

**PATIENT AND GENETICS HEALTHCARE PROVIDER ATTITUDES REGARDING  
RECONTACT**

by

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University of Pittsburgh, 2014

**ABSTRACT**

As genetic testing technologies continue to evolve, new opportunities for cancer risk assessment and prevention may become available. Because of this, it is necessary to evaluate the process of patient recontact for the purpose of offering additional genetic testing. Limited information exists regarding patients' expectations and preferences for recontact by their genetics providers. In addition, there is limited literature exploring the current practice of recontact by genetics providers and their attitudes regarding the duty to recontact patients. This study evaluated both patient and genetics providers' attitudes regarding recontact. Questionnaires were sent to 1000 patients previously tested for *BRCA1/2* between the years 2007-2012 at the UPMC Cancer Genetics Program that inquired about their expectations and preferences for recontact. Questionnaires were also sent to 490 members of the National Society of Genetic Counselors Cancer Risk Assessment Special Interest Group that inquired about current practice of patient recontact and attitudes regarding clinical practice guidelines and ethical responsibility to recontact patients. This study found that patients believed that their genetics providers hold more responsibility to keep patients updated about new genetic discoveries than other providers and the patients themselves. The data supports that patients' preferences for recontact include personalized information only when new information is discovered and preferences were not influenced by genetic testing results. In addition, the study found that genetics providers believe there is some

ethical duty to keep patients informed of new genetic information, and the majority of providers have previously recontacted patients for this purpose, but do not have formalized systems of recontact established. Resources, such as staff, monetary support, and database access were found to influence the practice of recontact by genetics providers, and the data suggests that database access is a significant component for genetics providers to have established systems of recontact. The majority of genetics providers did not believe patient recontact should be standard of care, however, desired clinical practice guidelines. This research is significant to the field of public health as it clarified patient expectations regarding recontact and has implications that may aid in the development of recontacting strategies for genetics providers.

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## 1.0 INTRODUCTION

This research study was conducted to assess patients' and cancer genetics providers' attitudes regarding the practice of recontact when new genetic discoveries have been made and/or new genetic testing becomes available.

The research study focused on patients who were previously tested for mutations in the *BRCA1* and *BRCA2* genes, which account for the majority of Hereditary Breast and Ovarian Cancer Syndrome (HBOC)<sup>1</sup>. HBOC is an autosomal dominant condition characterized by an increased risk for breast and ovarian cancer along with other cancers, including prostate, pancreas, and melanoma<sup>1</sup>. *BRCA1* and *BRCA2* are tumor suppressor genes, and mutations within those genes lead to an increased risk for tumor growth and development<sup>1</sup>. It is estimated that approximately 1/400 to 1/800 individuals carry a *BRCA1/2* mutation in the general population<sup>2</sup>. In addition, it is estimated that approximately 250,000 individuals undergo genetic testing for *BRCA1/2* each year<sup>3</sup>.

Individuals who are suspected of having a hereditary predisposition to certain cancers within their family are typically referred to a medical geneticist and/or genetic counselor. During a genetic counseling consultation, a detailed medical and family history are obtained. The National Comprehensive Cancer Network (NCCN) have specific guidelines for whom genetic testing should be offered to<sup>4</sup>. The NCCN guidelines take into account personal and family history of HBOC-related cancers. If a patient pursues genetic testing, they are often times notified of the results either by phone or an additional in person consultation. A summary of the patient's genetic

testing results and current cancer screening recommendations are provided to the patient, the patient's primary care physician, and if necessary, other doctors involved in the patient's care. When a patient's results reveal a positive gene mutation, this is often an answer for their personal and family cancer history. When a patient's results are negative (no mutation detected) or inconclusive, there is often much left to be answered. Due to the volume of patients who receive genetic counseling, it is not possible for genetics providers to recontact all patients who have a negative test result when new genetic testing becomes available. Therefore, most genetics providers will recommend that patients be responsible for recontact and that they should communicate with their primary care physicians or specialists regarding new information.

The American College of Medical Genetics (ACMG) have published guidelines that support this concept<sup>5</sup>. These guidelines state that it is the patient and the primary care physician's responsibility to seek up-to-date information regarding genetic testing. Only in situations where a genetic counselor or medical geneticist provides ongoing care, do they hold the primary responsibility. This is the minority of cases within a cancer genetics setting. The ACMG guidelines have been established to protect genetics health care providers from the burden of recontact and from liability issues that may be raised.

Understanding the patients' perspective for recontact is an important factor to consider when determining the success of such a policy. As genetic testing continues to evolve, especially with the evolution of next generation sequencing panels, whole exome and genome sequencing, the issue of recontact will become more complex. If the policy for the "duty to recontact" were to change, perhaps holding the genetics providers to a higher responsibility, it would be essential to know if and how patients would prefer to be recontacted. This study aims to understand patients' current expectations regarding recontact and their preferred methods of recontact if it were to be

initiated. Similarly, systems of recontact would need to be developed, taking into account the limited resources available to many genetics providers. This study was also designed to determine what methods genetics providers currently use for purposes of recontacting their patients and assessing their current attitudes regarding the responsibility to recontact patients.

### **1.1 SPECIFIC AIMS AND HYPOTHESES**

Specific Aim 1: Determine patients' expectations and preferences regarding recontact, including factors which influence their decision making, and whether preferences differ based on test results.

Hypothesis: Patients' perceptions of their primary care providers' knowledge of genetic testing influences their expectations for who is believed most responsible to provide information on new genetic discoveries. Different genetic testing results will influence patients' expectations and preferences for recontact.

Plan: Questionnaires will inquire about patient's relationship with their primary care providers, expectations for recontact by their primary care providers, preferences and motivations for recontact, and recall of recontact recommendations from prior genetics consultations. Survey responses will be analyzed to identify common trends.

Specific Aim 2: Determine current practices of cancer genetics providers regarding recontact for the purpose of additional genetic testing opportunities. Assess genetics providers' attitudes regarding the need for clinical practice guidelines concerning recontact and their attitudes in terms of ethical responsibility to recontact.



Hypothesis: Providers believe that patients hold the most responsibility for staying informed of new genetic discoveries. While genetics providers believe there is some duty to recontact patients, limited resources impact their ability and means to do so.

Plan: Questionnaires will inquire about whether methods of recontact have been established by genetic healthcare providers and if so, what methods have been utilized. Theoretical considerations regarding recontact will be analyzed.

## **1.2 HEREDITARY BREAST AND OVARIAN CANCER BACKGROUND**

### **1.2.1 Cancer Overview**

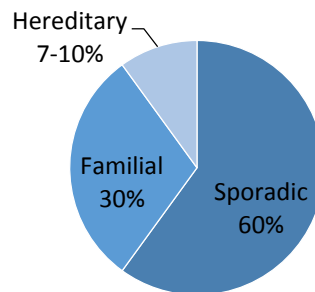
In the United States, approximately one-half of all men and one-third of all women are at risk of developing cancer throughout their lifetime<sup>6</sup>. Cancer arises from the accumulation of genetic mutations, either germline or somatic, in major cancer predisposition genes that are responsible for cell cycle progression and DNA repair<sup>7; 8</sup>. These genes include proto-oncogenes, tumor suppressor genes, and DNA repair genes<sup>7; 8</sup>.

Breast cancer is the second most common cancer among women in the United States<sup>6</sup>. It is estimated that approximately 1 in 8 women (12%) will develop invasive breast cancer throughout her lifetime, and the median age of diagnosis for breast cancer is 61 years<sup>6</sup>. The 5-year survival rate for breast cancer in women ranges from almost 100% (stage I) to 22% (stage IV)<sup>6</sup>. Male breast cancer is less common, and it is estimated that approximately 1 in 1000 (0.1%) men will develop breast cancer throughout his lifetime<sup>9</sup>. The 5-year survival rate for breast cancer in males ranges from 100% (stage I) to 20% (stage IV)<sup>9</sup>.

Ovarian cancer is the eighth most common cancer among women in the United States, excluding skin cancer. It is estimated that approximately 1 in 73 women (1.4%) will develop ovarian cancer throughout her lifetime and the median age of diagnosis for ovarian cancer is 63 years<sup>10</sup>. The 5-year survival rate for ovarian cancer ranges from 89% (stage I) to 18% (stage IV)<sup>10</sup>.

### 1.2.2 Cancer Etiology and Risk Factors

There are three main etiologies of the development of cancer, as shown by Figure 1. The development of cancer may be a sporadic occurrence, a familial predisposition, or a hereditary predisposition<sup>8, 11</sup>.



**Figure 1. Etiologies of Cancer**

The majority of cancers that occur are sporadic (60%), meaning that they occur by chance. Sporadic cancers are the result of the accumulation of somatic mutations in major cancer preposition genes<sup>8</sup>. These mutations are primarily acquired from environmental exposures and age related risk factors<sup>8</sup>. The most significant risk factors for the development of breast cancer are being female and aging<sup>6</sup>. Other factors that modify breast cancer risk within the general population are:

- Hormonal Factors<sup>6</sup>
  - Women with early menarche (<12 years) and older age at menopause (>55 years) have a slightly higher risk for developing breast cancer, which is thought to be related to the length of exposure time to cycling ovarian hormones<sup>12</sup>.
  - Age at first live birth (>35 years) is associated with increased risk for breast cancer (OR 1.26). In addition, women who've had two or more pregnancies have a decreased risk of breast cancer, while nulliparous women are at an increased risk, compared to uniparous women.<sup>13</sup>.
  - Breast feeding reduces breast cancer risk by approximately 4.3% for every 12 months and a greater reduction in risk is associated with longer duration<sup>14</sup>.
  - Oral contraceptive use is associated with a slightly elevated risk of developing breast cancer (RR:1.24) as compared to those who have never used oral contraceptives. The risk is normalized after 10 years of discontinued use<sup>15</sup>.
  - Long term non-menopausal hormone replacement therapy use has been associated with an increased risk of breast cancer (RR:1.35)<sup>16</sup>.
- Benign breast conditions<sup>6</sup>
  - Personal history of lobular carcinoma in situ (LCIS) can increase the risk of developing invasive breast cancer by 7-10 times that of women without a history of LCIS<sup>17</sup>.
  - Personal history of atypical ductal/lobular hyperplasia is associated with a 3-4 fold increased risk for breast cancer<sup>17; 18</sup>.
  - Women with dense breast tissue have a risk of breast cancer 4-6 times that of a women with less dense breast tissue<sup>19</sup>.

- Personal history of breast cancer<sup>6</sup>
  - A woman with breast cancer in one breast has a 3-4 fold increased risk of developing another primary breast cancer<sup>6</sup>.
- Exposures<sup>6</sup>
  - High-dose radiation therapy to the chest increases risk of breast cancer. The risk is highest when exposed during childhood or adolescence<sup>20</sup>.
  - In utero exposure to diethylstilbestrol (DES) increases breast cancer risk by approximately 3.9% in women older than 40 years<sup>21</sup>.
  - Consumption of 2-5 alcoholic drinks per day increases breast cancer risk by 1.5 times as compared to those who do not drink alcohol<sup>22</sup>.
- Family history of breast cancer<sup>6</sup>
  - The risk of developing breast cancer is 1.8 times higher for women with one 1<sup>st</sup> degree female relative with breast cancer<sup>23</sup>.
  - The risk of developing breast cancer is 2.9 times higher for women with two first degree relatives with breast cancer and 3.9 times higher for women with 3 or more first degree relatives with breast cancer<sup>23</sup>.

Risk factors associated with ovarian cancer in the general population include:

- Hormonal factors<sup>10</sup>
  - Having a first pregnancy after the age of 35 is twice as protective against ovarian cancer as a pregnancy younger than 25 years of age. One pregnancy lowers the risk by as much as 33%, and the risk decreases with each additional pregnancy<sup>24</sup>;  
25.

- Breastfeeding for 18 or more months may decrease the risk of ovarian cancer by up to 34%<sup>26</sup>.
- Oral contraceptive use for any period of time is associated with a 34% risk reduction in ovarian cancer and up to 60% risk reduction when used for 6 or more years<sup>24</sup>.
- Post-menopausal estrogen replacement therapy use for more than 10 years has been associated with an increased risk of ovarian cancer<sup>27</sup>.
- Clinical factors<sup>10</sup>
  - Chronic pelvic inflammatory disease and ovarian endometriosis are associated with a slight increased risk for ovarian cancer<sup>28; 29</sup>.
  - Tubal ligation is associated with a 34% reduction in ovarian cancer risk<sup>30</sup>
- Exposures<sup>10</sup>
  - Talcum powder usage within the perineal area increases the risk of ovarian cancer by up to 33%<sup>31</sup>.
- Family History of ovarian cancer<sup>10</sup>
  - The lifetime risk of developing ovarian cancer is 4.3 times higher for women with one 1<sup>st</sup> degree relative with ovarian cancer<sup>32; 33</sup>.

Approximately 30% of all cancer cases are familial<sup>8</sup>. Familial cancers are clusters of cancer within a family that occur in a higher frequency than would be expected by chance alone<sup>8</sup>. Familial cancers are the result of multiple genetic factors and multiple environmental factors interacting over time<sup>8</sup>. Familial cancers are variable in age of onset, but overall may occur at a slightly younger age than sporadic cancers<sup>8</sup>.

Approximately 7-10% of cancers are hereditary, meaning they are caused by inheriting a single genetic mutation<sup>8; 11</sup>. Many hereditary cancers develop when a germline mutation is inherited in a tumor suppressor gene, and the second copy of that particular gene acquires somatic mutations in the same cell<sup>7</sup>. This event is also known as the “Two Hit Hypothesis”, first proposed by Dr. Alfred Knudson in 1971 to describe inherited retinoblastoma<sup>11</sup>. Knudson proposed that inheriting one germline mutation (“first hit”) was not sufficient to cause carcinogenesis. Rather, an acquired mutation (“second hit”) within the other copy of the gene was required to lose control of cell division and lead to cancer development<sup>6</sup>.

### **1.2.3 Hereditary Breast and Ovarian Cancer Syndrome**

The majority of Hereditary Breast and Ovarian Cancer (HBOC) cases are caused by mutations within the tumor suppressor genes, *BRCA1* and *BRCA2*<sup>1</sup>. Mutations within *BRCA1/2* account for approximately 3-5% of all breast cancers and approximately 10-15% of all ovarian cancer cases<sup>34</sup>. The population frequency of mutations within the *BRCA1* and *BRCA2* genes is estimated to be between 1/400 to 1/800<sup>2</sup>. Mutations are found in all racial and ethnic populations. However, the prevalence of *BRCA1/2* mutations is higher in some founder populations, such as the Ashkenazi Jewish population, where it is estimated that the prevalence of carrying a *BRCA1/2* mutation is 1/40<sup>35</sup>. Other founder mutations have been identified in populations from the Netherlands, Sweden, Hungary, Iceland, and French Canada<sup>34</sup>.

#### **1.2.3.1 Genetics of HBOC**

The *BRCA1* gene is located on chromosome 17p21<sup>36</sup>. *BRCA1* encodes the breast cancer type 1 susceptibility protein<sup>37</sup>. *BRCA1* interacts with a number of other proteins involved cell cycle

progression, gene transcription regulation, double strand DNA damage response and ubiquitination<sup>37-39</sup>. The *BRCA2* gene is located on chromosome 13q12<sup>40</sup>. *BRCA2* encodes the breast cancer type 2 susceptibility protein. *BRCA2* interacts with other proteins, including those encoded by *RAD51* and *PALB2* to act in DNA repair of double stranded DNA breakage<sup>39; 40</sup>.

Greater than 1600 mutations have been identified in *BRCA1* and greater than 1800 mutations have been identified in *BRCA2*<sup>2</sup>. The most common types of mutations are frameshift deletions, insertions, and nonsense mutations resulting in premature truncation of protein transcription<sup>2</sup>. Approximately 12% of mutations in *BRCA1/2* are the result of large deletions or duplications<sup>41</sup>.

### **1.2.3.2 Clinical Presentation and Diagnosis**

Features that are suggestive of HBOC include early onset breast cancer (<50 years), bilateral breast cancer, epithelial ovarian cancer, breast and ovarian cancer diagnosed in the same individual, and male breast cancer<sup>4</sup>. In addition, HBOC-related cancers occurring in multiple family members across multiple generations within the same bloodline of a family are suggestive of HBOC.

Previous studies have been performed to understand the penetrance of *BRCA1/2* and associated cancer risks. *BRCA1/2* mutations have been shown to have the most impact on breast and ovarian cancer risk (Table 1). The lifetime risk for developing breast cancer for a woman with a *BRCA1/2* mutation ranges from 40-80%. In addition, the lifetime risk for developing ovarian cancer for a woman with a *BRCA1/2* mutation ranges from 20-40%. The range of cancer risk results from the incomplete penetrance seen with *BRCA1/2* mutations. Penetrance has been shown to vary within families with the same *BRCA1/2* mutation as well<sup>2</sup>. Both breast and ovarian cancer

risks appear higher in individuals with *BRCA1* mutations compared to individuals with *BRCA2* mutations<sup>42</sup>.

**Table 1. Lifetime Breast and Ovarian Cancer Risk Associated with *BRCA1/2* Mutations**

Cancer	General Population Risk	<i>BRCA1/2</i> Mutation
Breast Cancer	8-12% <sup>6</sup>	40-80% <sup>1</sup>
2 <sup>nd</sup> Breast Cancer	<10% <sup>43</sup>	2-3% per year <sup>44</sup>
Ovarian Cancer	<2% <sup>10</sup>	20-40% <sup>1</sup>

Additional studies have shown that mutations in *BRCA1/2* can increase the lifetime risk for other types of cancer (Table 2). In general, *BRCA2* carriers have an increased risk for male breast cancer, prostate cancer, pancreatic cancer, and melanoma above that of *BRCA1* carriers<sup>44</sup>.

**Table 2. Other Lifetime Cancer Risks Associated with *BRCA1/2* Mutations**

Cancer	General Population Risk <sup>45</sup>	<i>BRCA1/2</i> Mutation
Male Breast Cancer	<1%	7% <sup>46</sup>
Prostate Cancer	16%	20-39% <sup>1; 44</sup>
Pancreatic Cancer	<2%	2-7% <sup>1; 44</sup>
Melanoma	<2%	2-5% <sup>44</sup>

*BRCA1/2* related breast cancers have characteristic pathology. *BRCA1* related breast tumors are more likely to be of medullary histology and of high nuclear grade<sup>2</sup>. *BRCA1* tumors are also more likely to be “triple negative” than sporadic tumors, meaning that the tumor is estrogen and progesterone receptor negative and that the tumor does not demonstrate HER2/neu over-expression<sup>47</sup>. *BRCA2* related breast cancer tumors typically have an inconsistent phenotype, without a characteristic histological grade or tumor classification<sup>2</sup>. Nearly all ovarian cancers



associated with *BRCA1/2* mutations are epithelial in origin and have high grade serous histology<sup>2</sup>. The most commonly associated ovarian tumors are papillary serous adenocarcinomas. Ovarian tumors that originate from the germ cells or stromal tissue are not associated with mutations in *BRCA1/2*.

#### **1.2.4 Genetic Counseling for HBOC**

The goal of genetic counseling is to educate patients about their cancer risk, help them derive personal meaning from this information, and empower them to make informed decisions about genetic testing, cancer surveillance, and cancer prevention options<sup>8</sup>.

Genetic counseling consists of interpretation of personal and family history, cancer risk assessment, and psychosocial assessment<sup>8</sup>. If an individual is a candidate for genetic testing, informed consent is obtained. Informed consent includes proper education of cancer genetics including inheritance, discussion of medical management guidelines, information about the genetic testing process including possible test results, addressing economic and confidentiality concerns, discussing psychosocial issues associated with genetic testing, and identifying relevant resources/support for the patient<sup>48</sup>.

##### **1.2.4.1 Family history Interpretation and Cancer Risk Assessment**

Genetic risk assessment is the process of identifying individuals at an increased risk for familial or hereditary cancer predispositions<sup>8</sup>. Cancer risk assessment for HBOC includes analysis of the family pedigree, an individual's personal medical history, and relevant exposures<sup>48</sup>. A targeted three-generation family pedigree is a useful tool to identify features that are suggestive of HBOC. However, there can be instances where the family pedigree is not useful in determining an

individual's risk and may conceal the presence of a hereditary cancer syndrome<sup>48</sup>. These instances include limited knowledge of or access to family history information (including adoption), small family size, early deaths within a family (unrelated to cancer), or having predominately male relatives<sup>49</sup>.

There are several risk calculation models available to assess the likelihood of identifying a *BRCA1/2* mutation within a patient. Models such as *BRCAPRO* use Bayesian analysis of conditional probabilities to estimate the likelihood of a *BRCA1/2* mutation based on the individual's personal cancer history, family history, and Ashkenazi Jewish ancestry<sup>50</sup>. In addition, Myriad Prevalence Tables have been published, by Myriad Genetic Laboratories, using the data gained from their genetic testing services. Myriad Prevalence Tables estimate the likelihood of a *BRCA1/2* mutation based on an individual's personal cancer history, family history, and Ashkenazi Jewish ancestry and the prevalence rates of mutations among them<sup>51</sup>. A number of other *BRCA1/2* mutation probability models are available, including *PennII*, *BOADICEA*, and the Tyrer-Cuzick model<sup>48</sup>. These models incorporate various HBOC-related cancers in the patient, first and second degree relatives, along with ages of onset, and may include other personal factors<sup>52</sup>. The information determined by these risk calculation models provides an estimate for an individual's probability of carrying a *BRCA1/2* mutation, which may also be used to determine the appropriateness of genetic testing for certain individuals. Previously, the American Society of Clinical Oncology (ASCO) suggested that testing be considered for individuals whose estimated probability of to carry a *BRCA1/2* mutation was 10% or greater<sup>53</sup>. However, many centers use the National Comprehensive Cancer Network guidelines when considering genetic testing<sup>4</sup>.

#### **1.2.4.2 Differential Diagnosis**

As stated, HBOC accounts for the majority of hereditary breast and ovarian cancers. There are other less common hereditary cancer syndromes that include predispositions to breast and ovarian cancer<sup>52</sup>. Other hereditary cancer syndromes often have similar characteristics, including early onset cancers, high penetrant cancer risks, and follow an autosomal dominant pattern. Refer to Appendix A for an overview of other hereditary breast and ovarian cancer syndromes.

#### **1.2.4.3 Medical Management Options**

Management guidelines for individuals with HBOC are published by the National Comprehensive Cancer Network<sup>4</sup>. The guidelines for women with HBOC include:

##### **Breast cancer**

- Clinical breast exams, every 6-12 months, beginning at age 25
- Mammogram and breast MRI, annually, beginning at age 25
- Consider prophylactic mastectomy
- Consider chemoprevention options, such as selective estrogen receptor modulators (Tamoxifen) or aromatase inhibitors

##### **Ovarian cancer**

- Prophylactic bilateral salpingo-oophorectomy (BSO), upon completion of childbearing or between the ages of 35 and 40
- For those who do not elect to undergo prophylactic BSO, trans-vaginal ultrasound and CA-125 blood tests, every 6 months, beginning at age 30 or 5-10 years before the earliest ovarian cancer diagnosis in the family
- Consider chemoprevention options, such as oral contraceptives

The guidelines for men with HBOC include:

#### Breast cancer

- Clinical breast exam, every 6-12 months, beginning at age 35
- Consider baseline mammogram at age 40, and annual mammogram if excess or dense breast tissue is present

#### Prostate cancer

- Prostate cancer screening, including digital rectal exam and PSA measurements, annually, beginning at age 40

At this time, no specific guidelines exist for pancreatic cancer and melanoma. Screening may be individualized based on cancers observed in the family. Annual, full-body dermatological exams and ophthalmologic exams may be considered for melanoma screening. Endoscopic ultrasounds, MRIs or other investigational protocols may be considered for pancreatic cancer detection.

### **1.2.5 Genetic Testing for HBOC**

Molecular genetic testing for *BRCA1/2* is available to confirm the diagnosis of HBOC, as well as the identification of at-risk family members. Clinical testing has been available commercially since October 1996<sup>2</sup>.

#### **1.2.5.1 Recommendations and Guidelines for Genetic Testing**

Recommendations for genetic testing for cancer susceptibility are published by The American Society of Clinical Oncology<sup>53</sup>. These guidelines state that genetic testing should be offered when:

- There is a personal or family history suggestive of a hereditary cancer syndrome

- Genetic testing results can be adequately interpreted
- The results will aid in the diagnosis or impact medical management of the patient or at-risk family members

Testing criteria for HBOC are published by the National Comprehensive Cancer Network<sup>4</sup>. The testing criteria includes the following:

- Individual from a family with a known deleterious *BRCA1/2* mutation
- Individual with a personal history of breast cancer (including IDC and DCIS) and one or more of the following:
  - Breast cancer diagnosed  $\leq 45$  years
  - Two breast primaries, the first breast cancer diagnosed  $\leq 50$  years
  - Breast cancer diagnosed  $\leq 50$  years with  $\geq 1$  close blood relative with breast cancer at any age or with a limited family history
  - Breast cancer diagnosed  $\leq 60$  years and is triple negative breast cancer
  - Breast cancer diagnosed at any age with  $\geq 1$  close blood relative with breast cancer diagnosed  $\leq 50$  years
  - Breast cancer diagnosed at any age with  $\geq 2$  close blood relatives with breast cancer diagnosed at any age
  - Breast cancer diagnosed at any age with  $\geq 1$  close blood relative with epithelial ovarian cancer
  - Breast cancer diagnosed at any age with  $\geq 2$  close blood relatives with pancreatic cancer or aggressive prostate cancer at any age
  - Breast cancer diagnosed at any age and  $\geq 1$  close male blood relative with breast cancer

- Breast cancer diagnosed at any age of an ethnic background associated with higher mutation frequency (eg, Ashkenazi Jewish).
- Personal history of epithelial ovarian cancer
- Personal history of male breast cancer
- Personal history of pancreatic cancer or aggressive prostate cancer at any age with  $\geq 2$  close blood relatives with breast and/or ovarian and/or pancreatic or aggressive prostate cancer at any age
- Family history only
  - 1<sup>st</sup> or 2<sup>nd</sup> degree blood relative meeting any of the above criteria
  - 3<sup>rd</sup> degree relative with breast cancer and/or ovarian cancer with  $\geq 2$  close blood relatives with breast cancer (at least 1 diagnosed  $\leq 50$  years) and/or ovarian cancer

#### **1.2.5.2 Genetic Testing Methodologies**

The clinical methodologies for molecular genetic testing of *BRCA1/2* include sequence analysis, deletion/duplication analysis, and targeted mutational analysis. Testing is performed using DNA extracted from a peripheral blood sample or buccal sample<sup>2</sup>. Until recently, the majority of genetic testing for *BRCA1/2* was performed by Myriad Genetic Laboratories due to patent rights of the sequence analysis. In June 2013, the U.S. Supreme Court ruled that DNA fragments of the human genome are ineligible for patent rights<sup>54</sup>. Sequence analysis is now offered by more than nine labs in the United States.

Deletion/duplication analysis is available to identify large genomic rearrangement within *BRCA1* and *BRCA2* and is estimated to identify an additional 12% of mutations<sup>41; 55</sup>.

Targeted mutational analysis is available for detecting the three HBOC founder mutations of individuals of Ashkenazi Jewish ancestry<sup>2</sup>. Targeted 3-site analysis is estimated to detect 90% of mutations within this population. Site specific mutational analysis is also available to identify the presence of known familial mutations<sup>2</sup>.

With the advancements in next generation sequencing, panels have allowed the evaluation of multiple genes associated with other hereditary breast and ovarian cancers syndromes<sup>52</sup>. This approach has been useful for patients and families that present with features of more than one hereditary cancer syndrome. This makes testing for multiple genes more efficient and cost effective. While some of the genes included in these panels are well-described, several lesser known genes are included, for which cancer risks and medical management recommendations for mutations carriers are unclear at this time.

#### **1.2.5.3 Genetic Testing Strategies and Results Interpretation**

To ensure the most informative results, genetic testing for *BRCA1/2* is initiated for those with a personal history of breast and/or ovarian cancer whenever possible<sup>4</sup>. Comprehensive testing is indicated for the family member with the highest likelihood of carrying a *BRCA1/2* mutation. If more than one family member is affected, individuals with the youngest age of diagnosis, those with bilateral breast cancer, multiple primaries, and ovarian cancer have the strongest likelihood of being carriers<sup>4</sup>. If no mutation is identified in the most appropriate person to test within the family, testing other family members is not necessary or useful, thus conserving healthcare resources. If a mutation is identified, it allows for site-specific mutational analysis for other family members, and test results are informative even for those family members who are unaffected.

For individuals of Ashkenazi Jewish (AJ) descent, it is recommended that testing begin with targeted mutation analysis of the three specific founder mutations<sup>4</sup>. If no mutation is detected

with the 3-site mutation analysis and the individual meets NCCN criteria for HBOC, despite their Ashkenazi Jewish ancestry, follow up testing for comprehensive analysis is available. It is recommended that individuals within the AJ population be tested for all three AJ founder mutations, rather than site-specific testing for a known AJ mutation within their family<sup>4</sup>. This is due to the increased frequency of these mutations within the AJ population and the identification of two founder mutations within some AJ families.

There are four possible test results from *BRCA1/2* genetic testing<sup>4</sup>. A “true positive” result means that an individual is a carrier of a *BRCA1/2* mutation, which increases the risk for HBOC-related cancers. A “true negative” result means that an individual is not a carrier of a *BRCA1/2* mutation previously identified within the family. In the absence of a known family mutation, A “no mutation detected” result mean that an individual was not found to be a carrier of a *BRCA1/2* mutation and cancer risk is based on personal and family history. Lastly, a “variant of uncertain significance” (VUS), indicates identification of a subtle change within *BRCA1/2* for which the risk of HBOC-related cancers is unknown.

Disclosure of results should include personalized interpretation of results, including cancer risk assessment and identification of at risk family members<sup>48</sup>. This information should be conveyed for positive, negative, and inconclusive results.

#### **1.2.5.4 Benefits and Limitations of Genetic Testing**

ASCO recommends that genetic testing include pre-test counseling, including a discussion of possible benefits and limitations of testing<sup>53</sup>. The benefits of genetic testing for HBOC include the clarification of personalized cancer risks and risk management. Information about mutation status can aid in the making of informed decisions regarding medical management for both individuals with a personal history of cancer and those who do not. Another potential benefit of genetic testing



is the clarification of risk for other family members. Identification of a *BRCA1/2* mutation in one family member enables other at-risk family members to determine whether or not they share the same cancer risks.

Genetic testing for HBOC has limitations since only a small portion of these cancers will be due to an identifiable gene mutation and genetic testing is unable to identify all possible mutations. This means that a negative test result is most informative when there is a known mutation identified within a family. In the absence of a known family mutation, interpretation of a negative result may be limited, particularly when testing an unaffected individual. The possibility of identifying a VUS is approximately 2.9-7.8%<sup>56</sup>, depending upon the population tested. For those individuals, medical management decisions are based upon personal and family history. It is also possible that other genes are contributing to hereditary breast and ovarian cancer within a family. Other limitations of genetic testing include the inability for prevention and screening methodologies to detect all cancers at an early stage.

Individuals are often concerned about the risk of confidentiality and the risk of genetic discrimination by insurance companies<sup>57</sup>. In 1996, the Health Insurance Portability and Accountability Act (HIPAA) was enacted, which provides the protection of medical information, including genetic information for individuals within group health insurance plans<sup>58</sup>. In 2008, the Genetic Information Nondiscrimination Act (GINA) was enacted, which protects patients from potential discrimination from employers and health insurance companies based on genetic testing information<sup>57</sup>. The law does not protect individuals from discrimination in the context of life insurance, disability, and long-term care insurance providers.

### 1.2.6 Psychosocial Issues Related to HBOC

According to the National Society of Genetic Counselors' recommendations for genetic testing, psychosocial assessment of the patient should be included in both the pre- and post-test genetic counseling process<sup>48</sup>. This includes identifying the patient's motivation for genetic testing and assessing the patients understanding of information and testing process. Genetic testing may have a great impact on their medical management decisions, lifestyle, and relationships with others.

For individuals who have experienced an HBOC-related cancer, a positive test result can bring about a variety of emotions, both positive and negative<sup>59; 60</sup>. For some, a positive test result can provide an explanation for the cancer diagnosis. For others, a positive result may induce feelings of anxiousness, sadness, and fear related to additional cancer risks that are associated with having a *BRCA1/2* mutation. In addition, feelings of guilt regarding passing a mutation to children may result.

Approximately 20% of *BRCA1/2* mutation carrier women experience high distress after receiving their genetic testing results<sup>59</sup>. However, distress symptoms, including anxiety, sleeplessness, and changes in mood, were often minimal, did not affect everyday life activities, and greatly resolved after one year<sup>59</sup>.

Receiving a negative test result may bring similar emotions as a positive result. For most individuals, a negative test result is reassuring and brings relief from knowing they are not at a substantially increased risk for the development of HBOC-related cancers<sup>59</sup>. For others, a negative result can be associated with "survivor guilt", especially if a mutation has been previously identified within a family, and other family members, including siblings, have inherited the mutation<sup>61</sup>.

## **1.3 RECONTACTING PATIENTS IN CANCER GENETICS**

### **1.3.1 Possible Situations for Recontact**

There are several situations in which recontact of patients by their genetics providers has been considered, including reclassification of “variant of uncertain significance” test results and availability of additional testing options.

#### **1.3.1.1 Variants of Uncertain Significance (VUS)**

As uptake of genetic services and the utilization of genomic sequencing increases, the frequency in the number of unreported gene changes, where the clinical significance is uncertain, will increase as well<sup>62</sup>. The reporting of these novel sequence variants to physicians, genetics providers, and patients must include a clinical interpretation based on the current data available at the time of testing. Family studies and gene expression studies may be useful to clarify new variants, and clinical laboratories often work with researchers to classify these new variants as either harmful or benign<sup>63</sup>.

Because variants of uncertain significance are uncommon, knowledge of them is often restricted to a few laboratories, and they may not be published in the literature. Testing laboratories may be the most appropriate entity to modify the interpretation of a VUS. Therefore, testing laboratories should make an effort to contact physicians and/or ordering providers in the event that a VUS should be reclassified<sup>64</sup>. Reclassification of a VUS may help dissipate any psychological distress while clarifying cancer risks and helping to define the most appropriate medical management services for an individual<sup>65</sup>. At the present time, genetics providers and patients who

receive VUS results should discuss a plan for recontact in the event that new information becomes available<sup>62</sup>.

### **1.3.1.2 New Genetic Testing Methods**

Technical advances in genetic testing that include improved sensitivity of testing are relevant for patients who have undergone previous testing with a less sensitive test. For example, sequence analysis of *BRCA1/2* has been available since 1996 and since that time a number of changes have occurred to the testing process. In August 2006, Myriad Genetics<sup>®</sup> introduced a new component to *BRCA1/2* testing, called BART (BRACAnalysis Rearrangement Test<sup>®</sup>) which aimed to detect large genomic rearrangements in *BRCA1/2*<sup>55</sup>. When BART<sup>®</sup> was first introduced, Myriad Genetics established specific testing criteria based on personal and family history, offering testing to individuals with a greater than 30% risk of carrying a *BRCA1/2* mutation<sup>55</sup>. Current NCCN Criteria for HBOC recommends large rearrangement testing for all patients undergoing *BRCA1/2* sequencing, based on studies supporting the benefits of large rearrangement testing in individuals who do not have high pretest probabilities of carrying a mutations in *BRCA1/2*<sup>4;20</sup>. Currently, large rearrangement testing can be performed simultaneously with sequence analysis of *BRCA1/2*<sup>55</sup>. Because large rearrangement testing was determined to be a useful test for all individuals undergoing *BRCA1/2* sequencing, the question of recontact has been raised for those patients who had *BRCA1/2* sequence analysis before the introduction of large rearrangement testing<sup>66</sup>.

Until recently, only single gene tests were available for hereditary cancer syndromes. The introduction of next-generation sequencing has allowed for simultaneous testing of multiple hereditary cancer genes<sup>67</sup>. The main benefit of this approach is to carry out genetic testing in a cost effective manner for individuals whose personal and family histories are suspicious for more than one hereditary cancer syndrome. Testing for a panel of genes can lead to greater sensitivity for

assessing cancer risks compared to sequential genetic testing of individual genes and will be more cost effective. Improving risk assessment can aid clinicians in making more informed decisions about cancer prevention and screening by identifying individuals most likely to benefit from those interventions. In addition, cancer panel screening may detect mutations in genes that would not typically be considered for testing based on medical or cancer family history, thus allowing the ability to identify cancer risks that would not have previously been considered and for which management options can be developed. It's unlikely that an individual will meet criteria to warrant genetic testing for all of the genes included in a panel. However, it is estimated that approximately 30% of individuals with a mutation in a cancer predisposing gene will not have a family history significant enough to warrant testing due to incomplete penetrance, sex limited expression, or lack of personal/family history.<sup>67</sup> Offering cancer gene panels to a wider population to allow the ability to assess risks in individuals who do not meet the standard high risk criteria for offering genetic testing has been suggested<sup>68</sup>.

While there are many advantages to the utilization of multi-gene panels, there are still a number of challenges to recognize within the clinical setting. One challenge includes defining a target population to offer testing to in order to achieve the most appropriate use of resources. In addition, interpretation and communication of test results presents additional challenges<sup>68</sup>. This includes the possibility of multiple pathogenic mutations identified and the increased chance of identifying a variant of uncertain significance. Even with the identification of single pathogenic mutations within one gene, the ability to provide accurate cancer risks may be limited by the availability of such data. For less common low penetrant variants, large prospective studies that provide lifetime risk estimates of associated cancers are lacking. Implications of positive test results are also complex, as they differ for each gene and mutation detected. Availability of risk

reduction, prevention, and treatment options may vary widely depending on which gene is involved, especially for the lesser known low penetrant genes. For lower penetrance genes that lack established management guidelines, the clinical implications are less clear.

Over time, supporting evidence for cancer risks and management consensus will emerge as utilization of cancer gene panels increases and large-scale studies are coordinated. Just as individuals have elected to pursue large rearrangement testing after *BRCA1/2* sequence analysis, patients who have previously tested negative for *BRCA1/2* may also benefit from undergoing testing of other hereditary cancer genes.

### **1.3.2 ACMG Policy Statement: “Duty to Recontact”**

Due to the evolving nature of genetic testing availability, the American College of Medical Genetics (ACMG) introduced a policy statement regarding the responsibilities of recontact when new genetic information arises<sup>5</sup>. The policy states that after an initial genetics consultation, the referring physician, the designated primary care physician, and the patient should receive a written summary of the recommendations made, including recommendations for the patient to contact the genetics providers upon new advances in genetic testing<sup>5</sup>. In a small percentage of cases, where the medical genetics provider provides an on-going service, it is the medical geneticist’s responsibility to provide clinical updates to those patients. The policy also states that the patient should be properly counseled to share updates to their medical and family history with their primary care physician and/or genetics provider. This policy was established to identify whose responsibility it is to recontact patients, when the recontact should occur, and whether the patient is a responsible party in the process of obtaining new genetic information.

### **1.3.3 Primary Care Responsibilities**

The ACMG “Duty to Recontact” policy places the responsibility of keeping patients informed of genetic discoveries on the referring physician and/or the primary care physician, due to the continuous relationship they establish with their patients. Previous studies have observed several barriers that primary care physicians face regarding the delivery of genetic service information. Often times, primary care providers are overwhelmed in keeping up to date with advances in clinical genetics and genetic testing technologies. This includes a general lack of basic knowledge of genetics and lack of awareness of genetic services<sup>69</sup>.

As previously stated, identification of individuals at high risk for hereditary cancer syndromes requires an adequate family history assessment and can influence genetic testing recommendations. Studies have shown that while primary care physicians do utilize family history information as the primary tool for referral, family history information tends to be under-collected in clinical practice<sup>70</sup>. Physicians may be less adequately trained to obtain or document a complete family history, which includes cancer type and ages of diagnosis. Age of diagnosis is frequently omitted from family history interview questions<sup>70</sup>. Family history information is often less accurate when the complexity of family history increases, such as an increasing number of cancer diagnoses within a family. Other studies have reported physicians’ lacking skill in constructing a three-generation pedigree and interpreting cancer risks by pedigree analysis. Often times, lack of time spent with a patient is considered a barrier to the ability to collect such information. One observational study of 138 primary care physicians concluded that physicians spend less than two and a half minutes discussing family history information with patients<sup>69</sup>.

Overall, physicians demonstrate insufficient knowledge of hereditary breast and ovarian cancer and other hereditary cancer syndromes, lacking the ability to distinguish low and high risk

patients<sup>71</sup>. Physicians also lacked basic knowledge of hereditary cancer syndromes, including inheritance patterns and cancer risks. While physicians were comfortable referring to genetics providers, they had less knowledge of their availability and the services which were provided. Limited knowledge of the genetic testing process, including methods and costs of testing has also been observed.

#### **1.3.4 Patient Responsibilities**

The ACMG “Duty to Recontact” policy also places a large role of responsibility upon the patient to seek new information regarding genetic discoveries. Patients obligations include the action of contacting their physician or provider at previously agreed to periods of time for new information, making reasonable effort to understand the nature and implications of new information, and making reasonable use of resources available to keep themselves informed<sup>72; 73</sup>. In addition, patients may request additional consultations for clarification of information or if genetic counseling is needed.

#### **1.3.5 Genetics Providers Responsibility**

Despite the current ACMG policy, genetics professionals have struggled with the notion of their own “duty to recontact”. This phrase refers to the ethical and/or legal obligations of genetics service providers to recontact former patients regarding advances in genetic testing services that may be relevant to them<sup>74</sup>. There may be a continuing obligation to recontact the client when new information becomes available that would have an impact on that client’s decision making<sup>75</sup>.



There are several situations in which there may be an ethical obligation to recontact patients: 1) for an individual in whom a diagnosis is suspected, but not achieved, 2) when a more accurate diagnostic and/or prognostic test has been developed. 3) when new information may alter the prognosis or recurrence risk estimates<sup>74</sup>.

Attitudes regarding a moral obligation to recontact patient has previously been assessed. A study by Fitzpatrick et al, 1999 administered surveys to 1,000 randomly selected members of the American Society of Human Genetics, who were primarily physician geneticists (41%), Ph.D. geneticists (30%), and genetic counselors (18%)<sup>74</sup>. Respondents, overall, agreed that the responsibility for staying in contact with patients should be shared between all health professionals and patients. However, 46% of individuals agreed that recontacting patients should be the standard of care, while 43% answered that recontacting patients should not be the standard of care. This divide may be due to the consensus from genetics providers that recontact is ethically desirable in most cases; however, it is neither feasible nor practical<sup>76</sup>.

### **1.3.6 Current Practice and Limitations of Recontact**

Currently, there are no practice guidelines or standards of care to follow for patient recontact, so many genetics providers are left to follow their best clinical judgment<sup>77</sup>. In all situations, genetics providers' documentation should include a request to the patient to keep in touch, especially if their personal history or family history changes. A patient letter may also include statements about the potential future of genetic testing and availability of testing as technological advances arise<sup>63</sup>.

Strategies of recontact have been suggested, including identifying a target population to recontact by means of chart reviewing or extracting information from a database<sup>66</sup>. Once a target population is identified, an effort to recontact those individuals through various methods may be

achieved (personalized letters, phone calls, or newsletters) depending on the population size and resources available.

Some genetics providers have addressed their concerns regarding the limitations of recontact and have proposed methods for how to recontact patients successfully<sup>77</sup>. The use of an adequate clinical database that includes patient names, addresses, and genetic testing result may be essential for the ability to recontact patients. This information allows the ability to query appropriate individuals and readily perform a bulk mailing. The information presented to the patient must be presented in a clear, concise manner with as much information as possible about the new genetic test.

Genetics providers who initiate recontact should be prepared to handle an influx of additional patients. This would include availability of appointment times, in addition to regularly scheduled new patients. No matter how reliable the database, certain patients who should be notified may be missed, due to lack of current contact information, viability status, and human error of incorrect data entry. Addressing these issues can be very cumbersome and time consuming. While careful planning can reduce some of these issues, they will never be eliminated completely.

### **1.3.7 Patient Preference for Recontact**

Limited information exists regarding patient expectations and preferences concerning recontact to provide updated information regarding advances in cancer genetics. Griffin et al., 2007, conducted a study to evaluate the preferences for recontact of colon cancer genetics patients previously seen by the Colon Cancer Risk Assessment Clinic at Johns Hopkins Hospital. The study included recontact of former patients with information about recent advances in colon cancer genetics,

including large rearrangement testing and the discovery of the *MSH6* and *MUTYH* genes. Results of the study revealed that the majority of patients wanted an ongoing relationship with their genetics providers (63%), and preferred that contact be re-established by their genetics providers (65%). In addition, 51% of patients wanted to be contacted with information that was specifically relevant to their own personal medical history. Preferences for methods of recontact included personalized letter (51%), generalized letter (35%), and newsletter (14%). Only 1% of respondents believed that recontact should be initiated by their primary care provider. Respondents believed that the primary responsibility for updating patients belonged to the genetics providers, followed by their primary care physicians and gastroenterologists. Only 10% of respondents believed that the patient held primary responsibility for seeking updated information. Studies evaluating expectations and preferences of patients tested for other cancer predisposing genes have not yet been completed.

### **1.3.8 Patient's Right Not to Know**

It must also be considered that patients have the right to not seek additional information regarding their genetic health<sup>78</sup>. Autonomy includes the right to decide whether or not to seek information, and therefore, the right to remain uninformed. By re-initiating recontact, it may be violating the patients' right to privacy and "right not to know"<sup>78</sup>. When a patient is referred for a genetics consultation, he or she has the right to refuse the appointment. Approximately 10% of genetics patients do not appear for their scheduled appointments<sup>72</sup>. Nor can it be assumed that because a patient attended the initial genetics consultation that he or she would automatically wish to be recontacted with new information.

While informing patients of new information may allow for better medical management decisions, the possible negative impact of such recontact should be considered as well. This includes the impact it would have on the psychological and emotional state of the patient, in which recontact may arouse these emotions, which were previously laid to rest<sup>72</sup>

## **2.0 EXPERIMENTAL DESIGN AND METHODS**

### **2.1 QUESTIONNAIRES**

The questionnaires used for this study were created by members of the Cancer Genetics Program of the University of Pittsburgh Medical Center and reviewed by Francesmary Modugno, PhD, MPH of the University of Pittsburgh Department of Epidemiology. Questionnaires were approved for research purposes by the Institutional Review Board at the University of Pittsburgh, Pennsylvania. The “Evaluation of Patients’ Preferences for Recontact by Cancer Genetics Providers” survey (Appendix H) included 13 multi-tiered multiple choice and order ranking questions. The “Cancer Genetics Provider Attitudes Regarding Recontact” survey (Appendix E) included 13 multi-tiered multiple choice and short answer questions. Both surveys included the opportunity for participants to elaborate on their responses and include personal comments.

Questions and data used for this study were extracted from the two questionnaires. The patient survey contained four sections: 1.) evaluation of primary care relationship, 2.) expectations for recontact, 3.) preferences for recontact by genetics providers, 4.) factors that influence decision making regarding additional genetic testing. The healthcare provider survey contained three sections: 1.) Personal background, 2.) Current practice of recontacting patients, 3.) Theoretical consideration for recontacting patients.

## 2.2 PARTICIPANTS

A query was created with the UPMC Genetics Information System to identify patients tested for *BRCA1/2* between the years 2007-2012. Throughout these years, a total of 2,771 patients were tested for *BRCA1/2*. Of the individuals tested, 19.88% tested positive for a *BRCA1/2* mutation, 2.60% received a VUS result, and 77.52% tested negative for a *BRCA1/2* mutation (Table 3). A random sample of 1000 patients was selected using the random sample function in Microsoft Excel<sup>®</sup>. A review the UPMC electronic medical records was performed to confirm vital status and current contact information for the selected participants. As illustrated in Table 4, the random sample contained a comparable proportion of *BRCA1/2* positive, negative, and VUS results to the initial sample of patients.

**Table 3. Total Number of Patients Tested for *BRCA1/2* Throughout 2007-2012**

Years	Total # patients	Positive	%	VUS	%	Negative	%
2007	282	48	17.02	11	3.90	223	79.08
2008	466	123	26.39	10	2.15	333	71.46
2009	483	106	21.95	11	2.28	366	75.78
2010	515	91	17.67	10	1.94	414	80.39
2011	489	102	20.86	10	2.04	377	77.10
2012	536	81	15.11	20	3.73	435	81.16
Total	2771	551	<b>19.88</b>	72	<b>2.60</b>	2148	<b>77.52</b>

**Table 4. Randomly Selected Patient Population**

Years	Total # patients	Positive	%	VUS	%	Negative	%
2007-2012	1000	184	<b>18.40</b>	31	<b>3.10</b>	785	<b>78.50</b>

Current members of the National Society of Genetic Counselors “Familial Cancer Risk Genetic Counseling” Special Interest Group were selected to participate in the healthcare provider

portion of the study. This special interest group (SIG) was created for individuals who provide genetic counseling and cancer risk assessment. As of January 2013, there were 490 members of the NSGC Cancer SIG.

### **2.2.1 Recruitment**

Initially, the patient survey was distributed by mail to 500 randomly selected patients who were tested for *BRCA1/2* throughout the years of 2007-2012. To increase participation, the patient survey was distributed by mail to another 500 randomly selected patients. These individuals were patients tested for *BRCA1/2* in more recent years, throughout the years of 2010-2012. Participants were given unlimited time to return surveys and a follow up phone call was given to participants who had not returned their survey after one month.

The healthcare provider survey was distributed to the 490 members of the National Society of Genetic Counselors Cancer Special Interest Group via an electronic survey. Members were given a two-week follow-up notice and several follow up notices thereafter to increase participation.

Informed consent, including a signed consent form (Appendix G) or consent waiver (Appendix C ) was obtained from participants prior to completion of the questionnaires.

## **2.3 DATA CLEANING**

A data cleaning process was developed and performed on data from the surveys. The goal of data cleaning was to minimize making changes to or making assumptions about the data to preserve

the participants' responses in order to avoid making any questions unreliable. If a Yes/No question was blank but information was entered in corresponding "If yes" question or if an answer was entered for the "If no" question, the blank Yes/No variable was changed to "Yes" or changed to "No", respectively. Questions which were skipped or had comments written in stating a phrase similar to "Unsure" or "I can't remember" were regarded as such. In addition, if a respondent wrote in an answer in an "Other reasons" box, and it was similar to an already available answer, then the response was changed to the multiple choice option. Questions which were answered improperly were discarded for those participants. These situations most commonly included improper ranking of responsibility for recontact and selecting more than one answer for questions that required only one response. In addition, the final section of the questionnaire asked participants to fill it out only if they had received a "No mutation detected" or a "Variant of Unknown Significance Detected" result from their previous *BRCA1/2* testing. Answers were discarded for individuals who received a positive "Mutation Detected" result for *BRCA1/2* and still completed this section.

Because not all respondents answered every question, the total number of responses, represented by "n", are provided for each question in the Results section.



## **2.4 DATA ANALYSIS**

After data was collected from both survey populations, statistical analyses were performed using the statistical software package SPSS Statistics 21<sup>®</sup> and Microsoft Excel<sup>®</sup> formulas. Qualitative and descriptive statistics were produced for selected study characteristics. Chi-square and Fisher's exact tests were used to analyze and identify centralized themes within the data. A p-value of  $\leq 0.05$  was considered statistically significant.

## **3.0 RESULTS**

### **3.1 SPECIFIC AIM 1: PATIENTS**

#### **3.1.1 Response Rate**

In total, there were 254 complete surveys returned from 1000 randomly selected patients. The response rate for completion of the survey was 25.4%. An additional 18 surveys were discarded due to being undeliverable to the sender or for containing incomplete study documentation (lack of signed consent forms or survey). We can conclude that the responses of those who completed the survey are representative of the randomly selected patient population with 5.31% margin of error determined by the Krejcie and Morgan Table: “Determining Sample Size for a Given Population”<sup>79</sup>.

#### **3.1.2 Demographics**

Table 5 illustrates the characteristics of the participants by several categories including: gender, age, year of *BRCA1/2* testing, and *BRCA1/2* test results.

**Table 5. Characteristics of Patients**

Gender	Responses	%
Male	15	5.91
Female	239	94.09
Age	Responses	%
18-24	1	0.39
25-34	12	4.72
35-44	41	16.14
45-54	74	29.13
55-64	81	31.89
>65	45	17.72
Year	Responses	%
2007	12	4.72
2008	20	7.87
2009	27	10.63
2010	79	31.10
2011	52	20.47
2012	64	25.20
Result	Responses	%
Negative	194	76.38
Positive	49	19.29
VUS	11	4.33

Of the 254 individuals who responded, 94% were female and nearly 6% were male. The ages of the study participants were grouped and the groups ranged from 18 years to greater than 65 years. The majority of participants were over the age of 45 years, which is consistent with the age range for the population of patients that are typically referred for *BRCA1/2* testing. More responses were collected from individuals tested between 2010-2012, reflective of the larger proportion of patients selected from these years to participate in the study. Characteristics from patients who did not respond were similar, signifying there were no biasing demographic factors within the study population.

Response rates for each year the patients received genetic testing and the response rate for each *BRCA1/2* results group were analyzed separately (Tables 6 and 7). Response rates were

almost equally distributed, ranging from 20% to 34% for the five years that participants were selected from. Response rates were the highest (34.5%) among individuals who received a “variant of uncertain significance” result, and rates were similar between those who had received positive and negative results, at 26.6% and 24.7% respectively.

**Table 6. Patient Response Rate by Year**

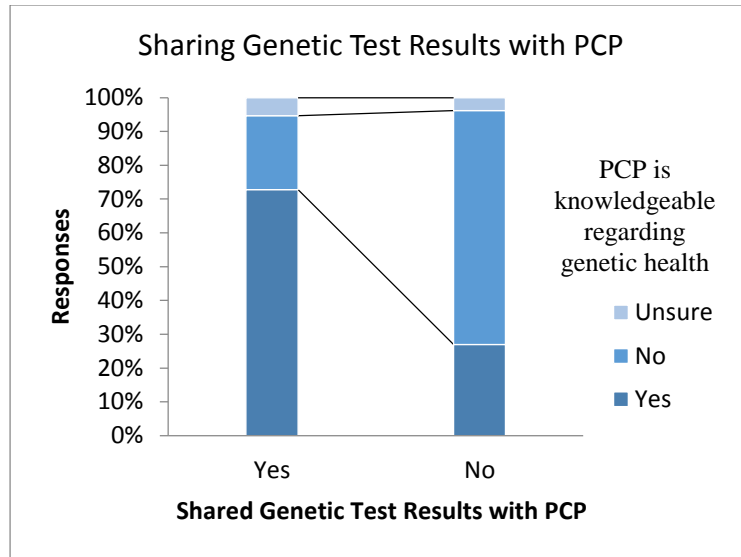
Year	Reponses	Total	%
2007	12	47	25.53
2008	20	78	25.64
2009	27	79	34.17
2010	79	274	28.83
2011	52	249	20.88
2012	64	273	23.44
Overall	254	1000	25.40

**Table 7. Patient Response Rate by *BRCA1/2* Results**

	Responses	Total	%
Positive	49	184	26.63
Negative	194	785	24.71
VUS	11	31	35.48
Overall	254	1000	25.40

### **3.1.3 Evaluation of Primary Care Physician and Specialist Relationship**

Of the 254 responses, 89.8% of patients reported seeing their primary care physician regularly. Of those individuals, 74.1% reported that they had shared their genetic test results with their PCP. Those who shared their genetic testing results with their PCP primarily (72.8%) believed that that their PCPs were knowledgeable regarding their genetic health. Whereas of the 22.8% of patients who did not share their genetic testing results with their PCP, only 26% believed that their providers were knowledgeable regarding their genetic health (Figure 2).



**Figure 2. Sharing Genetic Test Results with PCP and Perceived PCP Knowledge**

There was statistical significance (p-value <0.0001) showing a relationship between those who thought their PCP was knowledgeable regarding their genetic test results and their decision to share test results with those providers (Table 8).

**Table 8. Sharing Genetic Test Results with PCP vs. Perceived PCP Knowledge by Patients**

		Shared genetic test results	
		No (%)	Yes (%)
PCP knowledgeable regarding genetic health n=210	No	36 (17.1)	37 (17.6)
	Yes	14 (6.6)	123 (58.5)
p-value		<0.0001	

The same question was asked of the participants regarding their oncologist/breast specialist. In total, 79.9% reported seeing their specialists regularly. Of those individuals, 95.5% had shared their genetic testing results with their provider. Those who shared their genetic testing result with their specialist primarily believed (83.3%) that their provider was knowledgeable

regarding their genetic health. Of the 2.9% who did not share their results with their specialist, 88.3% believed that their providers were knowledgeable regarding their results.

In addition, there was no statistical significance showing a relationship between those who thought that their specialist was knowledgeable regarding their genetic test results and their decision to share test results with those providers. Tables illustrating these variables are located in Table 24 and Table 25 of Appendix I.

### **3.1.4 Expectations for Recontact**

The survey asked patients to determine whose primary responsibility it is to keep patients informed regarding new genetic discoveries by ranking the following: patient, primary care provider (PCP), specialist, and genetics provider (Table 9). Forty-eight percent responded that their genetics providers held the most responsibility, while 38.6% ranked their specialist as having the most responsibility. Only 7.7% of patients found themselves the most responsible, while patients found their PCP least responsible (5.1%).

**Table 9. Primary Responsibility for Recontact According to Patients**

n=254	Responses	%
Patient	15	7.73
PCP	10	5.15
Specialist	75	38.66
Genetics provider	94	48.45

Patients' expectations for recontact by their providers was compared with their responses regarding whether they shared their genetic testing results with their other providers and their perceived knowledge of the information. There were no differences observed between individuals

who believed their PCP or providers were or were not knowledgeable regarding their genetic health and which party they felt held the most responsibility for recontact (Table 26, Appendix I).

In addition, patients were asked to recall, at the time of their initial genetics consultation, whether their genetic counselor had suggested recontact if changes occurred with their personal or family's cancer history. Of the 250 patients who responded, 135 (54%) responded that they did not recall their genetic counselor's recommendation to recontact them, 89 (35.6%) did recall this information, and 26 (10.4%) were uncertain (Table 10). Responses from patients tested between 2007-2009 and patients tested between 2010-2012 was significantly different (p-value=0.05), suggesting that the patient's ability to recall this information was influenced by the time elapsed since their genetic testing (Table 11).

**Table 10. Recall to Recontact According to Patients**

n=250	Responses	%
No	135	54.00
Yes	89	35.60
Unsure	26	10.40

**Table 11. Recall to Recontact vs. Year of Testing**

	Recall			P-value
	No	Yes	Unsure	
2007-2009	37(63%)	13(22%)	9(15%)	0.05
2010-2012	98(51%)	76(39%)	20(10%)	

### 3.1.5 Preferences Regarding Recontact

The survey also examined patients' preferences for recontact including how often recontact should be initiated and by what method. Of the 250 individuals who responded, 76 (30%), indicated that recontact should be established regularly even if no new discoveries were made during that timeframe. The majority of those individuals (76.6%) indicated that recontact should be

established annually (Table 13). Forty-eight percent of individuals indicated that recontact should be established when the new information that became available was pertinent to the patient (Table 12). Personalized letters to only appropriate patients was the preferred method of recontact by 66% of individuals (Table 14) and 66% believed that specific information and how it pertained to the patient should be included in the information received by the patient upon recontact (Table 15).

**Table 12. Patient Preferences for Recontact: When**

n=250	Responses	%
Regularly, even if no new discoveries are made	76	30.04
When any new discoveries are made	48	18.97
When new discoveries are made that directly pertain to the patient	123	48.62
Unsure	3	1.19

**Table 13. Patient Preferences for Recontact: How Often**

n=76	Responses	%
> 1x/yr	8	10.53
Annually	56	73.68
Every 2-4y	5	6.58
Every 5y	3	3.95
Null	4	5.26



**Table 14. Patient Preferences for Recontact: Method**

n=250	Responses	%
Generalized letter to all patients	27	10.80
Telephone	17	6.80
Media release	0	0.00
Email	22	8.80
Personalized letter to only appropriate patients	165	66.00
Newsletter	3	1.20
Continually updated website	1	0.40
Did not answer properly	15	6.00

**Table 15. Patient Preferences for Recontact: Information Included in Recontact**

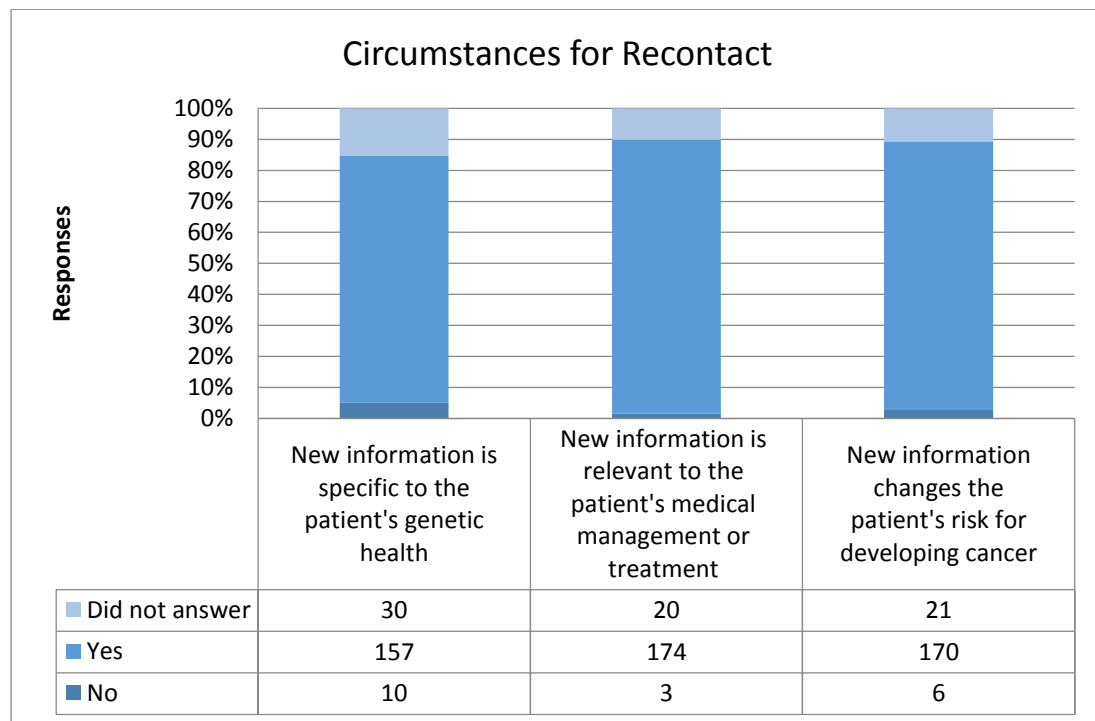
n=250	Responses	%
New information is available; ask patient to contact genetics if interested in more information	28	11.20
New information is available; identify resource where more information is available	30	12.00
Generally what new information has been identified	19	7.60
Specifically what new information has been identified and how it pertains to specific patient	165	66.00
Did not answer	8	3.20

Patients were also asked whether it should be established at a patient's first genetics consultation, whether he/she would like to be recontacted in the future if new information becomes available in the future. The majority of patients (96.8%) responded that this method should be practiced (Table 16).

**Table 16. Patient Preferences for Recontact Contract at First Consultation**

n=250	Responses	%
No	6	2.4
Yes	242	96.8
Unsure	2	0.8

In addition, patients were asked that if an individual answered “no” to be being recontacted at the initiation consult, were there any circumstances in which a provider should recontact the patient anyway. Of the 250 patients who responded, 29 (11.6%) patients indicated that there were no circumstances in which the genetics provider should recontact the patient. One hundred and ninety-seven patients (78.8%) indicated that there were certain circumstances which indicated a reason for recontact anyway, and 24 patients (9.6%) were uncertain or chose not to respond to the question. Of the individuals who indicated “yes”, the majority believed that recontact should be initiated when new information was specific to the patients’ health, medical management or treatment, or changed their risk of developing cancer (Figure 3). “Other” responses in favor of recontact included the ability to give patients a “second chance” for recontact, as their initial decision to not be recontacted may have been influenced by the overwhelming experience from their initial consultation.



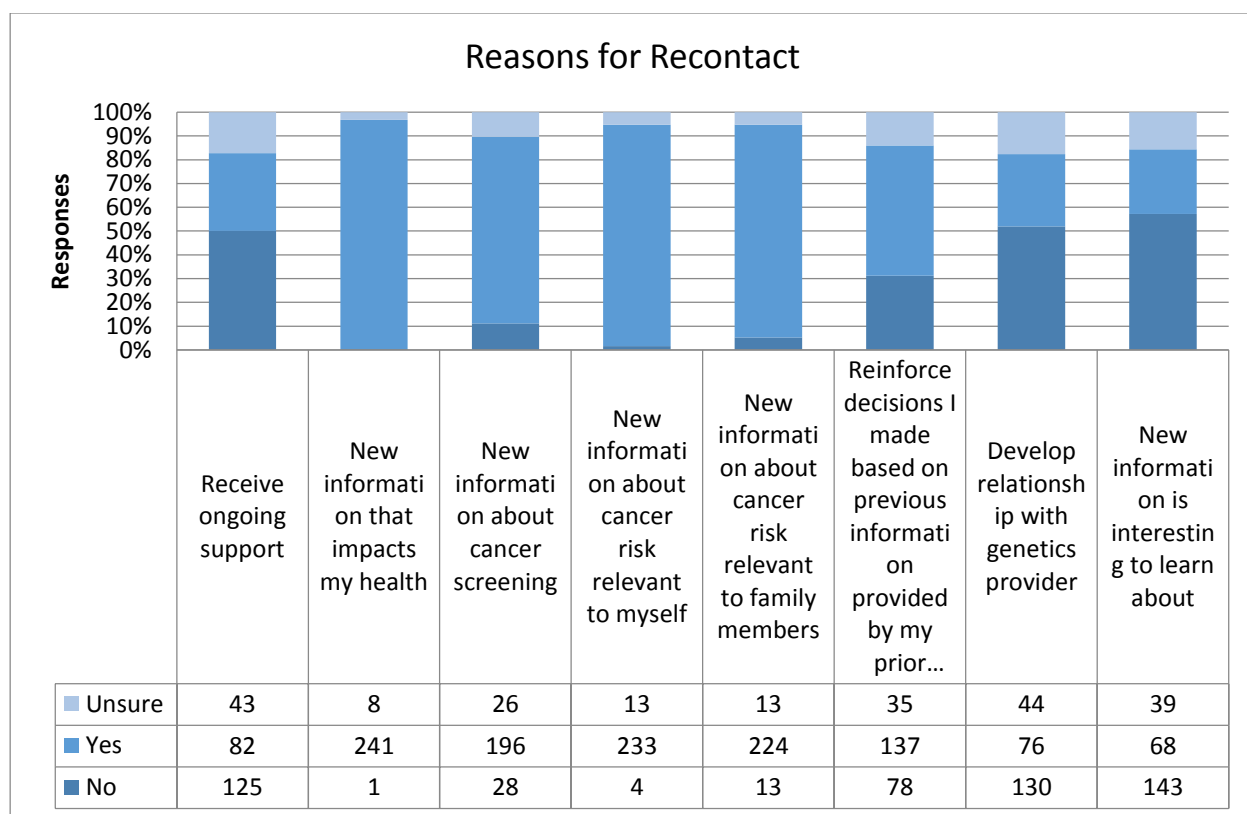
**Figure 3. Circumstances for Desired Recontact by Patients**

Other preferences regarding recontact included whether patients' interests in being recontacted would change if that meant an additional consultation with their genetics provider. Of the 253 individuals who indicated that genetics providers should recontact patients, 209 (83.6%) thought that an additional consultation would not affect their interest in being recontacted, 36 (14.4%) said that it would affect their interest, and 5 (2.0%) chose not to respond (Table 17).

**Table 17. Patient Interest for Recontact Changed when Additional Genetics Consultation is Required**

n=250	Responses	%
Yes	36	14.40
No	209	83.60
Did not answer	5	2.00

Patients were also provided with a list of conditions for recontact and were asked under which conditions they would want to be recontact by their genetics provider. Figure 4 outlines the responses. Overall, individuals believed that recontact was useful to learn about new information relevant to cancer risk for themselves and family members as well as information about cancer screening. Individuals believed that recontact was less useful to develop a relationship with their genetics providers or to receive ongoing support.



**Figure 4. Reasons for Recontact According to Patients**

### 3.1.6 Financial Factors that Influence Decision Making

Overall, 205 participants had previously received either a negative or VUS test result. Of those individuals, 174 (84.8%) said that they would be likely to pursue additional testing if they were told that new genetic testing were available (Table 18). Nearly 86% of individuals with a negative *BRCA* test result claimed they would be interested, while 63.6% of individuals with VUS test result claimed they would be interested in additional testing. Of the 174 individuals who said they would be interested in additional testing, the majority (80-92%) felt comfortable pursuing testing if tested were offered free of charge by either a research or clinical basis or if their insurance company would cover the cost of the test (Table 19). One hundred and twenty-four individuals indicated that they would be willing to pursue additional testing by paying out of pocket, as long as costs

were within reason (Table 20). Of this group, nearly 85% of individuals claimed that a reasonable cost for additional testing would be less than \$499. Only 9.6% of individuals were willing to pay out of pocket for additional testing, regardless of cost.

**Table 18. Interest in Additional Genetic Testing by *BRCA* Negative and VUS Patients**

	Would be interested in pursuing additional testing						
	Total	Yes	%	No	%	Unsure	%
Neg	194	167	86.08	23	11.86	4	2.06
VUS	11	7	63.64	2	18.18	2	18.18
Total	205	174	84.88	25	12.20	6	2.93

**Table 19. Financial Factors for Additional Genetic Testing for *BRCA* Negative and VUS Patients**

n=174	No	%	Yes	%	Unsure	%
Provided free of charge through research	5	2.87	156	89.66	13	7.47
Provided free of charge , but not through a research study	12	6.90	140	80.46	22	12.64
If my insurance would cover the cost of testing	4	2.30	161	92.53	9	5.17

**Table 20. Reasonable Cost of Additional Genetic Testing According to *BRCA* Negative and VUS Patients**

Reasonable cost (n=124)	Response	%
<100	53	42.74
100-499	52	41.94
500-999	10	8.06
>1000	5	4.03
Unsure	4	3.23
Regardless of cost (n=124)	Response	%
No	81	65.32
Yes	12	9.68
Unsure	31	25.00

### **3.1.7 Responses based on *BRCA* test results**

Each question was evaluated comparing individuals with *BRCA* positive, negative, and VUS results. This was done by comparing responses using Fisher's exact test. Though responses varied by each results group, there were no statistically significant differences between the three groups. These comparisons and corresponding p-values can be found in Tables 27-35 of Appendix I.

## **3.2 SPECIFIC AIM 2: CANCER GENETICS PROVIDERS**

### **3.2.1 Response Rate**

In total, there were 216 responses collected from the estimated 490 members of the NSGC Cancer Special Interest Group. Of the 216 responses, 3 surveys were discarded for incomplete survey responses. The response rate for the survey was 43.5%. We can conclude that the responses of those who completed the survey are representative of the randomly selected patient population with 5.05% margin of error determined by the Krejcie and Morgan Table: "Determining Sample Size for a Given Population"<sup>79</sup>.

### **3.2.2 Demographics**

Table 21 illustrates the characteristics of the participants by several categories including: profession title, action of regularly providing cancer risk assessment in their job, type of work setting, and length of time spent providing cancer risk assessment.

**Table 21. Characteristics of Healthcare Providers**

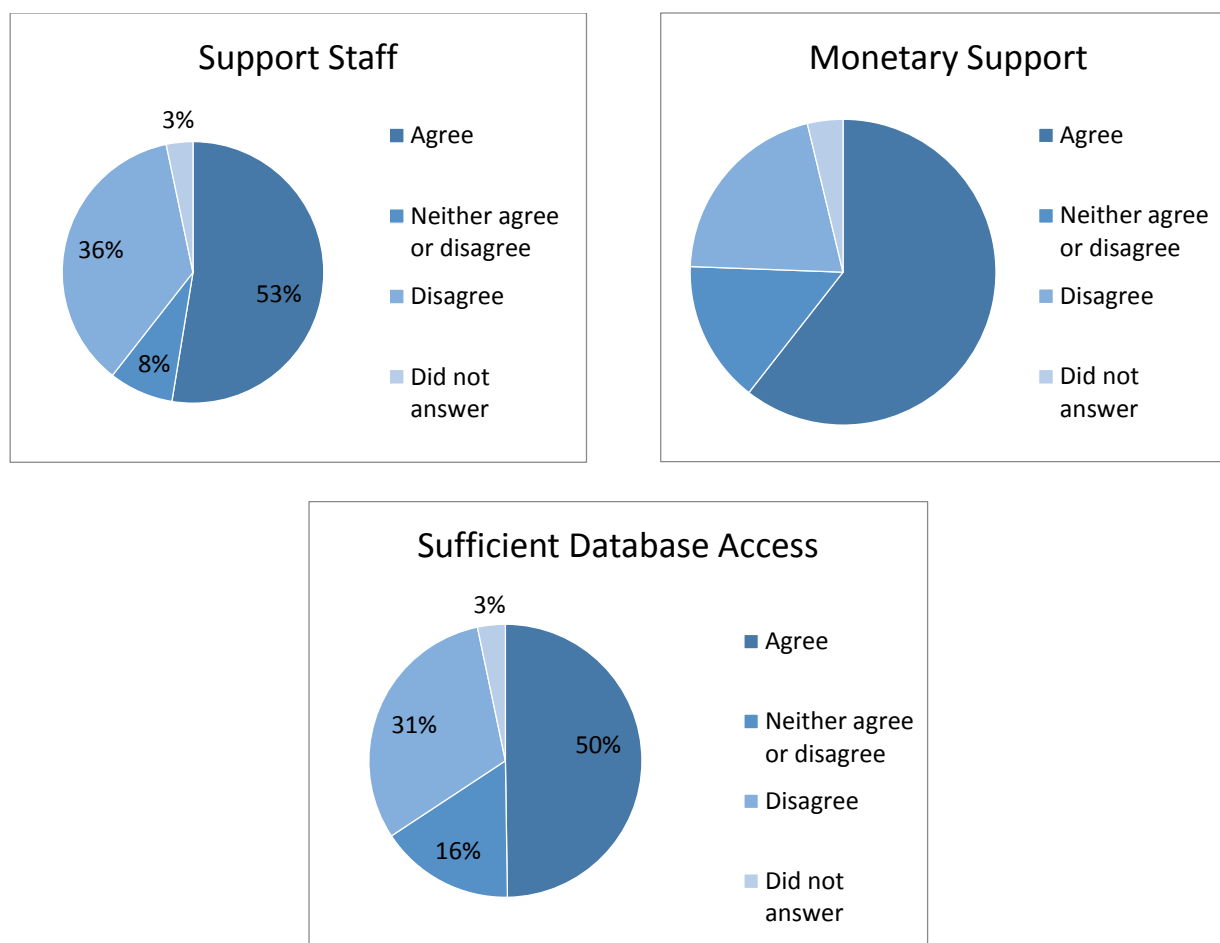
Profession	Number of Responses	%
Genetic Counselor	210	98.59
Geneticist	0	0.00
Physician	0	0.00
Physician Assistant	0	0.00
Nurse	0	0.00
Other	3	1.41
Regularly Provide Cancer Risk Assessment	Number of Responses	%
No	6	2.82
Yes	206	96.71
Other	1	0.47
Work Setting	Number of Responses	%
Independently	75	35.21
Within formal genetics department	136	63.85
Other	2	0.94
Length Providing Cancer Risk Assessment	Number of Responses	%
<1y	30	14.08
2-4y	59	27.70
5-9y	58	27.23
>10y	59	27.70
Other	7	3.29

Nearly all of the participants who completed the survey were genetic counselors (98.6%). Of the three respondents who chose “other”, two reported to be research assistants and one reported to be a genetic counseling intern. In addition, 96.7% responded that they regularly provide cancer risk assessment and 63.9% reported working within a formal genetics department. Number of years providing cancer risk assessment was divided in ranges. There was almost equal distribution, between these time frames. Demographic information for non-respondents was not available for this study sample.

### **3.2.3 Resources**

Respondents were asked to rate the following characteristics that describe the setting in which they provide cancer risk assessment (Figure 5). The majority of respondents either agreed or strongly agreed that they were provided with sufficient support staff (53%), financial support (60%), and sufficient database use (50%) within their work setting. Approximately one-third of respondents either disagreed or strongly disagreed that they were provided with these resources. Respondents were also able to select “neither agree or disagree” or chose not to respond.



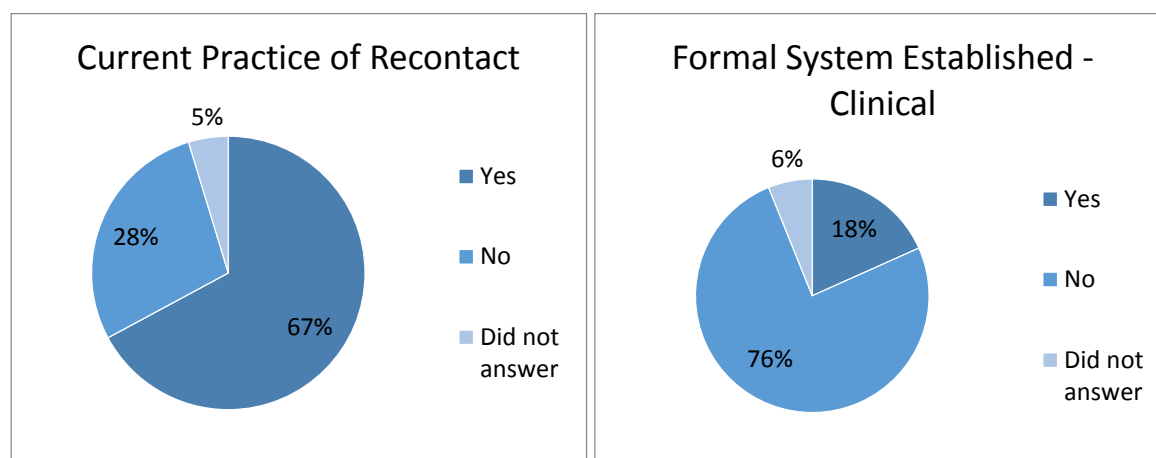


**Figure 5. Availability of Sufficient Resources According to Genetics Providers**

### 3.2.4 Current Practice of Recontact

Overall, 67% of respondents had said that they have recontacted patients for the purpose of offering additional genetic testing (Figure 6). In addition, the study revealed that only 18.3% of respondents had established formal systems of recontact for clinical purposes (Figure 6). Similar responses were observed for research purposes. Methods of recontact collected from the comments section of the survey included the use of generalized information sent to all patients via a newsletter format (mail or email) or information published on a departmental website. Other genetics providers used

a database to set reminders for specific patients whom they categorized as high risk and would benefit from additional testing. Other providers used a database to track which patients showed interest in additional testing from their initial consultations. Other individuals commented that their genetics division had collectively made decisions about pertinent groups of patients to recontact, either queried a database or did a chart review to identify eligible patients, and then contacted those patients via phone calls or personalized letters.



**Figure 6. Current Practice of Recontact by Genetics Providers**

When comparing responses from providers who have recontacted patients to those who have not, the level of support for resources was evaluated. There was a statistically significant difference in the practice of recontacting patients between those who indicated having adequate resources, including staff, monetary support, and a sufficient database (Table 22). Providers who reported having sufficient resources were more likely to recontact than those who did not report sufficient resources. This indicates a significant influence these resources have on the practice of patient recontact.

**Table 22. Genetics Providers Resources Influence on Recontact**

		Recontact (%)		P-value
		No	Yes	
Staff n=203	Disagree	30 (14.7)	47 (23.1)	<b>0.04</b>
	Neither Agree or Disagree	6 (29.5)	11 (5.4)	
	Agree	24 (11.8)	85 (41.8)	
Monetary n=202	Disagree	16 (7.9)	28 (13.8)	<b>0.005</b>
	Neither Agree or Disagree	16 (7.9)	16 (7.9)	
	Agree	28 (13.8)	98 (48.5)	
Database n=203	Disagree	22 (10.8)	44 (21.6)	<b>0.0124</b>
	Neither Agree or Disagree	16 (7.8)	18 (8.8)	
	Agree	22 (10.8)	81 (39.9)	

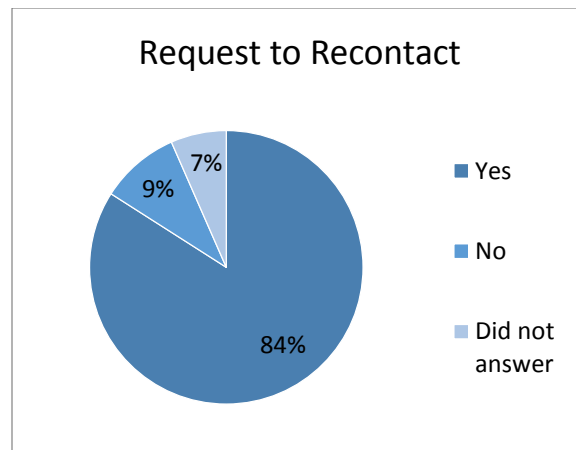
The same comparison was made regarding the degree of resources and provider's establishment of a formal system of recontact. The only statistically significant difference in having a formal system of recontact was for those who indicated having a sufficient database. Genetics providers who reported not having sufficient database access were less likely to recontact former patients than those who did report having a sufficient database. Degree of staff and monetary support did not influence the ability to have a formal system of recontact (Table 23).

**Table 23. Genetics Providers Resources Influence on Formal System of Recontact**

		Formal System (%)		P-value
		No	Yes	
Staff n=203	Disagree	66 (32.5)	10 (4.9)	0.1229
	Neither Agree or Disagree	14 (6.8)	2 (0.9)	
	Agree	80 (39.4)	26 (12.8)	
Monetary n=202	Disagree	39 (19.3)	8 (3.9)	0.2426
	Neither	29 (14.3)	3 (1.4)	
	Agree	95 (47.0)	27 (13.3)	
Database n=203	Disagree	59 (29.0)	6 (2.9)	<b>0.006</b>
	Neither	29 (14.2)	4 (1.9)	
	Agree	72 (35.4)	28 (13.7)	

Of the 213 respondents, 84% reported that they routinely direct patients to recontact their genetics providers for new information in the future (Figure 7). Approximately 9.4% reported that

they do not routinely direct patients to recontact them, while 6.6% chose not to respond to the question. Many individuals commented that this recommendation was conveyed in a letter to the patient, including the ability to recontact their genetics providers on a specific time line (annual, every 1-3 years), when there were changes noted within the family history, or when they heard about new information through the news or media. Others commented that they convey this information in person during a patient's appointment. Some providers allowed the option for patients to schedule an annual appointment or the option to receive a reminder card in the mail. Some individuals commented on the lack of interest in patients to follow through with the recommendation and often times they are better at remembering to recommend this when the patient shows more interest or when the family history is high risk.



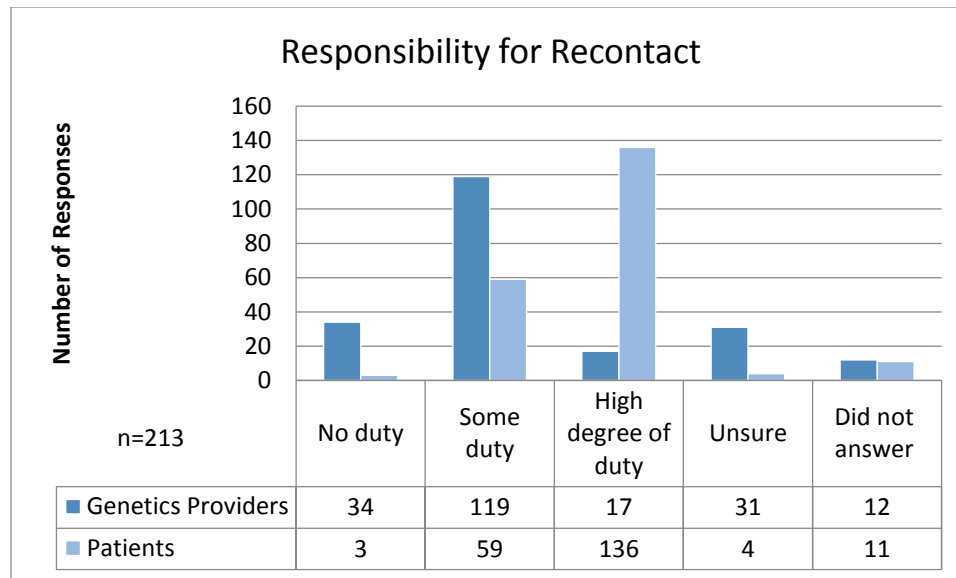
**Figure 7. Genetics Provider Routine Request for Patients Recontact**

### **3.2.5 Theoretical Considerations of Recontact**

Participants were asked to describe how much of an ethical duty genetics providers have to recontact former patients regarding new advances in genetics (Figure 8). Nearly 16% of genetics providers responded that they held no duty to recontact former patients, while 55.8% believed that

there was some duty to do so. Approximately 8% of respondents believed that there was a high degree of duty, while 14.5% were uncertain and 5.6% chose not to answer. Participants were also asked to rate how much responsibility patients have to keep in touch with their genetics providers to learn more information regarding advances in genetics. The majority of participants, 63.8%, agreed that there was a high degree of responsibility for the patient to seek out the new information. Less believed that there were either no responsibility or some responsibility of patients, 1.4% and 27.7%, respectively. Less than 2% were uncertain and 5% of respondents chose not to respond. Respondents commented that patient responsibility depended on the patient's personal interest and motivation for genetic testing and also the patient's need for genetic testing (high vs. low risk). Some genetics providers commented that they understood why patients would entrust a genetic counselor to hold the responsibility of recontact due to the intricacies of genetic testing information. Others commented about the burden felt by patients to recontact their provider multiple times over the course of years, possibly feeling embarrassed if no new information is available or feeling distress of the reminder that there is no known genetic cause.

Overall, there was no statistical difference for providers to recommend routine patient recontact between genetics providers who believed that patients had a higher responsibility to recontact than those who had less responsibility to recontact (Table 36, Appendix I)

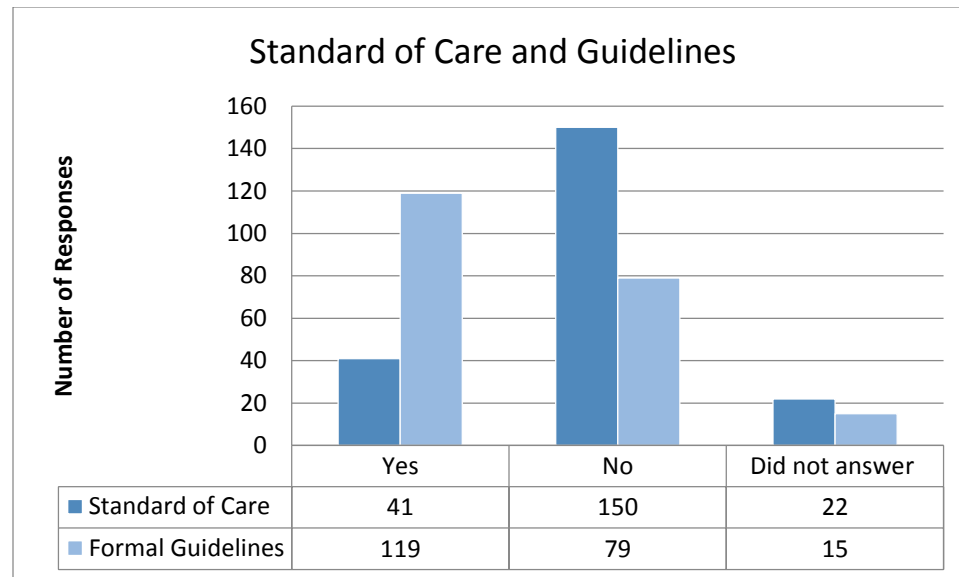


**Figure 8. Genetics Providers Attitudes Regarding Responsibility for Recontact by Patients and Genetics Providers**

Genetics providers were also asked whether recontacting patients about clinical testing advances should be the standard of care practice and whether formal guidelines should be established for the purpose of recontacting patients (Figure 9). Overall, 19.2% of respondents believed that recontact should be the standard of care, while 70.4% did not. For this question, 10.3% of participants chose not to respond. Comments from individuals who answered “yes” included beliefs that the notion was impractical due to lack of resources and infrastructure to do so. Comments from those who answered “no” aligned with belief of little duty to do so.

Overall, 55.9% of respondents believed that formal guidelines should be established, while 37.1% did not. For this question, 7% of participants chose not to respond. Comments from those who answered “yes”, included beliefs that formal guidelines would be helpful from a liability aspect, in which minimal responsibilities for recontact should be outlined, including who should be recontacted and what information should be conveyed to those individuals upon recontact. Others commented that guidelines would be useful, due to inconsistency in current practices.

Formal guidelines for recontact would be most useful if standards allowed flexibility in methods of recontact rather than mandated methods, and included strategies and suggestions for how to implement databases to quickly identify patients to recontact. Some respondents who answered “no” stated that ACMG policy guidelines were sufficient in outlining responsibilities and others stated that guidelines would quickly become unusable due to the rapid changes in technology.



**Figure 9. Genetics Providers Attitudes Regarding Recontact as Standard of Care and Desire for Formal Guidelines**

## **4.0 DISCUSSION**

This study was designed to determine patients' expectations and preferences for recontact by their genetics providers regarding new genetic tests that may become available. In addition, this study was designed to determine the utilization of recontact by genetics providers and survey the current methods used to do so. Implications of the study findings will aid in the development of recontacting strategies, as the availability of new genetic testing technologies expands. In addition, results may be useful in clarifying patient expectations for recontact to achieve better communication with patients regarding this process.

### **4.1 SPECIFIC AIM 1: PATIENTS**

The first aim of the study was to identify patients' current relationships with their primary care providers and specialists, identify patient expectations and preferences for recontact, and observe factors that may influence decisions to undergo additional genetic testing.

#### **4.1.1 Provider Relationships**

The study determined that patients were more likely to share their genetic testing results with their specialists than their primary care physicians. This observation may be biased due to the fact that the majority of individuals tested for *BRCA1/2* at the site where the study was performed are referred by a specialist, most commonly a gynecologist or oncologist. After a genetic counseling



appointment, a consult letter is sent to the referring physician, which is less likely to be the patients' PCP. Patients may also request that other physicians, including their PCP (if not the referring physician) be notified and have the option to discuss genetic testing results in person with their other providers. Therefore, patients may have had different interpretations of "sharing genetic test results", since this may have occurred through several methods of communication, either in person or through a consult letter via a genetics provider.

The study observed that patients who did not share their genetic testing results with their PCP were more likely to indicate that they did not believe their PCP was knowledgeable regarding their genetic health. Almost all of the patients had shared their genetic test results with a specialist. Therefore, there was no correlation observed between individuals who did not share their genetic test results with a specialist and their perceived knowledge of genetic information.

Notably, of 183 participants who reported having contact with both their PCP and specialist, only 3 did not share their genetic testing results with either their specialist or PCP and only 4 of 183 believed that neither their PCP nor specialist were knowledgeable. Therefore, the inability for patients to share results with a provider that they believed was knowledgeable would not impact a significant number of patients. While previous studies have proposed that healthcare providers have limited genetic knowledge, the data from this study suggests that participants believe their physician are informed and share their genetic testing results with them, signifying that PCP knowledge will not act as a barrier for disclosure as suggested by the ACMG policy to recontact. It may be that systems of recontact, through a genetics provider, could be most beneficial for patients who do not believe that their primary care physicians or specialists are knowledgeable of genetic information.

#### **4.1.2 Expectations for Recontact**

Overall, patients held their genetics providers responsible for providing them with updates, regardless of whether they believed their other healthcare providers were knowledgeable regarding their genetic testing results. There are several possibilities for this observation. Patients may hold their genetics provider to a higher standard than their other providers and themselves because as a provider who specializes in genetics, they expect those individuals to have the most expertise and knowledge regarding the topic. Because of this, patients have respect and are more confident in the information received from the genetics providers. Another reason could be the lack of communication established between the genetics provider and the patient regarding the process of receiving new information. At the cancer genetics program where the study was held, almost all patients seen between 2007 and 2012 were directed to recontact their genetics providers if changes occur within the cancer family history that may change the assessment of the family's risk. Specific statements requesting periodic recontact have been made in patient and physician correspondence since 2010 due to the evolution of genetic testing capabilities and the possible availability of new testing that could be of benefit to the patient and their family. The discrepancy in responsibility may then be due to patients not understanding the importance of this recommendation or due to the patient's inability to recall the recommendation, which was reported by 35% of patients in this study.

The proportion of patients in this study who believed that their specialists were most responsible for recontact was higher than expected when compared to responses in a similar study conducted with colon cancer patients. Griffin et al., 2007 surveyed 851 patients seen at the Colon Cancer Risk Assessment Clinic at Johns Hopkins Hospital to evaluate patients' expectations for recontact by their genetics providers. The study observed that the primary responsibility for

updating patients belonged to the genetics provider (62-67% of patients), followed by PCP (19-22%), then GI specialist (15-22%), and lastly the patient themselves (10%). The current study observed that only 48.4% of patients believed their genetics providers were most responsible, followed by their specialists (38.6%), then the patient themselves (7.7%), and last their PCP (5.1%). The new data suggests a more even divide in responsibility between genetics providers and specialists, less responsibility held by PCPs and an almost equal amount of responsibility held by patients themselves. Differences in these proportions may be due to variations in genetic counseling techniques between the two genetics programs and specific recommendations given about recontact. Alternatively, the observed differences may be due to differences in relationships between varying specialists (GI specialist vs. breast specialist), or gender (more males participated in colon cancer cohort).

Interestingly, only 5.1% of patients believed that their PCP was most responsible, yet the majority of respondents believed that their PCPs were knowledgeable regarding their genetic testing results. It is possible that knowledge of genetic health influences the perceptions of who holds more responsibility in recontacting patients when comparing all parties involved (genetics provider, specialist, PCP, and patient). However, when comparing a primary care physician to a specialist, the distinction maybe made by other factors, perhaps personal relationship with a specific provider, disease specific knowledge of a provider, and overall time spent with a provider (cancer patients may spend overall more time with an oncologist vs. PCP).

#### **4.1.3 Preferences for Recontact**

Patients' preferences for recontact were also compared to the Johns Hopkins study. This study found similar results to the colon cancer patient population, in that the majority of patients

preferred personalized letters sent to only appropriate patients and that the information directed to those patients should be specific to what new information exists, particularly pertaining to the patient. The majority of respondents desired to be recontacted only when new information was discovered that pertained directly to them.

In addition, both the current study and the colon cancer study showed that the majority of individuals thought that patients should be asked at the initial consultation whether they wished to be recontacted (96.8% and 92% respectively). In both studies, a large proportion of patients (78.8% and 47%) indicated that there were specific situations in which a patient should be recontacted regardless of whether they requested not to be recontacted. While one strategy to reduce liability issues is to recognize which patients would want to be recontacted, it may be problematic that some patients believe it is appropriate to disregard this contract under certain circumstances. There is subjectivity in determining which circumstances would be “significant enough” for recontacting patients who initially decline which also leads to the possibility of violating patients’ preferences and their right not to be recontacted.

The two studies also showed similar trends in reasons patients wished to be recontacted. More popular responses were for patients to be recontacted to receive new information regarding personal cancer risks and cancer risks to family members, information on cancer screening, and other information that may impact the overall health of the patient. Less common reasons for recontact included to develop a relationship with the genetics provider, reinforce decisions made during initial genetics consultation, and receive ongoing support.

#### **4.1.4 Factors Influencing Decision Making**

While considering patients preferences for recontact, cost of additional testing could be a key factor in the success of recontact and uptake of additional testing. Of the 205 participants with a VUS or negative *BRCA* result, the majority indicated an interest in undergoing additional testing if the option were available. Response rates were similar between the individuals who responded in this study compared to those within the colon cancer study. In both studies, patients were interested in additional testing if it were free through research or non-research based approaches. Approximately 71% indicated that they would be willing to pursue additional testing by paying out of pocket as long as costs were reasonable, and the majority indicated that reasonable costs would be less than \$499. Responses did not take into account individuals with “true negative” test results, meaning that a family mutation had already been identified and no additional testing would be indicated. Therefore, the proportion of patients interested in additional testing may be lower if those individuals been taken out of the analysis.

#### **4.1.5 Differences in Responses**

Differences in expectations and preferences for recontact between individuals who have received positive, negative, and inconclusive *BRCA1/2* test results were not observed in this study. The main limitation to this observation was the small proportion of respondents with VUS and positive test results. Further assessment is necessary to draw any further conclusions.

## **4.2 SPECIFIC AIM 2: CANCER GENETICS PROVIDERS**

The second aim of this study was to determine current practices and methods of recontacting patients held by genetic healthcare providers for the purpose of additional genetic testing opportunities. In addition, the study aimed to revisit the degree of responsibility felt by genetics providers regarding recontact of patients.

### **4.2.1 Current Practice of Recontact**

This study revealed that 67% of genetics providers have recontacted patients for the purpose of offering additional genetic testing and that 18% had established formal systems of recontact. The most recent study to determine practices of recontact was a study conducted in 1999 by Fitzpatrick et al. in which members of the American Society of Human Genetics were surveyed<sup>74</sup>. In that study, 61% reported that they had recontacted a patient regarding research advances in genetic testing. The previous study also reported that 13% of providers had developed formal systems of recontact for the specific purpose of recontacting patients. This suggests that over time, the rate of recontact has increased with the increase in opportunities for recontact (BART, additional testing). One could argue that this increase is not very dramatic for the degree of technological advances that have developed in interim of 15 years, possibly reflecting the barriers faced when recontacting patients.

Many of the barriers faced by genetics providers include limited resources. It is not surprising how much of an impact these types of resources have on the ability to recontact patients and this study supports that having sufficient staff, finances and database all impact a genetics providers' action to recontact patients. It is interesting that the only resource having a significant

influence on the ability to have a formalized system of recontact is a sufficient database. This study observed that formalized systems of recontact are less impacted by monetary support and staff, indicating the valuable role databases play in the process of recontacting patients and the value placed on recontact by the genetics providers. It is possible, in addition, that limited finances impacts the ability to invest in a sufficient database, while limited staff may also influence the ability to maintain and utilize database information. The comparison study by Fitzpatrick et al. did not inquire about resources available to those genetics providers; however, it is reasonable to suggest that resources provided to genetics programs may not have increased dramatically over the years, therefore contributing to the inability to invest in proper database systems and hence, a slow increased rate of recontact by providers.

#### **4.2.2 Theoretical Considerations**

The degree of ethical duty to recontact patients is consistent with the previous ASHG study, indicating that genetics providers believe there is “some degree of duty” to keep patients informed about technological advances. Genetics providers in the ASHG study also believed that the degree of responsibility was higher among patients than among the genetics providers themselves. This is consistent with the results of the current study, in which 63% of providers believed that patients had a high degree of responsibility for recontact, while only 8% of providers believed that genetics providers themselves had a high degree of responsibility for recontact.

This study observed that only 19.2% of genetics providers believed that recontacting patients should be the standard of care practice, while 70.4% did not. When the same question was asked in the 1999 ASHG survey, respondents showed less of a consensus: 43% believed that it should be a standard of care while 42% did not. Comments regarding standard of care practice

were similar between the two studies. Those who were in support of the decision indicated that it would only be feasible under certain circumstances, including those with sufficient assistance/resources. Those who indicated “no”, commented on similar limitations. This change in consensus overall, may be due to the experiences of recontact over time, noting first-hand the barriers to recontact and the inability to improve them throughout the years. Furthermore, the change in consensus may also be related to the degree of change that has occurred with regard to genetic testing in recent years and the amount of time and resources that would be required to frequently recontact an ever growing patient population.

In the current study, 55.9% of respondents indicated that formal guidelines should be established for recontact, with an overall trend that guidelines should include strategies for recontact. Previously, it has been observed that explicit guidelines do improve clinical practice, especially if the strategy developed is internal to the specialty<sup>80</sup>.

#### **4.2.2.1 Benefits and Limitations of Recontact**

This study observed several themes related to the perceived benefits and limitations of recontact. Comments regarding perceived benefits included providing improving quality of care for patients and the possibility of providing them with information that would reduce their uncertainty regarding medical management.

Comments regarding perceived limitations included the possibility of introducing more anxiety and stress for a patient through recontact and that information provided may create confusion for a patient. Other concerns were regarding privacy and patient autonomy. From a genetics provider perspective, limitations of recontact include limited time and staff, cost of information storage and retrieval, and lack of updated contact information for patients.



Some genetics providers believed that recontacting patients would introduce liability issues, especially in instances where patients could not be reached due to outdated contact information or potentially create unequal opportunities for additional testing based on which patients were selected to recontact.

#### **4.2.3 Differences in Expectations**

The two parts of the study indicate that patients assign a higher degree of duty to their genetics providers than genetics providers assign to themselves. This misalignment in expectations for recontact can create several areas of conflict. First, this situation can compromise the relationship between genetics providers and their patients resulting in dissatisfaction with their care. Second, the misalignment in expectations creates a potential for litigation, in which patients may be motivated by their unmet expectations for healthcare services.

Strategies to improve unmet expectations may include ways of increasing patients' awareness and responsibility for recontact. As shown by this study, the majority of patients do not recall being directed to contact their providers if there are changes to their personal or cancer family history. Mechanisms to help improve recall of this information may be useful. This may include altering delivery of this information and highlighting the importance of recontact. During a consultation, a patient may understand this recommendation, but also assume that a genetics provider may contact them with new information. Perhaps, a more comprehensive conversation regarding current recontact guidelines and the inability of a genetics provider to provide recontact services to all patients is worthwhile. A discussion on the topic of recontact during results disclosure, as well as its inclusion in the patient correspondence may help highlight the importance to a patient.

## **4.3 LIMITATIONS**

### **4.3.1 Survey and Analysis Methods**

Several limitations to the survey design were observed. The use of “ranking” questions had its limitations in this study. Some participants did not accurately answer these questions. It’s possible that this is due to lack of understanding of the directions. For instance, some individuals responded with an “X” for the individual(s) they believed most responsible for informing of genetic discoveries, instead of ranking the four providers 1-4 from most to least responsible. It is also possible that the inaccuracy of answers was due to the participant’s belief that no party was more or less responsible than another. For instance, some individuals selected “1” for all providers and the patient, indicating that all parties were equally responsible. Therefore, survey questions may or may not have been confusing for respondents. Perhaps switching between question types or requiring only one response for some questions and not others may have been a reason for the inconsistency in answers. Missing answers may reflect confusion or the lack of an appropriate response for respondents to select.

Individuals participating in the surveys were also allowed to skip questions. Therefore, blank responses may have been an indication that respondents were “unsure” of their response and chose to skip the question all together.

Specific to the patient survey, a branching format was used when inquiring whether participants see their primary care physicians regularly. If a participant indicated that he/she did not see their primary care physician or specialist regularly, they were no longer prompted to answer further questions about their relationship with that provider. However, patients may still have

shared their genetic test results with those providers and had varying opinions of the healthcare providers' knowledge with the subject matter.

Lastly, comments from participants were useful in qualitative analysis; however, they cannot be considered representative of the entire study population.

#### **4.3.2 Survey Populations**

Several limitations regarding the selected study populations were also observed. The patient population only included individuals tested for *BRCA1/2* throughout the years of 2007-2012 at the University of Pittsburgh Cancer Genetics Program. These criteria limit the diversity of the study population. Genetic counseling practices often differ between sites across the United States, including the capacity for different resources and the incorporation of different institutional regulations for genetic testing. Differences in the cost of care in specific areas may also influence patients' perspectives on genetic testing and the likelihood to pursue genetic counseling.

In addition, the patient population included only individuals tested for *BRCA1/2*. While this represents the large majority of patients seen by the cancer genetics providers, it does not include the perspectives of patients seen for other hereditary cancer predisposition syndromes.

The healthcare provider population included members of the NSGC Cancer SIG and their colleagues. The group is a paid-based membership that can have active members join at anytime and is not static. While the original estimate of the group was approximately 490 individuals, the number has likely fluctuated since that time. Because of this, it is difficult to assure that statistical significance has been met. In addition, the study population was aimed at all genetics health care providers; however, the NSGC Cancer SIG was primarily genetic counselors. Other providers,

such as medical geneticists, nurses, or others who are involved in cancer counseling could have been contacted as well and may have had a different perspective on the topic of recontact.

## **5.0 FUTURE RESEARCH OPPORTUNITIES**

Given the results of the study, many opportunities exist for future research studies. While this study observed the proportion of patients who share their genetic test results with other providers, further investigation of patients' relationships with their primary care providers and specialists would be useful. A more targeted approach may include asking patients if they've had an in person conversation with their providers regarding their genetic testing results. In addition, studies investigating patients' motivations behind not sharing genetic testing information with certain providers may be focused on more extensively, including other issues surrounding genetic testing (privacy, lack of interest/understanding of results, etc.).

This study also provided insight into patients' preferences for recontact by their genetics providers. Institutions already implementing recontact may find this information useful to improve their methods of recontact. Assessing patients' satisfaction with these methods may be useful in determining their success. Furthermore, institutions that do not have a policy of recontact may reconsider their position.

While this study aimed to determine differences in expectations and preferences based on patients with positive, negative, and inconclusive genetic test results, other factors may be incorporated in further studies. These may include personal cancer history and degree of risk based on family history (hereditary vs. familial vs. sporadic). It is possible that individuals with a personal history of cancer may have different perceptions of the need for recontact. Likewise, individuals with a strong family history of cancer may hold higher expectations for recontact compared to those who do not have a strong family history of cancer. Regression analysis could also be used to determine any trends in patient responses based on age

Gathering more information from institutions which do have formalized systems of recontact may also be useful. Further characterizing these systems by their methodologies (database query and direct contact vs. newsletter) should be established. This may help guide providers looking to develop methods of recontact.

## 6.0 CONCLUSIONS

From this research study, we conclude that patients believe that their genetics providers have more responsibility to keep patients updated about new genetic discoveries than other providers and the patients themselves. The data supports that patients' preferences for recontact include personalized letters to only appropriate patients only when new information is discovered and these preferences are consistent with the previous recontacting study. Financial factors influence a patient's desire for additional testing and they are more likely to undergo additional genetic testing when it is free or costs are less than \$499. Overall, there were no differences observed between patients who have received positive, negative, and inconclusive *BRCA1/2* test results.

In addition, we conclude that genetics providers believe that there is some ethical duty to keep patients informed of new genetic testing discoveries. The majority of genetics providers have recontacted patients for the purpose of additional testing; however, most do not have formalized systems of recontact and believe that recontact should not be a standard of care practice. In addition, lack of resources such as limited staff, monetary support, and database access impede the ability for genetics providers to recontact patients and suggests that the lack of a sufficient database system is a significant component for genetics providers who have established formalized systems of recontact.

## APPENDIX A: DIFFERENTIAL DIAGNOSES OF HEREDITARY BREAST AND OVARIAN CANCERS

Genetic Syndromes Associated with Breast Cancer <sup>1</sup>				
	Gene	Breast Cancer Risk	Associated Cancers	Associated Clinical Features
Li-Fraumeni Syndrome	TP53	30-50%	Soft tissue sarcomas Osteosarcoma Adrenocortical tumors Brain tumors Acute leukemia	
Cowden Syndrome	PTEN	25-50%	Thyroid Uterine Colon Renal	Mucocutaneous lesions Fibromas, lipomas Gastrointestinal hamartomas Macrocephaly
Hereditary Diffuse Gastric Cancer	CDH1	40% *lobular	Stomach Colon	Cleft lip and palate
Peutz-Jegher Syndrome	STK11	30-50%	Ovarian Colon Pancreatic	Small bowel polyposis Mucocutaneous pigmentation

Genetic Syndromes Associated with Ovarian Cancer <sup>81</sup>				
	Gene	Ovarian Cancer Risk	Associated Cancers	Associated Clinical Features
Peutz-Jegher Syndrome	STK11	18-21%	Breast Colon Pancreatic	Small bowel polyposis Mucocutaneous pigmentation
Lynch Syndrome	MLH1, MSH2, MSH6, PMS2, EPCAM	4-11%	Colon Uterine Stomach Urinary tract Small bowel Hepatobiliary	



## APPENDIX B: IRB APPROVAL LETTER



University of Pittsburgh  
*Institutional Review Board*

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

### Memorandum

To: Darcy Thull  
From: Christopher Ryan, PhD, Vice Chair  
Date: 8/5/2013  
IRB#: [MOD13010279-01](#) / PRO13010279  
Subject: Patient and Cancer Genetics Healthcare Provider Attitudes Regarding Recontact

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The University of Pittsburgh Institutional Review Board reviewed and approved the requested modifications by expedited review procedure authorized under 45 CFR 46.110 and 21 CFR 56.110.

Modification Approval Date: 8/5/2013  
Expiration Date: 3/27/2014

For studies being conducted in UPMC facilities, no clinical activities that are impacted by the modifications can be undertaken by investigators until they have received approval from the UPMC Fiscal Review Office.

Please note that it is the investigator's responsibility to report to the IRB any unanticipated problems involving risks to subjects or others [see 45 CFR 46.103(b)(5) and 21 CFR 56.108(b)]. Refer to the IRB Policy and Procedure Manual regarding the reporting requirements for unanticipated problems which include, but are not limited to, adverse events. If you have any questions about this process, please contact the Adverse Events Coordinator at 412-383-1480.

The protocol and consent forms, along with a brief progress report must be resubmitted at least one month prior to the renewal date noted above as required by FWA00006790 (University of Pittsburgh), FWA00006735 (University of Pittsburgh Medical Center), FWA00000600 (Children's Hospital of Pittsburgh), FWA00003567 (Magee-Womens Health Corporation), FWA00003338 (University of Pittsburgh Medical Center Cancer Institute).

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

## **APPENDIX C: INFORMED CONSENT FOR HEALTHCARE PROVIDERS**

The purpose of this study is to identify methods currently practiced by cancer genetics providers for the purpose of recontacting patients when new genetic discoveries are made or new genetic testing becomes available. In addition, the study will assess genetics providers' feelings regarding the duty to recontact. Approximately 700 cancer genetics healthcare providers will be invited to participate in this research study. If you agree to participate, you will be asked to complete a brief, online survey. Completion of the survey should take no longer than 15 minutes.

There is little risk involved in this study. All results generated through the electronic survey will be collected anonymously. Given the nature of the topic, it is possible that some questions may cause distress, as some individuals may feel uncomfortable thinking about the ethical implications of recontacting patients. Your participation in this study is completely voluntary and you may choose to exit the survey at any point.

There are no costs to you for participating in this study, and you will receive no direct benefit from participating in this study. It is possible that information gathered from this study will be of benefit to the genetic counseling profession and genetics healthcare procedures utilized in the future.

If you have questions about this research study, you may contact Darcy Thull, MS, CGC at (412) 641-1466.

If you have questions about your rights as a research subject, please contact the Human Subjects Protection Advocate at the University of Pittsburgh IRB Office, 1.866.212.2668.

I have read the above information and agree to participate in this research study.  
[click accept]

## **APPENDIX D: INTRODUCTORY LETTER FOR HEALTHCARE PROVIDERS**

Dear NSGC Cancer SIG member,

You are being invited to participate in a research study exploring cancer genetics providers' attitudes regarding recontact of patients. You were selected as a participant because you are a current member of the NSGC Cancer SIG.

This study is being conducted by Michelle O'Connor, a genetic counseling student at the University of Pittsburgh, under the direction of Darcy Thull, MS, CGC and Natalie Carter, MS, CGC. The study has IRB approval through the University of Pittsburgh.

The purpose of this study is to identify methods currently practiced by cancer genetics providers for recontacting patients when additional genetic testing options become available. In addition, we hope to better understand genetics providers' preferences and attitudes regarding the duty to recontact.

Previous studies have suggested mixed preferences from those working in the field of genetics regarding the responsibility to recontact patients. We wish to revisit this topic due to the complex and rapid emergence of new genetic technologies.

Participation in this study involves an online, anonymous survey that should take approximately 15 minutes to complete. Your participation is voluntary and you may choose to exit the survey at any point.

The survey link is \_\_\_\_\_.

Responses are kindly requested by \_\_\_\_\_.

Please feel free to contact us with any questions or concerns.

Thank you for your time,

Michelle O'Connor, BS

Darcy Thull, MS, CGC

Natalie Carter, MS, CGC

## **APPENDIX E: QUESTIONNAIRE FOR HEALTHCARE PROVIDERS**

<b>Section 1: Personal Background</b>	
1. What is your title/profession? <input type="checkbox"/> Genetic counselor <input type="checkbox"/> Geneticist <input type="checkbox"/> Physician (please specify type) _____ <input type="checkbox"/> Physician Assistant <input type="checkbox"/> Nurse <input type="checkbox"/> Other _____	
2. Do you regularly provide cancer risk assessment? <input type="checkbox"/> No <input type="checkbox"/> Yes	
	2a. In which type of setting do you provide cancer risk assessment? <input type="checkbox"/> Independently, without a formal genetics program <input type="checkbox"/> Within a formal genetics department <input type="checkbox"/> Other: _____
3. Please rate the following characteristics for accuracy as they would describe the setting in which you provide cancer risk assessment (scale 1-5, 1=strongly disagree, 2=disagree, 3=neither agree or disagree, 4=agree, 5=strongly agree) _____ I have sufficient amount of support staff to help carry out routine clinic duties _____ I have sufficient monetary support to help carry out routine clinic duties _____ I have a sufficient database system to adequately organize clinic and patient data	
4. How long have you been providing cancer risk assessment? <input type="checkbox"/> <1 year <input type="checkbox"/> 2-4 years <input type="checkbox"/> 5-9 years <input type="checkbox"/> >10 years	
<b>Section 2: Recontacting Patients: Current Practice</b>	
5. Have you or your department ever recontacted a patient(s) to invite them to participate in <i>research</i> for genetic testing? <input type="checkbox"/> No <input type="checkbox"/> Yes	
	5a. What was the approximate proportion of individuals who responded?
6. Have you or your department ever recontacted a patient(s) inviting them to undergo additional genetic testing ( <i>excluding research</i> )? <input type="checkbox"/> No <input type="checkbox"/> Yes	
	6a. What was the approximate proportion of individuals who responded?
7. Has your department established a formal system for the specific purpose of recontacting patients for participation in <i>research</i> for genetic testing? <input type="checkbox"/> No <input type="checkbox"/> Yes	
	7a. Please describe system:
8. Has your department established a formal system for the purpose of recontacting patients regarding additional genetic testing ( <i>excluding research</i> )? <input type="checkbox"/> No <input type="checkbox"/> Yes	
	8a. Please describe system:
9. Do you routinely direct patients to recontact you for updates regarding new genetic information or genetic testing that may become available in the future? <input type="checkbox"/> No <input type="checkbox"/> Yes	
<b>Section 3: Recontacting Patients: Theoretical Considerations</b>	
10. How much of an ethical duty do genetics service providers have to recontact former patients regarding new advances in genetics? (Please rate on a scale 1-5, 1=no duty and 5=greatest degree of duty): _____	
11. How much responsibility do patients have to keep in contact with genetics providers? (Please rate on a scale 1-5, 1=no responsibility and 5=greatest degree of responsibility): _____	
12. Should recontacting patients about clinical testing advances be the standard of care for genetics service providers? <input type="checkbox"/> No <input type="checkbox"/> Yes	
13. Do you believe formal guidelines should be established for the purpose of recontacting patients when new genetic testing becomes available? <input type="checkbox"/> No <input type="checkbox"/> Yes	
[Additional space provided for each section to allow for comments]	

## **APPENDIX F: INTRODUCTORY LETTER FOR PATIENTS**



# University of Pittsburgh

*University of Pittsburgh Cancer Institute  
Cancer Genetics Program*

Magee-Womens Hospital of UPMC  
300 Halket Street, Suite 1631  
Pittsburgh, PA 15213-3180  
Referrals: 1-800-454-8136  
Fax: 412-641-1132

Date

Dear \_\_\_\_\_,

Greetings from the Cancer Genetics Program at the University of Pittsburgh Medical Center! We are contacting you because you were seen in the UPMC Cancer Genetics Program and are eligible to participate in a brief research survey. You are being invited to participate in this survey because you were seen within the years 2007-2012 and have been tested for a BRCA1/2 mutation. The survey wishes to better understand your preferences regarding being recontacted by your genetics provider. The information gathered from this survey will help us better understand the needs of our patients in order to improve patient and genetics healthcare provider relationships.

Please be aware that the confidentiality of your medical information is very important to us. Personal identifiers (for example, your name) will be removed from the information used for the study. A special research code will be assigned and access to your identifiable medical information will be limited to the research staff.

Participation in this survey is voluntary and your participation will in no way affect your relationship with the University of Pittsburgh or UPMC.

We have enclosed a consent form that further explains the details of this study. If you wish to participate in the study, please follow the instructions below:

1. Review the green consent form.
2. Sign and date the green consent form (*page 4*).
3. Complete the 2-sided, green questionnaire.
4. Mail back the signed consent form and completed questionnaire in the pre-paid envelope.
5. Keep the white copy of the consent form for your records.

If you have questions regarding this information, please call the Cancer Genetics Program at any time at (412)- 641-1466.

Thank you for your consideration.

Sincerely,

Darcy L. Thull, MS  
Certified Genetic Counselor  
UPMC Cancer Genetics Program

Natalie Carter, MS  
Certified Genetic Counselor  
UPMC Cancer Genetics Program

Michelle O'Connor  
Research Assistant  
UPMC Cancer Genetics Program

## **APPENDIX G: INFORMED CONSENT FOR PATIENTS**





## **University of Pittsburgh**

### **CONSENT TO ACT AS A SUBJECT IN A RESEARCH STUDY**

**STUDY TITLE:** Evaluation of Patients' Preferences For Recontact by Cancer Genetics Providers

**PRINCIPAL INVESTIGATOR:**

Darcy Thull, MS, CGC  
UPMC Cancer Genetics Program  
Magee-Women's Hospital of UPMC  
300 Halket Street, Suite 1651  
Pittsburgh, PA 15213  
(412) 641-1466

Michelle O'Connor, BS  
Department of Human Genetics  
Graduate School of Public Health  
University of Pittsburgh  
Pittsburgh, PA 15261

**CO-INVESTIGATORS:**

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Graduate School of Public Health  
513 Parran, University of Pittsburgh  
Pittsburgh, PA 15261

M. Michael Barmada, PHD  
Department of Human Genetics  
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624 Parran, University of Pittsburgh  
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Kristin Zorn, MD  
Department of OB/GYN & Women's Health Services  
Gynecologic Oncology Division  
Magee-Women's Hospital of UPMC  
300 Halket Street  
Pittsburgh, PA 15213

**SOURCES OF SUPPORT:** UPMC Cancer Genetics Program



***Why is this study being done?***

The purpose of this study is to assess patients' relationships with their primary care physicians, specialists, and genetics health care providers as well as assess patients' preferences regarding recontact by their genetics providers in the future.

***Who is being asked to take part in this study?***

Men and women previously seen at UPMC Cancer Genetics Program for BRCA1/2 testing will be invited to participate in this research study.

***What are the procedures of this study?***

If you agree to participate in this research study, you will be asked to complete a brief pen and paper questionnaire. The questionnaire will take no more than 15 minutes to complete.

***What are the possible risks of this study?***

There is little risk involved in this study. No invasive procedures or medications are included. The major potential risk is a breach in confidentiality. If there is breach of confidentiality, knowledge of your genetic research data could potentially impact your future insurability, employability, or reproductive plans. A new federal law, called the Genetic Information Nondiscrimination Act (GINA), generally makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. This law generally will protect you in the following ways:

- Health insurance companies and group health plans may not request your genetic information that we get from this research.
- Health insurance companies and group health plans may not use your genetic information when making decisions regarding your eligibility or premiums.
- Employers with 15 or more employees may not use your genetic information that we get from this research when making a decision to hire, promote, or fire you when setting the terms of your employment.

Be aware that this new Federal law does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance.

The risk for a breach in confidentiality is minimal since the research staff have been thoroughly trained to protect your privacy. We will make every attempt to prevent a breach in privacy from happening by assigning a unique identification number for confidentiality purposes. This ID number which will not contain any of your personal identifiable information (full name, social security number) will be used for all data collected. All data collected will also be kept in locked file cabinets in a designated area in our office. Data collected for this study may also be stored electronically on a secure UPMC computer network. This information will only be accessible to the investigators and the research team.

***Are there any benefits to taking part in this study?***

Although you will receive no immediate direct benefit from participation in this study, the information gained from this study may be of benefit to you, your relatives, and future generations by improving relationships between patients and genetics service providers.

***Are there any costs to me if I participate in this study?***

There are no costs to you for participating in this study.



***Will I receive payment for participating in this study?***

You will not receive payment for taking part in this study. Participation in this study is voluntary.

***Will anyone know that I'm taking part of in this study?***

All records pertaining to your involvement in this study are kept strictly confidential and any data that includes your identity will be stored in locked filing cabinets at UPMC Cancer Genetics Program. A case number will indicate your identity on these records. Data collected may also be stored electronically on a secure UPMC computer network. This information will only be accessible to the investigators and the research team.

It is possible that authorized representatives from the University of Pittsburgh Research Conduct and Compliance Office (including the University of Pittsburgh IRB) may review your identifiable information (including your identifiable medical record information) for the purpose of monitoring the conduct of this study. Any information about you will be handled in a confidential (private) manner consistent with other hospital medical records. You will not be specifically identified in any publication of research results. However, in unusual cases your research records may be inspected by appropriate government agencies or be released in response to an order from a court of law. All research records will be kept indefinitely for this purpose.

***Will this research study involve the use or disclosure of my identifiable medical information?***

Yes, we are also requesting your authorization or permission to use your medical record information. This research study will involve the recording of identifiable medical information from your UPMC cancer genetics chart. The information that will be recorded will be limited to information concerning the results of genetic tests, medical history, and demographic information obtained from your previous genetic counseling consultation. This information will be used to ensure that accurate information is recorded and maintained in the collection of research data. This authorization is valid for an indefinite period of time. Identifiable information will be assigned a unique identification number for confidentiality purposes. This ID number which will not contain any of your personal identifiable information (full name, social security number) will be used for all data collected.

You should be aware that no information collected from this study will be placed in your medical records held at UPMC Cancer Genetics Program.

***Is my participation in this study voluntary?***

Yes, your participation in this study is completely voluntary. You may refuse to take part in it or you may stop participating at any time, even after signing this form. Any information obtained from you up to that point will, however, continue to be used by the research team. If you decide you no longer wish to continue to participate after you have signed this form, you should contact Darcy Thull, MS, CGC (412) 641-1466. You may also withdraw, at any time, your authorization to allow the research team to review your medical records, but if you do so, you will no longer be permitted to participate in this study.

Your decision will not affect your relationship with the University of Pittsburgh or your current or future medical care at a UPMC hospital.



\*\*\*\*\*

**VOLUNTARY CONSENT:**

All of the above has been explained to me and all of my current questions have been answered. I understand that, throughout my participation in this research study, I am encouraged to ask questions about the any aspect of this research study including the use and disclosure of my identifiable medical record information. Such future questions will be answered by members of the research team.

Any questions I have about my rights as a research participant or the research use of my medical information will be answered by the Human Subject Protection Advocate of the IRB Office, University of Pittsburgh (1-866-212-2668).

By signing this form, I agree to participate in this research study and for the use and disclosure of my medical record information for the purposes described above. A copy of this consent form will be given to me.

\_\_\_\_\_  
Participant's Printed Name

\_\_\_\_\_  
Participant's Signature

\_\_\_\_\_  
Date

**CERTIFICATION OF INFORMED CONSENT**

I certify that I have explained the nature and purpose of this research study to the above-named individual(s), and I have discussed the potential benefits and possible risks of study participation. Any questions the individual(s) have about this study have been answered, and we will always be available to address future questions as they arise.

\_\_\_\_\_  
Signature of Person Obtaining Consent

\_\_\_\_\_  
Date

\_\_\_\_\_  
Printed Name of Person Obtaining Consent

\_\_\_\_\_  
Role In Research Study



## **APPENDIX H: QUESTIONNAIRE FOR PATIENTS**



Section 1: Evaluation of Primary Care Physician Relationship	
1. Do you see a primary care physician regularly? <input type="checkbox"/> No <input type="checkbox"/> Yes	
<div style="border-left: 1px solid black; border-right: 1px solid black; height: 100px; position: relative;"> <div style="position: absolute; left: -5px; top: 0; bottom: 0; border-left: 1px solid black;"></div> <div style="position: absolute; right: -5px; top: 0; bottom: 0; border-right: 1px solid black;"></div> </div>	1a. How often do you seek care from your primary care physician (PCP)? <input type="checkbox"/> More than 1 time/year <input type="checkbox"/> Annually <input type="checkbox"/> Every 2-3 years <input type="checkbox"/> Every 4-5 years
	1b. Have you shared your genetic testing results with your PCP? <input type="checkbox"/> No <input type="checkbox"/> Yes
	1c. Do you feel that your PCP is knowledgeable regarding your genetic health? <input type="checkbox"/> No <input type="checkbox"/> Yes
2. Do you see an oncologist and/or a breast specialist regularly? <input type="checkbox"/> No <input type="checkbox"/> Yes	
<div style="border-left: 1px solid black; border-right: 1px solid black; height: 100px; position: relative;"> <div style="position: absolute; left: -5px; top: 0; bottom: 0; border-left: 1px solid black;"></div> <div style="position: absolute; right: -5px; top: 0; bottom: 0; border-right: 1px solid black;"></div> </div>	2a. How often do you seek care from your specialist? <input type="checkbox"/> More than 1 time/year <input type="checkbox"/> Annually <input type="checkbox"/> Every 2-3 years <input type="checkbox"/> Every 4-5 years
	2b. Have you shared your genetic testing results with your specialist? <input type="checkbox"/> No <input type="checkbox"/> Yes
	2c. Do you feel that your specialist is knowledgeable regarding your genetic health? <input type="checkbox"/> No <input type="checkbox"/> Yes
Section 2: Expectations for Recontact	
3. Whose primary responsibility do you think it is to keep patients updated about new genetic discoveries? (Please rank from 1-4, with 1=most responsible and 4=least responsible) <div style="margin-left: 20px;"> <input type="checkbox"/> Patient  <input type="checkbox"/> Primary care physician  <input type="checkbox"/> Specialist (includes oncologist or breast specialist)  <input type="checkbox"/> Genetic counselor/Geneticist </div>	
4. Should genetic counselors recontact patients regarding new genetic discoveries? <input type="checkbox"/> No <input type="checkbox"/> Yes <i>If no, please skip Section 3 and move on to question 12 of Section 4.</i>	
Section 3: Preferences for Recontact by Genetics Providers	
5. If genetic counselors were to recontact you, how often should it be done? <input type="checkbox"/> Regularly, even if no new discoveries are made <div style="margin-left: 20px;"> 4a. Please specify preferred time interval:  <input type="checkbox"/> more than 1 time/year    <input type="checkbox"/> Annually    <input type="checkbox"/> Every 2-4 years    <input type="checkbox"/> Every 5 years </div> <input type="checkbox"/> When any new discoveries are made <input type="checkbox"/> When new discoveries are made that directly pertain to the patient <input type="checkbox"/> Other: _____	
6. If genetic counselors were to recontact you, what method should be used? Please select one option. <div style="display: flex; justify-content: space-between;"> <div style="width: 45%;"> <input type="checkbox"/> Generalized letter to all patients  <input type="checkbox"/> Telephone  <input type="checkbox"/> Media release  <input type="checkbox"/> Email </div> <div style="width: 45%;"> <input type="checkbox"/> Personalized letter to only appropriate patients  <input type="checkbox"/> Newsletter  <input type="checkbox"/> Continually updated website  <input type="checkbox"/> Other: _____ </div> </div>	
7. What should the genetic counselor tell you when first recontacting you? <input type="checkbox"/> New information is available ; ask patient to contact genetics if interested in more information <input type="checkbox"/> New information is available; identify resource where more information is available <input type="checkbox"/> Generally what new information has been identified <input type="checkbox"/> Specifically what new information has been identified and how it pertains to specific patient	
8. During the patient's first genetic counseling appointment, the patient should establish whether he or she would like to be recontacted in the future if new information becomes available in the future. <input type="checkbox"/> No <input type="checkbox"/> Yes	

9. If patient answers "no" to being recontacted at the initial consult, is there any time a provider should recontact the patient anyway?	
<input type="checkbox"/> No <input type="checkbox"/> Yes	
	9a. Under what circumstances should a genetics provider contact the patient anyway?
	9a <sub>1</sub> . If the new information is specific to the patient's genetic health <input type="checkbox"/> No <input type="checkbox"/> Yes
	9a <sub>2</sub> . If the new information is relevant to the patient's medical management or treatment <input type="checkbox"/> No <input type="checkbox"/> Yes
	9a <sub>3</sub> . If the new information changes the patient's risk for developing cancer <input type="checkbox"/> No <input type="checkbox"/> Yes
	9a <sub>4</sub> . Other reasons:
10. What are reasons that you would want to be recontacted by your genetics provider?	
	10a. To receive ongoing support from genetics providers <input type="checkbox"/> No <input type="checkbox"/> Yes
	10b. To receive new information that impacts my health <input type="checkbox"/> No <input type="checkbox"/> Yes
	10c. To receive new information about cancer screening <input type="checkbox"/> No <input type="checkbox"/> Yes
	10d. To receive new information about cancer risk relevant to myself <input type="checkbox"/> No <input type="checkbox"/> Yes
	10e. To receive new information about cancer risk relevant to my family members <input type="checkbox"/> No <input type="checkbox"/> Yes
	10f. To reinforce decisions I made based on previous information provided by my prior consultation <input type="checkbox"/> No <input type="checkbox"/> Yes
	10g. To feel like I have a relationship with my genetics providers <input type="checkbox"/> No <input type="checkbox"/> Yes
	10h. New information is interesting to learn about, even if it doesn't apply to me <input type="checkbox"/> No <input type="checkbox"/> Yes
	10i. Other reasons:
	11. Because each person's medical care must be individualized, in most cases genetics providers would need to see you again to discuss the new information at length. Would this change your interest in being recontacted? <input type="checkbox"/> No <input type="checkbox"/> Yes
12. Did your genetic counselor suggest to recontact them if changes occur in your personal or family's <i>cancer</i> history? <input type="checkbox"/> No <input type="checkbox"/> Yes	
<b>Section 4: Factors That Influence Decision Making Regarding Additional Genetic Testing</b>	
<b><u>THIS SECTION IS FOR INDIVIDUALS WHO HAVE RECEIVED A TEST RESULT STATING THAT "NO MUTATION WAS DETECTED (NEGATIVE)" OR A "VARIANT OF UNKNOWN SIGNIFICANCE (VUS) WAS DETECTED"</u></b>	
13. If you were told that new genetic tests were available to you, would you be likely to pursue testing? <input type="checkbox"/> No <input type="checkbox"/> Yes	
	13a. Under what circumstances would you be likely to pursue testing?
	13a <sub>1</sub> . If it were provided free of charge through a research study <input type="checkbox"/> No <input type="checkbox"/> Yes
	13a <sub>2</sub> . If it were provided free of charge, but not through a research study <input type="checkbox"/> No <input type="checkbox"/> Yes
	13a <sub>3</sub> . If my insurance would cover the cost of testing <input type="checkbox"/> No <input type="checkbox"/> Yes
	13a <sub>4</sub> . I would be willing to pay-out-of-pocket if the cost were reasonable <input type="checkbox"/> No <input type="checkbox"/> Yes
	13a <sub>5</sub> . Define reasonable cost: <input type="checkbox"/> less than \$100 <input type="checkbox"/> \$100-499 <input type="checkbox"/> \$500-999 <input type="checkbox"/> \$1000 or more
	13a <sub>6</sub> . I would be willing to pay out of pocket, regardless of cost <input type="checkbox"/> No <input type="checkbox"/> Yes

## APPENDIX I: ADDITIONAL TABLES

### Aim 1: Patient Population

**Table 24. Patient Relationships with PCP and Specialist**

Do you see a PCP regularly?		
n=254	Responses	%
No	26	10.24
Yes	228	89.76
Unsure	0	0.00

Do you see a specialist regularly?		
n=254	Responses	%
No	50	19.69
Yes	203	79.92
Unsure	1	0.39

Have you shared your genetic testing results?		
n=228	Responses	%
No	52	22.81
Yes	169	74.12
Unsure	7	3.07

Have you shared your genetic results?		
n=203	Responses	%
No	6	2.96
Yes	194	95.57
Unsure	3	1.48

Do you feel your PCP is knowledgeable regarding your genetic health?	Did not share results with PCP		
	n=52	Responses	%
	No	36	69.23
	Yes	14	26.92
	Unsure	2	3.85
	Did share results with PCP		
	n=169	Responses	%
	No	37	21.89
	Yes	123	72.78
	Unsure	9	5.33

Do you feel your specialists is knowledgeable regarding your genetic health?	Did not share results with specialist		
	n=6	Responses	%
	No	1	16.67
	Yes	5	83.33
	Unsure	0	0.00
	Did share results with specialist		
	n=194	Responses	%
	No	8	4.12
	Yes	186	95.88
	Unsure	0	0.00



**Table 25. Sharing of Genetic Test Results with Specialist vs. Perceived Specialist Knowledge by Patients**

		Shared genetic test results with specialist	
		No (%)	Yes (%)
Do you feel your specialist is knowledgeable regarding genetic health N=200	No	1 (0.5)	8 (4.0)
	Yes	5 (2.5)	186 (93.0)

p-value 0.1032

**Table 26. Perceived PCP Knowledge vs. Perceived Responsibility for Recontact According to Patients**

Felt that PCP was knowledgeable n=164	Responsibility for Recontact				
		GC (%)	Specialist (%)	PCP (%)	Patient (%)
	No	22 (13.4)	26 (15.8)	5 (3.0)	2 (1.2)
	Yes	57 (34.7)	36 (21.9)	5 (3.0)	11 (6.7)

p-value =0.1001

**Comparison of Questionnaire Responses between *BRCA* Results Groups****Table 27. Perceived Primary Responsibility for Recontact by Patients vs. *BRCA* Result**

n=194	Patient (%)	PCP (%)	Specialist (%)	GC (%)
Negative	8 (4.1)	9 (4.6)	58 (29.8)	74 (38.1)
Positive	7 (3.6)	1 (0.5)	14 (7.2)	15 (7.7)
VUS	0 (0.0)	0 (0.0)	3 (1.5)	5 (2.5)

p-value 0.142

**Table 28. Preferred Timeframe for Recontact vs. *BRCA* Result**

n=247	Regularly, even if no new discoveries made (%)	When any new discoveries are made (%)	When new discoveries are made that directly pertain to patient (%)
Negative	50 (20.2)	39 (15.7)	101 (40.8)
Positive	22 (8.9)	7 (2.8)	17 (6.8)
VUS	4 (1.6)	2 (0.8)	5 (2.0)

p-value 0.084

**Table 29. Preferred Method of Recontact vs. *BRCA* Result**

n=254	Generalized letter to all patients (%)	Telephone (%)	Media Release (%)	Email (%)	Letter to appropriate patients (%)	News-letter (%)	Website (%)	No answer (%)
Negative	21 (8.2)	13 (5.1)	0 (0.0)	15 (5.9)	130 (51.1)	2 (0.7)	1 (0.3)	12 (4.7)
Positive	7 (2.7)	4 (1.5)	0 (0.0)	7 (2.7)	26 (10.2)	1 (0.3)	0 (0.0)	4 (1.5)
VUS	1 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	9 (3.5)	0 (0.0)	0 (0.0)	1 (0.3)

p-value 0.739

**Table 30. Preferred Information Included in Recontact vs. *BRCA* Result**

n=254	New information is available; ask patient to contact genetics if interested in more information (%)	New information is available; identify resource where more information is available (%)	Generally what information has been identified (%)	Specifically what information has been identified (%)	No answer (%)
Negative	24 (9.4)	20 (7.8)	13 (5.1)	128 (50.3)	9 (3.5)
Positive	2 (0.7)	9 (3.5)	6 (2.3)	30 (11.8)	2 (0.7)
VUS	2 (0.7)	1 (0.3)	0 (0.0)	7 (2.7)	1 (0.3)

p-value 0.253

**Table 31. Preferences for Contract for Recontact vs. *BRCA* Result**

n=249	No (%)	Yes (%)
Negative	6 (2.4)	186 (74.6)
Positive	0 (0.0)	46 (18.4)
VUS	0 (0.0)	11 (4.4)

p-value 0.401

**Table 32. Circumstances to Recontact Regardless of Patients Preference vs. *BRCA* Result**

n=226	No (%)	Yes (%)
Negative	25 (11.0)	152 (67.2)
Positive	5 (2.2)	34 (15.0)
VUS	0 (0.0)	10 (4.4)

p-value 0.439

**Table 33. Reasons to be Recontacted vs. *BRCA* Result**

		Negative (%)	Positive (%)	VUS (%)	P-value
Receive ongoing support n=207	No	103 (49.7)	17 (8.2)	5 (2.4)	0.08
	Yes	59 (28.5)	21 (10.1)	2 (0.9)	
New information that impacts my health n=242	No	1 (0.4)	0 (0.0)	0 (0.0)	0.878
	Yes	184 (76.0)	46 (19.0)	11 (4.5)	
New information about cancer screening n=224	No	24 (10.7)	2 (0.8)	2 (0.8)	0.171
	Yes	148 (66.0)	41 (18.3)	7 (3.1)	
New information about personal cancer risk n=237	No	3 (1.2)	1 (4.2)	0 (0.0)	0.876
	Yes	180 (75.9)	43 (18.1)	10 (4.2)	
New information about cancer risk for family members n=237	No	12 (5.0)	1 (4.2)	0 (0.0)	0.378
	Yes	170 (71.7)	43 (18.1)	11 (4.6)	
Reinforce decision making n=215	No	62 (28.8)	13 (6.0)	3 (1.3)	0.914
	Yes	106 (49.3)	26 (12.0)	5 (2.3)	
Relationship with Genetics Provider n=206	No	107 (51.9)	19 (9.2)	4 (1.9)	0.072
	Yes	52 (25.2)	20 (9.7)	4 (1.9)	
New information is interesting n=211	No	117 (55.4)	20 (9.4)	6 (2.8)	0.05
	Yes	47 (22.2)	19 (9.0)	2 (0.9)	

**Table 34. Patients Desire for Recontact and Required Additional Genetics Consultation vs. *BRCA* Result**

N=245	No (%)	Yes (%)
Negative	157 (64.0)	30 (12.2)
Positive	43 (17.5)	4 (1.6)
VUS	9 (3.6)	2 (0.8)

P-value 0.4

**Table 35. Patient Recall of Recontact Recommendations vs. *BRCA* Result**

N=224	No (%)	Yes (%)
Negative	103 (45.9)	67 (29.9)
Positive	26 (11.6)	17 (7.5)
VUS	6 (2.6)	5 (2.2)

p-value 0.92

## Aim 2: Genetics Provider Population

**Table 36. Perceived Patient Responsibility vs. Routine Recommendation to Recontact**

		Patient responsibility			P-value
		None (%)	Some (%)	High (%)	0.65
Routinely direct to recontact	No	0 (0.0)	4 (2.0)	15 (7.7)	
	Yes	1 (0.5)	53 (27.4)	120 (62.1)	

## **APPENDIX J: ADVISORY COMMITTEE**

**Thesis Advisor:** Darcy Thull, MS, CGC, Certified Genetic Counselor, Cancer Genetics Program, University of Pittsburgh Medical Center

**Thesis Committee Member:** Francesmary Modugno, Ph.D, Adjunct Assistant Professor, Department of Epidemiology, Graduate School of Public Health, University of Pittsburgh

**Thesis Committee Member:** M. Michael Barmada, Ph.D., Associate Professor, Department of Human Genetics, Graduate School of Public Health, University of Pittsburgh

**Advisory Committee Member:** Natalie Carter, MS, CGC, Certified Genetic Counselor, Cancer Genetics Program, University of Pittsburgh Medical Center

**Advisory Committee Member:** Kristin Zorn, MD, Assistant Professor, Department of Obstetrics, Gynecology, and Reproductive Sciences

**Advisory Committee Member:** Robin E. Grubs, Ph.D., CGC, Assistant Professor, Department of Human Genetics, Graduate School of Public Health, University of Pittsburgh

**Advisory Committee Member:** Elizabeth A. Gettig, MS, CGC, Associate Professor, Department of Human Genetics, Graduate School of Public Health, University of Pittsburgh

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