responsibility to keep patients informed. The provider that was most frequently expected to keep patients updated was the genetics provider (65%), followed by the primary care physician and gastroenterologist. When asked how often patients should be re-contacted, participants were evenly divided among three categories: "only when new discoveries are made that pertain directly to the re-contacted patient," "when any new discoveries are made," and "regularly, even if no new discoveries are made."

Although, as previously discussed, statements and research on the duty to re-contact exists, there has been no attempt to refine these statements and add to the research following the Supreme Court ruling on gene patents. Since this time, the prices of testing have dropped. NGS has emerged as the prominent technology, and large panel tests are becoming routine in hereditary cancer clinics. For these reasons, it is worthwhile to readdress the duty to re-contact former genetics patients, especially from a hereditary cancer standpoint.

1.5.1 Ethical Perspective. In hereditary cancer genetic counseling, it is not currently a standard of care to re-contact patients when there is new and relevant information or when newer diagnostic testing options become available. Many arguments from different ethical viewpoints, both in favor of and against re-contacting, have been made in the literature. The arguments focus mainly around three principles in healthcare: respect for patient autonomy, beneficence (do good), and nonmaleficence (do no harm) (Otten et al., 2015).

It has been argued that providing information to patients promotes autonomy by allowing these individuals to make informed decisions about their healthcare. By this argument, re-contacting patients when new and relevant information becomes available is indicated. In fact, many genetics providers believe that although it is not practical, re-contacting is desirable since it provides patients with the best care (Fitzpatrick et al., 1999), which falls under the principle of beneficence. However, respect of autonomy also includes the patient's right to remain uniformed (Hunter, Sharpe, Mullen, & Meschino, 2001). In some scenarios re-contacting may actually have the potential to cause harm to patients, which goes against the principle of nonmaleficence. For example, the decision about whether or not to undergo genetic testing for a hereditary cancer syndrome is made based on information provided at the time of the patient's appointment, and he or she may not desire to readdress the topic at a later point. In this situation, re-contacting a patient several years following an appointment may cause renewed anxiety for an issue that had already been laid to rest (Hunter, 2001).

Overall, there is a general consensus that there are both potential benefits and harms to re-contacting former patients. Information affects people differently. The type

of information being provided and the timing of such information likely influence the benefit or harm (Otten et al., 2015). Because of the potential emotional and psychological impact re-contacting may have, this is an avenue that would benefit from further exploration.

1.5.2 Legal Perspective. When examining the duty to re-contact former patients from a legal perspective, liability is a major concern. One argument supporting the practice of re-contacting former patients is that providers cannot be held liable for negligence for not providing updated information that may be medically relevant or actionable (Otten et al., 2015). In the past, providers have been held liable for failure to disclose subsequently discovered information about risks and side effects of medications and medical devices to former patients. However, there is currently no legal precedent requiring a complete disclosure of future knowledge pertaining to genetics (Hunter et al., 2001). Other arguments regarding the legal obligation to re-contact former patients state liability as a concern. In this argument, genetics service providers would be vulnerable to malpractice lawsuits if this duty was not fulfilled. Therefore, this obligation might not be in the best interests of the service providers (Otten et al., 2015). Furthermore, re-contacting may also go against a patient's desire or right to remain uniformed.

1.5.3 Current Landscape of Re-contacting. There is currently no consensus among professionals about whether or not patients should be re-contacted and, if so, how this should be accomplished. The only published guideline to date is the ACMG policy statement referenced previously (ACMG, 1999). A recent study aimed to address whether or not re-contacting was occurring and how it was being implemented in a population of genetic service providers in the United Kingdom (Carrieri et al., 2016). The majority of

participants in this study indicated they had experience with re-contacting but did not do so on a regular basis. They also did not routinely obtain consent from patients prior to re-contacting. The participating genetic service providers were most likely to re-contact patients if the information was viewed as clinically actionable. This included the availability of new diagnostic tests, new management guidelines, and reclassification of previous test results. Although the majority indicated they had updated patients with new information at some point, few stated their clinics had developed a system for re-contacting. Additionally, some participants stated they contacted the primary care provider with updated information while others contacted the patient directly.

No consensus exists between providers regarding which person is responsible for keeping patients informed (Otten et al., 2015). Cancer genetic evaluations typically involve one to three visits with a genetic counselor within a short period of time and include a risk assessment prior to testing (Riley et al., 2012). Long-term follow-up appointments are unusual, and no long-term patient-provider relationship is expected. This is different than other specialties where patients may get re-evaluated for the same condition on a regular basis. Especially in cancer genetics, it is unclear when a re-assessment needs to be made and by whom. Current healthcare practices are moving in the direction of interdisciplinary teams working together to provide patient care. This has further led to the question of whom, if anyone, bears the responsibility to re-contact patients. Is it the primary care physician who has an ongoing relationship with the patient; the referring physician who may only be working as a temporary specialist in the patient's care; or the genetic counselor who may be acting only as a consultant? Or is it

the patient's responsibility for maintaining the patient-provider relationship and actively inquiring about updates that affect medical management?

Many questions remain unanswered pertaining to the duty to re-contact patients regarding new genetic information, services, or insurance coverage. These questions are practical, legal, and ethical in nature. The purpose of the current study is to explore some of these questions surrounding the duty to re-contact, particularly through the interests and expectations of patients receiving genetic counseling and testing for hereditary cancer syndromes and the attitudes of physicians involved in their care. The intention is to elicit patient opinions on which circumstances warrant re-contacting, which healthcare provider should re-contact the patient, and the preferred method of re-contacting. An additional goal is to determine if there are common themes among patient and physician perspectives. To achieve this goal, this study will also survey physicians on their opinions.

Chapter 2: Manuscript

Re-contacting Cancer Genetic Counseling Patients: Expectations of Patients and Physicians[1]

2.1 Abstract

The landscape of cancer genetic counseling and testing is rapidly evolving. Genetic testing technology is improving, management guidelines are evolving, and genetic testing options are expanding. These frequent updates to the components of cancer genetics have increased the complexity of managing patient care over time. In particular, this raises questions on the duty to re-contact patients as new information becomes available. This study explored healthcare providers' duty to re-contact through the interests and expectations of patients, including which circumstances warrant re-contacting, which healthcare provider is responsible for re-contacting the patient, and the preferred method of re-contacting. Physicians' opinions on whether or not patients should be updated as well as the person responsible for updating were also explored. To answer the questions set forth in this study, we surveyed patients undergoing genetic counseling for a hereditary cancer condition and physicians who work with cancer genetic counselors. The study was limited by low response rate from patients so no statistically significant results could be confirmed. However, both groups indicated re-contacting patients with updates was desirable and assigned a high level of responsibility to providers for delivering these

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updates to patients. The majority of patient participants believed the duty to keep patients informed fell primarily on the genetic counselor and preferred the genetic counselor to initiate contact. In contrasts, physician participants indicated genetic counselors, referring physician, and a shared responsibility between these two providers most frequently as the responsible parties.

2.2 Introduction

The most significant risk factor for developing cancer excluding age is a positive family history of the disease. It is estimated up to 10% of all cancers are hereditary, meaning there is a germline mutation in a gene that confers an elevated cancer risk (van der Groep et al., 2011). In certain cases, the likelihood of developing cancer is greater than 80%. Genetic testing can have a significant impact on mutation carriers since management recommendations can be personalized to reduce cancer risk and cancer-related mortality (Feliubadaló et al., 2013). Mutation-based recommendations for screening and management purposes are made according to consensus guidelines developed by professional societies such as the National Comprehensive Cancer Network (NCCN), which formulate these guidelines based on current literature and professional opinions, and the guidelines are updated on an annual basis. However, the landscape of cancer genetics is rapidly evolving. The last few decades have seen an exponential growth in our understanding and knowledge of hereditary cancers, and an increasing number of cancer susceptibility genes are emerging. Furthermore, advancements in genetic testing technology have improved the sensitivity and reliability of these diagnostic tests (D'Argenio et al., 2015). While these factors have led to improved patient

care, frequent updates to the components of cancer genetics increases the complexity of caring for patients over time.

Genetic testing for mutations in cancer susceptibility genes was first incorporated into clinical practices around 1995 (Nelson, 1996). Testing at this time primarily focused on hereditary breast cancer and employed a single gene analysis strategy. Current genetic testing trends have evolved to include a broader approach when attempting to identify mutations in cancer susceptibility genes. Next Generation Sequencing (NGS) is the latest technology being widely integrated into clinical practices due to its ability to analyze multiple genes simultaneously and its improved detection rate. NGS has allowed the introduction of multigene panel tests, which is significant, as an increasing number of genes are being implicated in hereditary cancer syndromes, and additional cancer susceptibility genes with overlapping phenotypes are emerging.

Multigene panel tests were introduced into the clinical setting in 2012 (Lundy et al., 2014). At the time panel tests were introduced, laboratories were limited by which genes could legally be included on their cancer panels. This was a direct result of gene patents that were granted to various laboratories in the early to mid-1990s (Gold & Carbone, 2010). While these patents were upheld, patients who desired genetic testing for certain hereditary cancer conditions were required to go through the laboratory that owned the patents. In 2013, patents on human genes were overturned by the Supreme Court (Cook-Deegan et al., 2014). This has enabled other laboratories to include previously patented genes on their hereditary cancer panels, meaning patients and their genetics healthcare providers now have more choices on laboratory when ordering testing of cancer susceptibility genes.

Now that genetic testing technologies have improved and testing options have expanded and become more affordable, individuals with strong family histories of cancer who underwent genetic testing while it was in its early stages and found no causative genetic mutation may benefit from further testing. Genetic testing that examines a greater number of genes with a higher detection rate is beneficial for providing more personalized care since it has the potential to significantly impact risk assessment and management (Desmond et al., 2015). However, in some situations updates to the components of cancer genetic testing also raise ethical, legal, and practical concerns.

With continued advancements in genetic technology, the duty to re-contact patients as new information becomes available has been a major question plaguing clinicians. The duty to re-contact is defined in the genetics arena as the "ethical and/or legal obligation to re-contact former patients about new genetic information" (Otten et al., 2015). In cancer genetics, situations in which the duty to re-contact patients may become a concern include but are not limited to 1) when a hereditary predisposition had been suspected, but not discovered using previous testing techniques, and a new diagnostic test has become available (Fitzpatrick et al., 1999), 2) when a change in cancer screening and management guidelines occurs, and 3) when insurance guidelines change to allow additional genetic testing. Because of the potential emotional and psychological impact re-contacting may have, this is an avenue that would benefit from further exploration.

Additionally, current healthcare practices are moving in the direction of interdisciplinary teams working together to provide patient care. This has led to the question of who, if anyone, bears the responsibility to re-contact patients. Is it the

primary care physician, who has an ongoing relationship with the patient; the referring physician, who may only be working as a temporary specialist in the patient's care; or the genetic counselor, who may be acting only as a consultant? Or is it the patient's responsibility for maintaining the patient-provider relationship and actively inquiring about updates that affect medical management?

Previous research on this topic has attempted to address these and other questions. Overall, re-contacting patients with updated knowledge is deemed desirable by genetic service providers (Fitzpatrick et al., 1999) and is something that is currently being practiced, albeit on an irregular basis (Carrieri et al., 2016). Genetic service providers have indicated the responsibility of staying informed about advancements in genetics is shared between the patient and the genetic service provider as well as other healthcare professionals (Fitzpatrick et al., 1999). In a policy statement published by the ACMG, the primary care provider was indicated as the main liaison between patient and genetics provider due to the ongoing nature of their relationship, although the primary care provider was also to encourage the patient to independently inquire about updates as needed (ACMG, 1999). However, in a study which surveyed patients with colon cancer, participants indicated that it was the healthcare provider's responsibility to keep patients informed. These patients also indicated that they desired highly personalized updates (Griffin et al., 2007).

The purpose of this study was to explore the duty to re-contact, particularly through the interests and expectations of patients receiving genetic counseling and testing for hereditary cancer syndromes, and the attitudes of physicians involved in their care. The intention was to elicit patient opinions on which circumstances warrant re-

contacting, which healthcare provider should primarily be responsible for re-contacting the patient, and the preferred method of re-contacting. An additional goal was to determine if there were common themes among patient and physician perspectives.

2.3 Materials and Methods

2.3.1 Participants. The study was targeted at adults who had undergone genetic counseling for a hereditary cancer condition and physicians who work with genetic counselors as either referring physicians or as part of tumor boards.

Individuals were referred to a genetic counselor for a suspicious personal and/or family history of a hereditary cancer condition. Any patient who met with a cancer genetic counselor at the University of South Carolina between November 2015 and February 2016 and at the Greenville Hospital System between January 2016 and February 2016, either for an initial visit or for a follow-up results appointment, were invited to participate in the study if they met the inclusion criteria. The inclusion criteria for participation included patients who were 18 years of age or older, English speaking, and individuals with recognized competence to read and understand the written material. Undergoing genetic testing was not a requirement for participation.

Physicians associated with Palmetto Health Richland Hospital and Palmetto Health Baptist Hospital, both in Columbia, SC, were invited to participate in the study. The following physician specialties were targeted: oncology, surgery, obstetrics/gynecology (OB/Gyn), and primary care. These specialties were chosen since they are common referral sources to cancer genetic counseling.

2.3.2 Study Methods. Participation in this study entailed completing a questionnaire. The patient questionnaires were different from questionnaires provided to physicians.

Patients who were eligible to participate were informed of the study at the end of their genetic counseling session and were given an invitational letter (See Appendix A) by their genetic counselor. At that time, participants were also given a print copy of the questionnaire (See Appendix B) to be taken home and returned to our center via a self-addressed postage-paid envelope.

The patient questionnaire consisted of nineteen questions designed to assess participants' opinions regarding re-contacting. A section of Likert scale questions was used to assess patients' responses on which circumstances warrant re-contacting. Scenarios for re-contacting included the availability of newer diagnostic test options, when new research indicated a change in lifetime risk for developing cancer, when updates to testing results occurred, and following changes or updates to medical management or insurance guidelines. These Likert scale questions used a 1 to 4 scale of Strongly Disagree to Strongly Agree. Multiple choice questions were used to elicit opinions on which healthcare provider is primarily responsible for re-contacting the patient, the desired frequency and time period of re-contacting, and the preferred method of being updated. Basic demographic information was collected regarding the participants' age range, sex, reasons for being referred to cancer genetic counseling, whether or not they had had genetic testing, and which provider referred them to genetic counseling.

Print copies of the physician questionnaire were handed to every person that attended two breast and one gastric tumor boards. Tumor boards are multidisciplinary conferences where ongoing cancer cases are presented to establish and confirm treatment plans between various physician and non-physician specialists. Print copies were also

handed to all members at an obstetrical case conference, which are similarly attended by physician and non-physician specialists. Questionnaires at all meetings were completed and returned on site.

The physician questionnaire (See Appendix C) consisted of five multiple choice questions designed to assess the opinions of physicians regarding which circumstances, if any, warrant re-contacting and which healthcare provider is primarily responsible for updating patients with new information. Demographic information was collected regarding the participants' specialty, whether or not they had ever referred patients to a cancer genetic counselor, and whether or not they had ever personally updated patients with new information.

No personal identifying information was collected for either group of participants. Approval for this research study was obtained through the Institutional Review Board, Office of Research Compliance, of the University of South Carolina, Columbia, SC, in November, 2015 and through the Institutional Review Board, Office of Research Compliance, of the Greenville Health System, Greenville, SC, in January, 2016.

2.3.3 Data Analysis. Descriptive statistics including response frequencies and percentages were analyzed for both groups using SPSS, Version 23.0.0.2.

2.3.3.1 Patients. Demographic questions collected information from the patients regarding their sex, age range, whether or not genetic testing had been performed, referral process to genetic counseling, and personal and/or family history of cancer.

Descriptive statistical analyses were performed to provide data on demographic questions and response frequencies to the section of Likert scale questions inquiring about which circumstances warrant re-contacting. Response frequencies and percentages

were also calculated for multiple choice questions pertaining to how often and for what length of time participants indicated a desire to be re-contacted, the provider responsible for updating patients, and their preferred method of re-contacting. Additional comparisons were made between participants with a personal history of cancer with those who were unaffected to evaluate for any differences between the two groups with respect to participants' desired frequency of re-contacting and the time period in which they desired updates. Tables and charts were created to illustrate response frequencies and percentages to various questions.

2.3.3.2 Physicians. Demographic information regarding physician specialty, referral history to cancer genetic counseling, and previous experience with updating patients with new and relevant genetic information was collected from the physicians.

Response frequencies and percentages were provided for demographic information and multiple choice questions regarding physician opinions on 1) whether or not patients should be re-contacted; and 2) which provider was primarily thought to be responsible for re-contacting patients.

2.3.3.3 Patient and Physician Comparisons. A chi-square analysis was performed between patient and physician responses to the question regarding which provider is primarily responsible for updating patients to assess for statistically significant differences between the two groups. The response from each participant was assigned to one of five categories: genetic counselor, physician, a shared responsibility, patient, or unsure. Response frequencies for each of the five categories were recorded and differences between the two groups were analyzed.

2.4 Results

2.4.1 Patients. A total of 73 patients were invited to participate in the study. Eight participants completed and returned the questionnaire, yielding an 11% response rate. The majority of participants were female. Ages ranged from the 18-29 group to 70 years or older. Patients were referred to cancer genetic counseling for a personal and/or a family history of cancer, and referral sources came from a variety medical specialists, as well as one self-referral. For specific information on demographics, refer to Table 2.1.

All eight participants reported a desire to be contacted in the future regarding updates to the components of genetic testing and counseling discussed during their genetic counseling appointment. Patients were asked how frequently and for how many years following their initial appointment they desired to be updated with relevant information. When asked about the preferred frequency, 38% (n = 3) of patients indicated a desire to be update every six months and 63% (n = 5) stated a desire to be updated once a year. For the most part, they were similarly divided about the time period in which they desired updates, with 50% (n = 4) stating they desired to be kept updated for one year following their initial appointment and 38% (n = 3) indicating they desired updates for ten years. The remaining participant (n = 1) indicated a desire to be updated for five years following her initial appointment with a genetic counselor.

Responses to these questions were also compared between patients with a personal history of cancer (n = 3) and those who had never been diagnosed (n = 5). The small sample size limited exploration through chi-square analysis, but descriptive statistics are provided. The affected group was evenly divided between a desire to be contacted for a time period of either one, five, or ten years following their initial

appointment. In the unaffected group, 60% (n = 3) said they desired contact for one year following their initial appointment while 40% (n = 2) said they desired updates for a period of ten years. When asked about the desired frequency, 33% (n = 1) of the affected patients and 40% (n = 2) of unaffected patients indicated an update frequency of every six months. Among those who stated a desire for updates once a year, 67% (n = 2) were affected and 60% (n = 3) were unaffected. See Figure 2.1 and Figure 2.2.

Seven of eight patient participants, or 88%, believed the duty to keep patients informed fell primarily on the genetic counselor. The participant that did not select the genetic counselor as the responsible provider stated any knowledgeable person was an acceptable source of new information. When asked about maintaining the patient-provider relationship, all participants stated they preferred the healthcare provider to initiate contact with updates, instead of the patients contacting the provider themselves to inquire about new information. The preferred methods of notification by participants included phone call (n = 4), letter (n = 3), and email (n = 1). None of the participants indicated they desired to be updated by follow-up genetic counseling appointments or during appointments at high-risk clinics.

Seven of eight patient participants, or 88%, indicated they either agreed or strongly agreed with being updated when a newer diagnostic test becomes available, and when changes in cancer risk, test result status, or management guidelines occur. One participant selected strongly disagree to all of these questions. For the statements on updates to insurance guidelines and consenting at the initial appointment to future updates, 75% (n = 6) of participants either agreed or strongly agreed. The question participants agreed with least often pertained to being contacted on a regular basis to

provide updates on personal and/or family history. Thirty-eight percent (n = 3) of participants indicated they disagreed or strongly disagreed with this question while 63% (n = 5) either agreed or strongly agreed. Participants' responses to all of these questions are shown in Table 2.2.

2.4.2 Physicians. A total of 44 physician questionnaires were completed and returned. Of these questionnaires, two were omitted because they were completed by someone other than a physician, leaving a total of 42 physicians who participated in the study. The majority of physicians specialized in either OB/Gyn or surgery. Table 2.3 provides the physician demographics for the participants enrolled in the study.

Of the physicians surveyed in this study, 83% (n = 37) indicated they had referred patients to cancer genetic counseling at some point. The 17% (n = 7) of physicians who indicated they had never referred to genetic counseling included two pathologists, two out of the three radiologists, and one each from surgery, primary care, and OB/Gyn.

Physicians were asked whether or not patients who were previously seen for genetic counseling should be re-contacted when new and relevant genetic information becomes available, as well as whose primary responsibility it was to update patients. Eighty-six percent (n = 36) stated that patients should be re-contacted with updates, although the indications for re-contacting varied. The remaining 14% of participants (n = 6) who did not explicitly agree with re-contacting patients stated they were uncertain about whether or not re-contacting should occur. None of the participants indicated that patients should not be re-contacted when new information becomes available. The most frequent responses to whose primary responsibility it is to keep patients updated were genetic counselors (n = 16), referring physician (n = 10), and a shared responsibility

between these two providers (n = 9). See Table 2.4 below for specific information on physicians' responses to these questions.

Physician participants were asked whether or not they had ever updated patients with new information, and 67% (n = 28) indicated they had while 33% (n = 14) participants had not. Among those who had never re-contacted patients were three surgeons, two pathologists, two radiologists, six OB/Gyns, and one family medicine physician.

2.4.3 Patient and Physician Comparisons. Both the patient and physician groups were asked which provider was responsible for re-contacting patients with updated information. Patient and physician responses to this question are shown in Figure 2.1. While 88% (n = 7) of patient participants reported they expected updates to come from the genetic counselor, only 38% (n = 16) of physicians indicated the genetic counselor as the provider primarily responsible for re-contacting. Using chi-square analysis, comparison of patient responses to physician responses did not appear to be statistically significant, p = .139, but we cannot confirm this due to low patient sample size.

Physician responses regarding whose primary responsibility it is to update patients with new information were further categorized by specialty. Physicians in the following specialties more frequently indicated genetic counselors as the sole responsible provider: oncologists, surgeons, family medicine/primary care physicians, and radiologists. See Table 2.5 for more details.

2.5 Discussion

In this study we explored patient and physician opinions on which circumstances warrant re-contacting and who is the primary party responsible for providing new

information as it becomes available. We also explored the method of re-contacting preferred by patients.

2.5.1 Patient Responses. The patient group had a low response rate, despite the fact patients seemed interested when informed of the study. It is possible some patients intended to complete the questionnaire but did not get around to it. Additionally, it is possible that patients who answered "no" to the first question decided not to return the survey. The first question asked if they would like to be contacted in the future regarding updates to the components of genetic testing and counseling that were discussed. If they selected "no," they were asked to stop the survey. It is possible these patients did not return the questionnaire because they believed their answer made them ineligible to participate.

All eight patients who participated in the study stated they wished to be re-contacted in the future regarding updates to the components of genetic testing and counseling that were discussed at their appointment. The majority ($n = 6$) indicated they would be open to discussing their preference for future contact with the provider at their initial session. However, attaining consent for future, long-term contact is not a current standard of practice. A recent study which surveyed genetics providers in the United Kingdom found the majority did not routinely acquire permission to re-contact, citing a lack of resources to offer this service and concerns about raising the expectations of patients (Carrieri et al., 2016). While re-contact by a genetics provider seems to be preferred by patients, it is not currently widely done and may not be a practical task. One strategy for assisting in the practicality aspect may be developing technology, perhaps

based in an electronic medical record, to overcome these barriers traditionally associated with re-contacting patients.

The majority of participants in this study either agreed or strongly agreed with being updated for all the circumstances provided on the questionnaire. The circumstances participants responded to most favorably included being re-contacted with updates pertaining to the availability of newer diagnostic tests, changes in lifetime cancer risk based on new research, updates to test results, and changes in management guidelines such as how often to be screened and surgery recommendations. These circumstances were also listed among the most common reasons for re-contacting by genetics providers since these reasons were viewed as clinically actionable (Carrieri et al., 2016). It is likely that our patients also felt re-contact is best served by items that may have immediate effect on their medical management which was likely thoroughly discussed as part of the genetic counseling they received.

The question participants most strongly disagreed with pertained to the desire to be re-contacted on a regular basis to update providers to any changes in their own or their family's health. Interestingly, 75% ($n = 6$) of participants stated they desired to be re-contacted if insurance changed in a way that would allow for additional testing options that were unavailable at the time of their initial appointment. Even if guidelines for insurance do not change, updating the clinic with additional information on family members' medical histories or on newly diagnosed cancers is one way to potentially qualify for additional testing. It is possible that patients might not realize the importance of informing providers of such information. The National Society of Genetic Counselors (NSGC) notes in a position statement, "Collection and annual review of the FHH [Family

Health History] allows for risk assessment and can aid in diagnosis, decisions about health care, screening, genetic and other test selection, and interpretation of test results, in addition to the identification of at-risk relatives" (NSGC, n.d.) Patients need to be aware that changes in personal and family history can be a clinically actionable item. Perhaps, there is a role for genetic counselors and other health professionals in calling attention to this important fact. Another explanation could be that patients perceive updates to history as only potentially leading to a clinically actionable conclusion. Together, these results suggest patients desire highly personalized updates that are clinically actionable at the time of the update and are less interested in re-contact for other reasons.

Although all participants stated a desire for future updates, one participant strongly disagreed to being contacted for all the circumstances provided on the questionnaire. One possible explanation for this may have been the situations in which she would have desired re-contacting were not included on the questionnaire. It is also possible that she agreed with the notion of re-contacting patients in a general sense but did feel not this was relevant in her particular circumstance. This patient was between the age of 50-59 years and was referred to genetic counseling by her primary care physician based on her family history of breast cancer. An opportunity for an open-ended response might have provided more insight into her preferences.

Participants in this study indicated a desire to be re-contacted for a time period ranging from one to ten years following their initial genetic counseling appointment. The time period in which patients wish to be followed may be influenced by personal history. We found participants who were unaffected were less likely to indicate a desire for updates for further out than a year following their initial appointment. However, small

sample size limited exploration of this question, and we cannot claim any statistically significant results. Unfortunately, this study was unable to weigh the impact of a positive or negative test result on desired time period for future contact. This might be an area for future study.

A frequency of updates once every six months or one year was most appropriate according to participants. No one desired less frequent contact such as once every five or ten years. Two of the three participants in this study who stated they wanted updates as often as every six months were unaffected. A qualitative study surrounding why they wanted updates so frequently would be an informative supplement to our study. For unaffected patients, frequency of contact may be associated with closeness to an affected relative. For affected patients, the amount of time since cancer diagnosis may significantly influence the frequency with which they desire updates. For example, patients in the middle of treatment may desire more frequent updates due to perceived or actual relevance to their treatment and ongoing care.

Participants had a strong preference against in-person updates compared to updates via phone, email, or letter. No one indicated a desire to be updated during a follow-up genetic counseling appointment or during a high-risk cancer surveillance appointment. Perhaps participants did not want to be updated at a future genetic counseling appointment because it is inconvenient to schedule another appointment amongst busy lives. It is less clear as to why patients would not desire updates during regular high-risk cancer surveillance appointments. It is possible patients prefer to receive this information from the genetic counselor instead of the provider at the high-risk clinic.

It is also possible that many of our surveyed patients do not participate in a high-risk clinic, and thus, they do not see the relevance in this answer.

When asked whose primary responsibility it was to update patients with new information, participants were given the choice between genetic counselor, the physician who referred them to genetic counseling, or an option to provide their own answer. All patients agreed genetic counselors play an important role in updating patients, and all but one stated they expected updates to come from the genetic counselor. For the two participants referred by surgeons, it would make sense that they would prefer to be re-contacted by the genetic counselor instead of the referring physician since they would be unlikely to have an ongoing relationship with their surgeon. However, even when participants were referred by providers in which they are likely to have an ongoing relationship with (e.g., primary care physician, OB/Gyn, and gastroenterologist), the majority of patients preferred to be updated by the genetics provider over the physician. This could indicate trust in genetics professional, and a preference for specialized individuals.

2.5.2 Physician Responses. The majority of physicians in this study reported they had referred patients to a cancer genetic counselor at some point. However, it is possible those who referred may have been more likely to respond to the survey than those who have not referred. Nevertheless, this may still suggest the physicians included in this study value genetic counselors as non-physician medical specialists.

It was not surprising that both pathologists in this study were among the seven physicians who indicated they had never referred to cancer genetic counseling since pathologists typically do not have direct interaction with patients. It is also less common

for radiologists to refer even though they are involved in cancer care, as the referral usually comes from a specialist more involved in directing the patient's management following genetic testing. Surgeons and OB/Gyns are common sources of referrals. It is possible the surgeon that had never referred to genetic counseling in this study was a general surgeon and did not specialize in cancer care or was a surgeon new to practice. Additionally, it is within a physician's scope of practice to order genetic testing, so it is also possible the physicians that had never referred were ordering testing in their clinic instead of referring. It is unknown whether the genetics knowledge or awareness of the surveyed physicians had an impact on their referral patterns.

Overall, physicians in this study believed patients should be re-contacted when new and relevant genetic information becomes available and that it is the responsibility of the genetic counselor, referring physician, or a shared responsibility between these two providers. Consistent with their responses, most physicians stated they had experience with updating patients. However, the extent of these updates is unknown. The study surveying genetics providers in the United Kingdom found the majority of participants had re-contacted patients, although fewer claimed to have done so on a regular basis (Carrieri et al., 2016).

In our study, 33% (n = 14) of physicians, including three surgeons, two pathologists, six OB/Gyns, and one family medicine physician had never re-contacted patients. Again, it is not surprising that the surgeons and pathologists indicated they had never updated patients, since surgeons do not have an ongoing relationship with patients and pathologists may not have any patient interaction. It is more surprising that 29% of the OB/Gyns that were surveyed claimed to have never updated patients, while 71% of

physicians in this specialty indicated that patients should be updated. Additionally, one of the OB/Gyns and one of the surgeons included in this group of physicians who had never re-contacted patients also stated that the provider responsible for updating patients was the referring physician. Both of these physicians indicated they had referred to cancer genetic counseling at some point. It is possible these two physicians had never considered the duty to re-contact prior to participating in the study, but this disconnect warrants further investigation.

2.5.3 Patient and Physician Comparisons. All patients and the majority of physicians surveyed indicated that patients should be updated when there is new information. Both patients and physicians assigned a high level of responsibility to the providers for updating patients. Eighty-six percent of physicians assigned this duty solely to providers, while 5% claimed the responsibility should be shared between providers and patient. Only 2% (n = 1) stated it was the patient's responsibility to inquire about updates.

We were interested in comparing the percentage of patients who indicated genetic counselors as the provider primarily responsible for re-contacting patients to the percentage of physicians indicating likewise. All patient participants indicated a desire for the genetic counselor to be involved, either solely or as a shared responsibility. Some of the physician participants (n = 11) indicated the sole responsibility was on the physician. A small patient sample size prevented us from demonstrating that our responses were statistically significant, although it does not appear to be trending in this direction. We expect that a larger sample will help clarify answers to the goals set forth in this study.

The ACMG (1999) policy statement regarding the duty to re-contact genetics patients states there is a shared responsibility between genetics service providers, other healthcare professionals, and patients; however, the statement highlights the primary care provider as an important liaison between the patient and the recommendations of the genetic provider. Through their survey of physician and PhD geneticists and genetic counselors, Fitzpatrick et al. (1999) concluded that there is a shared responsibility between providers and patients to remain knowledgeable of updates. The differences between their participant population and that of this study may explain the discrepancy between findings in this and Fitzpatrick et al.'s (1999) study, since we surveyed a variety of physician types and did not limit our participants to genetic service providers.

Both the ACMG policy and the Fitzpatrick et al. (1999) study support a shared responsibility, acknowledging that physicians need to be providing regular updates to the patients. Combined with the feelings of our physicians in the study, we can point out the potential discrepancy between patients' feelings and that of their providers. The patients surveyed in this study suggested more interest in being updated by their genetic providers whereas physicians placed less responsibility on the genetics providers.

Initial data from our small patient sample supports a previous study conducted by Griffin et al. (2007) which found patients desired a longitudinal relationship with their providers and to be re-contacted when advancements in cancer genetic medicine occurred. Participants also stated it was the healthcare provider's responsibility to keep patients informed, with the genetics provider being most frequently selected as the provider expected to update patients.

Although physician participants in this study assigned a high level of responsibility to the provider for updating patients, there was no consistency among physicians as to which provider this responsibility fell upon. If all the providers involved in the care of a particular patient assume updates are being provided by another professional, then the patient may inadvertently receive no updates from any of his or her providers.

Study Limitations

Small patient participant sample size limited the types of quantitative analyses that could be performed and limited the statistical power. Low response rate could have been the result of confusion surrounding the first question where patients were asked to stop the survey if they did not wish to be contacted in the future regarding updates to the components of genetic testing and counseling discussed. If this were indeed the case, our population could be skewed towards those who desire re-contacting, and therefore be a misrepresentation of the larger cancer genetics patient population. Clarification of this question would be needed in the future. One possible avenue would involve collecting questionnaires while still in the clinic rather than by mail. We would also like more information across physician specialties.

Future Research

Qualitative studies, and even longitudinal quantitative studies, would be of great value to explore different factors that may potentially influence a patient's desire to be re-contacted in the future with updated information. Some specific areas of future exploration include how an individual's personal history of cancer, or lack there of, affected their desire to be re-contacted. This could also be explored in the context of

individuals or families with negative test results versus those with positive or uncertain results. A next step for this study could include patient focus groups to refine some of the questions based on the data collected from this study. We would also like to explore what type of updated information physicians are presenting to patients. This could determine the level of involvement required by genetic counselors when considering re-contacting patients.

2.6 Conclusions

This study has implications for the field of genetic counseling, as well as for other professions involved in cancer treatment, high-risk cancer surveillance programs, and the longitudinal care of patients. It has helped shed light on the expectations of individuals undergoing genetic counseling and testing for hereditary cancer conditions regarding their desire to remain informed of advancements in patient care. Similar to findings in previous studies, we found that patients desire highly personalized updates that are perceived as being clinically actionable and place the responsibility of acquiring updated knowledge primarily on the genetics provider. Likewise, we found physicians in specialties that commonly refer to cancer genetic counseling believe patients should be kept informed, and place the responsibility of updating on healthcare providers in general. However, there is no consensus on which providers are responsible for fulfilling this duty. Furthermore, the only guidelines that currently exist which attempt to address this issue may be outdated or not common knowledge among providers following the rapid advancements, accessibility, and uptake of genetic testing. Our study provides some initial, albeit limited, support of an update to these guidelines, considering our patients' point of view.

Table 2.1 Patient Demographics (*N* = 8)

Variable	*n*	Response	(%)
Age	1	18-29	(13%)
	1	30-39	(13%)
	1	40-49	(13%)
	2	50-59	(25%)
	2	60-69	(25%)
	1	70 or older	(13%)
Sex	7	Female	(88%)
	1	Male	(13%)
Cancer Status	3	Affected	(38%)
	5	Unaffected	(63%)
Referring Physician	1	Oncologist	(13%)
	2	Surgeon	(25%)
	1	Gastroenterologist	(13%)
	1	OB/Gyn	(13%)
	2	Primary Care	(25%)
	0	Radiologist	(0%)
	0	Pathologist	(0%)
	0	Maternal Fetal Medicine	(0%)
	1	Self-referred	(13%)

Percentage totals may not equal 100% due to rounding

Table 2.2 Patients' Level of Agreement with Reasons for Re-contacting (*N* = 8)

Statement	Patient Responses		
		n	(%)
I would like to be contacted if my genetic testing results came back negative (no mutation was found), and better testing options become available.	Strongly agree	5	(63%)
	Agree	2	(25%)
	Disagree	0	(0%)
	Strongly disagree	1	(13%)
I would like to be contacted if new research indicates there has been a change in my lifetime risk for developing cancer.	Strongly agree	5	(63%)
	Agree	2	(25%)
	Disagree	0	(0%)
	Strongly disagree	1	(13%)
I would like to be contacted if there has been a change or update to my test result.	Strongly agree	6	(75%)
	Agree	1	(13%)
	Disagree	0	(0%)
	Strongly disagree	1	(13%)
I would like to be contacted if there is a change for ME in medical management guidelines (i.e. how often to be screened, surgery recommendations).	Strongly agree	6	(75%)
	Agree	1	(13%)
	Disagree	0	(0%)
	Strongly disagree	1	(13%)
I would like to be contacted if there is a change for FAMILY MEMBERS in medical management guidelines (i.e. how often to be screened, surgery recommendations).	Strongly agree	6	(75%)
	Agree	1	(13%)
	Disagree	0	(0%)
	Strongly disagree	1	(13%)
I would like to be contacted on a regular basis to update the office on any changes to either my and my family's health.	Strongly agree	2	(25%)
	Agree	3	(38%)
	Disagree	1	(13%)
	Strongly disagree	2	(25%)
I would like to be contacted if my insurance changes in a way that would allow me to get more testing than I could based on today's insurance guidelines.	Strongly agree	2	(25%)
	Agree	4	(50%)
	Disagree	1	(13%)
	Strongly disagree	1	(13%)
I would like to be asked at my initial genetic counseling appointment about whether or not I wish to be contacted in the future.	Strongly agree	3	(38%)
	Agree	3	(38%)
	Disagree	1	(13%)
	Strongly disagree	1	(13%)

Percentage totals may not equal 100% due to rounding

Table 2.3 Physician Demographics (*N* = 42)

Variable	*n*	Response	(%)
Physician Specialty	4	Oncology	(10%)
	10	Surgery	(24%)
	0	Gastroenterology	(0%)
	21	OB/Gyn	(50%)
	0	Internal Medicine	(0%)
	1	Family Medicine/Primary Care	(2%)
	3	Radiology	(7%)
	2	Pathology	(5%)
	1	Maternal Fetal Medicine	(2%)

Table 2.4 Provider Responsible for Re-contacting Patients According to Physicians in Different Specialties (*N* = 42)

Variable	*n*	Response	(%)
Should patients be re-contacted when new information becomes available?	27	Yes to all new information	(64%)
	9	Yes, only when management guidelines change	(21%)
	0	Yes, only when new tests become available	(0%)
	0	No	(0%)
	6	Uncertain	(14%)
Whose primary responsibility is it to keep patients updated?	16	Genetic counselor/genetics provider	(38%)
	10	Referring physician	(24%)
	1	Oncologist	(2%)
	1	Patient	(2%)
	9	Physician and genetic counselor	(21%)
	2	Physician, genetic counselor, and patient	(5%)
	3	Unsure	(7%)

Percentage totals may not equal 100% due to rounding

Table 2.5 Provider Responsible for Re-contacting Patients (*N* = 42)

	Genetic Counselor		Physician		Shared		Patient		Unsure	
Specialty	*n*	(%)	*n*	(%)	*n*	(%)	*n*	(%)	*n*	(%)
Oncology	2	50%	2	50%	0	0%	0	0%	0	0%
Surgery	5	50%	2	20%	3	30%	0	0%	0	0%
OB/Gyns	6	29%	4	19%	7	33%	1	5%	3	14%
Family Medicine/Primary Care	1	100%	0	0%	0	0%	0	0%	0	0%
Radiology	2	67%	1	33%	0	0%	0	0%	0	0%
Pathology	0	0%	1	50%	1	50%	0	0%	0	0%
MFM	0	0%	1	100%	0	0%	0	0%	0	0%

Percentage totals may not equal 100% due to rounding

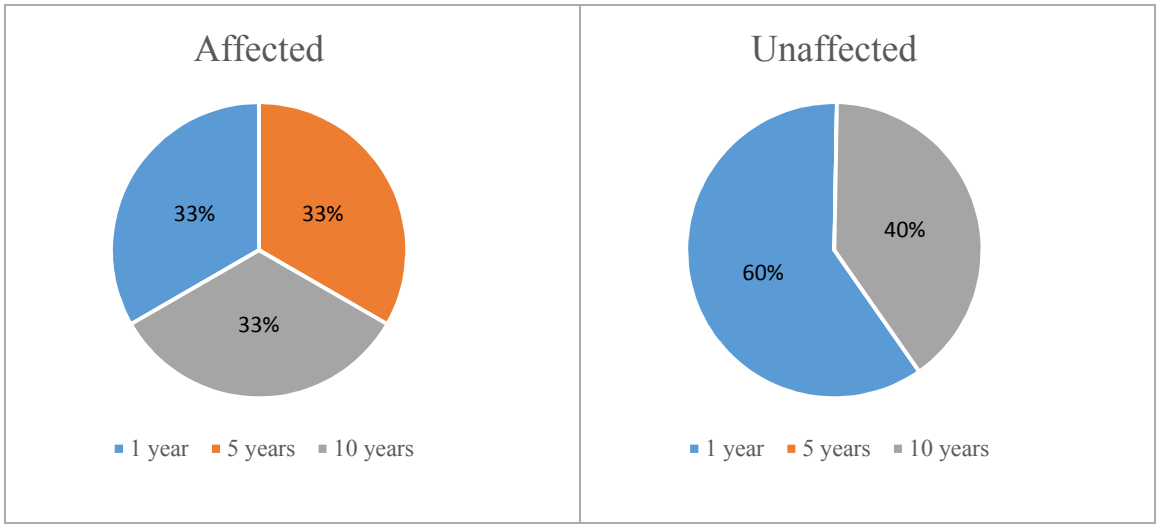

Figure 2.1 Desired Length of Follow-Up in Affected and Unaffected Participants

Statistically significant levels could not be calculated due to small patient sample size.

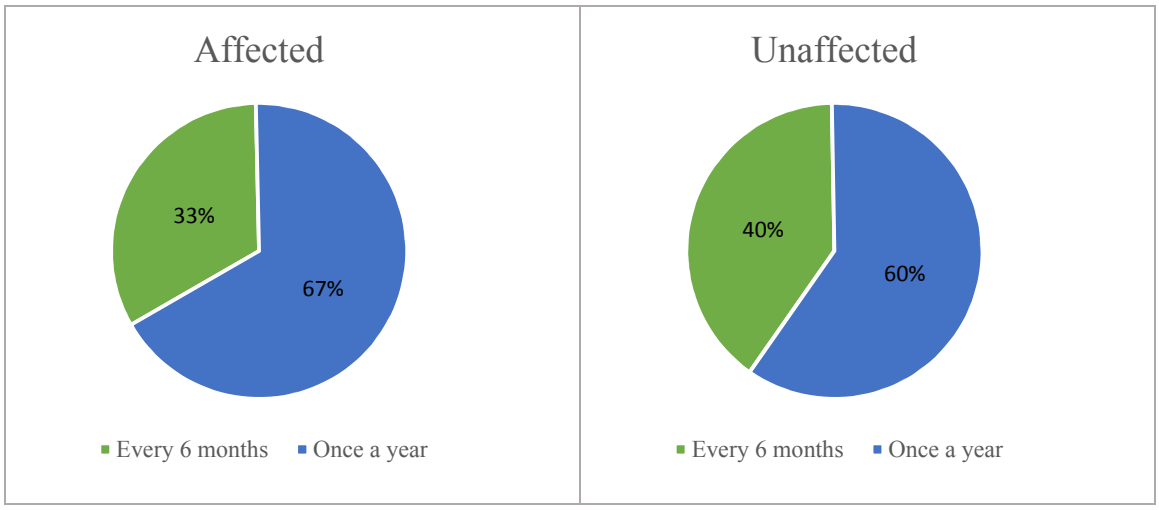

Figure 2.2 Desired Frequency of Updates in Affected and Unaffected Participants

Statistically significant levels could not be calculated due to small patient sample size.

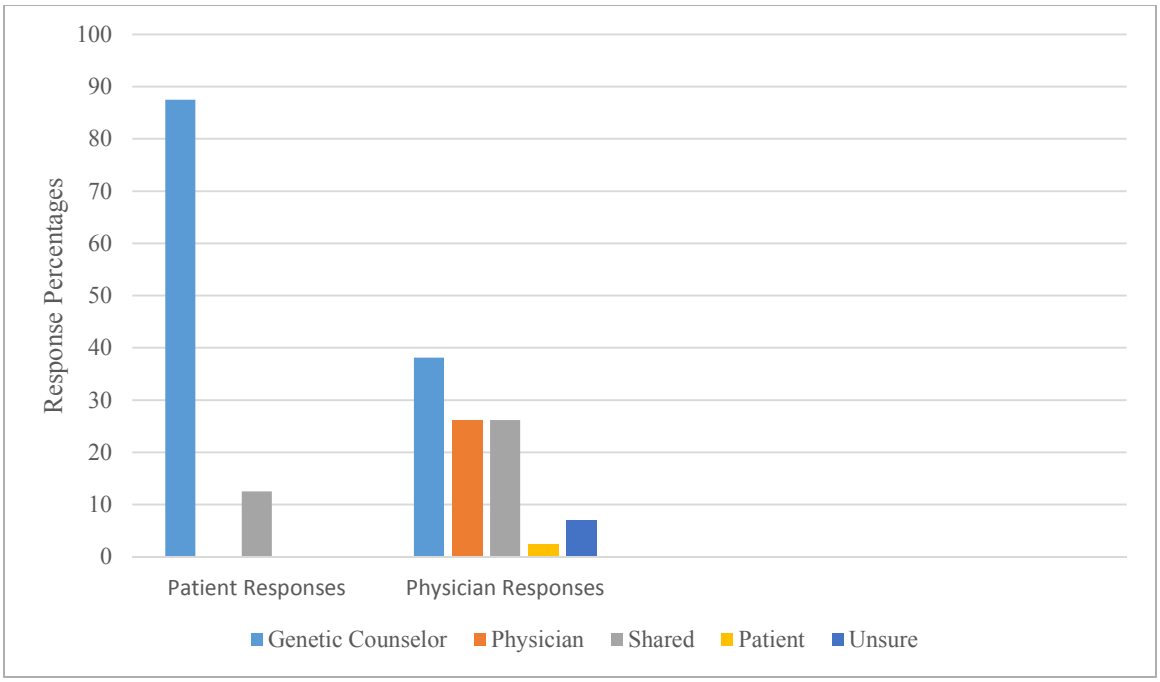

Figure 2.1 Person Responsible for Updating Patients

Note: Statistically significant levels could not be calculated due to small patient sample size.

Chapter 3: Conclusions

This study has implications for the field of genetic counseling, as well as for other professions involved in cancer treatment, high-risk cancer surveillance programs, and the longitudinal care of patients. It has helped shed light on the expectations of individuals undergoing genetic counseling and testing for hereditary cancer conditions regarding their desire to remain informed of advancements in patient care. Similar to findings in previous studies, we found patients desire highly personalized updates that are perceived as being clinically actionable, and place the responsibility of acquiring updated knowledge primarily on the genetics provider. Likewise, we found physicians in specialties that commonly refer to cancer genetic counseling believe patients should be kept informed, and place the responsibility of updating on healthcare providers in general. However, there is no consensus on which providers are responsible for fulfilling this duty. Furthermore, the only guidelines that currently exist which attempt to address this issue may be outdated or not common knowledge among providers following the rapid advancements, accessibility, and uptake of genetic testing.

References

American College of Medical Genetics (1999). Position Statement on Gene Patents and Accessibility of Gene Testing. Retrieved from https://www.acmg.net/StaticContent/StaticPages/Gene_Patents.pdf

Armstrong, K., Eisen, A., & Weber, B. (2000). Assessing the risk of breast cancer. *The New England Journal of Medicine*, *342*(8), 564–71. http://doi.org/10.1056/NEJM200002243420807

Barrow, E., Robinson, L., Alduaij, W., Shenton, A., Clancy, T., Lalloo, F., … Evans, D. G. (2009). Cumulative lifetime incidence of extracolonic cancers in Lynch syndrome: a report of 121 families with proven mutations. *Clinical Genetics*, *75*(2), 141–9. http://doi.org/10.1111/j.1399-0004.2008.01125.x

Berliner, J. L., Fay, A. M., Cummings, S. A., Burnett, B., & Tillmanns, T. (2013). NSGC practice guideline: risk assessment and genetic counseling for hereditary breast and ovarian cancer. *Journal of Genetic Counseling*, *22*(2), 155–63. http://doi.org/10.1007/s10897-012-9547-1

Bougeard, G., Renaux-Petel, M., Flaman, J.-M., Charbonnier, C., Fermey, P., Belotti, M., … Frebourg, T. (2015). Revisiting Li-Fraumeni Syndrome From TP53 Mutation Carriers. *Journal of Clinical Oncology*, *33*(21), 2345–52. http://doi.org/10.1200/JCO.2014.59.5728

Carrieri, D., Lucassen, A. M., Clarke, A. J., Dheensa, S., Doheny, S., Turnpenny, P. D., & Kelly, S. E. (2016). Re-contact in clinical practice: a survey of clinical genetics services in the United Kingdom. *Genetics in Medicine*. http://doi.org/10.1038/gim.2015.194

Casilli, F., Di Rocco, Z. C., Gad, S., Tournier, I., Stoppa-Lyonnet, D., Frebourg, T., & Tosi, M. (2002). Rapid detection of novel BRCA1 rearrangements in high-risk breast-ovarian cancer families using multiplex PCR of short fluorescent fragments. *Human Mutation*, *20*(3), 218–26. http://doi.org/10.1002/humu.10108

Cook-Deegan, R., & Niehaus, A. (2014). After Myriad: Genetic Testing in the Wake of Recent Supreme Court Decisions about Gene Patents. *Current Genetic Medicine Reports*, *2*(4), 223–241. http://doi.org/10.1007/s40142-014-0055-5

Cook-Deegan, R., DeRienzo, C., Carbone, J., Chandrasekharan, S., Heaney, C., & Conover, C. (2010). Impact of gene patents and licensing practices on access to genetic testing for inherited susceptibility to cancer: comparing breast and ovarian cancers with colon cancers. *Genetics in Medicine*, *12*(4 Suppl), S15–38. http://doi.org/10.1097/GIM.0b013e3181d5a67b

D'Argenio, V., Esposito, M. V., Telese, A., Precone, V., Starnone, F., Nunziato, M., … Salvatore, F. (2015). The molecular analysis of BRCA1 and BRCA2: Next-generation sequencing supersedes conventional approaches. *Clinica Chimica Acta*, *446*, 221–5. http://doi.org/10.1016/j.cca.2015.03.045

Desmond, A., Kurian, A. W., Gabree, M., Mills, M. A., Anderson, M. J., Kobayashi, Y., … Ellisen, L. W. (2015). Clinical Actionability of Multigene Panel Testing for Hereditary Breast and Ovarian Cancer Risk Assessment. *JAMA Oncology*, *1*(7), 943–51. http://doi.org/10.1001/jamaoncol.2015.2690

Doherty, J., Bonadies, D. C., & Matloff, E. T. (2015). Testing for Hereditary Breast Cancer: Panel or Targeted Testing? Experience from a Clinical Cancer Genetics Practice. *Journal of Genetic Counseling, 24*(4), 683–7. http://doi.org/10.1007/s10897-014-9796-2

Domchek, S. M. (2015). Evolution of genetic testing for inherited susceptibility to breast cancer. *Journal of Clinical Oncology*, *33*(4), 295–6. http://doi.org/10.1200/JCO.2014.59.3178

Feliubadaló, L., Lopez-Doriga, A., Castellsagué, E., del Valle, J., Menéndez, M., Tornero, E., … Lázaro, C. (2013). Next-generation sequencing meets genetic diagnostics: development of a comprehensive workflow for the analysis of BRCA1 and BRCA2 genes. *European Journal of Human Genetics*, *21*(8), 864–70. http://doi.org/10.1038/ejhg.2012.270

Fitzpatrick, J. L., Hahn, C., Costa, T., & Huggins, M. J. (1999). The duty to re-contact: attitudes of genetics service providers. *American Journal of Human Genetics*, *64*(3), 852–60. http://doi.org/10.1086/302293

Gold, E. R., & Carbone, J. (2010). Myriad Genetics: In the eye of the policy storm. *Genetics in Medicine*, *12*(4 Suppl), S39–70. http://doi.org/10.1097/GIM.0b013e3181d72661

Griffin, C. A., Axilbund, J. E., Codori, A. M., Deise, G., May, B., Pendergrass, C., … Giardiello, F. M. (2007). Patient preferences regarding re-contact by cancer genetics clinicians. *Familial Cancer*, *6*(3), 265–73. http://doi.org/10.1007/s10689-007-9117-0

Hall, J., Lee, M., Newman, B., Morrow, J., Anderson, L., Huey, B., & King, M. (1990). Linkage of early-onset familial breast cancer to chromosome 17q21. *Science*, *250*(4988), 1684–1689. http://doi.org/10.1126/science.2270482

Hall, M. J., Forman, A. D., Pilarski, R., Wiesner, G., & Giri, V. N. (2014). Gene Panel Testing for Inherited Cancer Risk. *Journal of National Comprehensive Cancer Network*, *12*(9), 1339–1346. Retrieved from http://www.jnccn.org.pallas2.tcl.sc.edu/content/12/9/1339.long

Hampel, H., Bennett, R. L., Buchanan, A., Pearlman, R., & Wiesner, G. L. (2015). A practice guideline from the American College of Medical Genetics and Genomics and the National Society of Genetic Counselors: referral indications for cancer predisposition assessment. *Genetics in Medicine*, *17*(1), 70–87. http://doi.org/10.1038/gim.2014.147

Hansford, S., Kaurah, P., Li-Chang, H., Woo, M., Senz, J., Pinheiro, H., … Huntsman, D. G. (2015). Hereditary Diffuse Gastric Cancer Syndrome. *JAMA Oncology*, *1*(1), 23. http://doi.org/10.1001/jamaoncol.2014.168

Hearle, N., Schumacher, V., Menko, F. H., Olschwang, S., Boardman, L. A., Gille, J. J. P., … Houlston, R. S. (2006). Frequency and spectrum of cancers in the Peutz-Jeghers syndrome. *Clinical Cancer Research*, *12*(10), 3209–15. http://doi.org/10.1158/1078-0432.CCR-06-0083

Hogervorst, F. B. L., Nederlof, P. M., Gille, J. J. P., McElgunn, C. J., Grippeling, M., Pruntel, R., … Pals, G. (2003). Large genomic deletions and duplications in the BRCA1 gene identified by a novel quantitative method. *Cancer Research*, *63*(7), 1449–53. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/12670888

Hunter, A. G., Sharpe, N., Mullen, M., & Meschino, W. S. (2001). Ethical, legal, and practical concerns about re-contacting patients to inform them of new information: the case in medical genetics. *American Journal of Medical Genetics*, *103*(4), 265–76. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/11746004

Lundy, M. G., Forman, A., Valverde, K., & Kessler, L. (2014). An investigation of genetic counselors' testing recommendations: pedigree analysis and the use of multiplex breast cancer panel testing. *Journal of Genetic Counseling*, *23*(4), 618–32. http://doi.org/10.1007/s10897-014-9692-9

Lynch, H. T., Snyder, C. L., Shaw, T. G., Heinen, C. D., & Hitchins, M. P. (2015). Milestones of Lynch syndrome: 1895-2015. *Nature Reviews. Cancer*, *15*(3), 181–94. http://doi.org/10.1038/nrc3878

Meldrum, C., Doyle, M. A., & Tothill, R. W. (2011). Next-generation sequencing for cancer diagnostics: a practical perspective. *The Clinical Biochemist*, *32*(4), 177–95. Retrieved from http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=3219767&tool=pmcentrez&rendertype=abstract

Montagna, M., Dalla Palma, M., Menin, C., Agata, S., De Nicolo, A., Chieco-Bianchi, L., & D'Andrea, E. (2003). Genomic rearrangements account for more than one-third of the BRCA1 mutations in northern Italian breast/ovarian cancer families. *Human Molecular Genetics*, *12*(9), 1055–61. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/12700174

Myriad Genetics Laboratories About Myriad Company Milestones. (n.d.). Retrieved April 05, 2016, from https://www.myriad.com/about-myriad/inside-myriad/company-milestones/

Myriad Genetics Laboratories. *Integrated BRACAnalysis to Include BART™*. Retrieved April 11, 2016 from http://d1izdzz43r5o67.cloudfront.net/sales-aids/Integrated+BRACAnalysis+to+Include+BART.pdf

National Society of Genetic Counselors Family Health History. (n.d.) Retrieved April 06, 2016, from http://nsgc.org/p/bl/et/blogaid=491

National Comprehensive Cancer Network. (2015). *NCCN Clinical Practice Guidelines in Oncology: Breast Cancer (v.2.2015)*. Retrieved from www.NCCN.com

National Comprehensive Cancer Network. (2016). *NCCN Clinical Practice Guidelines in Oncology: Breast Cancer (v.1.2016)*. Retrieved from www.NCCN.com

National Comprehensive Cancer Network. (2015). *NCCN Clinical Practice Guidelines in Oncology: Colorectal Cancer (v.2.2015)*. Retrieved from www.NCCN.com

Nelson, N. J. (1996). Caution Guides Genetic Testing for Hereditary Cancer Genes. Retrieved from https://repository.library.georgetown.edu/handle/10822/528788

Ngeow, J., Sesock, K., & Eng, C. (2015). Breast cancer risk and clinical implications for germline PTEN mutation carriers. *Breast Cancer Research and Treatment*. http://doi.org/10.1007/s10549-015-3665-z

Otten, E., Plantinga, M., Birnie, E., Verkerk, M. A., Lucassen, A. M., Ranchor, A. V, & Van Langen, I. M. (2015). Is there a duty to re-contact in light of new genetic technologies? A systematic review of the literature. *Genetics in Medicine*, *17*(8), 668–78. http://doi.org/10.1038/gim.2014.173

Printz, C. (2016). ACS updates breast cancer screening guidelines. *Cancer*, *122*(5), 663. http://doi.org/10.1002/cncr.29911

Puget, N., Stoppa-Lyonnet, D., Sinilnikova, O. M., Pages, S., Lynch, H. T., Lenoir, G. M., & Mazoyer, S. (1999). Screening for Germ-Line Rearrangements and Regulatory Mutations in *BRCA1* Led to the Identification of Four New Deletions. *Cancer Research*, *59*(2), 455–461. Retrieved from http://cancerres.aacrjournals.org/content/59/2/455.short

Riley, B. D., Culver, J. O., Skrzynia, C., Senter, L. A., Peters, J. A., Costalas, J. W., … Trepanier, A. M. (2012). Essential elements of genetic cancer risk assessment, counseling, and testing: updated recommendations of the National Society of Genetic Counselors. *Journal of Genetic Counseling*, *21*(2), 151–61. http://doi.org/10.1007/s10897-011-9462-x

Shannon, K. M., Rodgers, L. H., Chan-Smutko, G., Patel, D., Gabree, M., & Ryan, P. D. (2011). Which individuals undergoing BRACAnalysis need BART testing? *Cancer Genetics*, *204*(8), 416–22. http://doi.org/10.1016/j.cancergen.2011.07.005

Shiovitz, S., & Korde, L. A. (2015). Genetics of breast cancer: a topic in evolution. *Annals of Oncology*, *26*(7), 1291–9. http://doi.org/10.1093/annonc/mdv022

Smith, R. A., Andrews, K., Brooks, D., DeSantis, C. E., Fedewa, S. A., Lortet-Tieulent, J., … Wender, R. C. (2016). Cancer screening in the United States, 2016: A review of current American Cancer Society guidelines and current issues in cancer screening. *CA: A Cancer Journal for Clinicians*. http://doi.org/10.3322/caac.21336

Smith, R. A., Manassaram-Baptiste, D., Brooks, D., Doroshenk, M., Fedewa, S., Saslow, D., … Wender, R. (2015). Cancer screening in the United States, 2015: A review of current American Cancer Society guidelines and current issues in cancer screening. *CA: A Cancer Journal for Clinicians*, *65*(1), 30–54. http://doi.org/10.3322/caac.21261

Stuckey, A. R., & Onstad, M. A. (2015). Hereditary breast cancer: an update on risk assessment and genetic testing in 2015. *American Journal of Obstetrics and Gynecology*, *213*(2), 161–5. http://doi.org/10.1016/j.ajog.2015.03.003

Tan, M.-H., Mester, J. L., Ngeow, J., Rybicki, L. A., Orloff, M. S., & Eng, C. (2012). Lifetime cancer risks in individuals with germline PTEN mutations. *Clinical Cancer Research*, *18*(2), 400–7. http://doi.org/10.1158/1078-0432.CCR-11-2283

van der Groep, P., van der Wall, E., & van Diest, P. J. (2011). Pathology of hereditary breast cancer. *Cellular Oncology (Dordrecht)*, *34*(2), 71–88. http://doi.org/10.1007/s13402-011-0010-3

Walsh, T., Casadei, S., Coats, K. H., Swisher, E., Stray, S. M., Higgins, J., … King, M.-C. (2006). Spectrum of mutations in BRCA1, BRCA2, CHEK2, and TP53 in families at high risk of breast cancer. *JAMA*, *295*(12), 1379–88. http://doi.org/10.1001/jama.295.12.1379

Weischer, M., Bojesen, S. E., Tybjaerg-Hansen, A., Axelsson, C. K., & Nordestgaard, B. G. (2007). Increased risk of breast cancer associated with CHEK2*1100delC. *Journal of Clinical Oncology*, *25*(1), 57–63. http://doi.org/10.1200/JCO.2005.05.5160

Appendix A: Participant Introductory Letter

University of South Carolina School of Medicine
USC Genetic Counseling Program

Dear Potential Participant:

You are invited to participate in a graduate research study focusing on the duty to re-contact patients who undergo genetic counseling for hereditary cancer syndromes. I am a graduate student in the genetic counseling program at the University of South Carolina School of Medicine. My research investigates the preferences of patients that have undergone genetic counseling. The research involves completing and returning a questionnaire.

The questionnaire attempts to measure your interest in being re-contacted, the best method for being re-contacted, and whose responsibility it is to re-contact you. If you do not wish to answer a certain question, please skip that question and continue with the rest of the questionnaire. **Completing the questionnaire and stating that you desire to be re-contacted does not guarantee that you will be re-contacted in the future.** We are investigating that possibility with this research study, but do not currently have the ability to re-contact all patients with updates. We encourage you to re-contact us with any questions about your management or updates to your history.

All responses gathered from the questionnaires will be kept anonymous and confidential. You do not need to provide your name, contact information, or any other identifying information. We will not attempt to contact you again for this study after you complete the questionnaire. The results of this study might be published or presented at academic meetings; however, participants will not be identified.

Your participation in this research is voluntary. By completing the questionnaire, you are consenting that you have read and understand this information. At any time, you may withdraw from the study by not completing the questionnaire.

Thank you for your time and consideration to participate in this survey. Your responses may help genetic counselors gain a better understanding of the needs and expectations of their patients. If you have any questions regarding this research, you may contact either myself or my faculty adviser, Whitney Dobek, MS, CGC, using the contact information below. If you have any questions about your rights as a research participant, you may contact the Office of Research Compliance at the University of South Carolina at (803)777-7095.

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Appendix B: Patient Questionnaire

University of South Carolina School of Medicine
USC Genetic Counseling Program

1. Would you like to be contacted in the future regarding updates to the components of genetic testing and counseling that were discussed today?
   a) Yes
   b) No (if no, stop survey)

Questions #2-9 concern conditions under which you would or would not like to be contacted regarding the components of genetic testing and counseling that were discussed today. Please indicate your level of agreement for each question.

	Strongly Disagree	Disagree	Agree	Strongly Agree
2. I would like to be contacted if my genetic testing results came back negative (no mutation was found), and better testing options become available.	1	2	3	4
3. I would like to be contacted if new research indicates there has been a change in my lifetime risk for developing cancer.	1	2	3	4
4. I would like to be contacted if there has been a change or update to my test result.	1	2	3	4
5. I would like to be contacted if there is a change for ME in medical management guidelines (i.e. how often to be screened, surgery recommendations).	1	2	3	4

6. I would like to be contacted if there is a change FOR FAMILY MEMBERS in medical management guidelines (i.e. how often to be screened, surgery recommendations).	1	2	3	4
7. I would like to be contacted on a regular basis to update the office on any changes to either my and my family's health.	1	2	3	4
8. I would like to be contacted if my insurance changes in a way that would allow me to get more testing than I could based on today's insurance guidelines.	1	2	3	4
9. I would like to be asked at my initial genetic counseling appointment about whether or not I wish to be contacted in the future.	1	2	3	4

Questions #10-11 refer to how often you prefer to be contacted. Please select one answer for each question.

10. How frequently would you prefer to be updated with relevant information (e.g. better testing options, management changes, etc.)?

a) Every 6 months
b) Once a year
c) Once every 5 years
d) Once every 10 years
e) Other: _____

11. For how many years after your initial genetic counseling appointment would you like to be updated when new relevant information (e.g. better testing options, management changes, etc.) becomes available?

a) One year following appointment
b) Two years following appointment
c) Five years following appointment
d) Ten years following appointment
e) Other: _____

Questions #12-14 refer to methods that might be used to contact you. Please select **one answer** for each question.

12. Who would you expect to contact you with updates to the components of genetic testing and counseling discussed today? (Choose one)

a) The physician that referred you to genetic counseling
b) Genetic Counselor
c) Other: _____

13. Which method of notification would you prefer most? (Choose one)

a) Phone call
b) Letter
c) Email
d) During follow-up genetic counseling appointment
e) During high-risk clinic appointment
f) Other: _____

14. Which do you prefer regarding new information discussed in today's session? (Choose one)

a) You contact your provider to ask about new information as you desire it
b) Your genetic service provider contacts you when there is new information relevant to you

DEMOGRAPHICS

15. Please circle your age range.

a) 18-29
b) 30-39
c) 40-49
d) 50-59
e) 60-69
f) 70 or older

16. Please circle your sex.

a) Male
b) Female

17. Please indicate why you were referred to genetic counseling. (CIRCLE ALL that apply)

a) Breast cancer diagnosis
b) Family history of breast cancer
c) Colon cancer diagnosis
d) Family history of colorectal cancer
e) Known hereditary cancer gene mutation in family
f) Other: _____

18. Did you choose to do any genetic testing?

a) Yes
b) No

19. Which type of doctor referred you to genetic counseling?

a) OB/gyn
b) Oncologist
c) Surgeon
d) Primary care physician/family doctor
e) Self referral
f) Other: _____

Appendix C: Physician Questionnaire

University of South Carolina School of Medicine
USC Genetic Counseling Program

You are invited to participate in a **graduate research study** focusing on the duty to re-contact patients who undergo genetic counseling for hereditary cancer syndromes.

About the research: I am a graduate student in the genetic counseling program at the University of South Carolina School of Medicine. My research investigates how and for what reason patients who have undergone genetic counseling would like to be updated with new and relevant information. I am also interested in examining whether patient opinions are in line with the expectations of their physicians.

Your participation involves completing and returning a questionnaire. Your participation in this research is voluntary. By completing the questionnaire, you are consenting that you have read and understand this information. Your responses will help genetic counselors gain a better understanding of the needs and expectations of their patients.

Thank you for your time and consideration.

1. What is your specialty?

a) Oncologist
b) Surgeon
c) Gastroenterologist
d) OB/GYN
e) Internal medicine
f) Family medicine
g) Other: _____

2. Have you ever referred a patient for cancer genetic counseling?

a) Yes
b) No

3. Should patients previously seen for cancer genetic counseling be re-contacted when new and relevant genetic information is available (e.g. management guidelines change, new testing becomes available, etc.)?

a) Yes to all
b) Yes, management changes only
c) Yes, new testing only
d) No
e) Uncertain

4. Whose *primary* responsibility is it to keep patients updated on new genetic information?

a) Genetic counselor/genetics provider
b) Physician who referred to genetics
c) Patient
d) No one; the patient should <u>not</u> be updated
e) Other: _____

5. Have you ever informed patients when there is new and relevant genetic information available (e.g. management guidelines change, new testing available, etc.)?

a) Yes
b) No