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Assessing decision regret in the cancer genetics clinic

THESIS

Submitted in partial satisfaction of the requirements for the degree of

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by

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DEDICATION

For my parents, Denise and Mitchell Sarnoff

whose life experiences have inspired me to pursue this work

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ABSTRACT OF THE THESIS

Assessing decision regret in the cancer genetics clinic

by

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Patient-decision making plays a critical role in the hereditary cancer genetic testing process and creates an opportunity to experience decision regret. Motivations and feelings about genetic testing decisions are well-explored in the literature, but less is known about how patients feel about their decision to test after receiving results, particularly regarding regret.

We invited 1,596 English-speaking adults who had genetic counseling where testing was recommended for hereditary cancer risk at UCI Health (the clinical enterprise of the University of California, Irvine) between November 2014 and March 2023 and received 234 complete responses. Interestingly, when asked a yes/no question regarding test regret, 97% reported no regret, but on the validated Decision Regret Scale, 34% showed mild regret, and 7% had moderate to severe regret. Independently, those with biological children ($p = 0.01$), no personal history of cancer ($p = 0.01$), and some out-of-pocket cost ($p = 0.001$), commercial insurance ($p = 0.01$), and who were married or in a partnership ($p < 0.001$) were less likely to have regret. Level of regret was also correlated with education - those who had at least an undergraduate degree or

higher were less likely to have regret ($p = 0.01$). Importantly, education was our only variable that addressed socioeconomic status, so this may be a direct association, but other related variables may confound it. We assessed whether the level of regret differed between those who received a positive, negative, or uncertain test result. While those with positive test results appeared to have a higher regret rate, there were no statistically significant differences across the groups.

We explored whether current cancer diagnosis, genes associated with test results, if a change in medical care resulted, and various demographic factors were correlated with regret but did not find any significant associations.

Our data suggest that most individuals who choose to have genetic testing for hereditary cancer risk have little to no regret regarding their decision to test. Participants reported they lacked regret because genetic testing allowed them to learn of their cancer risk, make decisions about screening and management, and learn more information about their family members. Participants who reported regret said it was because they had to inform family members of their test results, had increased anxiety about developing cancer, and felt guilty that they may have passed something on to their children. Knowing that most patients do not have strong regret about genetic testing after learning their results, regardless of result type, allows genetic counselors to reassure their patients in their choices if they choose to proceed with genetic testing.

I. INTRODUCTION

1.1 Cancer genetics overview

All cancers are genetic in etiology due to mutations causing uncontrolled cell proliferation. Cancer develops when cellular DNA that promotes or prevents cell growth mutates, resulting in inappropriate cell replication. Genetic changes that lead to cancer can occur due to environmental exposures or by random chance (sporadic cancers) due to accumulating numbers of minor genetic changes throughout generations in a family as well as shared familial environments (familial cancers). Or, an individual may inherit a disease-causing genetic variant in a gene known to significantly increase the risk of cancer from a parent (hereditary cancers). Most cancers (approximately 75%) are sporadic, and about 15% to 20% fall into the familial category. Hundreds of genetic variants that increase cancer risk have been identified, yet only 5% to 10% of all cancers are hereditary ("Genetics of Cancer", 2022; "Genetic Test Fact", 2019). Many mutations that cause hereditary cancer syndromes follow an autosomal dominant inheritance pattern, are inherited from a parent, and can lead to different cancers with differing penetrance and age of onset ("Hereditary Cancer Syndromes", 2019). Occasionally, individuals may have a *de novo* mutation, meaning it was not inherited from either parent but rather occurred for the first time in the patient. For example, approximately 25% of individuals with Familial Adenomatous Polyposis (FAP), a colorectal cancer predisposition syndrome, have a *de novo* mutation in the *APC* gene (Talseth-Palmer, 2017). In particular, a 5-base pair (5bp) deletion at codon 1309 in *APC* (c.3927_3931del) is a common variant among *de novo* carriers (Talseth-Palmer, 2017). Also, it is estimated that 7% to 20% of *TP53* (a gene that codes for a regulatory protein that is often mutated in human cancers) pathogenic variants are *de novo* (Schneider et al.,

2019). *De novo* variants in other genes, such as *BRCA1*, *BRCA2*, and mismatch repair genes, have also been described (Antonucci et al., 2017; Zajo et al., 2020). Additionally, gene-to-gene interactions play a role in cancer development (Arshad & McDonald, 2021). For example, a pathogenic variant in a member of the *RAS* family (a group of genes that when mutated can cause uncontrolled cell death) variant can activate the *ATM* gene (associated with breast cancer, pancreatic cancer, and ataxia-telangiectasia) and allow DNA damage. However, a variant that inactivates *ATM* will suppress damaging *RAS* effects and result in synthetic viability of the cell. Similarly, effects from pathogenic variants in *VHL* (Von Hippel-Lindau tumor suppressor gene) are lessened by the inactivation of a second tumor suppressor gene, *RB1* (associated with hereditary retinoblastoma) (Ashworth et al., 2011).

Hundreds of genes are related to cancer development in the human body. When these genes are properly functioning, they protect against cancer development, working to regulate cell growth and suppress tumor growth. However, pathogenic variants impact the functioning of these genes and thus are related to increased cancer risk. Many genetic variants are related to increased risk for similar cancers. Hereditary breast and ovarian cancers are most often due to mutations in *BRCA1* and *BRCA2*, known as Hereditary Breast and Ovarian Cancer syndrome (HBOC) **(**"BRCA1 and BRCA2", 2020**).** Women with a *BRCA1* or *BRCA2* variant have a lifetime breast cancer risk of up to 72% compared to the general population lifetime risk of 12.9% ("BRCA Gene Mutations", 2020a, "Breast Cancer Risk in", 2020) and a lifetime ovarian cancer risk of up to 44% when compared to the general population lifetime risk of 1.2%. ("Breast Cancer Risk", 2020). Men with *BRCA* mutations also have an increased risk for breast and prostate cancer. All individuals with *BRCA* mutations are also at higher risk of developing other cancers such as pancreatic cancer. Other genes related to a high-risk of breast cancer include

TP53 (Li-Fraumeni syndrome), *PTEN* (Cowden syndrome), *STK11* (Peutz-Jeghers syndrome), *CDH1* (hereditary diffuse gastric cancer), and *PALB2* ("Breast Cancer Risk Factors", 2021). These genes are often included in high-risk breast cancer STAT panels typically ordered for individuals with new breast cancer diagnoses where treatment guidance based on genetic test results is beneficial. Variants in moderate-risk breast cancer genes increase one's risk for breast cancer, but the risk is not as high as variants in the previously mentioned genes. These genes include *ATM*, *BARD1*, *BRIP1*, *CHEK2*, *RAD51C*, *RAD51D*, among others. High-risk and moderate-risk breast cancer variants are also often related to gynecological cancers such as ovarian or uterine cancer.

Hereditary colon cancers are most commonly related to variants in mismatch repair genes (*MLH1*, *MSH2*, *MSH6*, *PMS2*, *EPCAM*), which cause Lynch syndrome, and genes associated with polyposis syndromes (most commonly *APC* and *MUTYH*). Individuals with Lynch syndrome have a colon cancer lifetime risk of up to 80% compared to the population lifetime risk of approximately 5% (Bhattacharaya & McHugh, 2023). However, the genes associated with Lynch syndrome have variable penetrance (i.e., identical genotypes do not always show the related phenotype or trait); thus, lifetime risk varies depending on the gene the variant is in. Lynch syndrome is also associated with up to a 60% lifetime risk of developing endometrial cancer and increased risk for ovarian, gastric, small bowel, urothelial, central nervous system, biliary tract, and pancreatic cancers (Bhattacharaya & McHugh, 2023). Individuals with pathogenic variants in *APC* can have a lifetime colon cancer risk as high as 100% and have an increased risk for other cancers such as duodenal cancer, gastric cancer, thyroid cancer and hepatoblastoma ("APC-Associated", 20202). However, those with moderate-risk *APC* variants,

such as *APC* p.I1307K, found in approximately 6% of the Ashkenazi Jewish population, have up to a 10% lifetime risk for colon cancer.

Germline pathogenic variants (a gene change in an egg or sperm that becomes incorporated into the DNA of every cell in the body of the offspring) are found in a variety of genes connected with other cancers, such as renal cancer (*FH*, *FLCN*, *MET*, *VHL*), pancreatic cancer (*ATM*, *BRCA1*, *BRCA2*, *STK11*, *PALB2*, *MLH1*, *MSH2*, *MSH6*, *PMS2*, *EPCAM*, *CDKN2A, TP53*), skin cancer (*CDKN2A*, *CDK4*), endocrine and neuroendocrine cancers (*MEN1*, *NF1*, *RET*, *SDHA*, *SDHB*, *SDHC*, *SDHD*), and central nervous system cancers (*NF1*, *NF2*, *TP53*, *TSC1*, *TSC2*).

1.2 Cancer genetic testing overview

Genetic testing for hereditary cancer risk looks for variants in a person's genes that make them more likely to develop cancer. ("Genetic Test Fact", 2019). This testing is typically recommended for individuals whose cancer diagnoses are suspicious for hereditary disease, those who have a known pathogenic variant in their family, those with a significant family history of cancer, and, in some cases, those who are curious about their own risks for cancer development. The testing explicitly assesses variants in genes that lead to a higher risk of developing certain types of cancers over a lifetime ("Genetic Test Fact", 2019). Genetic testing for hereditary cancer risk began in the late 1990s, with *BRCA1* and *BRCA2* testing as the only clinically available options, and was initially met with much hesitation (Hurst, 2014). Since then, knowledge, interest, and testing capabilities have increased markedly, but limitations still remain.

Hereditary cancer genetic testing provides a plethora of benefits for both patients and providers. For affected patients with a positive result, this testing can provide insight into treatment and management and an understanding of the cause of a diagnosis, allow for interventions to prevent future cancer(s) from developing and/or allow for early detection, and indicate that further familial genetic testing is appropriate ("Genetic Test Fact", 2019). For clinically unaffected patients, positive results can modify management and screening procedures and negative test results may provide peace of mind. However, it is essential to note the unaffected individual with a negative test result may have a pathogenic variant that was not identified by the testing method used or a pathogenic variant in a gene that was not included on the test panel, so cancer risk is not completely removed with a negative test result. Regardless of negative results, unaffected patients are recommended to follow cancer screening guidelines based on familial or average population risk. Despite these benefits, several negative aspects of genetic testing also exist. For example, individuals who have a variant of uncertain significance in a gene (a variant that has not been defined as either pathogenic or benign due to lack of sufficient information), must live their daily lives with the uncertainty of whether the variant increases their risks of developing cancer or not. The concept of guilt is also common in the realm of genetic testing. Those who receive positive results may experience extreme guilt knowing that they may have transmitted a pathogenic variant to a child, putting them at a higher risk for developing cancer (Murakami et al., 2001). Those who receive negative test results in a family with a known pathogenic variant may experience survivor guilt or guilt that they did not inherit that variant but another family member did (Murakami et al., 2001). Other potentially harmful aspects of the genetic testing process include the psychological stress of learning about

one's pathogenic variant, the cost of testing, and privacy and discrimination concerns ("Genetic Test Fact", 2019).

Genetic tests for hereditary cancer predisposition are ordered from various Clinical Laboratory Improvement Amendments (CLIA) certified laboratories, depending on the patient's personal and family history of cancer, and insurance plan. The National Comprehensive Cancer Network (NCCN) recommends genetic testing for individuals based on specific criteria for different hereditary cancer syndromes (e.g., Lynch syndrome, HBOC, Li-Fraumeni syndrome). If an individual meets criteria for genetic testing, their insurance will likely approve and cover the costs of the genetic test. If an individual does not meet NCCN criteria for testing, there is still the option to undergo testing, but there may be an associated out-of-pocket cost. On average, it takes approximately four to six weeks to get test results back, depending on the laboratory, insurance approval, and if rushing the order is requested

There are three typical outcomes of genetic testing – positive (the laboratory found a pathogenic or likely pathogenic variant that increases cancer risk), negative (the laboratory found no reportable variants), or a variant of uncertain significance (VUS), meaning that the laboratory found a change in an analyzed gene for which there is not enough information to know if that change is pathogenic or benign. It is also possible for an individual to receive both a positive and a VUS result(s) on a genetic test report. Notably, a positive test result does not mean an individual will develop cancer over their lifetime because most cancer predisposition syndromes have reduced penetrance. Several factors influence cancer development in addition to genetics, such as environmental exposures, age, sex, and lifestyle factors. For example, older individuals have an increased risk of developing cancer, and those who consume red meat have a higher likelihood of developing colon cancer. Another critical factor to consider is variable expressivity,

meaning that variants in the same gene can cause different types of cancers or other related features. These concepts must be taken into consideration when counseling individuals for positive results. This can potentially ease anxiety and is a reminder that a positive result is not necessarily a guarantee of cancer. Still, it is vital information that can be used to keep one as healthy as possible. In contrast, it is also crucial to remind patients with negative results that it is still possible to develop cancer at some point over their lifetime due to general population risk, familial risk, or the possibility of a missed pathogenic variant that has not yet been identified in the individual

1.3 Cancer genetic counseling

Genetic counselors' defined roles and responsibilities may differ amongst different sectors of the health care system. According to the Resta et al. (2006), the National Society of Genetic Counselors (2006) defines the process of genetic counseling as “helping people understand and adapt to the medical, psychological and familial implications of genetic contributions to disease. This process integrates the following: --Interpretation of family and medical histories to assess the chance of disease occurrence or recurrence. --Education about inheritance, testing, management, prevention, resources and research. --Counseling to promote informed choices and adaptation to the risk or condition”. Alternatively, the National Cancer Institute defines genetic counseling simply as “a communication process between a specially trained health professional and a person concerned about the genetic risk of disease. The person's family and personal medical history may be discussed, and counseling may lead to genetic testing” (“NCI Dictionary”, n.d.). The roles of a genetic counselor may differ depending on the clinical environment, such as in an oncology office, a laboratory, or a genetic counseling-only

department. It is recommended that those specifically concerned about their risk for hereditary cancer meet with a cancer genetic counselor to discuss their cancer risks and psychosocial concerns in order to make informed testing decisions.

Genetic counseling for hereditary cancer risk commonly follows the general process of provider referral followed by a pre-test appointment to obtain a personal and family history, decide which test would be most beneficial for the patient, and educate the patient about the potential risks and benefits of testing. Any healthcare provider can refer a patient for genetic counseling, but in some cases a patient may also seek out genetic counseling independently without a referral. Pre-test appointments can be held in-person or via-telehealth. Critical components of the personal and family history must be taken into consideration when assessing hereditary cancer risks. Significant aspects include first-and second-degree relatives with a history of cancer, type of cancer, any genetic testing results on relatives, age at diagnosis, age at death, treatment, and any preventative surgeries performed ("Hereditary Cancer Syndromes", 2019; "What is Genetic", 2022). Documenting family ancestry (Ashkenazi Jewish heritage, in particular) is critical due to the higher frequency of founder mutations in specific populations ("Hereditary Cancer Syndromes", 2019). After the personal and family history are obtained and assessed, recommendations for appropriate genetic testing are made. Potential risks, benefits, and limitations of testing are discussed, and consent for testing is obtained. Psychosocial issues are discussed with patients to address any concerns before undergoing genetic testing.

Testing options have evolved from single gene testing to large multi-gene panels, including multiple genes that can predispose an individual to specific types of cancer. For example, commonly ordered tests include a hereditary breast and gynecological panel covering up to 36 genes related to these cancers. A common hereditary cancer panel comprises 47 genes

associated with breast, ovarian, colon, uterine and other cancer predispositions. Larger panels, such as one that includes 84 genes related to these cancers and rarer cancers, such as kidney, thyroid and brain, also may be offered to patients. Patients may opt for smaller or more targeted panels if they only want to focus on genes related to cancers in their families. However, others may opt for larger, broader panels if they are information-seeking and prefer to have more extensive knowledge of risk.

Results disclosure appointments can take place via telehealth - ideally including both audio and video - or in-person. The contents of the results disclosure appointment differ depending on the type of test result received. Positive results disclosure appointments are usually more prolonged and involve what an individual should expect due to their genetic diagnosis. Screening and management guidelines are discussed, in addition to implications for family members, psychosocial counseling, and what the next steps entail. In most clinics, patients do not have long-term care from a genetic counselor. Once the results disclosure appointment is conducted, there is typically no continued follow-up with a genetic counselor or geneticist; however, the follow-up policy varies from clinic to clinic, and some clinics offer the option of longitudinal follow-up. Negative results disclosure appointments are relatively short, allowing space for the patients to ask questions and for the genetic counselor to provide management and screening recommendations based on specific risk models or corresponding family history. During the disclosure of a VUS result, it is explained that there is insufficient information to know if the specific variant is disease-causing or benign. Depending on the particular evidence for the variant, a lab may offer family resolution testing to obtain more evidence towards either a pathogenic or benign classification. If a VUS is identified on a genetic test report, it is necessary to inform individuals that as more research is done, these variants may be either upgraded to

pathogenic or downgraded to benign and are most often downgraded. From 2006 to 2016, it was found that 7.7% of reported VUS results in cancer related genes were reclassified - of these, 8.7% were upgraded to pathogenic/likely pathogenic and 91.2% were downgraded to benign/likely benign (Mersch et al., 2018). Reminding patients that a VUS is not medically actionable is crucial, but it cannot always be assumed to be a negative result. Patients are informed that if the VUS is reclassified, reasonable attempts will be made by the genetics clinic to provide updated results.

Individuals typically undergo genetic testing after they have been diagnosed with cancer, if they have a family history of cancer and do not have cancer themselves, if there is a known familial mutation, or if they are anxious about their own risk ("What is Genetic", 2022). Genetic testing is typically recommended for those who have multiple first-degree relatives with cancer, who have numerous individuals on the same side of the family with cancers/related cancers, family members with multiple similar or related cancers, who have family members with rare cancers (e.g., male breast cancer, medullary thyroid cancer or retinoblastoma), who are from different ancestral groups (e.g., there are three *BRCA1/BRCA2* Ashkenazi Jewish founder variants), who have features that are associated with cancer syndromes (e.g., many colon polyps), or have tumor testing that is suggestive of a germline variant (What is Genetic", 2022).

If an individual does not meet defined criteria for testing, testing is generally not recommended; however, patients may have the option to undergo testing if desired, depending upon insurance coverage, and whether out-of-pocket cost is acceptable to the patient. Test eligibility criteria have evolved significantly over the past decade and are expected to continue to expand, with the possibility that testing may be recommended without restriction someday.

Whether these tests are ordered depends on the provider, and whether the tests are covered by insurance depends on meeting NCCN testing criteria and insurance plan policies.

Direct-to-consumer (DTC) genetic testing has become a popular and accessible option for the general public. Yet, DTC testing should not replace formal genetic counseling and clinical testing ("What is Genetic", 2022). Learning results from a non-clinical setting, such as from a commercial company that provides DTC genetic testing, can fuel stress and may be inaccurate or inappropriate for an individual ("Genetic Testing Fact", 2019). Anyone interested in learning more about genetic risk for cancer should speak with their healthcare provider. However, with the popularity of DTC testing, it is unrealistic to prevent the global population from using these tests. If an individual opts for DTC testing, they should still contact their healthcare provider regardless of their results, especially because DTC testing is not comprehensive and uses less reliable technology, so it cannot accurately assess one's overall risk for developing cancer (What is Genetic", 2022). DTC testing for hereditary cancer risk usually uses single nucleotide polymorphism (SNP) technology ("Direct-to-consumer", 2022). SNP arrays assess for single nucleotide changes in the genome rather than actual causative variants, and the number and location of these SNPs varies from company to company; thus, this type of testing only looks at a small portion of the genome ("Direct-to-consumer", 2022). Another drawback is that even when DTC testing uses more comprehensive technologies, only predetermined variants are reported to patients ("Direct-to-consumer", 2022). For example, someone who is not of Ashkenazi Jewish ancestry who receives "negative" *BRCA1* and *BRCA2* results of DTC testing that only reports out the Ashkenazi Jewish founder variants, will get false reassurance, since they may still have a *BRCA1* or *BRCA2* that the company is not identifying. Genetic tests conducted in a clinical setting are more thorough because they use methods that include full gene sequencing and copy

number analysis and report any pathogenic/likely pathogenic and uncertain variants ("Direct-to-consumer", 2022).

1.4 Motivation for cancer genetic counseling and testing

Individual motivations for undergoing genetic counseling and testing for hereditary cancer risk have been well studied. How a person feels regarding genetic testing may differ between men and women, especially regarding genetic testing for *BRCA1* and *BRCA2* pathogenic variants. This may be in part because *BRCA1* and *BRCA2* are so highly linked to female breast and ovarian cancer, and research regarding these genes has been more dedicated to women than men (Ongaro et al., 2022). According to Gill et al. (2020) women typically attend genetics clinics for testing related to HBOC risk. Although most women are estimated to have a low risk of carrying a pathogenic variant related to HBOC, many still proceed with testing, largely due to family history, family experiences, or to fill in the gaps if family history is unknown (Gill et al., 2020). One study conducted by Annoni & Longhini (2022), suggests that men who are at-risk for *BRCA1* and *BRCA2* pathogenic variants are less likely to seek out genetic testing and take part in recommended screening. In fact, according to Peshkin et al. (2019), unaffected men undergo genetic testing for *BRCA1/BRCA2* pathogenic variants at about one-tenth of the rate noted in women. The findings by Annoni & Longhini (2022) suggest that men take a passive approach to screening and are less likely to obtain information about screening to manage their cancer risk. The study also indicates that men do not fully understand their risk regarding *BRCA1/BRCA2* pathogenic variants, strengthening the misconception that only women are at-risk for *BRCA1/BRCA2-related cancer*. Annoni & Longhini's study (2022) found that men are also left out of sensitive family conversations surrounding this topic, which

can fuel lack of awareness and general uncertainty. Men may also feel that *BRCA1/BRCA2* education materials are not tailored to their concerns, but their interest in genetic testing increases when they are provided with sufficient information (Peshkin et al., 2019). Therefore, it is crucial for healthcare providers to better identify at-risk men, educating men about their risk for carrying *BRCA1/BRCA2* variants and developing related cancers and referring to genetic counseling (Peshkin et al., 2019). However, it was found that factors contributing to men seeking genetic screening for *BRCA1* and *BRCA2* pathogenic variants are higher self-efficacy and perceived risk (Annoni & Longhini, 2022).

In a study involving 113 patients diagnosed with prostate cancer, the top reasons for seeking genetic testing were (1) to learn about the cancer risk of family members (98%), (2) to obtain information that can influence cancer treatment (93%), and (3) to learn more about the risk of other cancers in the future (92%) (Finn et al., 2022). Among 40 families in the Netherlands with a history of Lynch Syndrome, the most significant reasons for undergoing genetic testing were established surveillance programs (61%), to learn about personal Lynch Syndrome status (34%), and fear of getting cancer (14%) (Leenen et al., 2016). In a group of 30 adolescent and young adult cancer patients, 21 opted for genetic counseling because of its impact on other family members, family planning, learning about need for increased cancer screening, and easing concern about other cancer risks (Morand et al., 2022). Fear of cancer recurrence or occurrence also motivates affected individuals to seek genetic testing (Thomas et al., 2021). In general, family history of cancer is a common and significant reason for those seeking genetic counseling and testing (Kne et al., 2016).

In other cases, patients may choose to forgo genetic counseling and/or testing. It has been described that women who are at-risk for HBOC-related cancers do not seek out testing due

to lack of information about the relevance and purpose of genetic counseling services, not viewing genetic counseling as beneficial (influential factors include having children and not having female relatives), the lack of physician knowledge of genetics, having low perceived cancer risk, and believing that non-genetic factors caused their family history of cancer (Kne et al., 2016). Overall, having low perceived risk, not prioritizing genetic counseling, and seeing no benefit are common and well-studied reasons why women opt out of genetic counseling (Kne et al., 2016). For those counseled on Lynch Syndrome, genetic testing was declined because of potential life insurance and mortgage issues, being happy with their current life, and not having any physical symptoms (Leenen et al., 2016). Other factors that discourage patients from seeking genetic testing include potential emotional consequences and financial burden of increased healthcare (mainly if a positive result is found), lack of ability to assess personal cancer risk rationally, cost of testing, disclosing carrier status to blood relatives, and fear of insurance discrimination (Zimmermann et al., 2021).

1.5 Decision regret and genetic testing for hereditary cancer risk

Patient decision-making plays a critical role in the hereditary cancer genetic testing process. With this increased autonomy comes greater opportunity to experience decision regret (Brehaut et al., 2003). Decision regret is defined by Brehaut et al. (2003) as "distress or remorse after a [health care] decision". Motivations and feelings about making testing decisions are well-explored in existing literature. Still, much less is known about how patients feel about their decision to test after they receive their results. Patients may feel satisfied with their decision to test or may entirely regret it. According to Matarazzo et al. (2021), research on regret has seemingly halted in the last few years, possibly because the emotion of regret is well-understood

and further knowledge does not have to be developed.

Decision regret concerning cancer has been studied in the literature regarding prophylactic surgery, various cancer screening options (for breast, ovarian, colon, melanoma, and prostate cancers), different cancer treatments, and how decision aids impact decision regret for cancer genetic testing (Perez et al., 2016). Few studies exist that measure decision regret concerning cancer genetic test results, and they do not focus solely on regret or thoroughly investigate the relationship between regret, test result types, and the genes involved. Godino et al. (2018) explored the decision-making concepts and experiences of young adults choosing to have presymptomatic genetic testing due to a family history of cancer. No regret was evident, but the cohort only included young adults. Another study by Butterfield et al. (2019) examined the process of returning negative results for 11 medically actionable conditions (including cancer syndromes) and found that participants receiving negative results experienced no regret.

Some investigation has been completed on the relationship between test result type and level of decision regret, yet again, they have not been thorough investigations. Clift et al. (2018) found that individuals with a VUS result may be more likely to experience feelings of decision regret. Since one primary goal of genetic testing is to inform health care choices, an uncertain outcome does not provide helpful information about screening and management protocol (Clift et al., 2018). For example, when interviewing 27 individuals who received a VUS in a gene related to Lynch Syndrome, Solomon et al. (2017) found that two individuals experienced regret about testing. The uncertainty of outcomes, lack of defined protocol and management guidelines, and lack of consistency in how VUS results are handled throughout clinics likely fuels decision regret amongst patients with these types of results. Those with positive results in moderate-risk

cancer genes may have anxiety about their results, potentially leading to more feelings of regret towards genetic testing.

According to Reyes et al. (2022), those who were positive for *ATM* and *CHEK2* variants experienced uncertainty regarding risk management strategies. Pathogenic/likely pathogenic variants in *ATM* are associated with a 20% to 30% lifetime risk of breast cancer, and pathogenic/likely pathogenic variants in *CHEK2* are associated with a 20% to 40% lifetime risk of breast cancer when compared to the 12.9% lifetime risk in the general population (National Comprehensive Cancer Network, 2023). Increased screening recommendations in combination with these lower lifetime risks compared to other pathogenic variants may leave some individuals feeling conflicted about their level of concern. They may feel that they are in limbo regarding whether they will develop breast cancer or not.

1.6 Significance of research

Understanding patients' long-term feelings towards genetic cancer testing will help cancer genetic counselors better support their patients through the testing process. By knowing what types of results and outside demographic and personal factors impact the level of decision regret, providers can modify and personalize their counseling strategies when discussing possible results prior to testing and when conducting results disclosure. The findings from this research are a starting point to develop more streamlined counseling strategies for specific test results that may help patients feel more confident in their testing decisions and feel more secure in their decision to test afterwards.

Specialized care is crucial to the practice of genetic counseling. The findings of our research may identify groups that need more support when undergoing genetic testing for hereditary cancer risk. Findings may also identify which groups feel more confident in their decisions depending on what type of test result they receive. This may help genetic counselors prepare for more personalized conversations with patients based on specific demographic factors, personal factors, and test results, which better supports and meets patient needs.

This research deepens the cancer genetic counseling community's understanding of decision regret and the patient thought process regarding genetic testing. This resurgence of research surrounding decision regret allows genetic counselors to learn more about the possibility of patients regretting their choices, since it is a topic that does not frequently arise during genetic counseling appointments. Existing literature explores the concept of decision regret, yet in many different pieces across the board. We could not find published research that was completed in a cancer genetics clinic focusing on decision regret after testing for a variety of referral indications, which is what this study aims to do. This research should deepen genetic counselors' appreciation of the patient's experience and be a helpful addition to the existing literature on patient perspective on genetic testing.

1.7 Aims and hypotheses

This retrospective research aims to collect and analyze data on adult individuals who have had cancer genetic counseling where testing was recommended for hereditary cancer risk at a university medical cancer genetics clinic from November 2014 to March 2023 to:

1. Identify differences in decision regret between those who elected to have cancer genetic testing and those who did not. For those who chose testing, it will also assess differences

among those who received positive, negative, or VUS results on hereditary cancer panels or single-gene tests. For those who had positive test results, it will also assess differences in regret based on various genes involved in their test results.

2. Identify the impact of other variables—such as personal cancer history, gender, educational background, having children, how testing expense was covered, the out-of-pocket cost of testing, and reason for testing (cancer diagnosis, family history, testing due to anxiety)— on level of decision regret.

Based on evidence in the existing literature and previous experience with patients in this specific clinic population, it is hypothesized that approximately 1% of those with negative results, 15% of those with a VUS result, and 10% of those with a positive result will have some level of regret towards their decision to have hereditary cancer genetic testing. It is also hypothesized that those with positive results for moderate or low-risk cancer variants may have at least some regret. Finally, it is hypothesized that several other factors, such as having children, whether the appointment was in person or by telehealth, and reason for testing, will be related to decision regret.

II. METHODS

2.1 IRB protocol

This research study qualified for expedited review by the University of California, Irvine, Institutional Review Board and was approved under HS #1752 on January 25, 2023.

2.2 Retrospective data collection

2.2.1 Patient selection

This study included individuals who were 18 years or older at the time of their visit, spoke English, and had genetic counseling where testing was recommended for hereditary cancer risk at UCI Health between November 2014 and March 2023. This time frame was implemented to maintain continuity, since all patients during this time were seen by the same genetic counselor. Patients seen in the clinic were not eligible to participate if they were under 18, did not speak English, or if genetic testing was not recommended based on personal or family cancer history. Individuals were eligible to participate in the study only if it had been at least 4 weeks since receiving their genetic test results. Due to research time constraints, English was the only language included in this study, and English is the most common language spoken in the patient population of the UCI cancer genetic clinic.

2.2.2 Participant Recruitment

During recruitment, data was collected from the internal UCI Cancer Genetics Database (CaGen), the internal UCI FS-Cancer Genetics SharePoint, and electronic medical records

(EPIC). Between November 2014 and March 2023, information pertaining to 2,389 patients was examined from the UCI Cancer Genetics Database and the UCI FS-Cancer Genetics SharePoint.

Patient information including medical record number (MRN), last name, test result date, and category of test result (to assign study category and confirm eligibility) – positive, positive with additional VUS, negative, VUS, or did not elect to have testing for 2,343 patients with test results who were seen during this time was pulled from the UCI Cancer Genetics Database using the Power BI system. While result category was assessed, clinical utility of the test result was not assessed. Due to delays in database entry, information from 46 patients seen between 2022 and 2023 was taken directly from the UCI FS-Cancer Genetics SharePoint. Medical record numbers (MRN) were then queried in EPIC (the electronic medical record system used at UCI) to obtain patient email addresses from the demographics section.

After recruitment, last names, year of test completion, assigned group, and email addresses were entered into individual back-end data forms in REDCap. This back-end data form allowed for the data to be linked to participant responses via email at the time of de-identified data download. Patients were not contacted if they did not have an email address on file (180), were deceased (140), spoke a language other than English (58), were noted as having "other nongenetic result" (genetic diagnoses via colonoscopy, endoscopy, enteroscopy, and sigmoidoscopy 21) in the CaGen database, or did not meet other eligibility criteria (2). Based on eligibility criteria and availability of an email address, a participant list for contact was created in REDCap using collected email addresses and consisted of 1,596 unique potential participants in addition to 45 duplicate entries and one test entry (participant list totaled 1,642).

The validity of the CaGen database was assessed by randomly checking the accuracy of the test result type on 178 eligible patient genetic test reports, equating to 11.2% of the total

eligible patient records examined, and 100% of these records were accurate.

2.3 Data Collection Tools

The survey instrument (Appendix A) was designed to assess patient feelings about the genetic counseling process, patient recall about genetic counseling and their test results, and regret about having or not having genetic testing for hereditary cancer risk. Additionally, logistics of pre-test and post-test genetic counseling appointments were explored, such as who ordered testing, the mode of appointments, how genetic testing was paid for, and how much money was spent on genetic testing. Seven questions focused on demographics such as ethnicity, race, sex, education level, and having children. Six questions focused on cancer history and genetic test results. Eleven questions focused on the genetic counseling and testing process. Participants were also required to complete a validated five-question Decision Regret Scale (DRS, a validated scale assessing feelings of regret towards medical decisions) (Brehaut et al., 2003). The survey concluded with both close-ended and open-ended questions about feelings towards decision regret. The survey was administered between February 18, 2023 and March 28, 2023 through REDCap. In addition to the initial email blast, three follow-up emails were sent to potential study participants.

In addition to the informed consent section of the survey (Appendix B), an optional HIPAA Authorization form (Appendix C) via DocuSign was included at the end of the survey to obtain consent to confirm participant-reported genetic test results including test result type and, if applicable, the gene involved. For those who signed this consent form, their test result type was confirmed in the back-end data form in REDCAP, and the gene(s) noted on their genetic test report was added to this form. However, the clinical utility of the test result was not assessed.

All eligible participants had the opportunity to enter their email address in a separate Qualtrics survey (linked through the primary informed consent page) to be entered to win one of ten $20 Amazon gift cards. Winners were selected using a random number generator, and the cards were given to the randomly chosen participants in May 2023.

2.4 Data analysis

Data analysis was performed using IBM SPSS Software Version 29 for descriptive and inferential analyses. Descriptive analysis included all variables in the questionnaire. Counts and percentages were used for all categorical variables. Certain variables were condensed for analyses and DRS scores were converted to 100. The raw mean DRS scores were also used for analyses. Investigator determined category of test result types were used for analyses. Inferential analyses to determine difference in regret were carried out through both univariate and multivariate analyses. Univariate analyses were conducted using a Chi-Square test, Independent Samples T-Tests, and a One-way ANOVA. Multivariate analysis was conducted using binary logistic regression to explore how certain variables predict level of regret. The significance level for all statistical tests is a nominal p-value of 0.05.

Qualitative data from the final survey question number was analyzed using key words and coding into primary and subthemes.

III. RESULTS

3.1 Descriptive data

3.1.1 Demographics of study participants

The demographic characteristics of the study sample (n = 234) are detailed in Table 1. Regarding race, 76.5% of patients identified as White, 9.8% Asian, 6.4% more than one race, 3.8% preferred not to answer, 1.7% Black or African American, 1.3% did not report, and 0.4% American Indian/Alaska Native. For ethnicity, 80.3% of the population identified as not Hispanic or Latino, 17.5% Hispanic or Latino, 0.4% did not report, and 1.7% preferred not to answer. Most of the sample identified as female (74.4%), 24.8% as male, 0.4% as non-binary/third gender, and 0.4% did not report. Most respondents (68.4%) had received an undergraduate degree or higher, with 32.1% reporting an undergraduate degree, 20.9% having a master's degree, and 15.4% with a PhD, MD, JD, or other similar professional degree. Regarding relationship status, 62.0% of individuals were married, 19.2% single, 6.4% divorced, 6.4% widowed, 5.6% in a partnership, and 0.4% preferred not to say. Most respondents had biological children (65.4%), 32.1% had no children, 1.7% had adopted children, and 0.9% had stepchildren.

Out-of-pocket cost for genetic testing, payment method, and insurance type were assessed. Out-of-pocket cost was generally under $100, with 44.9% of patients paying nothing and 12.4% paying $100 or less. However, 32.5% of participants did not remember what they paid for testing. Most patients (73.9%) had some or all of their testing costs paid for by insurance coverage, 15.4% did not remember the payment method, 5.1% selected "other" as a payment method (one individual noted testing was covered by workers compensation, three individuals noted testing was done as part of a research study, and others noted a mix of partial insurance

coverage and partial self-pay), 3.0% had the testing laboratory cover their fee, and 2.6% opted for self-pay. Regarding insurance type, 65.8% reported having a commercial insurance plan, 25.4% had Medicare, 6.2% had Medicaid, and 2.7% had a health savings account.

As part of the recruitment process, we invited those who declined to test, but no one in the sample noted declining genetic testing. Additionally, as part of the recruitment process, individuals were grouped into categories based on their results - 55 (23.5%) had a positive result, 130 (55.6%) had a negative result, and 49 (20.9%) had a VUS result. Regarding the year genetic testing was complete, all but one individual had genetic testing done after 2013, and the majority (51.3%) were completed between 2020-2022.

Table 1. Demographic characteristics of study participants (N=234)

	n	(%)
Ethnicity		
Hispanic or Latino	41	(17.5%)
Not Hispanic or Latino	188	(80.3%)
Unknown/Not Reported	1	(0.4%)
Prefer not to answer	4	(1.7%)
Race		
American Indian/Alaska Native	1	(0.4%)
Asian	23	(9.8%)
Black or African American	4	(1.7%)
More than one race	15	(6.4%)
Unknown/Not reported	3	(1.3%)
Prefer not to answer	9	(3.8%)
Sex		
Female	175	(74.4%)
AFAB (Assigned Female at Birth)	1	(0.4%)
Male	58	(24.8%)
Gender		
Female	174	(74.4%)
Male	58	(24.8%)
Non-binary / third gender	1	(0.4%)
No answer	1	(0.4%)
Education		

Some high school	3	(1.3%)
High school graduate or GED	10	(4.3%)
Some college	43	(18.4%)
Associate degree	18	(7.7%)
Undergraduate degree (BS, BA)	75	(32.1%)
Master's degree	49	(20.9%)
PhD, MD, JD, or other similar professional degree	36	(15.4%)
Relationship Status		
Single	45	(19.2%)
Married	145	(62.0%)
Divorced	15	(6.4%)
In a partnership	13	(5.6%)
Widowed	15	(6.4%)
Prefer not to say	1	(0.4%)
Have Children		
Yes – biological	153	(65.4%)
Yes – adopted	4	(1.7%)
Yes – stepchildren	2	(0.9%)
No	75	(32.1%)
Genetic Testing Out-of-Pocket Cost		
I did not pay anything	105	(44.9%)
$100 or less	29	(12.4%)
$101 to $500	18	(7.7%)
$501 to $1,000	3	(1.3%)
$1,001 or more	3	(1.3%)
I don't remember	76	(32.5%)
Genetic Testing Payment Method		
Insurance coverage	173	(73.9%)
Self-pay	6	(2.6%)
Insurance did not cover, but lab did not charge	7	(3.0%)
Other	12	(5.1%)
I don't remember	36	(15.4%)
Insurance Type* (n = 261)		
Commercial Insurance	171	(65.8%)
Medicaid	16	(6.2%)
Medicare	66	(25.4%)
Health savings account	7	(2.7%)
Test Result Category (n = 234)		
Positive	55	(23.5%)
Negative	130	(55.6%)
VUS	49	(20.9%)
Year Test Complete		

2008	1	(0.4%)
2014	2	(0.9%)
2015	21	(9.0%)
2016	22	(9.4%)
2017	20	(8.5%)
2018	19	(8.1%)
2019	27	(11.5%)
2020	35	(15.0%)
2021	44	(18.8%)
2022	41	(17.5%)
2023	1	(0.4%)
Unavailable	1	(0.4%)

**n is larger than expected because participants were allowed to select more than one option*

3.1.2 Participant cancer history

Personal cancer history is detailed in Table 2. Most participants did not have cancer at the time of participating in the study (81.2%), while 12.8% reported that they currently had cancer, and 6.0% did not know if they currently had cancer. Whether or not individuals previously had cancer was a near-even split, with 51.3% reporting having cancer and 48.7% reporting never having cancer. The presence of multiple colon polyps is a red flag for hereditary cancer predisposition, so we also asked about this history. Most participants did not have a personal history of 10 or more colon polyps (72.6%), while 12.8% reported having 10 or more colon polyps, and 14.5% did not know. One-hundred thirty participants (55.6%) reported on what type of cancer they were diagnosed with either previously or currently. Participants were allowed to select more than one option, yielding a total number of 206 responses. Of these, 13.1% reported either previously or currently having breast cancer, colon cancer 11.2%, skin cancer 13.3%, prostate cancer 9.1%, uterine cancer 8.3%, and ovarian cancer 7.3%.

Table 2. Participant cancer history (N=234)

	n	(%)
Currently Have Cancer		
Yes	30	(12.8%)
No	190	(81.2%)
I don't know	14	(6.0%)
Previously Had Cancer		
Yes	120	(51.3%)
No	114	(48.7%)
History of 10+ Colon Polyps		
Yes	30	(12.8%)
No	170	(72.6%)
I don't know	34	(14.5%)
Cancer Diagnoses (n = 131, 55.7% of study population)*		
Bile duct	2	(1.0%)
Brain	1	(0.5%)
Breast	27	(13.1%)
Colon	23	(11.2%)
Endocrine**	8	(3.9%)
Esophageal	1	(0.5%)
Other hematologic cancer	1	(0.5%)
Leukemia and/or Lymphoma	6	(2.9%)
Lung	1	(0.5%)
Ovarian	15	(7.3%)
Pancreatic	5	(3.0%)
Prostate	15	(9.1%)
Renal	8	(3.9%)
Skin***	22	(13.3%)
Stomach	3	(1.5%)
Uterine	17	(8.3%)
Other gynecological cancer****	4	(1.9%)
Other cancer	6	(2.9%)

**participants were allowed to select more than one option*
***includes thyroid cancer, paraganglioma, and pheochromocytoma*
****includes melanoma, basal cell, and squamous cell*
*****includes fallopian tube and cervical cancers*

3.1.3 Participant genetic test result details

Table 3 summarizes participant genetic test result details. Two-hundred twenty-six participants (96.6%) received genetic test results, while eight (3.4%) did not. Although these eight individuals reported not receiving genetic test results, all have genetic test results in their medical record that were reviewed during the recruitment process. Of those who reported not receiving their test results, two individuals reported that their insurance did not cover testing and they did not want to pay for it. One participant reported that their results were not ready yet, one reported a sample failure, one did not remember receiving their results, and one reported that genetic testing was not offered, though they do have a negative genetic result in their medical records. A decision was made not to exclude this individual because testing was actually recommended, which was among the criteria for inclusion.

Individuals were given the opportunity to self-report their test results. Regarding test result type, 21.5% reported that they had a positive test result, 56.6% reported a negative test result, 10.7% reported a VUS result, 9.9% did not remember their test result, and 1.2% reported never receiving test results. For those who self-reported a positive result, 16 (30.2%) reported a variant in a gene associated with a high risk of breast and gynecological cancer, 13 (24.5%) had a variant associated with a moderate-risk of breast cancer, 11 (20.8%) had a variant related to colon cancer, two (3.8%) had a variant related to other cancers, and 11 (20.8%) did not remember the gene on their positive test report. Of those who reported a VUS, 57.1% did not remember the gene associated with their result.

Table 3. Participant genetic test result details (N=234)

	n	(%)
Received Genetic Test Results		
Yes	226	(96.6%)

No	8	(3.4%)
Why Results Not Received		
My insurance would not cover testing and I was not comfortable paying for it	2	(0.9%)
The results are not ready yet	1	(0.4%)
I submitted a blood or saliva sample, but the test did not work	1	(0.4%)
I don't remember receiving the results	1	(0.4%)
Genetic testing was not offered to me	1	(0.4%)
Other	2	(0.9%)
Self-Reported Test Results Category		
Positive	52	(21.5%)
Negative	137	(55.6%)
VUS	29	(10.7%)
Don't remember results	24	(9.9%)
Did not receive results	3	(1.2%)
Self-Reported Positive Categories (n = 53)*		
High-risk breast and gyn cancer genes	16	(30.2%)
Moderate-risk breast cancer genes	13	(24.5%)
Colon cancer genes	11	(20.8%)
Other gene	2	(3.8%)
Don't remember gene	11	(20.8%)
Self-Reported Pathogenic/Likely Pathogenic Variants (n = 53)		
APC	1	(1.8%)
ATM	5	(9.1%)
BARD1	1	(1.8%)
BRCA1	6	(10.9%)
BRCA2	10	(18.2%)
BRIP1	1	(1.8%)
CHEK2	6	(10.9%)
MLH1	2	(3.6%)
MSH2	2	(3.6%)
MSH6	3	(5.5%)
MUTYH	2	(3.6%)
PMS2	2	(3.6%)
STK11	1	(1.8%)
VHL	1	(1.8%)
Other gene	1	(1.8%)
Don't remember gene	11	(20.0%)
Self-Reported VUS Genes (n = 26)		
BRCA1	2	(7.1%)

BRCA2	2	(7.1%)
CDKN2A	1	(3.6%)
MEN1	1	(3.6%)
MSH3	1	(3.6%)
MSH6	1	(3.6%)
MUTYH	2	(7.1%)
SDHD	1	(3.6%)
Other gene	1	(3.6%)
Don't remember gene	16	(57.1%)

**n is larger than expected because participants were allowed to select more than one option*
**high-risk breast/gyn includes BRCA1, BRCA2, STK11. One person in this group selected both BRCA1 and BRCA2.*
**moderate-risk breast cancer genes include ATM, BARD1, BRIP1, CHEK2*
**colon-cancer related genes include APC, MLH1, MSH2, MSH6, MUTYH, PMS2. One person in this group selected both MLH1 and MSH6.*
**other genes include MEN1, NF1, SDHA, VHL*

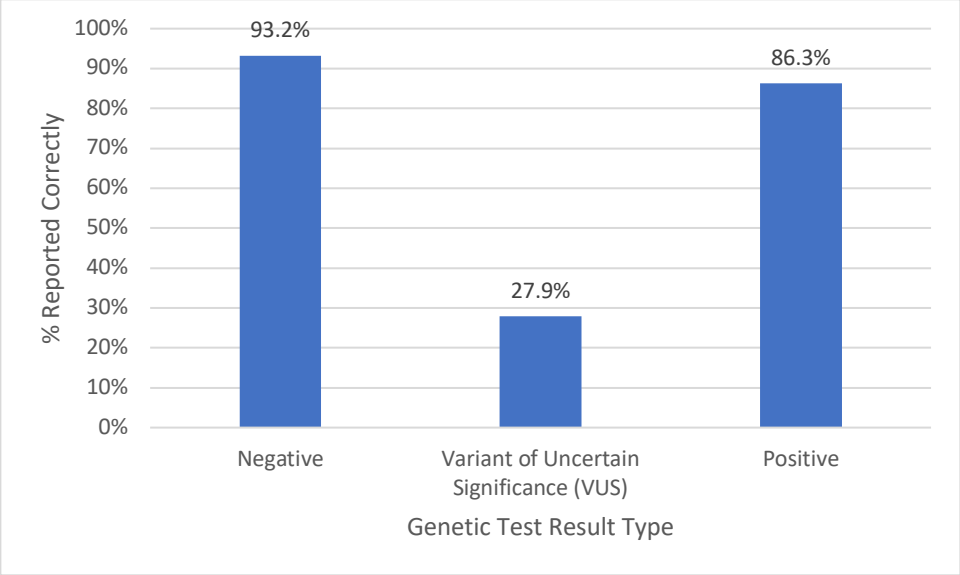
The accuracy of participant-reported genetic test result type was explored (Table 4 and Figure 1). A total of 212 (90.6%) individuals self-reported genetic test results. Fifty-two (22.2%) reported a positive result, 137 (58.5%) reported a negative result, and 23 (9.8%) reported a VUS. This differed from the distribution of results as determined by study eligibility criteria ($p<0.001$). When compared to the actual category of results (determined from medical records as part of study eligibility criteria), it was found that 86.3% of those with a positive result correctly reported a positive result and 93.2% with a negative result correctly reported a negative result, but only 27.9% with a VUS result correctly reported a VUS. It should be noted that the clinical utility of these test results was not examined, so someone may have self-reported a negative result when, in reality, their result was a clinically irrelevant VUS (such as a heterozygous VUS in genes like *NBN* or *MUTYH* that are related to autosomal recessive conditions).

Table 4. Self-reported genetic test results vs. investigator determined genetic test results

		Investigator Determined Test Result			
		Negative	**VUS**	**Positive**	**Total**
Self-reported test result	**Negative**	110	24	3	137
	VUS	7	12	4	23
	Positive	1	7	44	52
	Total	118	43	51	212

Shaded boxes indicate number of individuals who correctly reported their test result type

Figure 1. Accuracy of self-reported genetic test results



*Positive and negative test results were generally reported correctly, but VUS results were more likely to be incorrectly reported. *Chi-square test revealed significant difference between self-reported and actual test results $\chi 2$ (d.f.) = 81.64 (2), $p < 0.001$*

3.1.4 Participant genetic test appointment experience details

Details surrounding the genetic test appointment experience are presented in Table 5. Regarding ordering provider, 49.1% reported that their testing was ordered by a UCI Health physician, 28.2% by a UCI Health genetic counselor, 8.5% by a physician outside of UCI Health, 1.3% by a genetic counselor outside of UCI Health, 3.4% by someone else, and 9.4% did not

remember. Most individuals (74.8%) reported that they had a pre-test appointment. Of those individuals, 55.1% had an in-person appointment, 11.5% had a video conference appointment, and 8.1% had an appointment via telephone; 12.8% reported not having a pre-test appointment, and 12.4% did not remember having an appointment. Most participants (85%) reported having a post-test appointment to discuss their genetic test results. Of those, 44.4% had an in-person appointment with a genetic counselor, 15.0% had a telephone call with a genetic counselor, 12.4% had a video conference with a genetic counselor, 7.7% had an in-person appointment with a physician, 2.6% had a video conference with a physician, 1.7% had a telephone call with a physician, 0.9% had a telephone call with a nurse or medical assistant, and 0.4% had an in-person appointment with a nurse or medical assistant. Regarding who first disclosed test results, 54.3% of individuals first learned about their test results from a genetic counselor, 32.9% from a physician, 1.7% from a nurse, and 11.1% did not remember. Most participants (87.2%) remember discussing their test results in detail, and 12.8% did not. Of those who did not report having a post-test appointment, 0.9% were sent their test results via the MyChart patient portal and did not speak to anyone about results, 6.0% did not have a post-test appointment, and 8.1% did not remember if they had a post-test appointment.

Participants were given nine possible reasons why they decided to have genetic testing and were allowed to select more than one reason. All 234 participants responded, with a total of 441 reasons. Out of the reported reasons, the most common were that someone in their family has or had cancer (38.3%), they wanted to know if their family members have an increased genetic chance to have cancer (16.8%), and there is a known genetic risk in their family (16.3%). Individuals were then asked to choose their primary reason for genetic testing from the same list of options; 35.9% chose to have testing because someone in their family has or had cancer,

23.9% due a personal history of cancer, 20.1% because of a known genetic risk in their family, 12.4% because they wanted to know if their family members had an increased genetic chance to have cancer, 0.9% for family planning, and 0.4% because they were worried about developing cancer despite having a negative family history of cancer. On the other hand, 6.0% of participants indicated that they did not know why they had testing but chose to do so their doctor recommended it. Participants were asked if their medical care was modified by their genetic test results and were allowed to select more than one answer from a list of possible ways their care may have changed. Out of 241 selections, 56.4% reported no change in medical care, 13.7% had no change in medical care but thought it may change in the future, 17.4% had increased cancer screening based on test results, 2.5% decided to have prophylactic surgery, 2.5% indicated that it changed their cancer treatment plan, and 0.8% reported starting to take cancer risk-reducing medication. Three individuals (3.3%) responded "other" regarding whether medical care changed; their explanations were not having hysterectomy, not having to worry about getting breast or cervical cancer, and making dietary and exercise modifications.

Table 5. Participant genetic test appointment experience details (N=234)

	n	(%)
Ordering Provider		
UCI Health genetic counselor	66	(28.2%)
UCI Health physician	115	(49.1%)
A physician outside of UCI Health	20	(8.5%)
A genetic counselor outside of UCI Health	3	(1.3%)
Other	8	(3.4%)
I don't remember	22	(9.4%)
Pre-test Appointment		
Yes, in-person appointment	129	(55.1%)
Yes, video conferencing	27	(11.5%)
Yes, phone call	19	(8.1%)
No	30	(12.8%)
I don't remember	29	(12.4%)
Post-test Appointment		

Yes, in-person appointment with GC	104	(44.4%)
Yes, video conference with GC	29	(12.4%)
Yes, telephone with GC	35	(15.0%)
Yes, in-person appointment with physician	18	(7.7%)
Yes, video conference with physician	6	(2.6%)
Yes, telephone with a physician	4	(1.7%)
Yes, in-person appointment with nurse/MA	1	(0.4%)
Yes, telephone with a nurse/MA	2	(0.9%)
My results were sent via MyChart and I did not speak to anyone about results	2	(0.9%)
No	14	(6.0%)
I don't remember	19	(8.1%)
Who First Disclosed Test Results		
Genetic counselor	127	(54.3%)
Physician	77	(32.9%)
Nurse	4	(1.7%)
I don't remember	26	(11.1%)
Remember Discussing Test Results in Detail		
Yes	204	(87.2%)
No	30	(12.8%)
Reasons For Genetic Testing* (n = 441)		
I have a personal history of cancer	93	(21.1%)
There is a known genetic risk (such as a gene mutation) for cancer in my family	72	(16.3%)
Someone in my family has or had cancer	169	(38.3%)
I don't have a family history of cancer, but I'm curious about my chance of developing cancer	1	(0.2%)
I don't have cancer or have a family history of cancer, but I'm worried about developing cancer	1	(0.2%)
This information may help me make decisions about having children	11	(2.5%)
I or someone in my family ordered my genetic test from a company online	1	(0.2%)
I had testing to know if my family members have an increased genetic chance to have cancer	74	(16.8%)
I don't know, but my doctor recommended testing	19	(4.3%)
Primary Reason for Genetic Testing		
I have a personal history of cancer	56	(23.9%)
There is a known genetic risk (such as a gene mutation) for cancer in my family	47	(20.1%)
Someone in my family has or had cancer	84	(35.9%)
I don't have cancer or have a family history of cancer, but I'm worried about developing cancer	1	(0.4%)
This information may help me make decisions about having children	2	(0.9%)

I or someone in my family ordered my genetic test from a company online	1	(0.4%)
I had testing to know if my family members have an increased genetic chance to have cancer	29	(12.4%)
I don't know, but my doctor recommended testing	14	(6.0%)
Did Medical Care Change Based on Results* (n = 246)		
Yes – increased cancer screening	46	(18.7%)
Yes – I decided to have prophylactic surgery	7	(2.8%)
Yes – started taking cancer risk-reducing medication	2	(0.8%)
Yes – changed my cancer treatment plan	6	(2.4%)
Yes – other	8	(3.3%)
No, but it might change in the future	33	(13.4%)
No	136	(55.3%)
I don't know	8	(3.3%)

**n is larger than expected as participants were allowed to select more than one option*

3.1.5 Participant test regret details

Specifics regarding patient test regret are detailed in Table 6. When given the choices of yes or no, 96.6% of patients reported having no regret about genetic testing, and 3.4% reported having regret. With respect to recommending genetic testing to someone else, 96.6% of participants would recommend and 3.4% would not. Participants were given six possible reasons why they do not regret undergoing genetic testing and were allowed to select multiple answers. Two-hundred twenty-six participants responded with a total of 431 reasons: 34.8% said genetic testing gave them helpful information for their family, 27.6% said they have no regret because they know more about their personal risk for developing cancer, 22.3% said it eased their anxiety about developing cancer, 7.2% said they were able to change their medical management based on genetic testing, 5.3% said it helped them make decisions about having children, and 2.8% reported other reasons for having no regret. Participants who indicated that they did regret genetic testing were given 11 possible reasons as to why and were allowed to select multiple

answers. Eight participants responded with a total of 21 reasons: 19.0% said that genetic testing increased their anxiety about developing cancer, 19.0% said they had regret because they had to tell their family members, 9.5% had regret because of guilt that they might have passed something to their children, 9.5% because their medical management did not change, and 9.5% because they felt like testing was a burden on their family.

Table 6. Participant decision regret details (N=234)

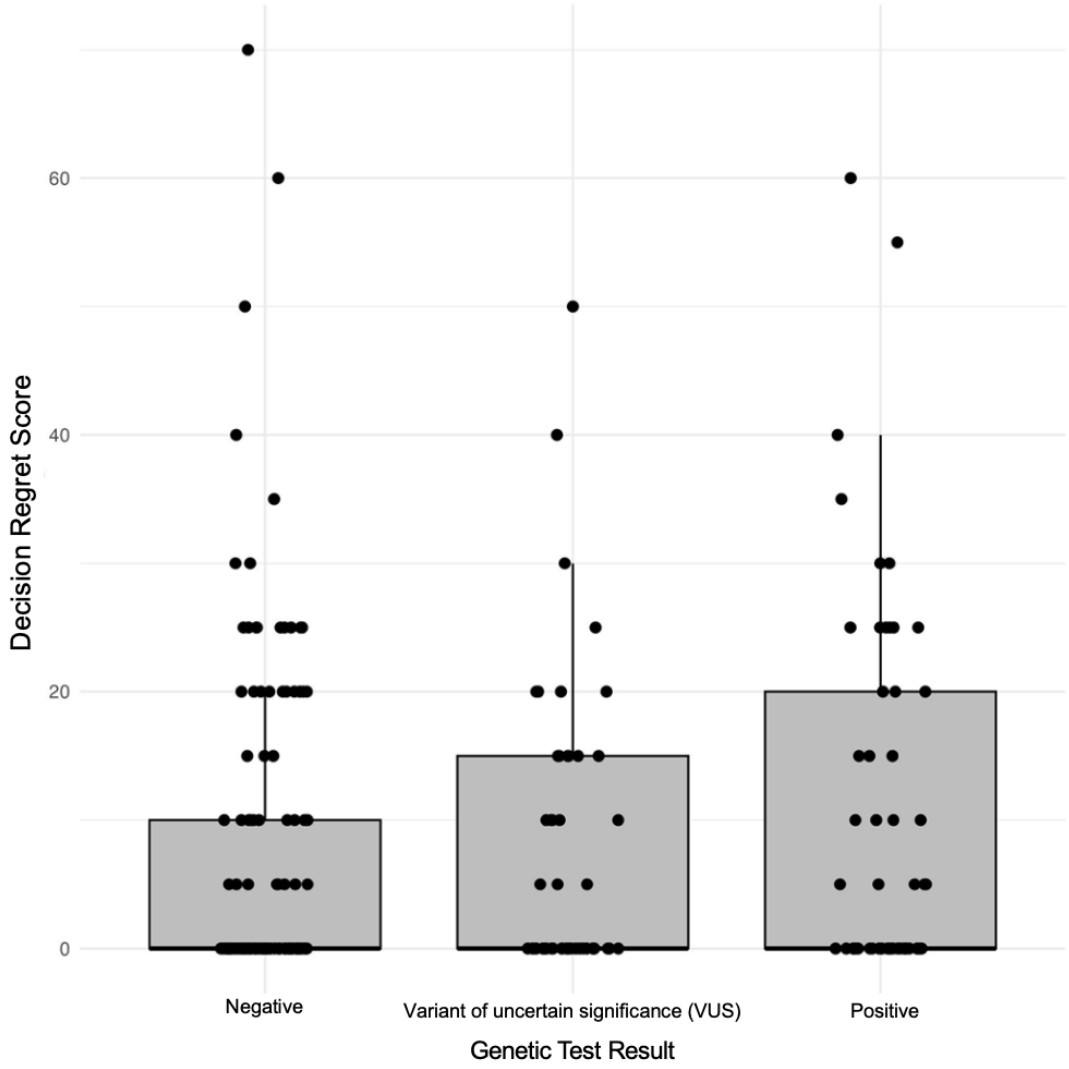
	n	(%)
Have Regrets About Testing		
Yes	8	(3.4%)
No	226	(96.6%)
Would Recommend Testing to Someone Else		
Yes	226	(96.6%)
No	8	(3.4%)
Reasons for Not Having Regret* (n = 431)		
I was able to change medical management	31	(7.2%)
It eased anxiety about developing cancer	96	(22.3%)
I now know more about risk for developing cancer	119	(27.6%)
It gave me helpful information for my family	150	(34.8%)
It helped me make decisions about having children	23	(5.3%)
Other	12	(2.8%)
Reasons for Having Regret (n = 21)		
It increased anxiety about developing cancer	4	(19.0%)
It made me think something is wrong with my body	1	(4.8%)
I don't fully understand my test results	1	(4.8%)
I feel guilty I could have passed something to my children	2	(9.5%)
It changed my medical treatment and/or management	1	(4.8%)
It did not change my medical treatment and/or management	2	(9.5%)
I had to tell my family members about my test results	4	(19.0%)
It was a burden to myself	1	(4.8%)
It was a burden to my family	2	(9.5%)
I'm now concerned about losing my health/life insurance	1	(4.8%)
Other	2	(9.5%)

**n is different than expected as participants were allowed to select more than one option*

3.1.6 Decision regret scale

Data from the DRS are detailed in Figure 2. Final DRS scores were converted to a score ranging from 0 to 100 by taking the means of all five answers, subtracting 1, and multiplying by 25 (O'Connor, 1996). There are no current consensus cutoff points for the DRS, but a recent metanalysis categorized scores as follows: A score of 0 is considered no regret, 1–24 is mild regret, and greater than or equal to 25 is moderate to severe regret (Berecca-Perez et al, 2016). Therefore, regret was also categorized into two groups for analyses, where 0 equates to no regret and a score of 5 or more equates to at least some regret. Regret was categorized into yes or no, and also into categories of none, mild, and moderate to severe. When categorized into two groups, 59% had no regret, and 41% had at least some regret. When categorized into three groups, 58.0% had no regret, 34.2% had mild regret and 6.8% had moderate to severe regret.

Figure 2. Decision regret scale score distribution



Individual DRS scores (out of 100) are shown by investigator determined genetic test result type. Dots represent individual participants. Rectangles represent the 25th through 75th quartiles of each group and whiskers represent the spread of DRS scores.

3.2 Statistical Analysis

In addition to descriptive statistics, group demographics were compared by level of regret to identify significant differences using Chi-Square analysis, independent samples t-tests, and

binary logistic regression. To maximize statistical power, certain variables were condensed for statistical analyses and are detailed in Table 7.

Table 7. Condensed variables for statistical analyses

	n	(%)
Ethnicity (n = 229)*		
Hispanic or Latino	41	(17.9%)
Not Hispanic or Latino	188	(82.1%)
Gender (n = 232)*		
Female	174	(75%)
Male	58	(25%)
Education		
No undergraduate degree	74	(31.6%)
At least an undergraduate degree	160	(68.4%)
Children (n = 228)*		
Have biological children	153	(67.1%)
Do not have biological children	75	(32.9%)
Insurance Type (n = 233)*		
Commercial insurance	173	(74.2%)
Medicaid or Medicare	60	(25.8%)
Cost of Genetic Test (n = 158)*		
Zero out-of-pocket cost	105	(66.5%)
Some out-of-pocket cost	53	(33.5%)
Personal Cancer History (n = 230)*		
Personal history of cancer	130	(56.5%)
No personal history of cancer	100	(43.5%)
Appointment Delivery Mode (Pre-test) (n = 175)*		
In-person appointment	129	(73.7%)
Telehealth appointment	46	(26.3%)
Appointment Delivery Mode (Post-test) (n = 199)*		
In-person appointment	123	(61.8%)
Telehealth appointment	76	(38.2%)
Medical Care Change Based on Results (n = 226)*		
Medical care changed	59	(26.1%)
Medical care did not change	167	(73.9%)

**n is different than original study population because individuals who did not select a definite answer were omitted from the category*

Those with lower levels of regret were significantly more likely to have an undergraduate degree ($p = 0.01$), have biological children ($p = 0.01$), and be married or in a partnership ($p < 0.001$) (Table 8). Chi-Square tests revealed no significant differences between level of regret and ethnicity ($p = 0.24$), pre-test appointment delivery mode ($p = 0.17$), post-test appointment delivery mode ($p = 0.20$), and change in medical care ($p = 0.86$). Those with lower levels of regret were significantly more likely to have at least some out-of-pocket cost ($p < 0.001$) and commercial insurance ($p = 0.01$). No significant differences were identified between gender and level of regret ($p = 0.15$). One-way ANOVA revealed no significant differences between the time period during which the test was completed (between 2014-2016, between 2017-2019, between 2020-2023) and mean DRS ($p = 0.33$).

Table 8. Comparisons between demographic characteristics and regret

Patient Demographics	**No Regret**	**Some Regret**	**$\chi 2$ (d.f.)**	**p-value***
Ethnicity				
N = 229				
Hispanic or Latino	21	20	1.38 (1)	0.24
Not Hispanic or Latino	115	73		
Pre-test appointment delivery mode				
N = 175				
In-person appointment	82	47	1.84 (1)	0.17
Telehealth appointment	24	22		
Post-test appointment delivery mode				
N = 199				
In-person appointment	79	44	1.54 (1)	0.20
Telehealth appointment	42	34		
Change in medical care				
N = 226				
Medical care changed	35	24	0.02 (1)	0.86
Medical care did not change	97	70		

Education *N=234* No undergraduate degree At least an undergraduate degree	 35 103	 39 57	6.09 (1)	0.01
Children *N = 233* Have biological children Do not have biological children	 99 36	 54 39	5.81 (1)	0.01
Marital Status *N = 203* Single Married or in a partnership	 16 102	 29 56	12.10 (1)	< 0.001
	N	**Mean DRS (SD)**	**t (d.f.)**	**p-value****
Insurance *N=233* Commercial insurance Medicaid or Medicare	 173 60	 1.28 (0.47) 1.41 (0.62)	-1.76 (231)	0.01
Cost of Genetic Test *N = 158* Zero out-of-pocket cost Some out-of-pocket cost	 105 53	 1.41 (0.62) 1.15 (0.27)	2.93 (156)	< 0.001
Gender *N = 232* Female Male	 174 58	 1.33 (0.54) 1.29 (0.40)	0.51 (230)	0.15
	N	**Mean DRS (SD)**	**F (d.f.)**	**p-value*****
Year of test completion *N=232* 2014-2016 2017-2019 2020-2023	 45 66 121	 1.35 (0.49) 1.23 (0.40) 1.34 (0.55)	1.11 (2)	0.33

**From chi-square*
***From independent t-test*
****From ANOVA*

Those with lower levels of regret were significantly more likely to have no personal history of cancer (p = 0.01) (Table 9). One-way ANOVA revealed no significant differences in mean DRS among those with a history of only breast, colon, or skin cancer (p = 0.67). A two-

sample t-test revealed no significant difference sin regret between those with a history of only colon or breast cancer (p = 0.82).

Table 9: Comparisons between cancer history and regret

Participant Cancer History	**N**	**Mean DRS (SD)**	**t (d.f.)**	**p-value****
Ever had cancer				
N = 230				
Personal history of cancer	130	1.34 (0.58)	1.31 (228)	0.01
No personal history of cancer	100	1.26 (0.03)		
Type of cancer				
N = 47				
Only breast cancer	25	1.41 (0.71)	-0.10 (43)	0.82
Only colon cancer	20	1.43 (0.72)		
	N	**Mean DRS (SD)**	**F (d.f.)**	**p-value*****
Type of cancer				
N = 66				
Only breast cancer	25	1.40 (0.71)	0.40 (2)	0.67
Only colon cancer	20	1.43 (0.72)		
Only skin cancer	21	1.36 (0.63)		

***From independent t-test*
****From ANOVA*

Regret was compared across different test result categories (Table 10). Chi-square test revealed no significant differences in regret between those with a pathogenic variant related to breast cancer vs. colon cancer (p = 0.18), and no significant differences in regret between those with high-risk breast vs. moderate-risk breast cancer variants (p = 0.70).

Mean DRS did not appear to differ between those with a positive vs. negative/VUS result (p = 0.06). However, based on p = 0.06, it appears that the association between higher regret and a positive test result is trending. Mean DRS did not differ between those with a positive/negative vs. VUS result (p = 0.34). One-way ANOVA revealed no significant differences between a positive, negative, or VUS result and mean DRS (p = 0.29).

Table 10. Comparisons between genetic test experience and regret

	No Regret	Some Regret	χ2 (d.f.)	p-value*
Pathogenic variant *N = 24*				
High-risk breast cancer variant	10	6	1.34 (1)	0.24
Colon cancer variant	3	5		
Pathogenic variant *N = 29*				
High-risk breast cancer variant	10	6	0.14 (1)	0.70
Moderate-risk breast cancer variant	9	4		
Pathogenic variant *N = 38*				
Breast cancer variant	18	10	1.78 (1)	0.18
Colon cancer variant	4	6		
	N	**Mean DRS (SD)**	**t (d.f.)**	**p-value****
Test result type *N = 234*				
Positive result	55	1.41 (0.58)	1.55 (232)	0.06
Negative/VUS result	179	1.29 (0.49)		
Positive/Negative result	185	1.32 (0.53)	0.15 (232)	0.34
VUS result	49	1.31 (0.45)		
	N	**Mean DRS (SD)**	**F (d.f.)**	**p-value*****
Test result type *N = 234*				
Positive	55	1.41 (0.58)	1.24 (2)	0.29
Negative	130	1.28 (0.50)		
VUS	49	1.31 (0.45)		

**From chi-square*
***From independent t-test*
****From ANOVA*

Multiple binary logistic regression models were run to determine the impact of education, having biological children, result type, and appointment delivery mode on regret (Table 11). Model 1 revealed that individuals with at least an undergraduate degree were half as likely to

experience regret and that education level was responsible for 3.4% of the variance in decision regret. Model 2 revealed that the combination of having at least an undergraduate degree and having biological children was associated with having less regret. Model 2 showed that education and having biological children were responsible for 6.5% of the variance in decision regret. Model 3 revealed this same concept and that the combination of education, having biological children, and test result type accounted for 8.4% of the variance in regret. Model 4 revealed that when controlling for post-test appointment delivery mode, there was a statistically significant decrease in regret among those with a negative result ($p < 0.05$) as compared to those with a positive result. In combination, education, having biological children, post-test appointment delivery mode, and test result type accounted for 12.6% of the variance in regret level.

Table 11. Logistic regression examining impact of education, parental status, test category, and post-test appointment delivery mode on level of decision regret

	Odds Ratio [95% CI]			
	Model 1	Model 2	Model 3	Model 4
Education				
No undergraduate degree vs. have undergraduate degree	0.49 [0.284, 0.869]*	0.50 [0.285, 0.985]*	0.50 [0.283, 0.898]*	0.46 [0.239, 0.892]*
Parental Status				
Have biological children vs. no biological children		1.99 [1.129, 3.521]*	1.97 [1.112, 3.494]*	2.11 [1.127, 3.956]*
Genetic test result category				
Positive vs. Negative result			0.55 [0.283, 1.08]	0.43 [0.209, 0.891]*
Positive vs. VUS result			1.07 [0.548, 2.091]	1.19 [0.581, 2.433]
Post-test appointment delivery mode				
In-person appointment vs. telehealth appointment				0.12 [0.878, 3.104]
R^2	3.4%	6.5%	8.4%	12.6%

Note. CI=confidence interval *p<.05
Reference variables: No undergraduate degree, having biological children, positive test result, in-person appointment

Note. CI=confidence interval *p<0.05. Reference variables: No undergraduate degree, having biological children, positive test result, in-person appointment

3.3 Qualitative analysis

The last survey question was an open-ended opportunity for participants to discuss in more detail why they would or would not recommend genetic testing for hereditary cancer risk to someone else. One hundred sixty-six responses were analyzed and coded, revealing seven themes related to why individuals would recommend genetic testing and one theme related to why individuals would not recommend genetic testing to someone else. All quotations are detailed in Appendix D.

Theme 1: Early detection and prevention

Participants expressed that early cancer detection and prevention was the primary reason for recommending genetic testing to others.

One participant reported:

> "This is a monumentally important and potential life changing piece of science. If this form of testing had been around, it could have saved many of my family members who carry an MSH2 mutation among others… I cannot express how responsible this testing is for single handedly changing our lives and how much the genetic counselors have helped to equip myself and other with the knowledge necessary to accept and live a full life, with screenings."

This individual explained that genetic testing allowed her and her siblings to learn their genetic variants, increase screening, and identify early-stage cancer.

Another participant with a familial *BRCA2* variant reported:

> "I would recommend genetic testing because it gives you the information to do something about it if you test positive. My mom tested positive for the BRCA 2 gene mutation and had a full hysterectomy and double mastectomy because her risk was not if but when. So I was tested and it was negative. I am at a normal risk for cancer, but not prone to anything in particular. To know your risk is to know what to do. You have the power of choice rather than an unknown."

One participant reported:

> "Having the power to do a double mastectomy to essentially eliminate any chance of it coming back was a huge benefit. Especially as a mother. My one challenge- insurance took too long to approve it so I ended up having two surgeries - I would have gone straight to mastectomy had I known. Very frustrating."

Other participants mentioned recommending testing because you can "get a head start", "avoid or identify cancer early", and that it is "better to know and watch then not know and do nothing".

Theme 2: Provide information for family members

Having the ability to inform family members of their cancer risk was also a powerful reason for individuals recommending genetic testing to others.

Participants reported:

> "If I would have gotten results that showed a higher risk I would have known to have more frequent follow up and shared the information with my health care providers. I would have been able to share the risk information with my loved ones. Having received results that showed no increase risk markers present I have shared the information with my health team and family members (my family members have done their own testing due to the prevalence of cancers in our families). I just feel like having the knowledge allows for better planning and risk management."
>
> "Your family will benefit and know what to be aware of"
>
> "It was important to me that I be able to tell my sister and daughters (brothers and son) if they were more likely to have breast cancer. I understood that my breast cancer means they all have a slightly higher risk but if I had the brca (sic)gene it would have been a much higher risk to all my loved ones."
>
> "If you have the opportunity to know if your immediate family or future children may be diagnosed with cancer, why wouldn't you take the test? There is incredibly low risk and only provides benefits."
>
> "I'm proactive about my health care. This allowed me to learn of any future risks and provided information that was valuable to my two daughters who also were tested. And they tested positive for the same PMS2 mutation."

Theme 3: Learn personal cancer risk

Obtaining more information about personal cancer history risk was also an apparent theme as to why participants would recommend genetic testing to others. Several participants answered, "knowledge is power" regarding genetic testing.

Other participants reported:

"It's better to know than to not know. Obviously I was happy the test result came back negative, but I still would have wanted to know if it were positive"

"It was helpful to know i do not have a genetic risk of cancer"

"It is better to know what the risks of getting cancer are and what I can do to proactively screen for it going forward. My mother recently died from cancer and my father has Lynch Syndrome. I do not have Lynch Syndrome but have been proactive in screening for colorectal cancer with Cologuard and will schedule a colonoscopy when it is recommended."

"It is better to have the knowledge of your risk of cancer than to ignore it."

Theme 4: Testing for peace of mind

Participants recommended testing for peace of mind regarding cancer risk.

Participants reported:

"Getting genetic testing gave me peace of mind that I would not otherwise have had. I know some people might rather not know, but for me personally, having more information gave me the tools I needed to make major life decisions. Even if the result had been that my cancer was genetic and the likelihood of my child having it was high, I still would have wanted to know in order to make informed decisions about the future."

"It gave me peace of mind not just for me but also for my children"

"If negative, anxiety is lessened. If positive, needed steps can be made to prolong life and/or find issues quickly."

"It would ease any anxiety and not leave a 'what if?' floating around in my head."

Theme 5: Health and lifestyle reasons

Testing to modify health and lifestyle choices also came up for some participants.

Participants reported:

"Regardless of the results I would have been better informed to make decisions about my health based on the results."

"Knowing your results gives you an advantage on what to do with your health."

"Chance to make better decisions about medical care and lifestyle changes."

"I just wanted to know what my risk factor was and be proactive about my health, especially since I have a congenital heart defect"

"It's better to know and might help with lifestyle and diet changes."

Theme 6: Getting an answer

The concept of "getting an answer," especially regarding diagnosis, was also a reason that individuals recommend testing.

Participants reported:

"To help you as well as research teams find answers"

"I think it's good to know and could answer questions"

Theme 7: Guiding treatment

Several participants mentioned genetic testing's impact on cancer treatment. Some participants reported:

"Knowing that my cancer was BRCA related allowed for more precise drug therapy choices. It gave me insight into the etiology of my disease and allowed me to discuss with male family members."

"It will help with any additional treatment choices like Trial meds."

"I would recommend because knowing can alter your course"

Theme 8: Testing was unhelpful

The one central theme that arose between those who would not recommend testing to others is that the testing itself was unhelpful.

One participant listed reasons of why they both would and would not recommend testing. Their reasoning for not recommending testing were as follows:

> "I would also NOT recommend because there is clearly a polyp genetic issue in my family but no specific gene was found for me, so it was not very helpful to understanding my current medical issues."

Another participant reported:

> "I went in with a family history that pointed towards Lynch syndrome. Was told I did not have Lynch Syndrome and how no signs of cancer but 5 months later I was diagnosed with the same cancer of family member(s)"

One other participant reported:

> "I came up negative it does not make a difference to me and I'm beyond the age of having children. Dr wanted it to determine treatment."

Other concepts that arose from those who would not recommend testing were that some individuals could not handle the truth regarding genetic test results, that insurance coverage for testing is an issue, and that testing can be an emotional burden.

IV. DISCUSSION

4.1 Evaluation of factors associated with regret

This study examined demographic factors, personal cancer history, personal genetic counseling experience, and genetic test results and their impact on the level of decision regret towards their decision to have genetic testing for hereditary cancer predisposition.

Specific demographic characteristics, such as having at least an undergraduate degree ($p = 0.01$), having biological children ($p = 0.01$), and being married or in a partnership ($p = 0.001$), were associated with a lower level of regret. The relationship between a higher education level and a lower regret level makes sense, because higher health literacy can affect understanding of personal genomic risk (Haga et al., 2013). Understanding one's test result allows individuals to comprehend better what this means for their health, leading to less regret about their decisions. As noted in the qualitative findings, many individuals noted obtaining information for their children as a significant motivator for testing. With this, it makes sense that those with biological children have less regret as they learn information for their families through genetic testing. Marriage or partnership provides extra support throughout and after the genetic testing experience. Therefore, these individuals may experience less regret because they have their partner to speak to and process test results with. Other factors that were related to having less regret were having some out-of-pocket costs for testing ($p < 0.001$) and having commercial insurance ($p = 0.01$). Lower levels of regret may be related to having some out-of-pocket cost for testing because payment for testing may reveal more desire to test. Those who reported having no out-of-pocket cost may have moved forward with the process simply because it was free of charge, and they may not have as much buy-in. Commercial insurance may be related to less regret, because those with commercial insurance plans may have better coverage than those with

Medicare or Medicaid. Additionally, those with commercial insurance potentially have higher levels of education; therefore, this result may be confounded by education level. However, some testing laboratories offer free testing for Medicare or Medicaid holders, so this may have been an incidental finding.

Analyzing cancer history and level of regret revealed an association between having a personal history of cancer and a higher level of regret about their decision to have genetic testing ($p = 0.01$). Those with a personal history of cancer and a negative result may have a higher level of regret because their genetic test failed to provide a clear answer for why their cancer developed. Therefore, they may feel that testing was a waste of time and was not informative for themselves or their families. Those with a history of cancer may feel regret in other areas, such as treatment decisions or regrets of lifestyle choices, which impacts their feelings of regret towards genetic testing. No significant differences in regret were seen amongst different cancer diagnoses; however, our sample sizes of these individual groups were small, and this would be exciting to explore in a larger study population.

Overall, there was no significant relationship between positive, negative, or VUS results and level of regret ($p = 0.29$). This may be due to a skewed distribution of mostly negative results (positive = 23.5%, negative = 55.6%, VUS = 20.9%). However, it was found that appointment delivery mode has an impact on level of regret when it comes to those with negative results ($p = 0.02$). Those with positive and negative results were combined to analyze against VUS results to explore certain versus uncertain results, but no difference was apparent ($p = 0.34$). Those with negative and VUS results were combined for analysis because these results are clinically treated the same. When comparing the level of regret between those with a positive result and those with a negative or VUS result, statistical analysis revealed a trend in positive

results being related to a higher level of regret ($p = 0.06$). This is an important finding because pathogenic variants are typically associated with increased screening and management and likely explain cancer etiology; however, individuals may feel more regret as their anxiety surrounding cancer development can increase, and the recommendation of sharing results with family members may be nerve-wracking for some.

Some discrepancy in the accuracy of self-reported genetic test results was revealed. It was found that 78.3% of individuals correctly reported their genetic test result type. Those with a VUS were most likely to incorrectly report their result (only 27.9% of those with a VUS accurately reported this), and they were more likely to report to incorrectly report negative result than incorrectly report a positive result. This may reflect how VUS results are treated clinically, which is most cases is as a negative result until proven otherwise. However, notable finding emphasizes the importance of ensuring patients understand their genetic test results. For example, if an individual has a VUS that gets upgraded to likely pathogenic/pathogenic but believes their result is negative, they may be shocked to learn this information and not comprehend how that happened, and may also not be as likely to follow up to monitor for variant reclassifications over time. However, because the clinical utility of the test results was not analyzed, some of this discrepancy could be due to participants remembering the overall actionability of the test result. For example, if a participant had a heterozygous VUS in a gene associated with an autosomal recessive condition, their result would be negative in a clinical setting. These findings suggest that patients do not always correctly remember their genetic test results and that genetic counselors must pay close attention to patient understanding to ensure correct long-term recall.

Binary logistic regression revealed that post-test appointment delivery mode impacted the degree of regret among those who had a negative result. When considering this, it was found that in-person post-test results disclosures were associated with less regret in those with negative results as opposed to telehealth post-test results disclosures ($p = 0.02$). In the cancer genetics clinic setting, it is trending that most negative results disclosure appointments are conducted via telehealth. While this tends to be most convenient for both patients and providers, given the shorter nature of these appointments, our data suggests that in-person discussions may have more benefit than telehealth for those with negative results regarding regret.

It is important to note that across all analyses, having biological children and having at least an undergraduate degree were associated with a lower level of regret regardless of result type. Therefore, genetic counselors knowing this information about their patients may be crucial to counseling with an outcome of less regret. During family history review in the clinical setting, genetic counselors learn whether patients have biological children and can add this to their assessment of potential patient regret and tailor their counseling accordingly. On the other hand, not all genetic counselors will learn the exact education level of their patients, and not all clinics have questionnaires that inquire about the highest level of education. If genetic counselors do not have specific information about a patient's education level, they should pay particular attention to informing patients about implications of testing to compensate for possible lack of higher education with the goal of lowering potential regret. With this, it is helpful to inquire about this information beforehand, because it is beneficial for genetic counselors to tailor appointments more toward the patient's education level in order to diminish regret regarding testing decisions.

Another aspect to consider is the timing of testing in relation to our survey. Although no significant difference was found between the year test was performed and level of regret ($p =$

0.33), one individual with a pathogenic variant identified on a test done in 2008 had a much higher level of regret than most of the sample (DRS = 55/100). Therefore, as more individuals come into the cancer genetics clinic with older results seeking updated genetic testing, patients may acknowledge that they already regret their previous genetic testing. With this, it may be beneficial to ask about a patient's previous genetic counseling and testing experience to explore and possibly mitigate regret. Regret is a variable concept that can change depending on the amount of time passed after a decision, life experiences since making the decision, and various other factors; therefore, it is crucial to explore this with patients who have previously had genetic testing or counseling.

Exploring specific reasons why individuals did not have regret revealed that most participants did not have regret because it provided helpful information for their family, gave more insight into personal cancer risk, and eased anxiety about developing cancer. This information highlights the importance of personal and family risk assessment during genetic counseling appointments. With this, providing a thorough personal and family cancer risk assessment in both pre-test and post-test appointments may help patients feel less regret after the process is complete. While having many individuals report that genetic testing eased their anxiety about developing cancer is a favorable outcome, it is a good reminder that it is critical to ensure understanding of baseline and familial cancer risk in all individuals, despite having negative testing. Interestingly, few individuals reported that genetic testing for hereditary cancer risk assisted in making family planning decisions. This is an important finding, because it is possible that most individuals seeking genetic counseling for hereditary cancer risk may not be doing so directly for family planning purposes unless otherwise stated. However, this number may be low due to the population's demographics such as age, which was not reported in this

study; since people being seen in a cancer clinic tend to be older in general, it is likely that participants were older than the average age of individuals actively undergoing family planning.

A small number of individuals (7.2%) reported having no regret because their medical management changed based on test results, such as having increased cancer screening or making prophylactic surgery decisions. This small number is likely due to fewer individuals in the sample who tested positive for a pathogenic/likely pathogenic variant. Interestingly, the most reported reason for not having regret was obtaining helpful information for family members. These results are likely skewed since many of the population had biological children. This high frequency may suggest that undergoing genetic testing to obtain information for family members may be equally, if not more, important for patients as finding out about personal genetic risk. These findings are in line with the findings by Sun et al. (2020), where the desire to create awareness for self and family was an encouraging factor for undergoing genetic testing for hereditary cancer risk. This is also in line with findings by both Armstrong et al. (1997) and Hallowell (1999) indicating that women who chose to undergo *BRCA1/BRCA2* testing were more likely to want information for their family members, noting that this reason for undergoing testing has existed for many years.

Although few individuals reported regret, this investigation revealed increased anxiety about cancer development, guilt about passing something to children, and disclosing results to family members were reasons for regret amongst those who had it. These findings indicate that addressing anxiety about cancer development during results disclosure sessions in those with positive results may help lessen regret and open further conversations regarding early detection and prevention. Additionally, these results reveal the importance of discussing the option of family letters with patients to help them disclose results to their relatives. During results

disclosure appointments, patients may not feel comfortable discussing their discomfort with speaking with family members about their results. Therefore, genetic counselors can and should provide family letters to help with this process. These results also show that guilt can be associated with passing a pathogenic/likely pathogenic variant on to children. With this, genetic counselors must remind patients that they cannot control what genes they may have passed down to their children and what genes they inherit from their parents. In addition, genetic counselors must also inform patients about the availability of fertility options such as preimplantation genetic testing (PGT) and prenatal genetic diagnosis for their future pregnancies

4.2 Study limitations and future research implications

It is crucial to note several limitations of this research. Due to time and cost constraints, Spanish speakers were excluded from this study. Since Spanish is the second most common language spoken in the United States, it is necessary to include Spanish speakers in future studies. Including other languages that are less commonly spoken was not expected to yield sufficient power and would not allow data analysis for actual effect. The results of this study can serve as baseline data to design a follow-up study that aims to explicitly enroll non-English speaking participants. The study population lacked diversity; 80.3% are not Hispanic or Latino, 76.5% are white, 74.8% are female, 68.4% have at least an undergraduate degree, 62.0% are married, and 65.4% have biological children. This lack of diversity likely skewed the results and lessened the ability to apply the findings to other populations. Importantly, different distributions of regret may be present in a more diverse patient population.

Participants were not asked their age in order to be as inclusive as possible and to maintain anonymity. Since this clinic population is older, an age of 90 years or older would

become an identifying piece of protected health information. However, understanding how age relates to regret may provide important information for genetic counselors.

The same genetic counselor saw all patients in this population in the UCI Health system. Therefore, these findings may be influenced by this and may not represent the genetic counseling and testing experience across other clinics and in other health systems. However, this is also a strength of the research, because seeing the same provider allows for continuity of care amongst the sample population.

Other limitations include outreach being conducted only via email. Not all patients had an email address on file in EPIC. Additionally, survey-related emails may have gone to spam folders or may have gone to email addresses that patients do not frequently check. Not all participants may be technologically savvy enough to complete an online survey and additional online consent forms. Similarly, filling out forms may be challenging if individuals only have a cell phone and no larger devices such as a tablet or computer.

Since the feeling of regret is variable and can impact thoughts and actions, this survey topic may have appealed more to those who did not have regret, causing the results of the study to be skewed. Additionally, it is possible that patients felt regret immediately upon learning their genetic test results but that their regret had dissipated by the time that they participated in this research.

Patients were allowed to self-report their genetic test results including both result type and the gene involved. From clinical experience, and as the results show, patients do not always remember details about their genetic test results. In this research, investigator determined categories of test results (positive, negative, VUS) were used for analysis, but self-reported

pathogenic/likely pathogenic variants were used for data analysis because this detail about result type was not obtained as part of study eligibility. Therefore, any findings using self-reported pathogenic/likely pathogenic variants may be inaccurate; however, reassuringly, 86.2% of participant-reported positive results were actually positive.

Similarly, individuals may entirely forget about their genetic counseling experience due to factors that were not assessed (for instance, cognitive abilities) and others that were (such as time since testing was done). Lack of memory may impact their responses since some individuals participated in this research years after undergoing genetic testing and counseling. For example, one participant with a confirmed negative test report from 2020 reported that genetic testing was not offered to them. Due to the way the questionnaire was developed, there was no way of learning more about this discrepancy. However, this participant was kept in the sample population because they did have a genetic test result, and their genetic counseling experiences are still valid. Therefore, regarding study design, consenting patients for study participation at their pre-test appointment and sending out questionnaires four weeks after the disclosure of results on a rolling basis might have led to more accurate results. This would not incorporate individuals who experienced regret after a more extended period; however, this would address the level of regret in patients during a critical time window after first learning results, allowing genetic counselors to potentially assist in mitigating patient regret.

Understanding decision regret in other specialty areas, such as prenatal, cardiology, neurology, and general adult genetics, is helpful for the genetic counseling community. For example, in the specialty of pediatric genetics (specifically regarding parent regret and whole genome sequencing for the children), Liang et al. (2021) found that 45% of 121 parents had no regret, 38% had mild regret, and 17% had moderate or higher regret. This distribution is similar

to our research (58.0% had no regret, 34.2% had mild regret, and 6.8% had moderate to severe regret); therefore, it is possible that as this topic of regret is studied more extensively, this may be a commonly found distribution of regret towards genetic testing of all types. Similar to our research, Goldman et al. (2019) found that decision regret was associated with the number of living children for those undergoing preimplantation genetic testing for aneuploidy (PGT-A). This finding suggests that the number of biological children may impact the level of regret across multiple specialty areas in genetics. Goldman et al. (2019) found that regret for those undergoing PGT-A was low (similar to our findings), and Bordet et al. (2020) found little regret for those undergoing predictive genetic testing for hereditary heart disease, suggesting that decision regret may be low across all genetics specialties, but further research is needed.

It is also beneficial to assess decision regret in cancer clinics in other geographic areas and other healthcare institutions, such as privately owned ones. Other potential areas of exploration are investigating decision regret amongst individuals who had a reclassified VUS result. Designing a study with a larger sample population with more evenly distributed result times may yield more information.

4.3 Conclusions

While the sparse existing literature on the topic of decisional regret in hereditary cancer genetic testing suggests that individuals may have little to no regret when undergoing genetic testing, studies have not been inclusive but rather have only considered individuals of a certain age or those with a particular cancer diagnosis. However, findings from our research are similar to that of Godino et al. (2018) and Butterfield et al. (2019) in that most of those with negative results had no regret. Similarly, Clift et al. (2018) found that VUS results may be associated with

decision regret. Although it did not have the highest association in our study, we still identified that 45% of those with a VUS had some level of regret, resulting in similar findings. Aspinwall et al. (2013) found that individuals at-risk for hereditary melanoma and pancreatic cancer had no regret regarding genetic counseling and testing. As in our study, this suggests that regret for hereditary cancer genetic testing may be low across the general patient population.

Although most individuals reported having little to no regret, certain factors were found to play a role in having less regret about genetic testing for hereditary cancer risk. Independently, having at least an undergraduate degree, having biological children, having no personal history of cancer, having commercial insurance, paying some out-of-pocket cost, and being married or in a partnership are all associated with having less regret. Knowing that most patients have mild to no regret after learning their test results, regardless of result type, allows genetic counselors to reassure their patients in their choices if they choose to proceed with genetic testing. Additionally, understanding which factors may be related to more and less regret can help genetic counselors personalize their sessions to address specific concerns and reduce future regret. Although abstract, patient regret is a feeling that genetic counselors will continue to confront. Therefore, the genetics community must better understand it, learn how to assess regret potential, and become versed in supporting patients who may experience it.

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APPENDIX A

Study questionnaire

If you would like to participate in this study, **are over the age of 18, and live in the United States,** complete the verification below to start the survey.

a. I agree

Section 2: Demographics

1. Ethnicity
   a. Hispanic or Latino
   b. NOT Hispanic or Latino
   c. Unknown/Not Reported
   d. Prefer not to answer

2. Race
   a. American Indian/Alaska Native
   b. Asian
   c. Black or African American
   d. Native Hawaiian or Other Pacific Islander
   e. White
   f. More than one race
   g. Unknown/Not reported
   h. Prefer not to answer

3. What is your sex?
   a. Female
   b. AFAB (Assigned Female at Birth)
   c. Male
   d. AMAB (Assigned Male at Birth)
   e. Intersex
   f. Prefer not to say
   g. Other (write in)

4. Gender (describe how you identify)
   a. Female
   b. Male
   c. Non-binary / third gender
   d. Prefer not to say

6. What is your highest level of education?

   a. Some high school

b. High school graduate or GED
c. Some college
d. Associate Degree
e. Undergraduate Degree (BS, BA, etc)
f. Master's Degree
g. PhD, MD, JD, or other similar professional degree

7. Relationship status

a. Single
b. Married
c. Divorced
d. In a partnership
e. Widowed
f. Prefer not to say

8. Do you have any children, including those who may have died?

a. Yes – biological
b. Yes – adopted
c. Yes – from a donor egg or sperm
d. Yes – stepchildren
e. No

9. Do you currently have cancer?

a. Yes
b. No
c. I don't know

10. Have you previously had cancer?

a. Yes
b. No

11. What type of cancer do you have or did you have before? (if applicable, select more than one) (only display if answer to 1 or 2 is yes)

a. Bile duct cancer
b. Brain cancer
c. Breast cancer
d. Colon cancer
e. Esophageal cancer
f. Leukemia and/or Lymphoma
g. Lung cancer
h. Ovarian cancer

i. Pancreatic cancer
j. Prostate cancer
k. Renal cancer
l. Stomach cancer
m. Testicular cancer
n. Uterine cancer
o. Other (fill in)

12. Have you had 10 or more colon polyps?

a. Yes
b. No
c. I don't know

13. Have you received genetic test results for hereditary cancer risk?

a. Yes (go to 2)
b. No (go to 1b)
c. (IF NO to question 1) Why have you not received results? (then jump to Section 5)

a) I declined testing
b) My insurance would not cover testing and I was not comfortable paying for it
c) The results are not ready yet
d) I submitted a blood or saliva sample, but the test did not work
e) I did not submit a blood or saliva sample
f) I don't remember receiving results
g) Genetic testing was not offered to me
h) Other (write-in)

14. What was your genetic test result? (can select more than one)

Note: If you do not remember your result, do not worry. At the end of this survey, everyone will have a chance to give permission for the lead researcher to look at your test results and collect the information.

a. Positive (my genetic test showed a pathogenic or likely pathogenic variant) (display question 3)
b. Negative (my genetic test was normal) (skip to question 5)
c. Unclear (my genetic test showed one or more variants of uncertain significance – the lab found a change in a gene, but it's unknown if it causes disease) (display question 4)
d. I don't remember (skip to question 5)
e. I did not receive results (skip to question 6)

15. In which gene(s) did you have a **positive** test result?

I don't remember

AIP

ALK

APC

ATM

AXIN2

BAP1

BARD1

BLM

BMPR1A

BRCA1

BRCA2

BRIP1

CASR

CDC73

CDH1

CDKN1B

CDKN1C

CDKN2A

CEBPA

CHEK2

CTNNA1

DICER1

DIS3L2

EGFR

EPCAM

FANCA

FANCC

FANCM

FH

FLCN

GATA2

GPC3

GALNT12

GREM1

HOXB13

HRAS

KIT

MAX

MEN1

MET

MITF

MLH1

MRE11A

MSH2

MSH3

MSH6

MUTYH

NBN

NF1

NF2

NTHL1

PALB2

PDGFRA

PHOX2B

PMS2

POLD1

POLE

POT1

PRKAR1A

PTCH1

PTEN

RAD50

RAD51C

RAD51D

RB1

RECQL4

RET

RUNX1

SDHA

SDHAF2

SDHB

SDHC

SDHD

SMAD4

SMARCA4

SMARCB1

SMARCE1

STK11

SUFU

TERC

TERT

TMEM127

TP53

TSC1

TSC2

VHL

WRN

WT1

XRCC2

Other

16. In which gene(s) did you have a **VUS** test result?

I don't remember

AIP

ALK

APC

ATM

AXIN2

BAP1

BARD1

BLM

BMPR1A

BRCA1

BRCA2

BRIP1

CASR

CDC73

CDH1

CDKN1B

CDKN1C

CDKN2A

CEBPA

CHEK2

CTNNA1

DICER1

DIS3L2

EGFR

EPCAM

FANCA

FANCC

FANCM

FH

FLCN

GATA2

GPC3

GALNT12

GREM1

HOXB13

HRAS

KIT

MAX

MEN1

MET

MITF

MLH1

MRE11A

MSH2

MSH3

MSH6

MUTYH

NBN

NF1

NF2

NTHL1

PALB2

PDGFRA

PHOX2B

PMS2

POLD1

POLE

POT1

PRKAR1A

PTCH1

PTEN

RAD50

RAD51C

RAD51D

RB1

RECQL4

RET

RUNX1

SDHA

SDHAF2

SDHB

SDHC

SDHD

SMAD4

SMARCA4

SMARCB1

SMARCE1

STK11

SUFU

TERC

TERT

TMEM127

TP53

TSC1

TSC2

VHL

WRN

WT1

XRCC2

Other

17. Do you remember discussing your test results in detail with a genetic counselor? A genetic counselor is an individual who is trained to assess individual or family risk for a variety of inherited conditions.

a. Yes
b. No

18. Why did you have cancer genetic testing? (if applicable, can select more than one)

a. I have a personal history of cancer
b. There is a known genetic risk (such as a gene mutation) for cancer in my family
c. Someone in my family has or had cancer
d. I don't have a family history of cancer, but I'm curious about my chance of developing cancer
e. I don't have cancer or have a family history of cancer, but I'm worried about developing cancer
f. This information may help me make decisions about having children
g. I or someone in my family ordered my genetic test from a company online

h. I had testing to know if my family members have an increased genetic chance to have cancer.
i. I don't know, but my doctor recommended testing

19. What was your primary reason for having cancer genetic testing? (select only one) only show if someone selected more than one option in question 6)

a. I have a personal history of cancer
b. There is a known genetic risk (such as a gene mutation) for cancer in my family
c. Someone in my family has or had cancer
d. I don't have a family history of cancer, but I'm curious about my chance of developing cancer
e. I don't have cancer or have a family history of cancer, but I'm worried about developing cancer
f. This information may help me make decisions about having children
g. I or someone in my family ordered my genetic test from a company online
h. I had testing to know if my family members have an increased genetic chance to have cancer.
i. I don't know, but my doctor recommended testing

20. Did you have an appointment with someone (for example, a genetic counselor) who explained the pros and cons of testing *before* you decided to have your genetic test for hereditary cancer risk?

a. Yes, in-person appointment
b. Yes, video conferencing
c. Yes, phone call
d. I did not have an appointment with a genetic counselor before I had my genetic testing
e. I don't remember

21. Who ordered your genetic test for hereditary cancer risk?

a. UCI Health genetic counselor
b. UCI Health physician
c. A physician outside of UCI Health
d. A genetic counselor outside of UCI Health
e. Other (fill in)
f. I don't remember

22. Who first told you about your genetic test results?

a. Genetic counselor
b. Physician

c. Nurse
d. I don't remember

23. Did you have an appointment to discuss your hereditary cancer genetic test results in detail?

a. Yes, in-person appointment with a genetic counselor
b. Yes, in-person appointment with a physician
c. Yes, in-person appointment with a nurse/medical assistant
d. Yes, video conference with a genetic counselor
e. Yes, video conference with a physician
f. Yes, video conference with a nurse/medical assistant
g. Yes, telephone with a genetic counselor
h. Yes, telephone with a physician
i. Yes, telephone with a nurse/medical assistant
j. My results were sent via MyChart and I did not speak to anyone about my test results
k. I don't remember

24. Did your medical care change based on your genetic test results? (select all that apply)

a. Yes – increased cancer screening
b. Yes – I decided to have prophylactic surgery
c. Yes – started taking cancer risk-reducing medication
d. Yes – changed my cancer treatment plan
e. Yes – other (have fill in option)
f. No, but it might change in the future
g. No
h. I don't know

25. How was your genetic testing paid for?

a. Insurance coverage
b. Self-Pay
c. Insurance did not cover, but the lab did not charge me for the test
d. Other (have fill in option)
e. I don't remember

26. How much did you or your family pay out-of-pocket for your hereditary cancer genetic test?

a. I did not pay anything
b. $100 or less
c. $101 to $500
d. $501 to $1,000
e. $1,001 or more
f. I don't remember

27. What is your insurance coverage?

a). Commercial insurance

b) Medicaid

c) Medicare

d) Health savings account

e) I do not have insurance coverage

28. Please think about the decision you made to have hereditary cancer genetic testing. Please show how you feel about these statements by selecting a number from 1 (strongly agree) to 5 (strongly disagree) which best fits your views about your decision

		1	2	3	4	5
1.	It was the right decision	Strongly Agree	Agree	Neither Agree Nor Disagree	Disagree	Strongly Disagree
2.	I regret the choice that was made	Strongly Agree	Agree	Neither Agree Nor Disagree	Disagree	Strongly Disagree
3.	I would go for the same choice if I had to do it over again	Strongly Agree	Agree	Neither Agree Nor Disagree	Disagree	Strongly Disagree
4.	The choice did me a lot of harm	Strongly Agree	Agree	Neither Agree Nor Disagree	Disagree	Strongly Disagree
5.	The decision was a wise one	Strongly Agree	Agree	Neither Agree Nor Disagree	Disagree	Strongly Disagree

29. Do you have any regrets about your choice to undergo cancer genetic testing?

a. Yes
b. No

IF NO: Which factor(s) contributed to you not having regret about having genetic testing for hereditary cancer risk:

a. I was able to change my medical management
b. It eased my anxiety about developing cancer
c. I now know more about my risk for developing cancer
d. It gave me helpful information for my family
e. It helped me make decisions about having children
f. Other: Write-in

IF YES: Which factor(s) contributed to you having regret about your choice to have genetic testing for hereditary cancer risk:

a. It increased my anxiety about developing cancer
b. I know more about my risk for developing cancer
c. It made me think something is wrong with my body
d. I don't fully understand my test results
e. I feel guilty I could have passed something to my children
f. It changed my medical treatment and/or management
g. It did not change my medical treatment and/or management
h. I had to tell my family members about my test results
i. It was a burden to myself
j. It was a burden to my family
k. Cost of testing
l. I'm now concerned about losing my health/life insurance
m. I'm now concerned about my test results affecting my job status
n. Other: Write-in

30. Based on your personal experience, would you recommend genetic testing for hereditary cancer risk to someone else?

a. Yes
b. No

31. **Open-ended:** Please tell us in more detail why you would or would not recommend genetic testing for hereditary cancer risk to someone else.

We are asking everyone who takes this survey to please give us permission to look at your genetic test report so we can make sure we have the correct information.

Even if you already entered this information, this will allow us to double-check it. This is completely optional.

You can give us your permission by clicking this link so you can sign the consent form on your computer:

APPENDIX B

Secondary informed consent form

UCI IRB: Biomed Consent – November 2021

UNIVERSITY OF CALIFORNIA, IRVINE
CONSENT TO ACT AS A HUMAN RESEARCH SUBJECT

Assessing decisional regret in the cancer genetics clinic

Lead Researcher
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SUMMARY OF KEY INFORMATION:

The information provided in this box includes a brief yet complete summary of key information about the research, presented first as required by the federal regulations. Some sections that require additional information may be repeated later in this document.

Participation is Voluntary
You are being asked to participate in a research study. Participation is completely voluntary. Please read the information below and ask questions about anything that you do not understand. A researcher listed above will be available to answer your questions.

Study Purpose
You are being asked to participate in a research study to understand how individuals feel about their decision to have genetic testing for hereditary cancer syndromes Thank you for participating in our survey. We invite you to participate in this research further by granting permission for the Lead Researcher to view and confirm your genetic test results for hereditary cancer risk.

Study Procedures
Genetic test results viewed are from testing that was completed at UCI Health between November 2014 and March 2023. This will allow the Lead Researcher to confirm the accuracy of the genetic test result you provided in the survey or to look at your genetic test results if you do not remember them. Confirming these test results allows our research to be as accurate as possible. These genetic test results are located in your UCI medical record, and will be used for the research purposes mentioned above. The Lead Researcher will only view your genetic test report, and nothing else in your medical record.

Expected Duration
Participation in this study concludes after choosing to consent or not consent to the Lead Researcher viewing your genetic test results in your UCI medical record.

Risks of Participation
Possible risks/discomfort associated with this portion of the study is a potential breach of confidentiality. To minimize risk, information is collected and stored through a secure program, and information that is collected (genetic test results) will be de-identified before analysis and destroyed after use. The risk for breach of confidentiality is significantly less than 1%.

Benefits to Participants
There are no direct benefits from participation in this portion of the research. However, it will help our research be more accurate, and your participation may help us understand how patients feel about genetic testing after they receive their results, depending on what type of result they receive.

Benefits to Others or Society
This research may provide guidance for genetic counselors to help support their patients as they make informed decisions about their own genetic testing for hereditary cancer risk.

Alternative Procedures or Treatments
There are no alternative treatments or procedures available. The only alternative is not to participate in this portion of the research

WHY IS THIS RESEARCH STUDY BEING DONE?
You are being asked to participate in a research study to understand how individuals feel about their decision to have genetic testing for hereditary cancer syndromes. Thank you for participating in our survey. We invite you to participate in this research further by granting permission for the Lead Researcher to view and confirm your genetic test results for hereditary cancer risk. Genetic test results viewed are from testing that was completed at UCI Health between November 2014 and March 2023. This will allow the Lead Researcher to confirm the accuracy of the genetic test result you provided in the survey or to look at your genetic test results if you do not remember them. Confirming these test results allows our research to be as accurate as possible. These genetic test results are located in your UCI medical record, and will be used for the research purposes mentioned above. The Lead Researcher will only view your genetic test report, and nothing else in your medical record.

HOW MANY PEOPLE WILL TAKE PART IN THIS STUDY?
Approximately 200 participants will take part in the research at UCI.

AM I ELIGIBLE TO PARTICIPATE IN THIS STUDY?

Inclusion Requirements
You can participate in this study if you are over the age of 18, live in the United States, speak, read, and write English or Spanish, and have had cancer genetic counseling where testing was recommended/performed/interpreted for hereditary cancer risk at UCI between November 2014 and March 2023.

Exclusion Requirements
You cannot participate in this study if you are under 18 years of age, do not speak, read, and write English or Spanish, and have not received genetic counseling at UCI.

HOW LONG WILL THE STUDY GO ON?
Participation in this study concludes after choosing to consent or not consent to the Lead Researcher viewing your genetic test results in your UCI medical record.

WHAT ARE THE POSSIBLE SIDE EFFECTS OR RISKS RELATED TO THE STUDY?
Possible risks/discomfort associated with this portion of the study is a potential breach of confidentiality. To minimize risk, information is collected and stored through a secure program, and information that is collected (genetic test results) will be de-identified before analysis and destroyed after use. The risk for breach of confidentiality is significantly less than 1%.

WILL I BE PAID FOR TAKING PART IN THIS STUDY?

Compensation
You can choose to opt into a raffle to win one of 10 available $20 Amazon electronic gift cards. To enter this raffle, you may submit your email address here (link to separate survey), if you did not do so already. Email addresses will be assigned a number, and a random number generator will be used to select the 10 winners. Electronic gift cards will be emailed to winners by June 2023. All email addresses collected will be destroyed after the prizes have been awarded.

Reimbursement
You will not receive reimbursement for any out of pocket expenses, such as parking or transportation fees.

WHAT ARE THE COSTS OF TAKING PART IN THIS STUDY?
There is no cost to you for participation in this study.

WHAT HAPPENS IF I WANT TO STOP TAKING PART IN THIS STUDY?
You are free to withdraw from this study at any time. **If you decide to withdraw from this study, you should notify the research team immediately**.

If you elect to withdraw, you may choose to terminate the continued use or disclosure of your protected health information (PHI) for research purposes. The request to end the use or disclosure of your PHI should be made in writing.

HOW WILL INFORMATION ABOUT ME AND MY PARTICIPATION BE KEPT?

Subject Identifiable Data
Genetic test results will be kept with the research data. At the time of data download and analysis, genetic test results will not be linked with any identifiers.

Data Storage
Research data will be stored electronically through REDCap and stored on a secure, HIPAA compliant server housed at UCI.

Data Retention
In accordance with UC Office of the President policy, information will be retained for 10 years after the end of the calendar year in which the research is completed.

WHO WILL HAVE ACCESS TO MY STUDY DATA?
The research team, authorized UCI personnel, and regulatory entities such as the Food and Drug Administration (FDA) and the Office of Human Research Protections (OHRP), may have access to your study records to protect your safety and welfare.

While the research team will make every effort to keep your personal information confidential, it is possible that an unauthorized person might see it. We cannot guarantee total privacy.

Future Research Use
Researchers will use your genetic test results to conduct this study; your personal information will be removed when the data are analyzed. Your genetic test results gathered during this research study will

only be used for this study. We will not ask you for additional permission to share this de-identified information. If this research is published in a medical journal, your personal information will be removed first.

ARE THERE OTHER ISSUES TO CONSIDER IN DECIDING WHETHER TO PARTICIPATE IN THIS STUDY?

Genetics
In the event of an unexpected breach of confidentiality, a federal law called the Genetic Information Non-Discrimination Act (GINA) will help protect you from health insurance or employment discrimination based on genetic information obtained about you. In California, state law (CalGINA) requires that employers with 5 or more employees may not use your genetic information, obtained from this research when making a decision to hire, promote, or fire you or when setting the terms of your employment. However, these laws do not protect you against discrimination by companies that sell life insurance, disability insurance, or long-term care insurance.

If you would like more information about the federal GINA law go to:
http://www.genome.gov/Pages/PolicyEthics/GeneticDiscrimination/GINAInfoDoc.pdf or CalGINA:
http://www.leginfo.ca.gov/pub/11-12/bill/sen/sb_0551-0600/sb_559_bill_20110906_chaptered.pdf

WHO CAN ANSWER MY QUESTIONS ABOUT THE STUDY?
If you have any comments, concerns, or questions regarding the conduct of this research, please contact the research team listed at the top of this form.

If you wish to ask questions about the study or your rights as a research participant to someone other than the researchers or if you wish to voice any suggestions, problems or concerns you may have about the study, please contact the UCI Institutional Review Board by phone, (949) 824-6068 or (949) 824-2125, by e-mail at IRB@research.uci.edu or at 160 Aldrich Hall, Irvine, CA 92697-7600.

What is an IRB? An Institutional Review Board (IRB) is a committee made up of scientists and non-scientists. The IRB's role is to protect the rights and welfare of human subjects involved in research. The IRB also assures that the research complies with applicable regulations, laws, and institutional policies.

HOW DO I AGREE TO PARTICIPATE IN THIS STUDY?
You should not sign and date this consent form until all of your questions about this study have been answered by a member of the research team listed at the top of this form. You will be given a copy of this signed and dated consent form, and the attached "Experimental Subject's Bill of Rights" to keep. **Participation in this study is voluntary.** You may refuse to answer any question or discontinue your involvement at any time without penalty or loss of benefits to which you might otherwise be entitled. Your decision will not affect your future relationship with UCI or your quality of care at the UCI Medical Center.

If, during the course of this study, significant new information becomes available that may relate to your willingness to continue to participate, this information will be provided to you by the research team listed at the top of the form.

Your signature below indicates you have read the information in this consent form and have had a chance to ask any questions you have about this study.

Note: If the research described in this form involves your protected health information (PHI), you will be asked to sign separate UC HIPAA Research Authorization form for the use of your PHI.

I agree to participate in the study.

_____	_____
Subject Signature	**Date**
_____	
Printed Name of Subject	
_____	_____
Signature of Person Obtaining Informed Consent	**Date**
_____	
Printed Name of Person Obtaining Informed Consent	

UNIVERSITY OF CALIFORNIA, IRVINE
Experimental Subject's Bill of Rights

The rights listed below are the right of every individual asked to participate in a research study. You have the right:

1. To be told about the nature and purpose of the study.

2. To be told about the procedures to be followed in the research study, and whether any of the drugs, devices, or procedures is different from what would be used in standard practice.

3. To receive a description of any side effects, discomforts, or risks that you can reasonably expect to occur during the study.

4. To be told of any benefits that you may reasonably expect from the participation in the study, if applicable.

5. To receive a description of any alternative procedures, drugs, or devices that might be helpful, and their risks and benefits compared to the proposed procedures, drugs or devices.

6. To be told of what sort of medical treatment, if any, will be available if any complications should arise.

7. To be given a chance to ask any questions concerning the research study both before agreeing to participate and at any time during the course of the study.

8. To refuse to participate in the research study. Participation is voluntary. You may refuse to answer any question or discontinue your involvement at any time without penalty or loss of benefits to which you might otherwise be entitled. Your decision will not affect your right to receive the care you would receive if you were not in the experiment.

9. To receive a copy of the signed and dated written consent form and a copy of this form.

10. To be given the opportunity to freely decide whether or not to consent to the research study without any force, coercion, or undue influence.

If you have any concerns or questions regarding the research study you should contact the research team listed at the top of the consent form.

If you are unable to reach a member of the research team and have general questions, or you have concerns or complaints about the research study, research team, or questions about your rights as a research subject, please contact the UCI's Human Research Protections unit in the Office of Research by calling (949) 824-6068 or (949) 824-2125 Monday – Friday, 8 am – 5 pm; or by e-mail at IRB@research.uci.edu; or by writing us at 160 Aldrich Hall, Irvine, CA 92697-7600.

APPENDIX C

Participant HIPAA Authorization Form

UCI IRB # 1752

University of California Irvine Health
Permission to Use Personal Health Information for Research

Study Title (or IRB Approval Number if study title may breach subject's privacy): Assessing decisional regret in the cancer genetics clinic

Principal Investigator Name: Emily Sarnoff, MS

Sponsor/Funding Agency (if funded): National Society of Genetic Counselors – Cancer SIG

A. What is the purpose of this form?

State and federal privacy laws protect the use and release of your health information. Under these laws, the University of California or your health care provider cannot release your health information for research purposes unless you give your permission. Your information will be released to the research team which includes the researchers, people hired by the University or the sponsor to do the research and people with authority to oversee the research. If you decide to give your permission and to participate in the study, you must sign this form as well as the Consent Form. This form describes the different ways that health care providers can share your information with the researcher, research team, sponsor and people with oversight responsibility. The research team will use and protect your information as described in the attached Consent Form. However, once your health information is released by UC Irvine Health it may not be protected by the privacy laws and might be shared with others. If you have questions, ask a member of the research team.

B. What Personal Health Information will be released?

If you give your permission and sign this form, you are allowing your health care provider to release the following medical records containing your Personal Health Information. Your Personal Health Information includes health information in your medical records, financial records and other information that can identify you.

☐ Entire Medical Record

☐ Ambulatory Clinic Records

☐ Progress Notes

☒ Other Test Reports

☐ Other (describe):

(Description of Other Health Information)

☐ Lab & Pathology Reports

☐ Dental Records

☐ Operative Reports

☐ Discharge Summary

☐ Consultations

☐ Emergency Department Records

☐ Financial Records

☐ Imaging Reports

☐ History & Physical Exams

☐ Psychological Tests

C. Do I have to give my permission for certain specific uses?

Yes. The following information will only be released if you give your specific permission by putting your initials on the line(s).

_____I agree to the release of information pertaining to drug and alcohol abuse, diagnosis or treatment.

_____I agree to the release of HIV/AIDS testing information.

_____I agree to the release of genetic testing information.

_____I agree to the release of information pertaining to mental health diagnosis or treatment.

D. Who will disclose and/or receive my Personal Health Information?

Your Personal Health Information may be shared with these people for the following purposes:

1. To the research team for the research described in the attached Consent Form;
2. To others at UC with authority to oversee the research
3. To others who are required by law to review the quality and safety of the research, including: U.S. government agencies, such as the Food and Drug Administration or the Office of Human Research Protections, the research sponsor or the sponsor's representatives, or government agencies in other countries.

E. How will my Personal Health Information be shared for the research?

If you agree to be in this study, the research team may share your Personal Health Information in the following ways:

1. To perform the research
2. Share it with researchers in the U.S. or other countries;
3. Use it to improve the design of future studies;

4. Share it with business partners of the sponsor; or
5. File applications with U.S. or foreign government agencies to get approval for new drugs or health care products.

F. Am I required to sign this document?

No, you are not required to sign this document. You will receive the same clinical care if you do not sign this document. However, if you do not sign the document, you will not be able to participate in this research study.

G. Optional research activity

If the research I am agreeing to participate in has additional optional research activity such as the creation of a database, a tissue repository or other activities, as explained to me in the informed consent process, I understand I can choose to agree to have my information shared for those activities or not.

☐ I agree to allow my information to be disclosed for the additional optional research activities explained in the informed consent process.

H. Does my permission expire?

This permission to release your Personal Health Information expires when the research ends and all required study monitoring is over.

I. Can I cancel my permission?

You can cancel your permission at any time. You can do this in two ways. You can write to the researcher or you can ask someone on the research team to give you a form to fill out to cancel your permission. If you cancel your permission, you may no longer be in the research study. You may want to ask someone on the research team if canceling will affect your medical treatment. If you cancel, information that was already collected and disclosed about you may continue to be used for limited purposes. Also, if the law requires it, the sponsor and government agencies may continue to look at your medical records to review the quality or safety of the study.

J. Signature

Subject

If you agree to the use and release of your Personal Health Information, please print your name and sign below. You will be given a signed copy of this form.

_____
Subject's Name (print)—*required*

_____ _____
Subject's Signature Date

Parent or Legally Authorized Representative

If you agree to the use and release of the above named subject's Personal Health Information, please print your name and sign below.

_____ _____
Parent or Legally Authorized Representative's Name (print) Relationship to Subject

_____ _____
Parent or Legally Authorized Representative's Signature Date

Witness

If this form is being read to the subject because s/he cannot read the form, a witness must be present and is required to print his/her name and sign here:

_____
Witness' Name (print)

_____ _____
Witness' Signature Date

APPENDIX D

Participant responses to final survey question

<u>Would Recommend Genetic Testing (Themes)</u>:

Early Detection/Prevention
*includes mentions of prophylactic surgery
*includes mention of "preparing"
*includes screening and management reasons

Provide Knowledge of Cancer Risk for Family Members

Knowledge of Personal Cancer **Risk**

Peace of Mind/Ease Anxiety

Health & Lifestyle Reasons

Getting an Answer

Guide Treatment

<u>Would Not Recommend Genetic Testing (Themes)</u>:

Unhelpful

Can't Handle Truth

Insurance

Emotional Burden

Record ID	Response
1256	You want to be able to advise your relatives if there are potential genetic problems. For instance, if there is a sink hole in the road to your family house you want to advise everyone and take proper action to prevent anyone from driving into it. With genetics you are just making family members aware of potential problems.
489	You should know your statistical odds of various cancers and thereby make informed decisions. You should also be taught how statistics and medical k owledge change over time (in case of difficult results).
1556	You have to find out for your kids and family. Give them a head start.
1192	You can take action ahead of time if needed.
38	Would, for Peace of mind

1146	Would recommend: early detection, monitoring and preventive medical treatments. Family members could be made aware of potential medical issues they might need to address or be tested for. Early detection/ treatment.
1133	Would recommend to get genetic testing to see the possible risks and then have more information on how to proceed.
920	Would recommend so one can ask their PCP for screening referrals
1294	Would recommend because some cancers are not evident until too late such as pancreatic cancer
560	When my mother developed cancer in the late 70's it was considered a death sentence. She suffer through her ordeal however, I was told there were signs early on that were either ignored or over looked. Cancer research and treatment has come along way since then and I want as much information for both myself and my children and their children
578	was a very simple test and knowing about potential risks would only help you make health decisions
1524	Two reasons. 1- Public health it's easier to get tested and move to preventive screening than to address an existing cancer 2- Lifestyle choices. It is better to know and lead a fulfilling life understating your risk than to fall ill for something that can be potentially addressed
1120	To help you prepare for the future
564	To help you as well as research teams find answers.
1557	This opened the door for family to get tested. One of my two daughters tested positive. My mother tested positive...maternal family members were then eligible to get test and be informed.
1277	This is a monumentally important and potential life changing piece of science. If this form of testing had been around, it could have saved many of my family members who carry an MSH2 mutation among others. This mutation could have given my family screening recommendations and prolonged many lives. Because of this testing, my siblings and I have been able to identify our specific mutations and screen accordingly. This screenings have caught cancer and it was treated promptly whereas without the testing, these precious lives would have been cut short like the family members before them. I cannot express how responsible this testing is for single handedly changing our lives and how much the genetic counselors have helped to equip myself and other with the knowledge necessary to accept and live a full life, with screenings.
1099	They could act accordingly
788	there is a several generation history of cancer, primarily colon, in my fathers family. I felt better feeling that I am probably not passing this on to my children. Also, if I did have a genetic tendency, I would be more vigilant on PE as needed.
1408	The results are valuable for yourself and family members.
259	The reason I took the test was my daughter tested positive for a gene mutation. My other two daughters tested nergative -1 through Kaiser and one through their health plan in Oregon. My former husband refuses to be tested.

1429	The not knowing is filled with anxiety and stress. Information is power. I was lucky that my information was negative, but i had a plan of how I was going to go forward if it was positive.
1438	The more information you have gives you power to decide what medical testing you will need in the future, as well as your family.
1219	The knowledge helps plan for myself and my family members in advance of any possible cancer diagnosis
716	The counselor took great care in explaining the genetic reasoning for the test. Unfortunately I was dealing with another life issue - retiring from my career - that made me less focused on the details of this process.
505	Technology has allowed individuals to chance the path their cancer could take them. It also allows families to educate themselves on the potential risks they may have in the future.
836 (0)	Some people can't handle the truth, also who has insurance that actually covers this.
1126	so you can prepare
961	Retinoblastoma can be sporadic or hereditary. If the cancer is hereditary, there is a very high likelihood of passing it on to your children and it affecting both eyes early in childhood. If I knew that my cancer was hereditary, I would have seriously considered not having biological children as I would not want them to go through what I went through, especially if the risk for losing both eyes was high. Getting genetic testing gave me peace of mind that I would not otherwise have had. I know some people might rather not know, but for me personally, having more information gave me the tools I needed to make major life decisions. Even if the result had been that my cancer was genetic and the likelihood of my child having it was high, I still would have wanted to know in order to make informed decisions about the future.
1149	Regardless of the results I would have been better informed to make decisions about my health based on the results. If I would have gotten results that showed a higher risk I would have known to have more frequent follow up and shared the information with my health care providers. I would have been able to share the risk information with my loved ones. Having received results that showed no increase risk markers present I have shared the information with my health team and family members (my family members have done their own testing due to the prevalence of cancers in our families). I just feel like having the knowledge allows for better planning and risk management.
1628	Recommended to have a piece of mind
381	recommend but want to do more in details with insurance covered. my tests was limited
1261	Recommend - knowing your results gives you an advantage on what to do with your heallth.
1144	possiblely lowering risk , knowing what I am at risk for.
967	Peace of mind regarding my children and there children.
301	Peace of mind and chance to make better decisions about medical care and lifestyle changes.
646	Peace of mind

449	One problem that is not detailed above: When one informs relatives that they may carry a genetic risk factor, it is disturbing when they ignore this information even when it might carry a risk for their children and grandchildren.
1131	NONE
691	My mother died of colon cancer at 48 and I wanted to know if it was genetic. I found out that it was not gave me a great sense of relief.
427	My mother died of cancer at age 55. I developed postrate cancer and had a surgery at age 60. I was curious if it is heredity or not,
1370	My brother also tested positive for CHEK2 and we informed all our cousins. Their responses were very varied. Some appreciated the info and others were reluctant to discuss. Also this gene variant is less well understood and it was hard to explain
1641	Knowledge is power. If you are able to know you have a genetic mutation that puts you at higher risk for cancer, then it can give you a sense of power to be able to deal with that increased risk. You can start screening for cancer and ultimately reduce your chance of actually dying from cancer if the screening is appropriately followed.
1460	Knowledge is power. As a cancer survivor it's so important to know not only for yourself but your family if there is any genetic predisposition.
484	Knowledge is power to act in the best interest of yourself and family.
986	Knowledge is power and knowing the potential increased risk gives me extra insight to pursue surveillance. I have found certain doctors to be very pushy about recommending surgery instead of surveillance. I don't like that. But, I am strong enough in my self and knowing what I want in terms of treatment. So, I move forward with confidence in my decisions.
228	Knowledge is power
1100	Knowledge is power
666	Knowing the risks helps to make informed decisions.
374	Knowing the information gives an opportunity for family to be more vigilant about monitoring symptoms
1170	Knowing that my cancer was BRCA related allowed for more precise drug therapy choices. It gave me insight into the etiology of my disease and allowed me to discuss with male family members.
471	Knowing risks can help to mitigate them
730	knowing can help you adjust...getting the proper screenings...see the right specialists...be more in tune with your body and your family will benefit and know what to be aware of...a little peace of mind
1598	Just to know where you stand in the big picture helps so much. My mom had no known family history of cancer, but she developed both breast and ovarian cancer. My dad's side of the family had lots of cancer issues. I just wanted to know what my risk factor was and be proactive about my health, especially since I have a congenital heart defect. That automatically puts me in the 'high risk' category for procedures and significant treatments, so of course I'd want to know. Mind you, the testing resulted in showing I didn't have the genes, but

	environmental issues are still always a contributor. I want to make sure I'm prepared.
829	It's peace of mind and helps you manage your medical decisions.
1240	It's important to know your risk. Whether it eases the anxiety of developing it by learning you are not predisposed, or you learn you are predisposed and you can start to take appropriate action to love a long and healthy life.
1593	It's good to know about our family health history but there should be some counseling involved because it can lead to depression.
511	it's better to know...
256	It's better to know than to not know. Obviously I was happy the test result came back negative, but I still would have wanted to know if it were positive
464	It's better to know and might help with lifestyle and diet changes.
1228	It's always good to know what the reality is .
390	It's a personal decision but not for everyone.
1400	it. was nice for my cousins to know that my cancer was not hereditary. grandpa had same cancer as me.
403	It will help with any additional treatment choices like Trial meds. It helps your family make informed decisions about their health
1151	It was stressful to do the test not knowing what to expect, but also a relief to find out that my family is at no greater risk of cancer because of any genetic markers.
743	It was important to me that I be able to tell my sister and daughters (brothers and son) if they were more likely to have breast cancer. I understood that my breast cancer means they all have a slightly higher risk but if I had the brca gene it would have been a much higher risk to all my loved ones.
526	It was helpful to know i do not have a genetic risk of cancer
963	It was helpful for me to undergo genetic testing after learning that my mother has BRCA1 and knowing my chances for having the gene mutation were 50%. I am even more grateful now, 2 years after testing, because my doctors were able to detect that I have early stage breast cancer which would not have been the case if I didn't have increased cancer screenings after learning about my BRCA1 mutation. However, I did experience increased anxiety and a feeling of helplessness after receiving the BRCA results because I was 31 years old at the time I received the genetic testing, which is younger than most doctors recommend undergoing prophylactic surgeries. It was also a lot of stress to deal with while finishing my PhD and I wished that I had been given resources to join a support group or talk to a therapist to process the emotional journey of having the BRCA mutation. I would definitely recommend that others get the genetic testing if there is a family history of cancer, but would also warn them that having a positive result of a gene mutation is an emotional burden. At the same time, knowledge is power and it allows the individual to take action and undergo regular cancer screenings and possibly make a lifestyle change to have the best outcomes.
567 (0)	It was a brief results conversation. Didn't feel much was discussed.
712	It is important for people to know their risks and take appropriate action to manage care so they have a choice to living a long and healthy life. For me,

	genetic testing forewarned me about inherent risks in my heredity. I only wished I took appropriate action immediately after I knew of my test results.
408	It is Breyer to know if you have a higher risk by testing and try to better take care of your health
989	It is better to know what the risks of getting cancer are and what I can do to proactively screen for it going forward. My mother recently died from cancer and my father has Lynch Syndrome. I do not have Lynch Syndrome but have been proactive in screening for colorectal cancer with Cologuard and will schedule a colonoscopy when it is recommended. I get annual dermatological screenings for skin cancer, because it is important that I manage anything that arises instead of allowing it to get out of hand. I would rather be prepared and have nothing happen than to be caught off guard and told that I have stage 4 cancer or something shocking like that.
1245	It is better to have the knowledge of your risk of cancer than to ignore it. I am proactive about my health.
75	It helps you make decisions about your own health and can help your children in the future. I would have done prophylactic surgery if there was a significant probability of getting cancer in the future. And children can test earlier for cancer than recommended based on genetics.
1423	It helps us all become more vigilant with screenings, exams, etc.
871	It helps ease your mind to know
1317	It helps both you and your doctor to make better health recommedations/decisions.
1417	It gives you and your doctors a better idea of what to look for. I don't see a problem with having too much information.
1491	It gave me peace of mind not just for me but also for my children
1237	It doesn't hurt to have more information about your family hereditary information.
392	It could save someone's life. May someone change their mind about going for check ups.
733	It can support appropriate monitoring and early intervention should a problem arise.
1114	It allows one to take steps to mitigate future risk
1553	It allowed me to take preventative measures that I otherwise wouldn't have done
1145	It a proactive helpful advantage to staying healthy.
1508	Informed people can make intelligent decisions and share pertinent data with family members. One can also encourage other family members to get tested if his/her results merit that.
894	In was a relief to know that my children, ,grandchildren,nieces, etc. are not predisposed to have cancer. Since I'm unaware of any cancer history.
628	If you have the opportunity to know if your immediate family or future children may be diagnosed with cancer, why wouldn't you take the test? There is incredibly low risk and only provides benefits.
1279	If the person asking about testing was outside my family and had the same hit rate of hereditary family members with various cancers (like myself) asked,

	then yes, I would recommend it. Otherwise, the genetic mutation doesn't really explain why we have such a high incident of all types of cancer in my family. It does help to know that.
1263	If someone was getting multiple skin cancers and melanomas as I have, I would reccommend because you have information for future and how to deal with any upcoming. Share with family
1479	If negative, anxiety is lessened. If positive, needed steps can be made to prolong life and/or find issues quickly.
1369	if I had the test earlier, I might have made different choices about building a family, and I might have felt less anxiety.
1167	if cases are mounting in your family, it puts you at ease...but, then, I had no known markers.
1128	I'm proactive about my health care. This allowed me to learn of any future risks and provided information that was valuable to my two daughters who also were tested. And they tested positive for the same PMS2 mutation.
145	I would recommend they discuss the pros and cons with their physician, therapist, and/or genetic counselor (rather than recommend testing outright). I personally think more information is helpful for making healthcare decisions, and the testing eased my anxiety about developing breast cancer. However, I might feel differently if my results were positive (e.g., my anxiety might increase). It is also hard to say how the additional information might impact behavior. For example, the negative test result may have also given me a false sense of security. I might get fewer breast exams or check less often than I would have without testing.
330	I would recommend testing to help people pinpoint medical care. I would also NOT recommend because there is clearly a polyp genetic issue in my family but no specific gene was found for me, so it was not very helpful to understanding my current medical issues.
591	I would recommend it to help educate someone about their risk of developing cancer and to help prevent or plan for medical care if there is a risk of developing cancer.
241	I would recommend genetic testing for anyone who has a personal history of cancer or family history of cancer. The results can ease your mind, help modify your testing frequency, and adjust your lifestyle to prevent cancer.
23	I would recommend genetic testing but it is up to the individual if they feel like it is necessary.
1588	I would recommend genetic testing because it gives you the information to do something about it if you test positive. My mom tested positive for the BRCA 2 gene mutation and had a full hysterectomy and double mastectomy because her risk was not if but when. So I was tested and it was negative. I am at a normal risk for cancer, but not prone to anything in particular. To know your risk is to know what to do. You have the power of choice rather than an unknown.
618	I would recommend for science purposes, and also for information for your family members as we move forward. If results had turned out differently then at least I would know what I could do to change my life eating habits.

758	I would recommend but am not sure if the test could be more comprehensive and cover more genetic possibilities. The test was recommended because my mother lived to 88 and my dad to 96 i was raised on an organic dairy farm was a nurse and school teacher and I ended up with 3 different cancers. If I remember nothing turned up so still a mystery. Having 3 kids and 8 grandkids we would like to know if there was any hereditary markers
938	I would recommend because knowing can alter your course
757	i would recommend because having the data and information could be helpful. i understood what the results could be and whether it came back positive or negative, it would ease any anxiety and not leave a 'what if?' floating around in my head. would recommend for anyone who had cancer or family history of cancer.
901	I would recommend and it would definitely help family members.
1631	I would rather know if I have genetic risks for colon and other cancers for both myself and my children.
1268	I would change your life! Coming from a family with a cancer history, it was a relief to know I do not carry the gene. For this reason, I would encourage anyone on the fence to be aware instead of fearful.
1504 (0)	I went in with a family history that pointed towards Lynch syndrome. Was told I did not have Lynch Syndrome and how no signs of cancer but 5 months later I was diagnosed with the same cancer of family member .
379	I was sent to get testing as I was diagnosed with melanoma at an early age, then again about 7 years later - also I had family history. My main goal was to inform my family members to be more diligent if needed.
31	I want to know if I have increased risk, which may the only thing that gets my HMO to do increased screening and take my potential risk more setiously
731	I think it's good to know and could answer questions
287	I think if there is cancer in your family it is helpful to see if others should undergo screenings. I understand my results were good so it is easier for me to say I would do it again.
735	I think I just got tested for Lynch syndrome. I forgot already it's been a long time.
1404	I think having the knowledge allows a patient/person to make better-informed decisions.
25	I think everyone should get tested if there is a possibilities of a cancer gene in their bloodline. It's way more helpful to know if you do or do not than not knowing at all.
872	I strongly recommend since cancer is so commend to hear now and if you can prepare yourself or make life changes to help decrease the chance It's totally worth it.
1129	I recommend genetic testing. Finding out that I was ATM positive, I was referred to a breast cancer specialist. I had a double mastectomy which saved my life. Years before (2.1.2013) I had a Whipple Surgery at UCI from EUS surveillance.

914	I recommend genetic testing because it is a painless and reassuring experience that gave nepeace of mind about my future
487	I recommend genetic testing as such information can help my children in the future.
66	I personally like having more information, so it would be helpful for others who have that preference too.
410	I originally did testing bc I was told my biological father overseas had colon cancer. Later, I discovered this to not be accurate. My results came back negative. With that panel, the BRCA mutation for breast cancer was also negative. No one in my family has had cancer. I was diagnosed with aggressive triple negative breast cancer last year. Unaware that there are different types of breast cancer, since my BRCA was negative i thought I was in the clear. Then I discovered a lump and have been treating my BC. I think the results that are given about how it was obtained by the lab processing etc is confusing and isn't really relevant to a patient specifically. As a patient I just want to be screened for all different types of cancer, since clearly you can get cancer and not even have the genetics for it. There was also findings that I was told 'isn't a lot of research in yet' so they didn't really know but it was discovered. It would be helpful to have a follow up on that and be updated, once the proper information has been 'discovered'. Seems odd to have a strain of something show up and be told they don't know the risks of that. Was told bc I am half middle eastern that that could be why. Still confused on this and did not find that part helpful. However, I think everyone should do genetic testing. Some answers are better than none. Once I was diagnosed w BC I did contact my genetic counselor informing Bf her and requesting a full BC panel be run on me. She didn't seem informed as to which would be the best panel to run on me which I would think is kinda basic since so many people are diagnosed w BC. Not sure if she is only specialized in testing for one type of cancer or not but I could have been referred to someone else if that was the case. It was really overwhelming being newly diagnosed and not feeling like I could rely on follow up genetic testing from UCI. She also recommended that i could ask my doctor at hoag or city of hope to be apart of a clinical trial.. this helped me not at all when i was trying to figure out genetic testing. Because of the lack of support with navigating this, i decided not to do my cancer treatment at UCI. Cancer is a huge issue and should be handled w care w providers who take it seriously. It delayed beginning treatment bc i needed more genetic testing done. I tried to be proactive by contacting her ahead of time. I ended up doing genetic testing with a different hospital bc of this and got way more results. It might just be because you guys use Ambry; i find a lot of physicians actually aren't that impressed by their reports. Side note: I also found 23&me helpful. Again, people should do genetic testing no matter what. Why not know what you can get a 'head start' on to prevent instead of being blinded. Of course there is always my scenario where I didn't test positive for the BRCA or HER 2 genes and still ended up with triple negative breast cancer. That was nothing I could prepare for, even with how proactive I am about my treatments.

1555	I lost my mother to ovarian cancer. My dad had been job hopping and because of that we did not have health insurance. She began having pain and when we applied for Medical and took her to the ER the ovarian cancer had already metastasized. My mother was cautious of her health but without insurance she could not go in for regular check ups for about 2 years. Once it was found it was too late. She fought the cancer for 2 years but eventually passed away from it. When she passed my physician insisted me and my two older sisters get genetic testing done. So, we did. One of my sisters and myself found out we are BRCA 1 positive. It was scary but the physicians explained that now that we were aware we could start screenings and monitoring early. Knowing our genetic testing results helped shape decisions in our life in regards to child bearing and managing our health. After my mother's death, my aunt, her sister, developed breast cancer. Thus my cousins were also advised to get genetic testing. We found out one of our cousins is also BRCA1 positive. I would recommend getting tested because it can definitely help you manage your health. It also makes you think about life differently. It feels like there is a monster looming in the future to come out and grab you at some point but it also makes me enjoy life by the day. Nobody knows when their last day will be but when your aware of a cancerous genetic mutation in your body you are a little more realistic about how much time you can enjoy life. I don't mean this to sound negative. I am grateful for knowing. I admit I hate appointments for screening and early mammograms, those days feel a little grayer. However, when the appointments are over, I walk out of medical building and really look at how blue the sky is and how green the trees are and how I can still see them. Sorry if it sounds schmaltzy but its really how it feels for me living life knowing cancer is possible some day but at least not for today.
1459	I have let my kids and grandkids know their risks.
1630	I have daughters that need to know their risk
772	I have already had genetic testing, that's why I didn't ask for it again. I already had the specific test. I am grateful I had the genetic testing.
717	I have a stong history of cancer in my family. I would want to know if I am or my children are at risk to develop it
860	I had uterine cancer and 2 year later my sister had colon cancer. There could have been a gene in our family that would have made both of us more susceptible to the other's cancer. I was tested for that gene and didn't have it. My risk of colon cancel could have gone up to 80% and I would have needed a colonoscopy every year. So good news for me.
571	I had to have the genetic test so that my daughter could get a MRI for breast cancer prevention. Her current insurance would not cover the MRI since my previous genetic test (2007) showed no genetic defect.
387	i had my test done because my brother came positive to a gene and my husband has cancer and was worried i carried a gene and wanted to know for my daughter and also so we could be more on the lookout for any signs as my husband never had any symptoms and we did everyyear his annual physical and he stii end up with colorectal cancer stage 3 did not wanted to have any other surprises and also be aware of any possibility for my daughter.

657	I feel that the more knowledge a person has about their health the better. Whether it's good news or bad news it's always better to know.
1142	I feel that leaving it unknown until it shows itself is not good way to go.
798	I feel that genetic testing empowers me and my family to make informed decisions and prepare for possible health issues. I believe it is important to be prepared and genetic testing coupled with periodic cancer screenings could help us avoid or identify cancer early.
239	I feel it's important to understand how the cancer can come about, in your family, it will help better understand your family and fight cancer and maybe help my family if I do have children.
1527	I feel empowered to know about my high risk of pancreatic cancer - better to know and watch then nit know and do nothing.
279	I don't understand why you wouldn't want to know if your family and kids need to be more cautious
104	I could tell my daughter about risk factors
1405	I constantly recommend genetic testing to my family and friends, especially those with close family predispositions. I believe it is very important to know and be educated in our health decisions. It has put my mind at ease for one concern and made me more aware or vigilant for another.
1421 (0)	I came up negative it does not make a difference to me and I'm beyond the age of having children. Dr wanted it to determine treatment.
1583	I believe the knowledge is useful. Knowing I have the increased potential, I just increase my screening visits. The intended plan is to mitigate any developments early. I would recommend to others for the same reason.
1526	I believe that having a genetic test will help me and my family to understand my risk for the cancer
1420	Helps with treatment planning. Informative for family.
771	Helps me make informed decisions about my future
692	Helpful
900	Helped ease my mind about my rare diagnosis.
1617	Help with management, it will help me control the development of cancer by having regular colonoscopies, removal of polyps before they turn into cancer
1437	Having the power to do a double mastectomy to essentially eliminate any chance of it coming back was a huge benefit. Especially as a mother. My one challenge- insurance took too long to approve it so I ended up having two surgeries - I would have gone straight to mastectomy had I known. Very frustrating.
391	Having lost a parent to cancer, another parent who had cancer and my sister's diagnosis with fallopian tube cancer.
353	Had my results been different, I would be better prepared for an increased risk of cancer, mentally, and perhaps done more screening or looked into preventative measures
388	Good information for responsible healthcare management
7	Give a clearer answer
1442	Genetic testing can provide useful information about proceeding with one's own preventative measures or their family member's.

870	Genetic testing allowed me to inform my children who were all tested. And it let me know my risk of other cancers.
124	For screening and planning purposes.
602	For my family
1612	Ease the mind for what the future holds
780	Definitely needs to be done to determine what type of cancer, or what future cancer Dx you may have .
1595	Coming from parents that were orphaned I did not have any family history. Now my family and their children will know to get screened based on the lynch syndrome and increased risk of cancer. Proactive is better than reactive.
328	Catching cancer early is key. Knowing you're pre-disposed and can start screening early is helpful.
223	can take prophylactic actions in some cases, also increased detection may find cancer at earlier stages
1016	By getting tested and realizing I do not have the genetic mutation that has caused my family's pancreatic cancer it has significantly reduced my anxiety about developing the cancer or passing those genes onto my children.
1013	Better to know than not
928	Better to know and plan ahead
460	Better safe than sorry. Good to have more information.
128	As long as insurance companies don't use such tests to deny coverage, I would recommend it. But I think the genomics era needs to give way to the epigenomics era - genetic risks are not being evaluated in relation to social-enviro factors . I'm addition, people aren't being educated in this country to understand scientific tests and results.
791	As an Ashkenazi Jews with a family history of breast cancer I wanted to make sure that I wasn't carrying the breast cancer genes
1161	As a grandmother I feel it's important my grandchildren understand what is a possible genetic condition l have 2 sisters and a brother that carry the gene was told that it can skip generations my son is fine but I have 2 biological granddaughters that it may effect
456	Allows one to modify cancer screening according to risk based on family history and so children are aware at an early age. My dad passed away at an early age and was not aware of his medical history details since my parents divorced so it was good for me to know my risk for cancer (paternal family history of cancer)
544	All 3 of my siblings (3 sisters) as well as my father died from 4 different cancers. My nieces and a nephew tested positive for BRC1 mutation. I wanted this information for my children as well as myself. I highly recommend genetic testing if you have a history of cancer in your family.
298	ability to screen earlier if gene is detected