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Predictors of Patient Attendance for Follow-Up Cancer Genetic Counseling Appointments

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Predictors of Patient Attendance for Follow-Up Cancer Genetic Counseling Appointments

THESIS

submitted in partial satisfaction of the requirements
for the degree of

MASTER OF SCIENCE

in Genetic Counseling

by

Jessica Elin Spiewak

Thesis Committee:
Professor Moyra Smith, MD, PhD, Chair
Adjunct Professor Pamela Flodman, MSc, MS
Assistant Clinical Professor Deepika Nathan, MS

2019

DEDICATION

To my selfless parents, Phil and Dawn, and my effervescent sister, Becky.

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I would like to thank my thesis committee, Dr. Moyra Smith, Pamela Flodman, and Deepika Nathan. I am thankful for the time Dr. Smith regularly spent with me to discuss hypotheses and scientific literature. She challenged me to consider how research in our field can best be utilized to improve patient-care. Dr. Smith is a rare example of someone who manages to be both brilliant and exceptionally kind. I am grateful for Pamela Flodman's generosity and guidance. She has dedicated her valuable time to both my genetic counseling training and my thesis. I am inspired by her focus on advocating for others, patients and students included, and by her ability to extract real meaning from complex datasets. I would like to thank Deepika Nathan for her insights from the clinical perspective for this project.

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ABSTRACT OF THE THESIS

Predictors of Patient Attendance for Follow-Up Cancer Genetic Counseling Appointments

By

Jessica Elin Spiewak

Master of Science in Genetic Counseling

University of California, Irvine, 2019

Professor Moyra Smith, MD, PhD, Chair

Medical providers often interact with and provide care for their patients over the course of several visits. In the cancer genetic counseling setting, many patients choose to have genetic testing for mutations that confer a heritable predisposition for cancer. Follow-up genetic counseling is integral for disclosing genetic testing results and discussing the patient's cancer screening regimen and recommendations for at-risk family members in the context of genetic testing results. Previous research has revealed the barriers to an initial cancer genetic counseling visit and uptake of genetic testing, but less is known about patients who miss follow-up visits. This retrospective chart review compared demographic factors, aspects of patients' medical history, family cancer history, and information covered during genetic counseling for patients who had an initial cancer genetic counseling visit in 2016-2017 and attended their scheduled follow-up visit to those who missed their follow-up visit. Patient sex, ethnicity, age, personal cancer history, initial visit referral indication, type of genetic testing ordered, and proportion of first and second-degree relatives affected with cancer did not differ between patients who attended and patients who missed their testing results disclosure visit. However, female patients

who had biological children were statistically more likely to attend their follow-up appointment compared to childless women, and this trend was present but not statistically significant for men who had children compared to childless men. Identifying predictors of follow-up visit patient attendance highlights the need for alternate delivery methods in genetic counseling, such as written materials, and video or telephone counseling.

I. INTRODUCTION

1.1 Cancer genetics

In 2018, an estimated 1,735,350 Americans were diagnosed with cancer, and 609,640 died from cancer (SEER Program 2018). Cancer originates from a tumor, which is a growing mass of aberrant cells. Tumor cells that have the potential to invade surrounding tissue are considered malignant, meaning cancerous, rather than benign. All cancers are caused by mutations. Mutations are alterations in the DNA sequence or regulatory elements of a gene that disrupt the normal expression of a gene. Mutations accumulate in a person's cells with time as he or she is exposed to different environmental factors, such as UV rays, occupational exposures, certain viruses or bacterial infections, tobacco, a high-fat diet, and alcohol. Tumors are often caused by accumulated genetic mutations in genes called tumor suppressor genes that normally control basic cell growth, proliferation, survival, and DNA repair, thereby preventing abnormal cells from developing into a tumor. Biallelic mutations causing loss of function in both copies of a tumor suppressor gene in the same cell can lead to tumor development and cancer.

While all cancers are genetic in origin, they can be classified into one of three types: sporadic, familial, and hereditary. Most cancers are sporadic, meaning a person randomly accumulated cancer-causing mutations over their lifetime. Sporadic cancers tend to be in individuals with an older age of diagnosis who do not have a strong family history of cancer. About 20% of cancer is familial, meaning there is a cluster of individuals in the family with cancer, but a single inherited genetic predisposition is not identified. Approximately 5-10% of cancers are hereditary, meaning they are caused in part by a germline cancer-susceptibility mutation that was likely inherited from a parent (Garber and Offit 2005). An individual with an inherited cancer syndrome is born with a cancer-predisposing mutation in every cell of his or her

body. As such, these individuals have an increased risk to develop cancer. Families with an inherited cancer syndrome typically have earlier ages of cancer onset, may include individuals with multiple primary tumors, or a rare type of tumor. Some cancer-predisposing mutations increase the risk for cancer in several different organs (for example, breast, ovarian, pancreatic cancer and melanoma among other types with a *BRCA2* mutation), so a family history with multiple individuals with related cancers may also suggest a single inherited genetic predisposition. Individuals who have personal and/or family history suggestive of a hereditary cancer syndrome may qualify for a genetic evaluation and genetic testing, typically performed by a cancer genetic counselor.

1.2. Cancer genetic counseling protocol

1.2.1 Cancer genetic counseling discussion points during an initial visit

Cancer genetic counselors assess a patient's risk to have a cancer-predisposing mutation based on his or her personal medical history and family history. The counselor will explain to the patient whether he or she is at risk for a genetic predisposition for cancer, and if genetic testing is clinically indicated, the counselor will also explain genetic testing options, risks and benefits of testing, and the implications for possible results of testing. This is called pre-test counseling. Multiple professional societies including the National Society of Genetic Counselors (NSGC) and the American Society of Clinical Oncology (ASCO) recommend pretest counseling (Riley et al. 2012; Robson et al. 2015). Discussion between the provider and patient during pretest counseling should include:

- Collection of the patient's medical history and a three-generation family history. Individuals who have a family history of multiple family members with cancer diagnoses, one or multiple family members with an early-onset diagnosis, or multiple primary

tumors, or diagnosis of a rare cancer may be at increased risk for a cancer predisposition syndrome. Additionally, family history of related individuals with the same or related cancer diagnoses are likely at increased risk. For example, a patient with who has multiple related family members with breast cancer is likely at higher risk to have a breast cancer-predisposing mutation than a patient with one family member with a breast cancer diagnosis at an average age of onset.

- Explanation of the patient's cancer risk based on the patient's medical and family history, which may also include risk assessment through an empiric cancer risk model (e.g. Tyrer-Cuzick (Tyrer et al. 2004), BOADICEA (Antoniou et al. 2004), BRCAPRO (Parmigiani et al. 1998)). There are many different models that calculate the risk for a person to develop a specific cancer and/or to have a cancer-predisposing mutation. Traditionally, models were based primarily on personal and family history, however some now also account for other risk factors such as breast-density and reproductive history (Cintolo-Gonzalez et al. 2017; Usher-Smith et al. 2016).
- The utility of genetic testing and appropriate genetic testing options in the context of the patient's personal and family history.
- Possible results of genetic testing, including 1) positive, meaning a pathogenic mutation was detected in a cancer-predisposing gene and there may be recommended changes in medical management and cancer screening course, as well as implications for at-risk family members 2) negative, meaning no pathogenic mutations were detected in the tested genes, and 3) variant of uncertain significance (VUS) was detected, meaning there is a difference in the sequence of one of the patient's genes for which there is not enough data to determine whether it is cancer-predisposing or harmless variation.

- The possibility for unexpected results, for instance, an identified pathogenic mutation in a gene that predisposes to a type of cancer that was previously assessed to be of low likelihood based on personal and family history. With the advent of next-generation sequencing (NGS) panel testing, many providers offer testing of multiple genes simultaneously. While testing more genes can provide more information for the patient, it also increases the likelihood of an unexpected result (Desmond et al. 2015; Laduca et al. 2014; Tung et al. 2015) or a result for which there are unclear medical management guidelines (Maxwell et al. 2015).
- The possibility for an uninformative test result. If a patient has a strong family history of cancer, but her cancer NGS panel is negative and there is no known familial mutation, the possibility of a genetic predisposition for cancer is not ruled out and she may still be at increased risk (Loman et al. 2003). NGS panels cannot detect every possible mutation for the tested genes, and there are likely genetic and non-genetic risk factors not tested by the panel which may confer risk. Non-genetic risk factors may include a strong family history of cancer, breast density (in the context of breast cancer risk), hormonal factors, lifestyle factors such as alcohol consumption, smoking, and diet, and polygenic risk scores (A. Lee et al. 2019). Polygenic risk scores describe the associated combined cancer risk of many single DNA basepairs which are individually correlated with either increased or decreased cancer risk.
- Limits of, and protections granted by the Genetic Information Nondiscrimination Act (GINA), (US Congress 2008) which prohibits health insurers from using an enrollee's genetic information to determine coverage, eligibility, or premiums. GINA also prohibits employers from discriminating against employees based on genetic information.

However, employers with fewer than 15 employees are exempt from the employment aspects of GINA, and military medical insurance has a separate, different set of protections.

Pretest genetic counseling in the cancer setting has been shown to have several benefits. Women with breast cancer reported increased knowledge of Hereditary Breast and Ovarian Cancer syndrome after pretest genetic counseling (Christie et al. 2012; Schlich-Bakker et al. 2006). Similarly, studies have also shown that individuals at risk for breast cancer have a more accurate perception of their risk after cancer genetic counseling (reviewed in Meiser and Halliday 2002; Smerecnik et al. 2009), although a few studies with small sample sizes found no difference in risk perception accuracy (Pieterse et al. 2006; Rothemund et al. 2001).

1.3 Posttest genetic counseling

After cancer genetic testing is ordered, genetic testing results and the implications of those results must be communicated to the patients. Some genetic counselors convey this information by phone, while others schedule an in-person follow-up visit with the patient (Wham et al. 2010). The role of the genetic counselor in genetic testing results disclosure and posttest counseling includes (Riley et al. 2012):

- Disclose the genetic testing results.
- Explain the limitations of the genetic test.
- If the test result is positive, explain the cancer risk and any other medical risks associated with the identified mutation. It is also important to discuss any recommended changes in cancer screening associated with that mutation, and any prophylactic surgical options if

appropriate. For example, if a woman has a mutation in a gene that substantially increases her risk for ovarian cancer, a risk-reducing salpingo-oophorectomy (removal of the fallopian tubes and ovaries) may be an option (NCCN 2018). For positive results the genetic counselor should explain which relatives of the patient are at risk to have the same mutation, and also provide materials to help the patient inform his or her relatives (e.x. a family letter, referral to genetics clinic). The genetic counselor should also provide support resources for the patient.

- If the test result is negative, explain whether the patient is at any increased risk for cancer based on personal and family history alone.
- If the test result reports a variant of uncertain significance, explain that medical decisions are not recommended based on this result because there is currently insufficient evidence to determine whether it is cancer-predisposing or harmless variation (Richards et al. 2015).
- Answer questions the patient has about the testing and/or cancer screening recommendations.
- The genetic counselor should make referrals as appropriate to providers who can surveil high-risk individuals.

In some cancer genetics clinics, patients who have a positive genetic testing result and/or a variant of uncertain significance are routinely recommended for follow-up genetic counseling 6-12 months after their results disclosure appointment. The purpose of a follow-up visit for patients with a variant of uncertain significance is for the genetic counselor to determine whether the variant has been reclassified as either benign or disease causing, and if so, the implications

for medical management and family members. For patients who tested positive on their genetic testing, the purpose of a follow-up visit was typically to review testing for family members and to further discuss cancer screening for the patient in the context of their mutation.

1.4. Barriers to cancer genetic counseling referrals and uptake

There are clear guidelines for when patients should be referred for a genetic cancer evaluation (Gupta et al. 2017; Hampel et al. 2015; NCCN 2018). Whether a qualified patient is referred for cancer genetic counseling depends on both the referring provider's ability to elicit relevant medical history and family history from the patient, and on the provider's ability to determine whether cancer genetic counseling is clinically indicated for that patient. Studies have shown that a proportion of general practitioners did not document an adequate family history of cancer, and medical documentation often underreported family history of cancer compared to the patient's actual self-reported family history (Grover et al. 2004; Lanceley et al. 2012). Another barrier to genetic counseling referral is the lack of awareness of available genetics providers that has been reported by some general practitioners, especially in rural areas where the distance to a genetics clinic may be greater (Koil et al. 2003; Sweet et al. 2002). Additionally, not every patient who is referred to a cancer genetic counselor will choose to meet with one. Having a breast cancer diagnosis at a younger age, having female children, and having a high-risk family history of cancer are all factors associated with increased uptake for cancer genetic counseling (Ayme et al. 2014). It is important that the medical community be aware of and work towards lowering the barriers to an initial cancer genetic counseling visit for at-risk patients.

1.5 Predictors for genetic testing uptake

Previous literature has identified predictors of uptake of genetic testing for patients who are referred to cancer genetic counseling and are offered genetic testing. Factors associated with higher genetic testing uptake for women being evaluated for breast and/or ovarian cancer include higher perceived breast or ovarian cancer risk (Andrews et al. 2004), a personal history of breast or ovarian cancer (Andrews et al. 2004; Julian-Reynier et al. 2000), having children (especially daughters when breast and ovarian cancer are being considered) (Ayme et al. 2014; S. C. Lee et al. 2002; Meijers-Heijboer et al. 2000), and having a greater number of relatives affected with cancer (Biesecker et al. 2000). Patients who are being evaluated for a genetic risk for colon cancer are also more likely to opt for genetic testing if they are personally affected with cancer and have more relatives who have had cancer (Codori et al. 1999; Hadley et al. 2003).

Demographic factors such as the patient's age and sex have less consistent data regarding genetic testing uptake. Some studies have shown significantly increased uptake for women compared to men (especially when risk for hereditary breast and ovarian cancer syndrome is being considered) (Lerman et al. 1997; Meijers-Heijboer et al. 2000), while others show no significant difference (Biesecker et al. 2000; Botkin et al. 2003). Similarly, some studies reveal that younger patients are less likely to choose genetic testing during an initial cancer genetic counseling visit (Biesecker et al. 2000) while other studies show no significant difference (Aktan-Collan et al. 2000; S. C. Lee et al. 2002).

1.6. Aims of this study

The estimated proportion of individuals who do not return for follow-up cancer genetic counseling after an initial appointment has not been addressed by currently available published literature. Furthermore, which patients are at risk to miss follow-up is unknown. If we can

understand the population that is most likely to forgo follow-up appointments, genetic counselors can develop methods and tools to ensure posttest recommendations and follow-up care are conveyed to at-risk individuals. This retrospective chart reviews aims to collect data on patients seen through a cancer genetic counseling service in a university medical center setting over a two-year period, in order to:

1. Identify the proportion of individuals who attend an initial cancer genetic counseling visit, but do not attend their scheduled follow-up appointment(s).
2. Identify factors that predict whether a patient will return to their scheduled follow-up genetic counseling visit. Understanding the group of patients at higher risk to miss follow-up appointments can elucidate how to better communicate post-test recommendations. I hypothesize demographic factors, personal medical history, and the proportion of the patient's family members who have had cancer are predictors of follow-up visit attendance. I will compare these variables between individuals who attended their in-person genetic testing results disclosure counseling session to those who did not.

II. METHODS

2.1. IRB Protocol

This research protocol was reviewed by the Institutional Review Board of the University of California, Irvine under Exempt Registration HS#2019-4952.

2.2 Retrospective Chart Review

2.2.1 Patient Chart Selection

The initial study population included all patients aged 18 years and older who had an initial new-patient consult with a UCI cancer genetic counselor between January 1st, 2016 and December 31st, 2017. These cases were identified by reviewing the electronic cancer genetic counseling schedule from this time period through the Quest (AllScripts) electronic medical record system, used until November 4th, 2017 at UCI, and the Epic electronic medical record system from November 4, 2017 through December 2017. This time period ensured that there had been at least 16 months since each patient's initial appointment at the time of data analysis, leaving ample time for information from follow-up visits to be included in the dataset. These patients were all seen by the same genetic counselor at either the Chao Family Comprehensive Cancer Center, University of California, Irvine Medical Center in Orange, CA or the Comprehensive Digestive Disease Center, University of California, Irvine Medical Center in Costa Mesa, CA. There were 419 patients that met these initial criteria. Within this cohort of 419 patients, 15 were excluded due to substantial missing information, such as a missing pedigree or clinic note for a genetic counseling encounter. The final number of patient charts reviewed in this study was 404. Of the 404 patients that qualified for this study, 356 were scheduled for at least one follow-up genetic counseling visit, and 291 elected genetic testing during the first

appointment. Each patient was given a study ID number that was used for the data collection spreadsheet, and the code that links the study ID number to the patient identifier was stored separately from the data collection spreadsheet.

2.2.2 Data Collected from Consult Notes in the Electronic Medical Record

For each patient chart in this study, demographic information, personal medical history, and aspects of the cancer genetic counseling visit were collected from the electronic medical record.

Demographic information that was collected from each chart includes:

- The age of the patient at the time of the initial cancer genetic counseling appointment
- The sex of the patient reported at the time of the initial cancer genetic counseling appointment.
- The ethnicity of the patient as reported by the patient was collected. Patient ethnicities in this study included:
    - Ashkenazi Jewish
    - Asian
    - Black
    - Indian subcontinent, which included Bangladeshi, Indian, and Pakistani individuals
    - Hispanic
    - Middle Eastern, which included Afghan, Iranian, and Iraqi individuals
    - White, which means the patient reported European ancestry on both maternal and paternal sides of the family

    - Unknown
    - Mixed, meaning that the patient reported being part of two or more of the previous categories.
- Parent-status of the patient was collected, meaning whether the patient had biological children at the time of the initial appointment. If a patient had children, the number of male and female children was also noted.

Aspects of each patient's personal medical history and cancer genetic counseling visit information was collected, including:

- Personal history of cancer as noted in clinic notes and pathology records when available in the electronic medical record. The patient's cancer history at the time of the initial genetic counseling appointment was classified as:
    - No history of cancer
    - Current cancer diagnosis
    - Past cancer diagnosis, meaning the patient was considered cancer-free
    - Both a current cancer diagnosis and past cancer diagnosis, meaning the patient currently had cancer but also had previously had cancer that had been in remission at one point. Patients that had current and past cancer diagnoses included individuals who had a recurrence of the same cancer as well as individuals who had a new cancer derived from a different primary tumor as their past cancer.
- Other personal medical history that was considered relevant to assessing whether someone is at-risk for a hereditary cancer syndrome was collected, including colon

polyps, benign tumors, clinical diagnoses of hereditary cancer syndromes such as Neurofibromatosis Type I, and precancerous moles.

- Whether the patient was self-referred or referred by a medical professional to cancer genetic counseling was noted. If the patient was referred by a medical professional, the specialty of that provider was collected.
- Primary referral indication was collected for each initial visit. Primary referral indication was categorized as either due to personal medical history, family history of cancer, or a combination of both.
- The type of insurance the patient had during the first cancer genetic counseling visit was collected. Insurance types included PPO, HMO, Medicare, Medi-Cal (California's state Medicaid program), and Tricare.
- Whether or not the patient had a family member who had had genetic testing was documented, and if that relative was positive for a pathogenic variant in a cancer predisposition gene, the gene name was noted.
- If a patient was referred for cancer genetic counseling and had already had genetic testing, the test result was documented.
- The dates of the initial cancer genetic counseling visit and follow-up visits were collected from each patient chart, and the time between visits was calculated.
- The type of test that was ordered and the test result were both collected for patients who previously had genetic testing or had testing during the course of cancer genetic counseling. Most patients had a gene sequencing panel of at least two genes, and for these patients the type of gene panel was recorded. Other types of genetic testing included targeted familial testing, meaning a patient was tested solely for a genetic

mutation that was previously identified in a family member. Some patients had single gene testing, typically because they had a hereditary cancer syndrome clinical diagnosis or there was clinical suspicion for only one type of hereditary cancer syndrome.

- The mode of disclosure of testing results (either by phone or during an in-person appointment) was collected.
- If a patient had been scheduled for a follow-up visit, the reason for doing so as documented by the genetic counselor in the previous visit's clinic note was recorded.

2.2.3 Data Collected from Patient Pedigrees

A detailed three-generation pedigree was collected for each patient at every cancer genetic counseling initial appointment. For this study, the proportion of adult first-degree, second-degree, and third-degree relatives of the patient who had ever been diagnosed with cancer, typically by per patient report, was calculated from each family history. First degree relatives include parents, full-siblings, and the children of a person. Second-degree relatives include half-siblings, aunts and uncles, grandparents, grandchildren, and nieces and nephews. The most common third-degree relatives reported were first-cousins, half-aunts and half-uncles, great-aunts and great-uncles, and great-grandparents. Some pedigrees did not specify the number of individuals in one or more sibships, which was documented as "n" number of individuals on the pedigree. Every "n" number of relatives was counted as two relatives, because standard pedigree practice is to only use "n" to represent >1 relative; however, there is no maximum number of relatives "n" can represent. While assigning "n" the value of two is likely

conservative and an underestimate, the average number of relatives “n” truly represents is unknown.

2.2.4 Data Analysis

IBM SPSS software version 25 (IBM 2017) was used to calculate both descriptive and inferential analyses. Examples of descriptive statistics calculated in this study include the frequencies of patient demographic data, basic referral information, and the type of genetic testing that was performed. Inferential analyses included comparison of categories within each independent variable and the outcome of whether a person attended their follow-up visit. Statistical analyses included chi-square analysis or Fisher’s exact test for categorical independent variables, and student’s t-test for continuous independent variables. Levene’s test for equal variances was employed prior to conducting each t-test. Statistical significance is reported for each analysis as a nominal p-value, and a p-value <0.05 was considered significant. For this exploratory analysis, no correction was made for multiple comparisons.

III. RESULTS

3.1 Descriptive Data

Between January 1st, 2016 and December 31st, 2017, 404 new adult patients were seen by a UCI cancer genetic counselor and qualified for this retrospective chart review. Of these 404 patients, 356 were scheduled for a follow-up visit after their initial cancer genetic counseling appointment and used for analyses in this study. The majority of patients in this study were female (84%), White (43%), Hispanic (20%), or Asian (18%), and were parents to biological children (70%) (Table 1 and Figure 1A-C). When categorized by men and women, 73% of male patients were fathers and 70% of women were mothers to biological children (Table 1 and Figure 1C). Most patients had a personal history of cancer, either a current diagnosis (39%), or a previous cancer diagnosis (22%) (Table 1 and Figure 1D). Of the total patients, 33% had never had cancer and were referred either due to a family history of cancer or due to personal medical history such colon polyps (Table 1 and Figure 1D). Most patients were referred to genetic counseling by a physician (91%) due to both their personal medical history and family history of cancer (61%) (Table 1 and Figure 1E-F).

Table 1: Patient demographics and referral information of patients scheduled for a follow-up visit after an initial cancer genetic counseling session at UCI

Patient Sex

	Number	Percent
Female	300	84
Male	56	16
Total (n)	356	100

Table 1 cont.

Patient Ethnicity

	Number	Percent
Ashkenazi Jewish	17	5
Asian	63	18
Black	5	1
Hispanic	71	20
Indian subcontinent	5	1
Middle Eastern	20	6
Mixed	20	6
Unknown	1	0.3
White	154	43
Total (n)	356	100

Total Patient Parent-status

	Number	Percent
No Children	105	30
Has Children	251	70
Total (n)	356	100

Male Patient Parent-status

	Number	Percent
No Children	15	27
Has Children	41	73
Total (n)	56	100

Female Patient Parent-status

	Number	Percent
No Children	90	30
Has Children	210	70
Total (n)	300	100

Patient Personal Cancer History

	Number	Percent
Current	139	39
Previous	78	22
Current and Previous	22	6
None	117	33
Total (n)	356	100

Table 1 cont.

Referral Indication

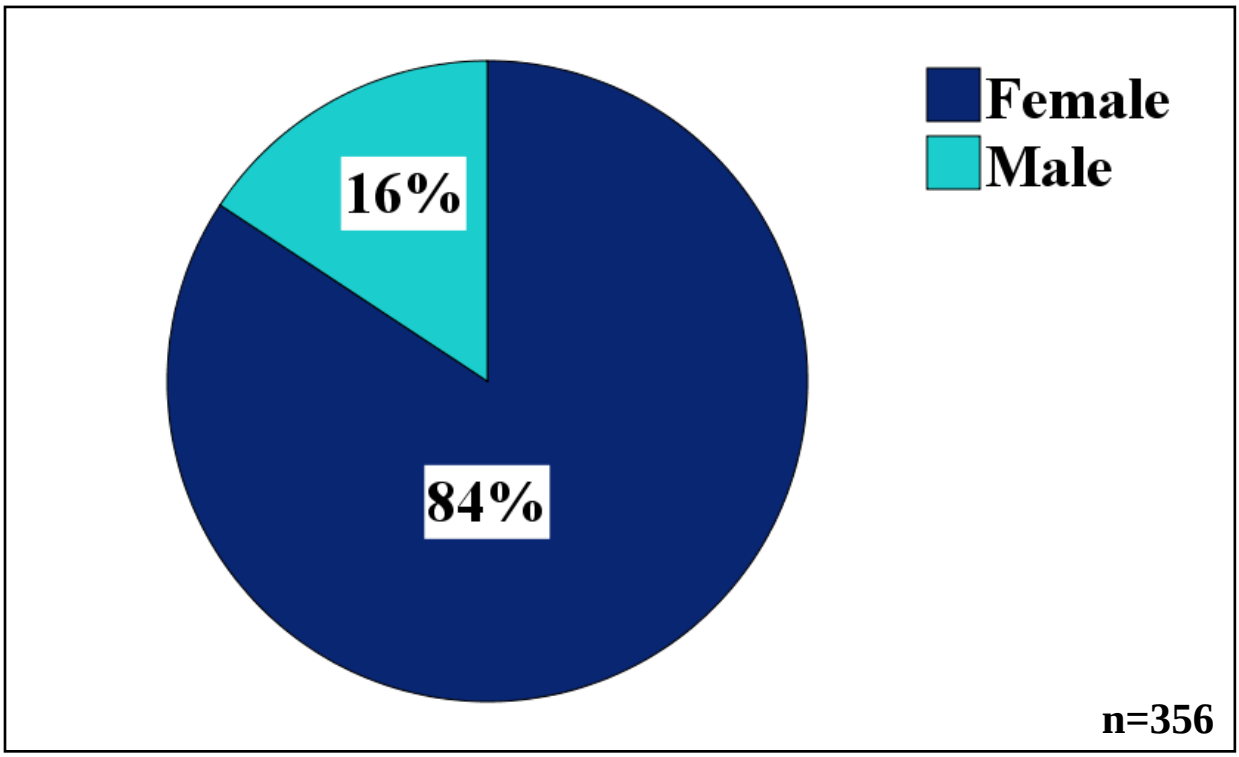
	Number	Percent
Personal history	45	13
Family history	95	27
Both	216	61
Total (n)	356	100

Referral Source

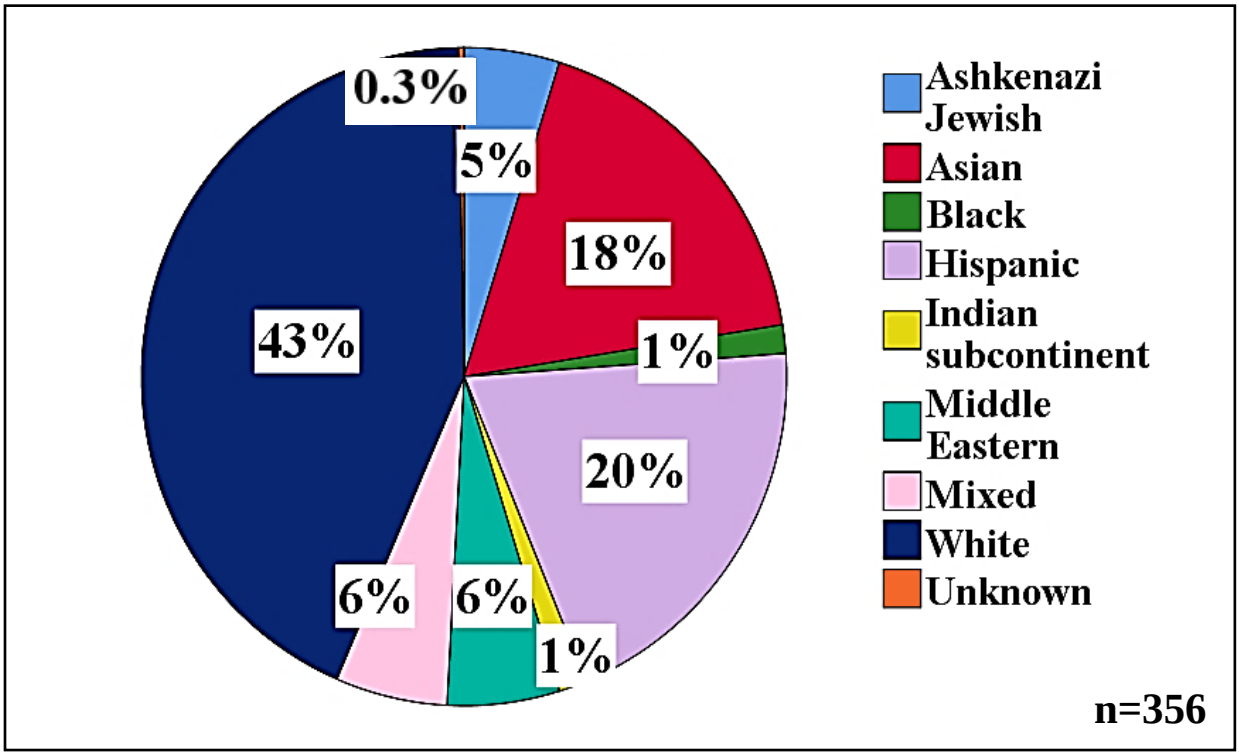
	Number	Percent
Physician	324	91
Self	31	9
Total (n)*	355	100

*Referral Source was undocumented for one patient.

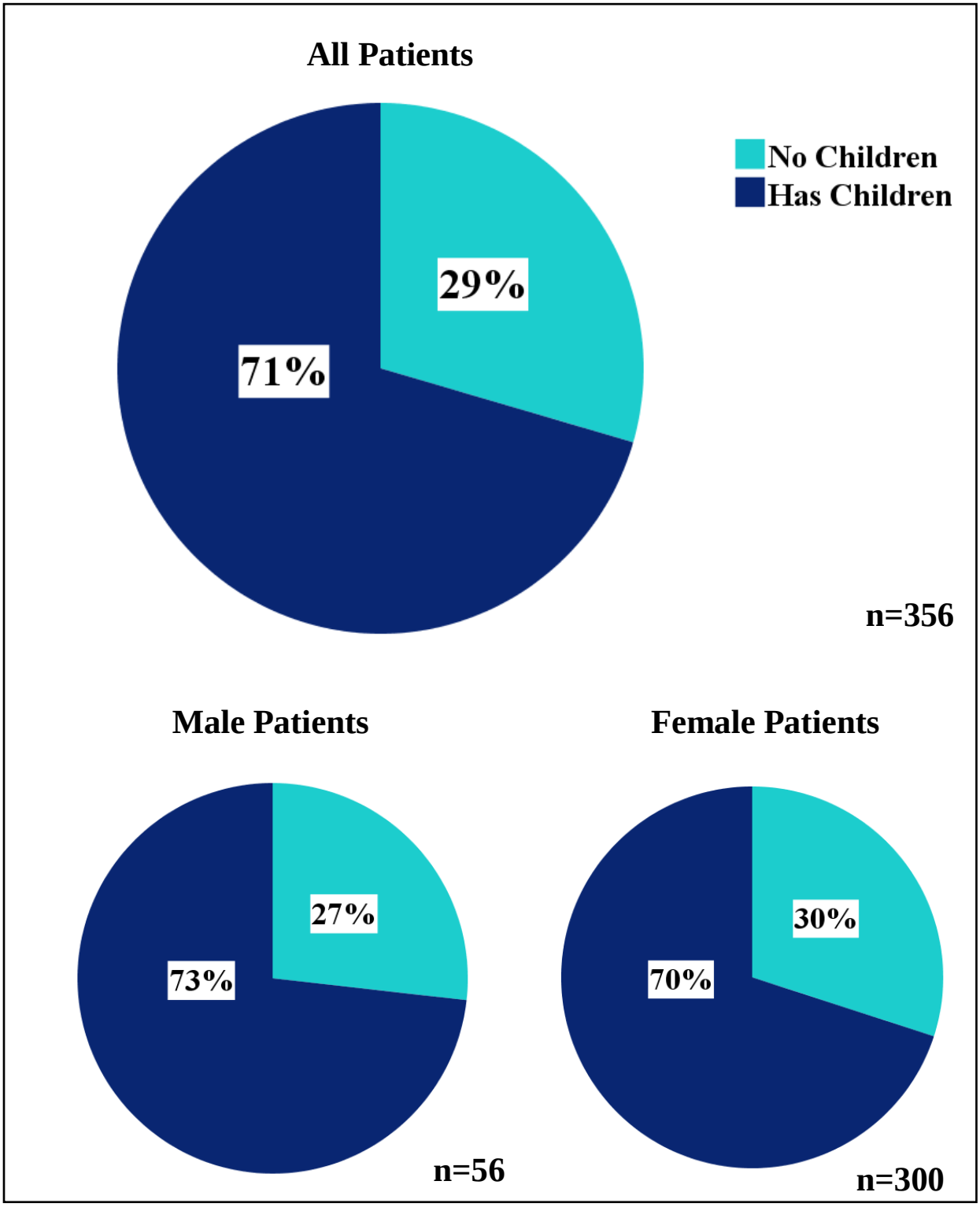
1A) Patient Sex



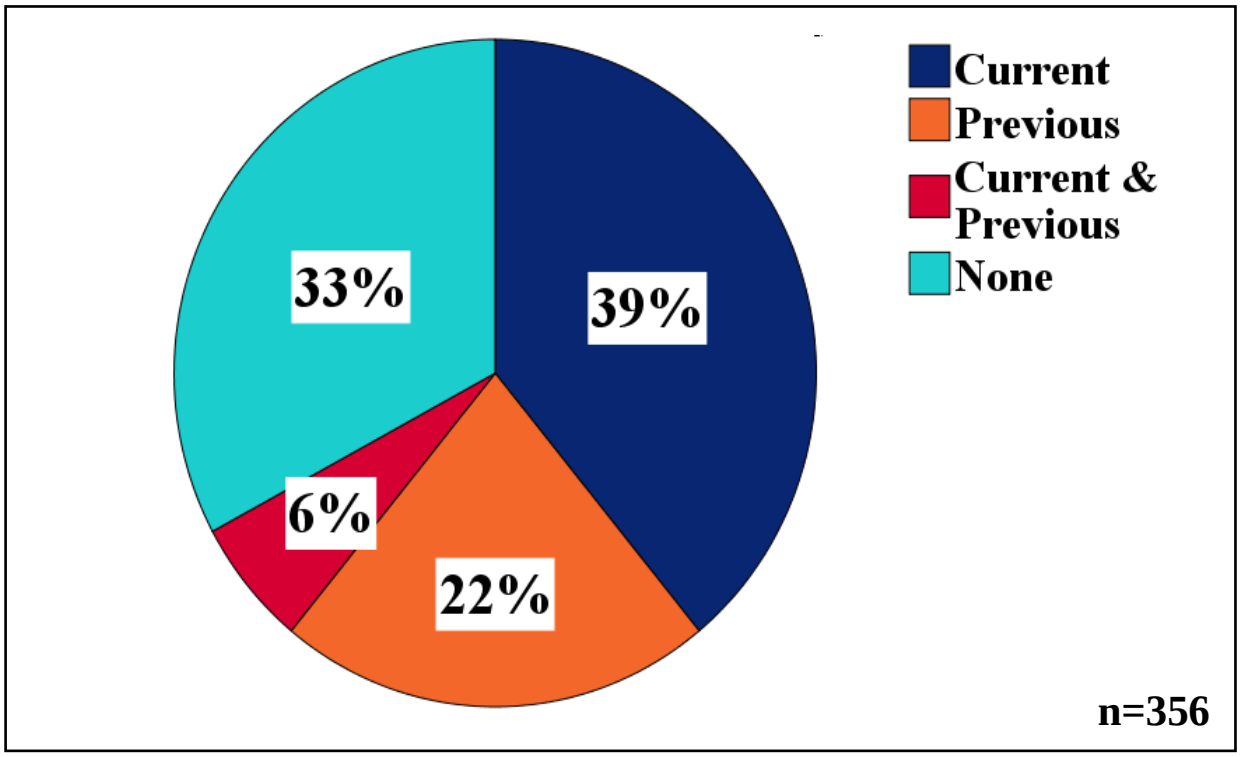
1B) Patient Ethnicity



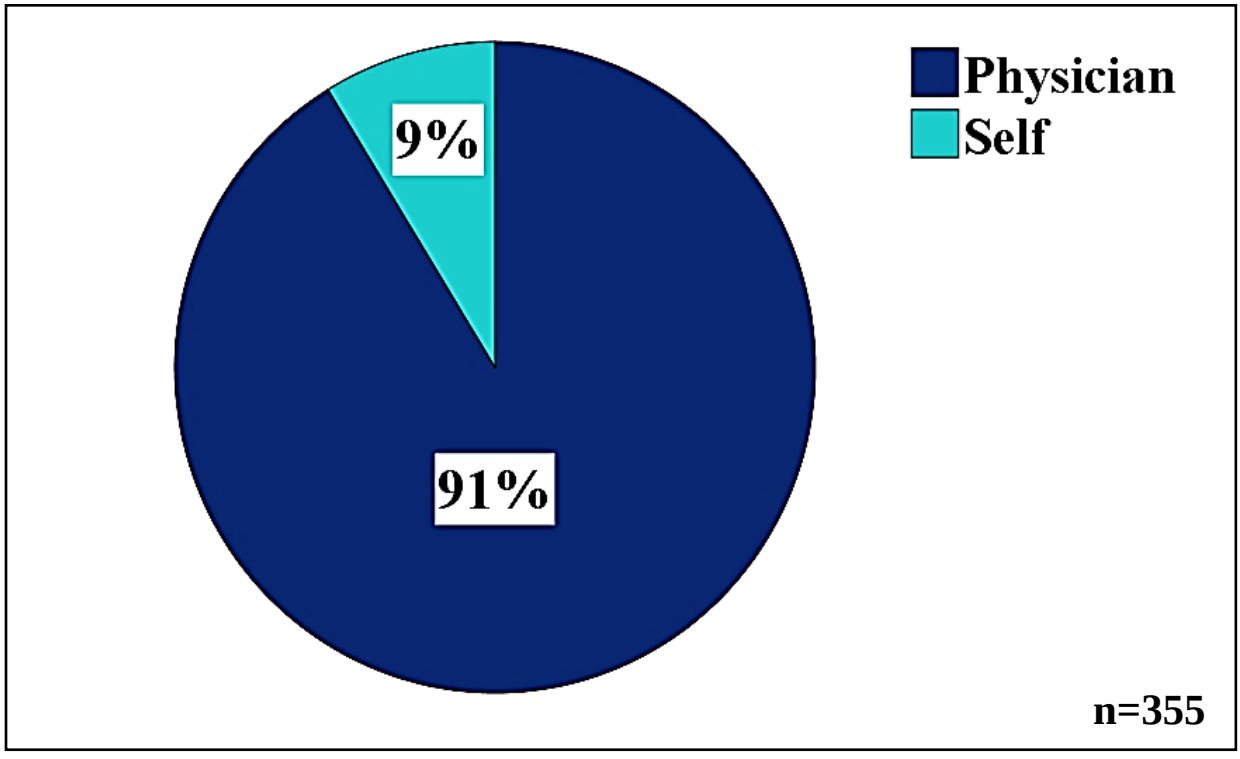
1C) Patient Parent-status



1D) Patient Personal Cancer History



1E) Referral Source for Initial Genetic Counseling Appointment



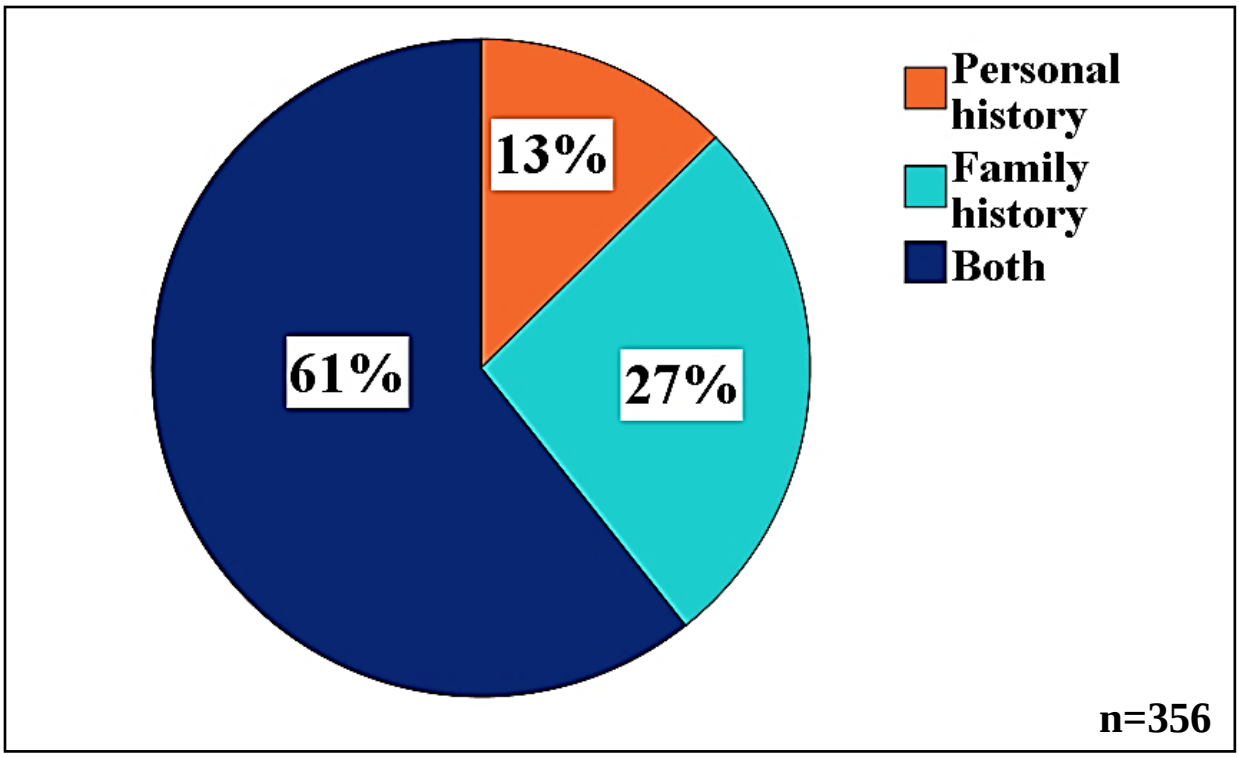


Figure 1: Frequencies of sex, ethnicity, personal cancer history, referral source, and referral indication for the 356 patients that attended an initial cancer genetic counseling visit and were scheduled for a return appointment. 1A) The percentage of male and female patients included in this study. **1B)** There was a range of ethnicities represented in the patients that attended an initial cancer genetic counseling session, with the majority being White, Hispanic, or Asian. **1C)** Most patients in this study were parents to biological children, which was true for both male and female patients. **1D)** Patient cancer history was categorized as either having a current diagnosis of cancer, a previous diagnosis which is no longer in effect, no cancer history, or a current cancer diagnosis and previous cancer diagnosis. Patients that qualified as having a current and previous diagnosis may have had two different primary cancers, or a recurrence of the same cancer. **1E)** Patients were either referred to cancer genetic counseling by a physician or were self-referred. **1F)** The possible referral indications for the initial genetic counseling appointment include family history of cancer, personal history only, which includes cancer diagnoses and/or other features suggestive of a cancer predisposing mutation such as colon polyps, or a combination of both personal medical history and family history.

The average age of the patients at the initial cancer genetic counseling visit was 52-years-old, and the average age of the patients did not differ significantly between men and women ($t(354\ d.f.) = -1.741$, $p=0.083$) (Table 2A and Figure 2A). While the overall mean age did not

differ between men and women, there is an apparent small peak in the age 25-50 age range compared to men (Figure 2B). Therefore, we tested via chi-square analysis whether the number of women and men who aged 50 and younger at the initial genetic counseling visit differed from the expected frequencies under an assumption of no association between age and sex. Categorizing patient-age as 50 and younger and 51 and older is also a clinically important age cutoff; NCCN guidelines recommended genetic evaluation for women who have had breast cancer at age 50 or younger, which may influence the age distribution of women who are referred for cancer genetic counseling. However, chi-square analysis found no significant association in this sample between age (categorized as 50 or younger versus 51 and older) and sex (χ^2 (1 d.f.) =2.288, p=0.130) (Table 2B).

Table 2: Age distribution for male and female patients who attended an initial visit and were scheduled for a follow-up visit

Table 2A

Mean Age of Patient by Sex

Sex	Mean	N	Std. Dev.
Female	51.7	300	14.7
Male	55.4	56	13.5
Total (n)	52.3	356	14.5

t (354 d.f.) =-1.741, p=0.083

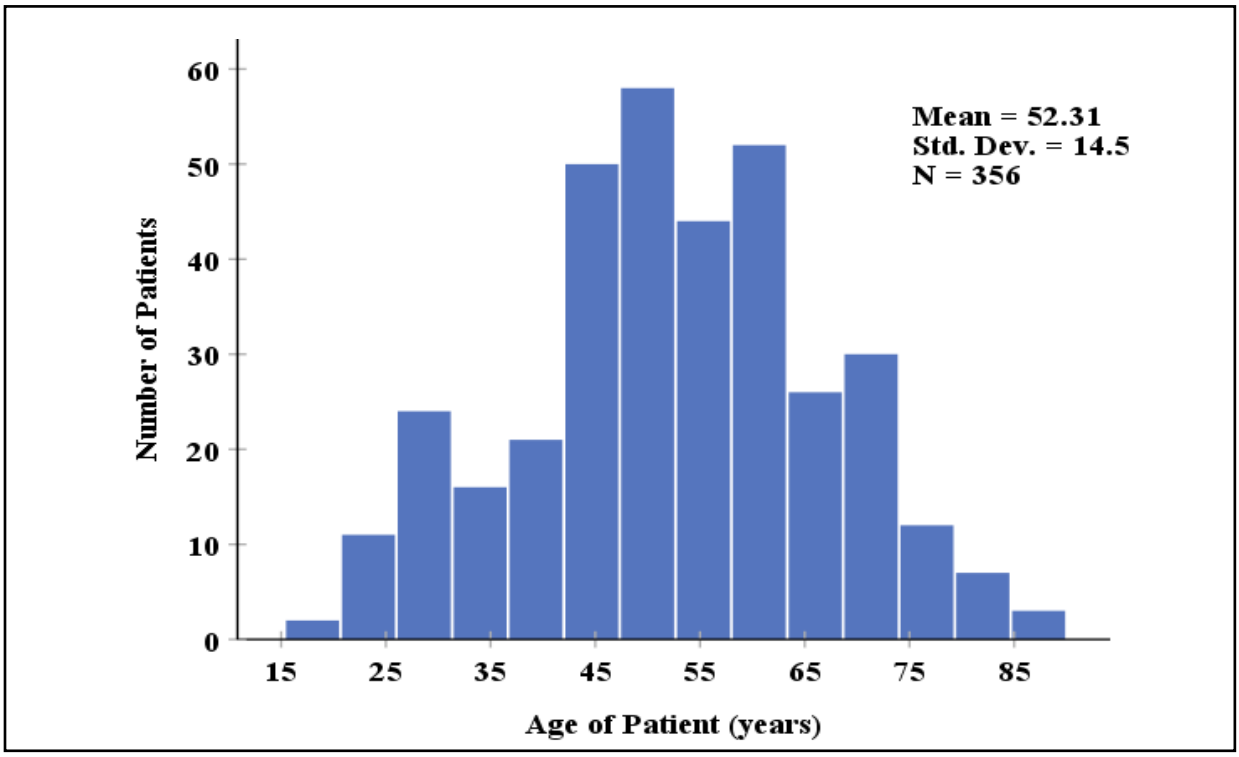
Table 2B

Patients over age 50 by Sex

		Sex		
		Female	Male	Total
Age	>50	161	36	197
	≤50	139	20	159
Total (n)		300	56	356

χ^2 (1 d.f.) =2.288, p=0.130

2A) Age Distribution of Patients



2B) Age Distribution of Patients by Sex

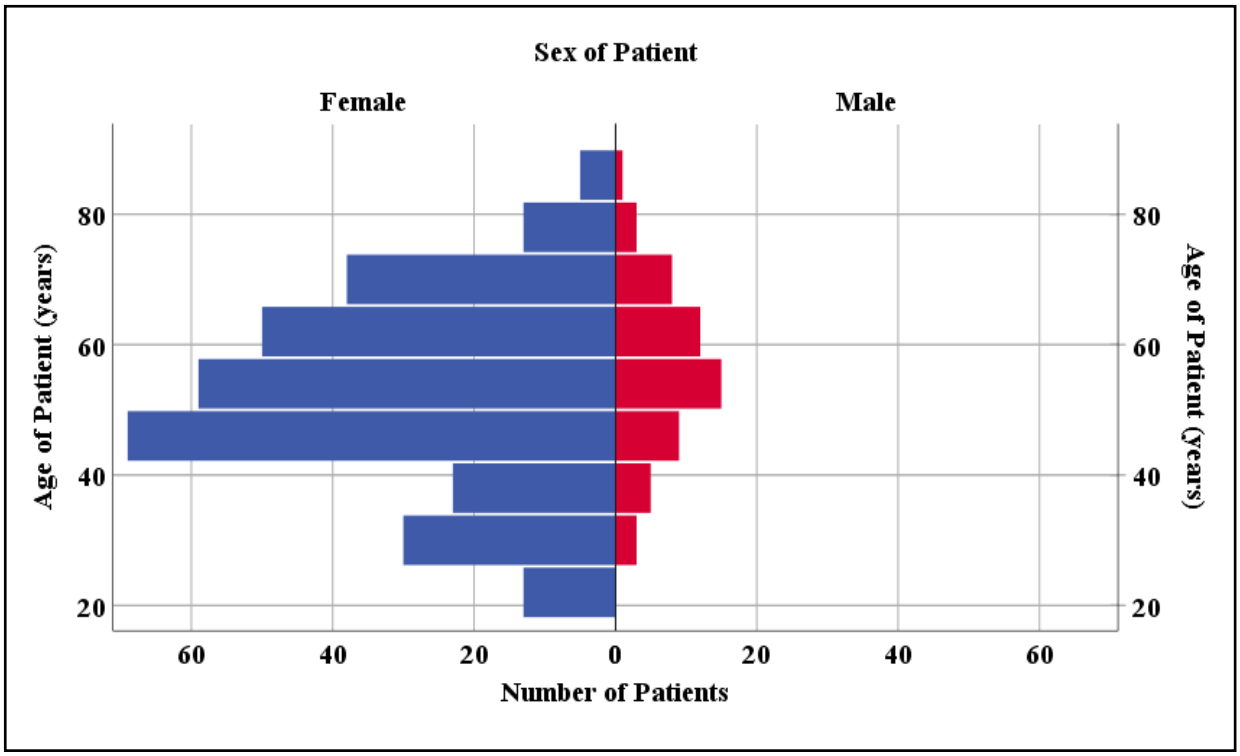


Figure 2: Age distribution of patients who attended an initial visit and were scheduled for a follow-up visit. 2A) The mean age of the 356 patients who attended an initial cancer genetic counseling visit and were scheduled for follow-up is 52.3 years old. **2B)** The age distribution of male and female patients was determined to be of equal variance and equal means.

Most of the patients seen during this period had cancer genetic testing during their initial cancer genetic counseling visit or came to their initial visit having already had cancer genetic testing. Most patients had gene panel testing (80%) (Table 3A and Figure 3A). The biggest proportion of panels were broad and targeted cancers of different organs ("multi-organ"), and the next most common panel ordered targeted breast cancer-related genes (23%) (Table 3B and Figure 3B). Approximately 7% had site-specific mutation testing, meaning testing for only one mutation in one gene (Table 3A and Figure 3A). These patients typically had a family member who had a known cancer-predisposing mutation and were being tested for that same mutation only (Appendix A). About 3% of patients had testing for only one gene, typically because their personal history and/or family history were consistent with one syndrome caused by mutations in only one gene (Table 3A and Figure 3A). For example, individuals with history of retinoblastoma and no other personal or family history of cancer were offered *RB1* testing because there are no other genes known to be associated with retinoblastoma at this time (Appendix B). A small proportion of patients who had a follow-up visit scheduled after an initial cancer genetic counseling session did not have genetic testing during or before the first visit (9%) (Table 3A and Figure 3A). Some of these patients did not have genetic testing because there was a different family member who would be more informative to test first, either because that person had a cancer history or was more closely related to an individual with cancer than our patient was. In these cases, the patient was scheduled to return to clinic after his or her family member underwent genetic counseling and possibly genetic testing, or after it was determined

that the family member was not going to proceed with genetic counseling or testing. Other patients who did not have genetic testing during or before their initial visit may have been missing critical records, such as past genetic testing results or the testing results of a family member. These patients were asked to bring these results to a follow-up visit during which genetic testing may be offered, understanding that testing could proceed without obtaining the previous testing results, but that testing would most likely be more informative if results from an affected family member were available.

Table 3: The type of genetic testing patients had either before their initial visit or ordered during their first genetic counseling appointment

Table 3A
Type of Genetic Test Ordered

	Number	Percent
Site-specific mutation†	25	7
None	33	9
Panel‡	282	80
Single Gene	11	3
Total (n)*	351	100

*Type of genetic test was undocumented for 5 patients.
† "Site-specific mutation" refers to testing one mutation in one gene, typically one previously identified in a family member.
‡ "Panel" testing means testing of at least two genes.

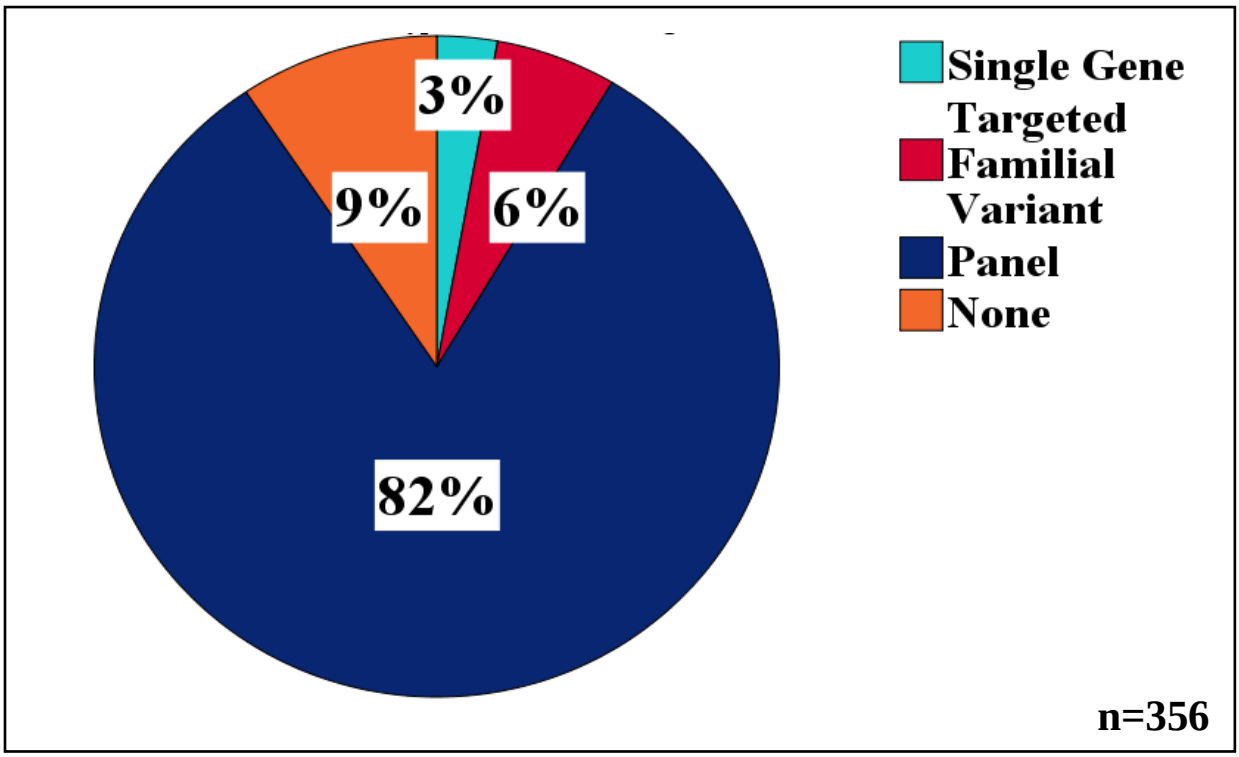
Table 3B

Type of Gene Sequencing Panel Ordered

	Number	Percent
Breast	64	23
Colon	24	9
Multi-organ*	91	32
Melanoma	4	1
Ovarian	37	13
Ovarian and Uterine	47	17
Pancreatic	2	0.7
Paraganglioma	1	0.4
Prostate	1	0.4
Renal	10	4
Uterine	1	0.4
Total (n)	282	100

*"Multi-organ" refers to broad panels that include multiple cancer sites and syndromes that are unrelated.

3A) Type of Genetic Testing Ordered



3B) Type of Gene Panel Ordered

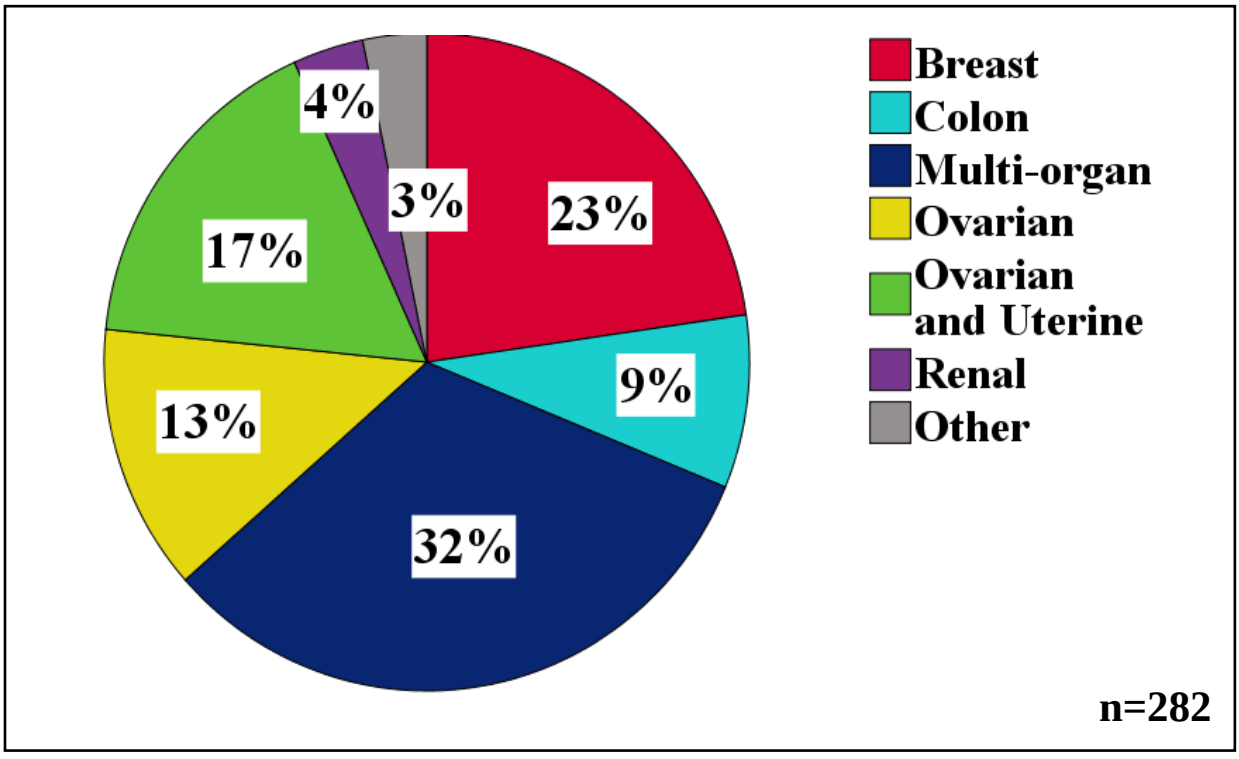


Figure 3: Type of genetic testing ordered for patients who attended an initial cancer genetic counseling visit and were scheduled for a follow-up visit. 3A) Patients had either no genetic testing, panel testing (meaning two or more genes were tested concurrently), single gene testing, or targeted familial variant testing (meaning testing for one mutation that had been identified previously in a family member). **3B)** There were multiple types of genetic testing panels utilized for the 282 patients that had panel testing. Panels typically included genes in which mutations cause a particular type of cancer, however some were broader ("multi-organ").

3.2 Analyses of factors hypothesized to predict patient follow-up visit attendance

During 2016 and 2017, there were 291 patients who were offered and elected to have cancer genetic testing at their initial visit, the results of which were to be disclosed at a follow-up visit. Of these patients, 225 attended their scheduled results disclosure visit (225/291 = 77%). Of the 225 patients who attended their scheduled results disclosure visit, 82 were scheduled for another follow-up visit to further discuss whether there were updates in medical management and/or family testing recommendations due to a cancer-predisposing mutation, or to discuss whether there was updated information on a variant of uncertain significance that had been detected on testing. There was a large drop-off in attendance between the results-return follow-up visit and the next return visit, with a 17% attendance rate (14/82) (Figure 4, Row A). For the 82 patients scheduled for an additional follow-up appointment, the reasons for this appointment as documented by the genetic counselor were either to discuss whether there was an update in variant of uncertain significance classification (37/82 = 45%), whether there were updates in cancer screening and medical management for patients with a cancer-predisposing mutation (20/82 = 25%), or another reason such as discussing the possibility of additional genetic testing or revisiting the topic of testing relevant family members (25/82 = 30%) (Figure 5).

There were 33 patients in the study period that did not have genetic testing ordered during or before the first genetic counseling visit. These patients intended to get more information from a family member, such as their genetic testing results before proceeding with

testing themselves. If they were unable or unwilling to coordinate with their family, genetic testing was typically offered to them. All 33 of these patients were scheduled for a return visit, of which 10 attended (30%) to revisit genetic testing (Figure 4, Row B).

Another alternate genetic counseling track included 32 patients who already had genetic testing ordered and the results disclosed by another provider by the time of the initial cancer genetic counseling visit. The purpose of their initial visit with the genetic counselor was to discuss the implications of a positive genetic testing result or a detected variant of uncertain significance. These patients were all scheduled for a follow-up genetic counseling visit to further discuss the personal and familial implications of their positive genetic testing or to discuss any updated variant of uncertain significance information. Of these of 32 patients, 8 attended (25%) their follow-up cancer genetic counseling appointment (Figure 4, Row C).

4) Cancer Genetic Counseling Visit Tracks and Attendance Rates

	Initial Visit	Follow-up Visit	Follow-up Visit
A	Based on family and/or personal history, genetic testing is offered and ordered **291**	Genetic testing results return **225/291 (77%)**	Update management Family testing Update VUS **14/82 (17%)**
B	More information is needed before offering testing **33**	Patient brings records, testing possibly offered **10/33 (30%)**	
C	Discuss genetic testing results ordered by another provider **32**	Update VUS status Update management Family member testing strategy **8/32 (25%)**	

Figure 4: The number of patients who attended initial cancer genetic counseling visits and follow-up visits. There are typically three possible visit tracks that each cancer genetic counseling patient underwent during the study period. Most patients followed track A, in which the patient was offered genetic testing by the genetic counselor based on analysis of the patient's personal and family history, and the patient elected testing and had a sample drawn the same day. A follow-up appointment to disclose and discuss the genetic testing results was scheduled for one month after the initial visit. 82 of the patients who attended their results return appointment were scheduled for another follow-up visit 6-12 months later, typically because the patient was positive for a cancer-predisposition gene and personal and family management guidelines were to be discussed at the next visit, or because the patient had a variant of uncertain significance (VUS) and updated information and classification status were to be discussed. Patients on track B did not have a sample drawn for genetic testing at the first genetic counseling visit, usually because they were not the ideal candidate for testing in the family or additional records were needed before ordering testing such as a family member's testing results. These patients were scheduled for a follow-up visit 2-6 months later to re-evaluate the possibility of genetic testing once the patient gathered more information or if it was determined that the patient would not be able to gather more information. Patients who followed track C came to the initial cancer genetic counseling appointment having already had genetic testing through a different provider and were referred to further discuss implications of the test results for personal medical management and for family members. All 32 of these patients were scheduled for a follow-up appointment in 6-12 months to further discuss medical recommendations based on the patient's positive test result, or possible reclassification of a variant of uncertain significance result. The number of patients who attended each type of visit is shown in bold.

5) Stated Reason for Recommended Follow-up Visit after Genetic Testing Results Disclosure Visit

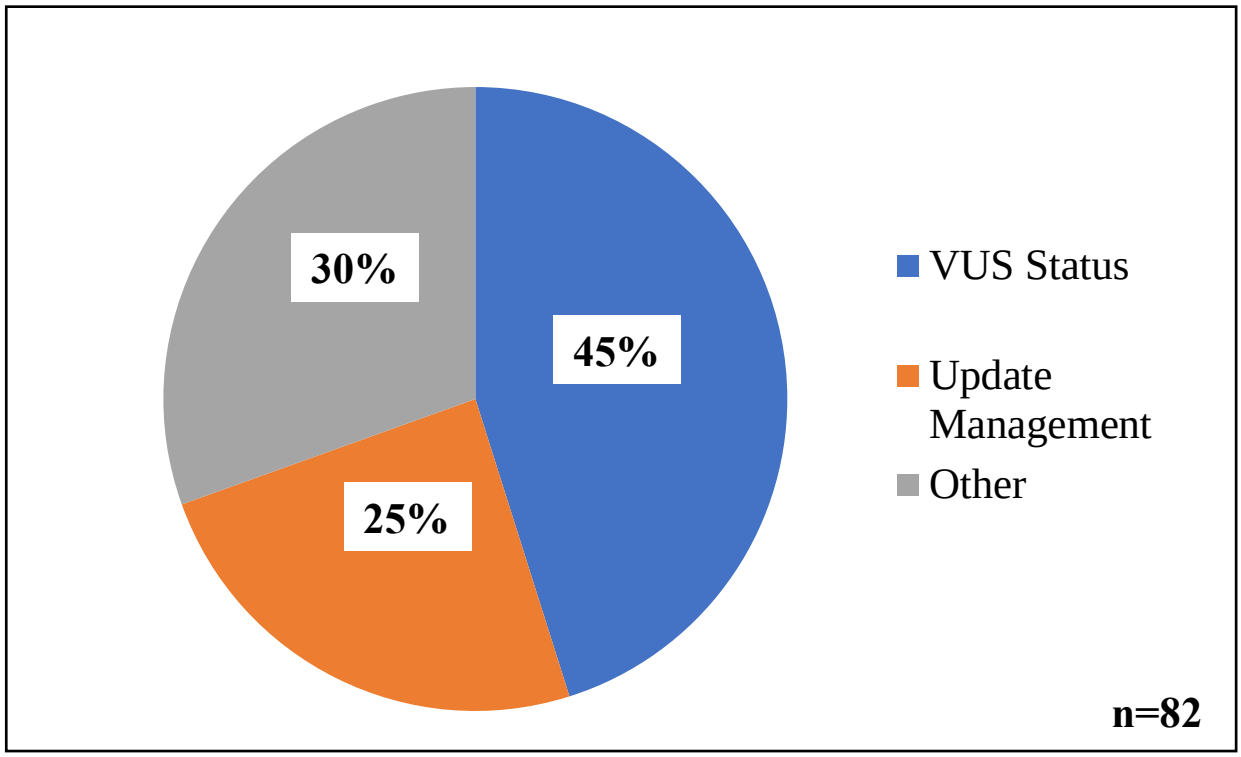


Figure 5: Referral indications for a cancer genetic counseling follow-up visit after the results disclosure visit. Of the 291 patients who attended their genetic testing results disclosure visit, 82 were recommended by the genetic counselor to have another follow-up visit. The documented reasons for the follow-up visit include reviewing whether there is an update in classification status of a variant of uncertain significance, reviewing whether there are updated medical management guidelines for the patient's cancer-predisposing mutation, or for other reasons which include but are not limited to discussing genetic testing for family members or additional testing options for the patient.

To determine predictors of whether a patient is at high-risk to miss their follow-up visit, we compared demographics, personal medical history, and family cancer history among patients who attended and patients who missed their results disclosure visit after an initial cancer genetic counseling visit. Patients who previously had genetic testing ordered by another provider and those who did not have genetic testing ordered at the initial visit were excluded because these small populations of patients may have very different motivations for returning to clinic

compared to those who are returning to receive and discuss their genetic testing results. Of the 291 patients scheduled for a results disclosure visit, 77% of patients (225/291) attended and 23% of patients missed their appointment, and therefore received their results by another mechanism (either by phone call, or from their referring provider (66/291) (Figure 6).

6) Results Disclosure Visit Attendance

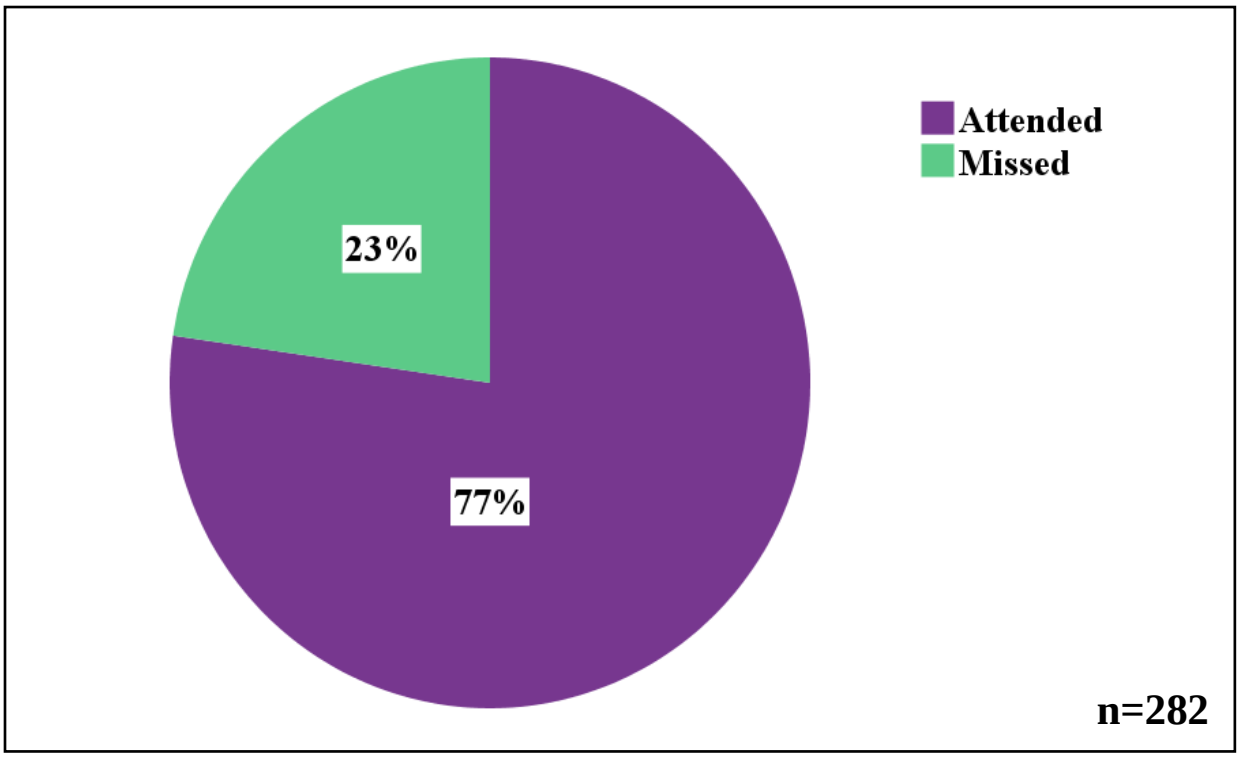


Figure 6: Attendance frequency for results disclosure return visits. Of the 356 patients who attended an initial cancer genetic counseling appointment during the study period, 291 had a sample drawn for genetic testing at the first visit. 77% of those patients attended their results-disclosure follow-up visit, and 23% did not attend their scheduled visit.

Demographic information that was collected and compared amongst patients who attended and missed their results disclosure visit include the sex, ethnicity, and age of the patient. Chi-square analysis showed there was no significant difference in the attendance rate for the genetic testing results disclosure visit for between men and women (χ^2 (1 d.f.) =0.173, p=0.677)

(Table 4A and Figure 7A). Additionally, there was no difference in individuals of Asian, Hispanic, and White ethnicity (other ethnicities did not have a large enough sample size for statistical analysis) (χ^2 (2 d.f.) =2.371, p=0.306) (Table 4B and Figure 7B). The median age for patients who attended their appointment was 57 years and the range was 65 years, from age 20 to 85 years-old. The median age was 54 years for patients who missed their appointment and range was 69 years, from age 18 to age 87 years-old (Figure 8). The mean age for those who attended their results disclosure visit (53 years) and those who missed the appointment (56 years) was not statistically different (t(289 d.f.) =-1.325, p=0.186) (Table 4C). These results suggest the patient's sex, ethnicity, and age are not predictive of whether they will attend their genetic testing results disclosure appointment.

Table 4: **Demographic factors of patients who attended and who missed results their results disclosure visit**

Table 4A

Results Return Attendance by Patient Sex

		Results Disclosure Visit Attendance		
		Attended	Percent	Total
Sex	Female	186	77	242
	Male	39	80	49
Total (n)		225		291

χ^2 (1 d.f.) =0.173, p=0.677

Table 4B

Results Return Attendance by Patient Ethnicity

		Results Disclosure Visit Attendance		
		Attended	Percent	Total
Ethnicity	Asian	38	83	46
	Hispanic	45	80	56
	White	94	73	129
Total (n)*		177		231

χ^2 (2 d.f.) =2.371, p=0.306

*Ashkenazi Jewish, Black, Indian subcontinent, Middle Eastern, mixed, and unknown ethnicities were excluded because of insufficient sample size for chi-square analysis.

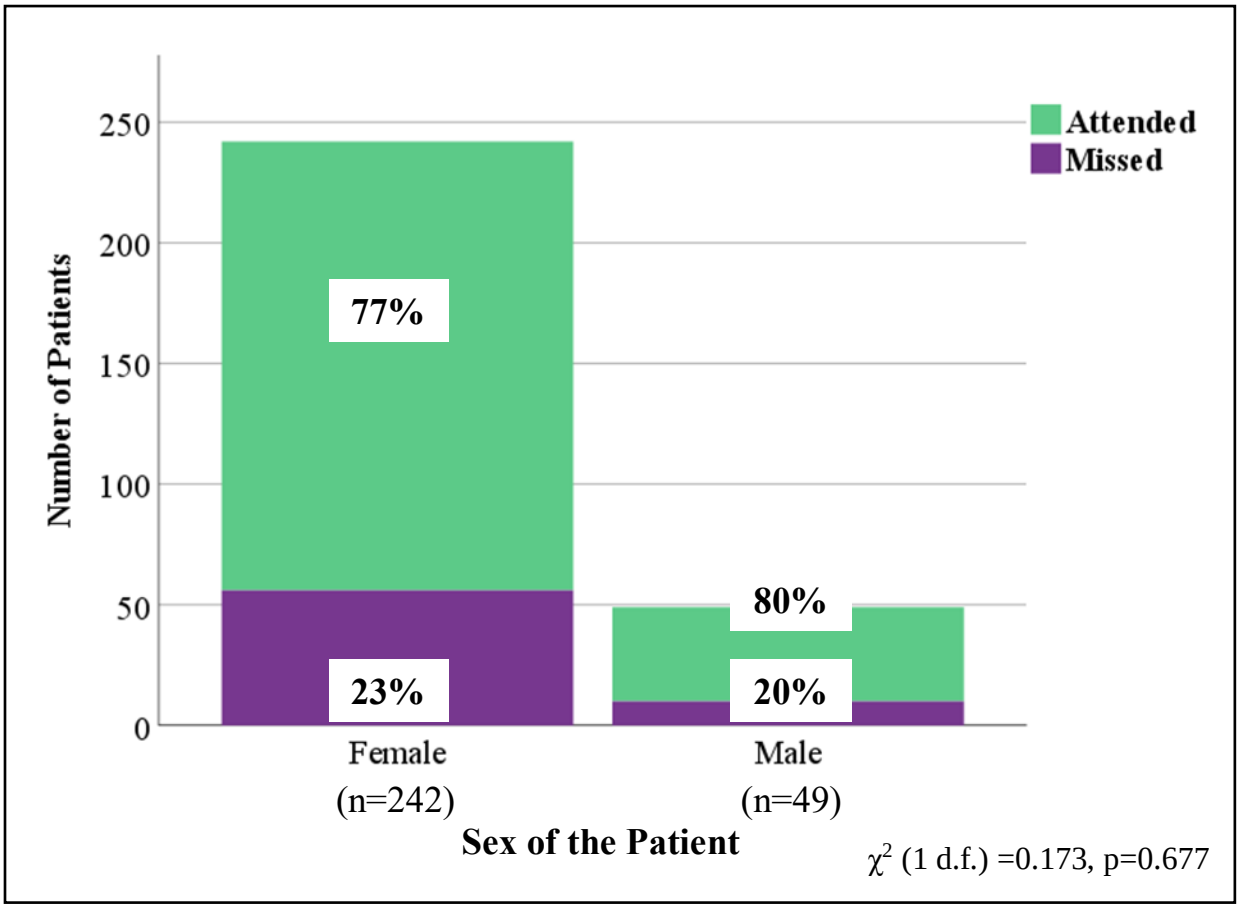
Table 4C

Results Disclosure Visit Attendance by Age of Patient

	Results Disclosure Visit Attendance	N	Mean	Std. Dev.
Age	Attended	225	53.4	14.0
	Missed	66	56.0	15.2

t(289 d.f.) =-1.325, p=0.186

7A) Results Disclosure Visit Attendance Rates by Patient Sex



7B) Results Disclosure Visit Attendance Rates by Patient Ethnicity

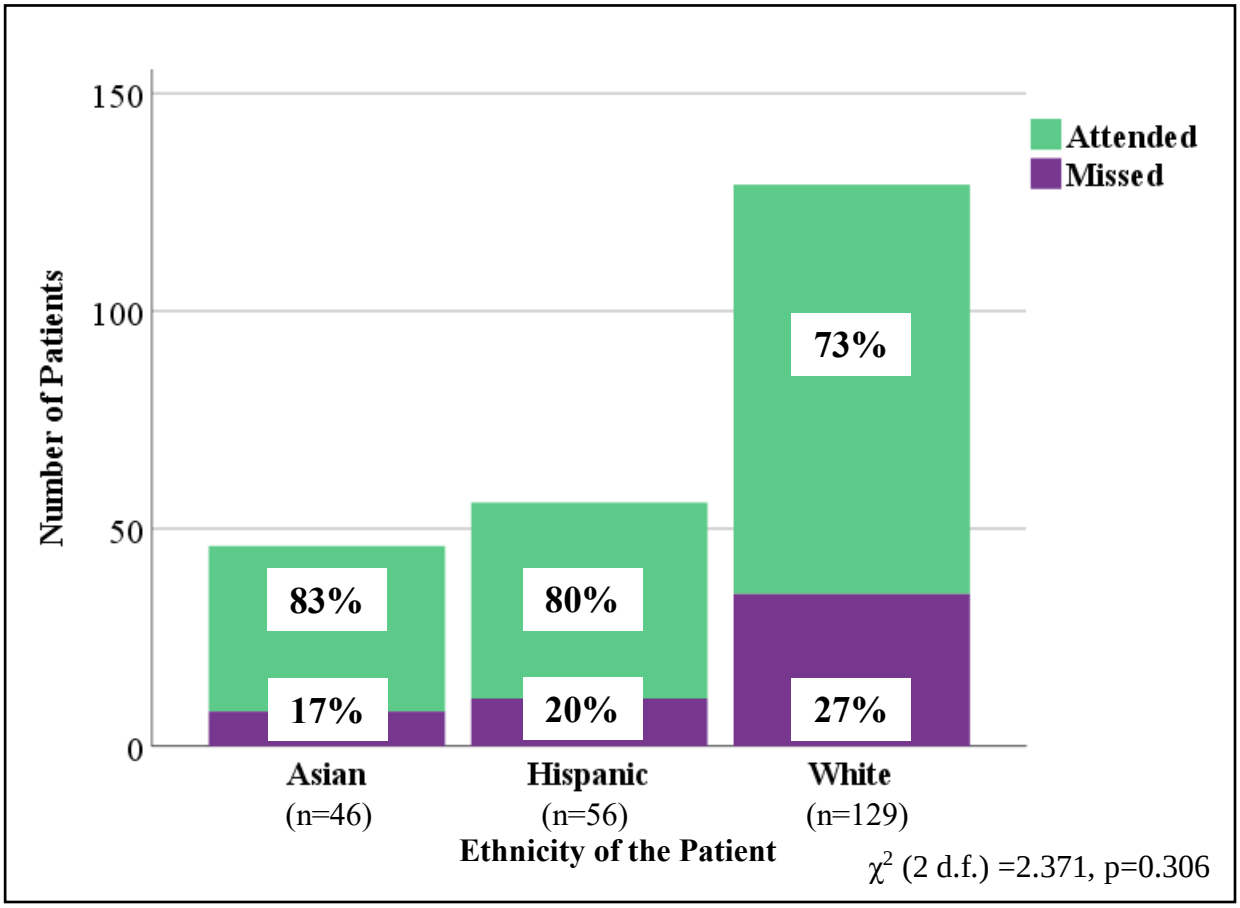


Figure 7: Comparisons of patient sex, ethnicity, and mean ages of age for patients who missed and who attended their results disclosure visit 7A. Chi-square analysis found that the attendance rate between men and women was no different than expected. **7B.** Chi-square analysis determined results disclosure attendance did not differ between different ethnicities from the expected attendance rate.

8) Patient Age Distribution by Results Disclosure Attendance

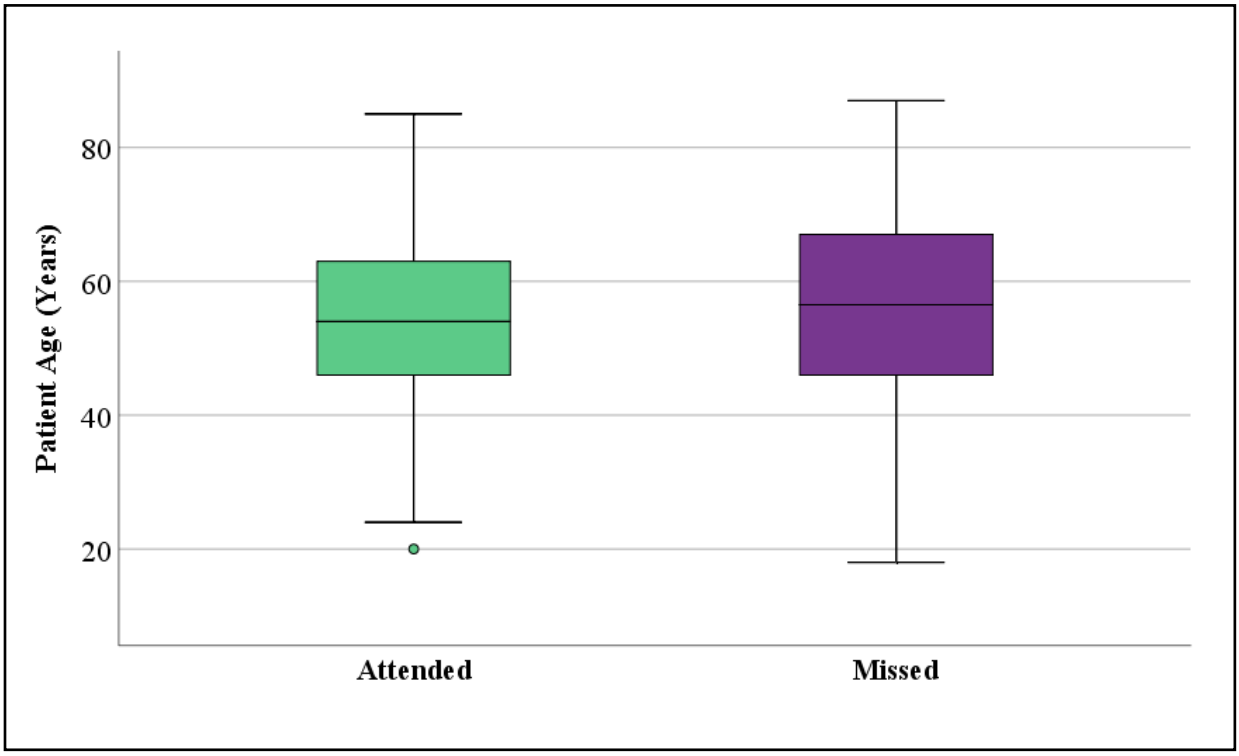


Figure 8: The distribution of ages of patients who missed and patients who attended their results disclosure visit. The medians are represented by the black line in the middle of each box, 54 years for the attended visit group, 57 years for the missed visit group. Each box represents the 25th to the 75th percentile age range. The bars represent the minimum and maximum values with the exception of one outlier (green dot), which is defined as any value 1.5 box lengths from the median.

To determine whether there is a relationship between the patient's personal experience with cancer and cancer genetic testing and results disclosure visit attendance, we preformed chi-square analysis to compare patients who attended their visit to those who missed their visit. A reasonable hypothesis might be that a patient who has a personal history of cancer would be more likely to attend his or her results return visit, perhaps out of a greater concern or perceived risk for a cancer-predisposing mutation; however, chi-square analysis found no significant difference in attendance rate in patients who currently have cancer (81% attended), who previously had had cancer (76% attended), and who have never had cancer (73% attended)

(Table 5 and Figure 9A) (χ^2 (2 d.f.) =1.820, p=0.403). Similarly, results disclosure attendance rate did not differ between different referral indications for the initial cancer genetic counseling visit. 85% of patients who had been referred due to their personal medical history attended their results disclosure visit, compared to 76% of patients who were referred due to family history, and 77% of the patients referred due to both a personal and family history (χ^2 (2 d.f.) =1.221, p=0.543) (Table 5 and Figure 9B). Additionally, the type of genetic test that was ordered either prior to the initial genetic counseling visit or during the first visit does not appear to influence results disclosure attendance (χ^2 (1 d.f.) =0.052, p=0.820) (Table 5 and Figure 9C).

Table 5: Frequencies of personal medical history factors of patients who attended and who missed results their results disclosure visit.

Results Disclosure Attendance by Patient Personal Cancer History

		Results Disclosure Visit Attendance		
		Attended	Percent	Total
Cancer history	Current*	109	81	135
	Previous	56	76	74
	None	60	73	82
Total (n)		225		291

χ^2 (2 d.f.) =1.820, p=0.403

*Individuals who had both a current and previous cancer diagnosis were included in the current category for this analysis.

Results Disclosure Attendance by Referral Indication

		Results Disclosure Visit Attendance		
		Attended	Percent	Total
Referral indication	Personal History	28	85	33
	Family History	50	76	66
	Both	147	77	192
Total (n)		225		291

χ^2 (2 d.f.) =1.221, p=0.543

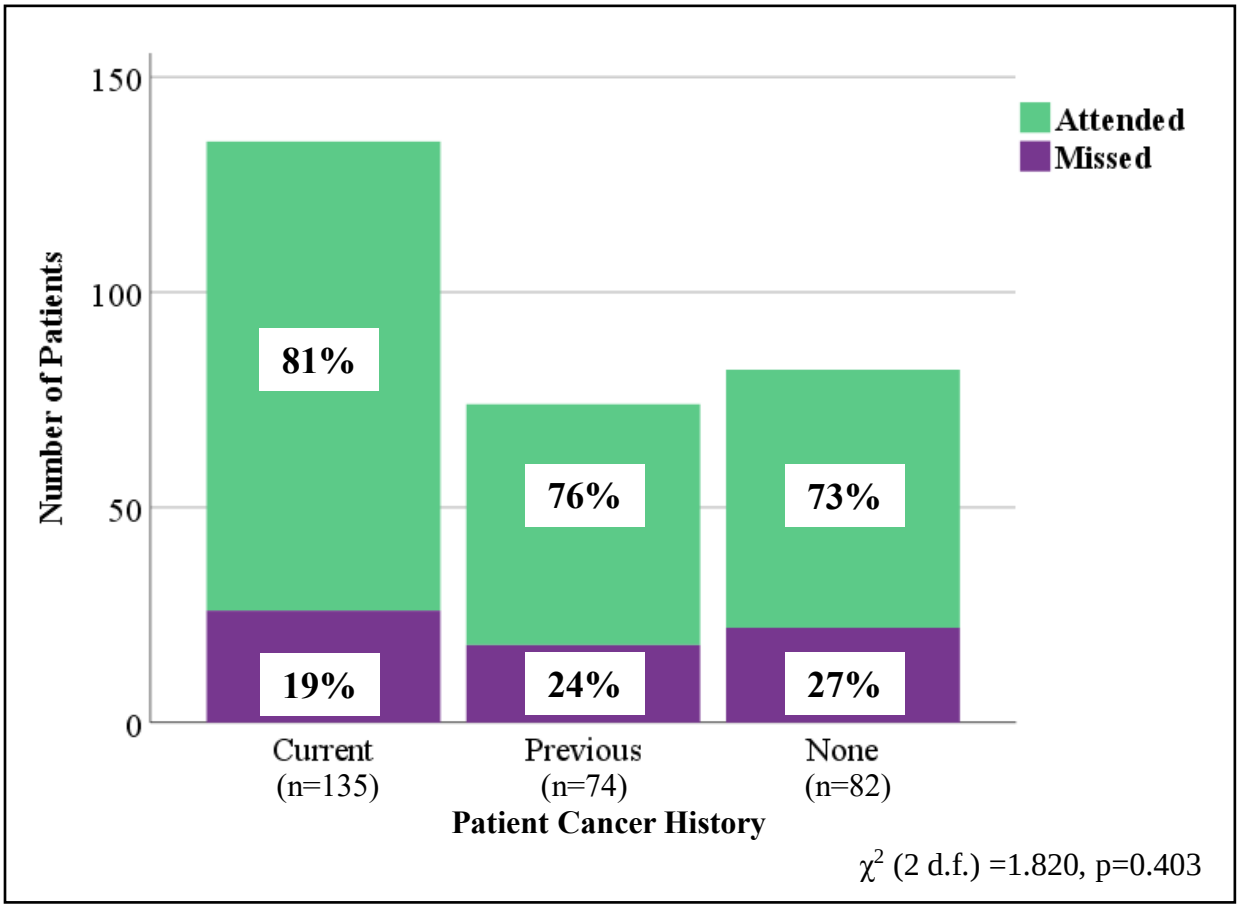
Results Disclosure Visit Attendance by Genetic Testing Type Ordered

		Results Disclosure Visit Attendance		
		Attended	Percent	Total
Test type	Panel	200	81	258
	Targeted*	25	73	33
Total (n)		225		291

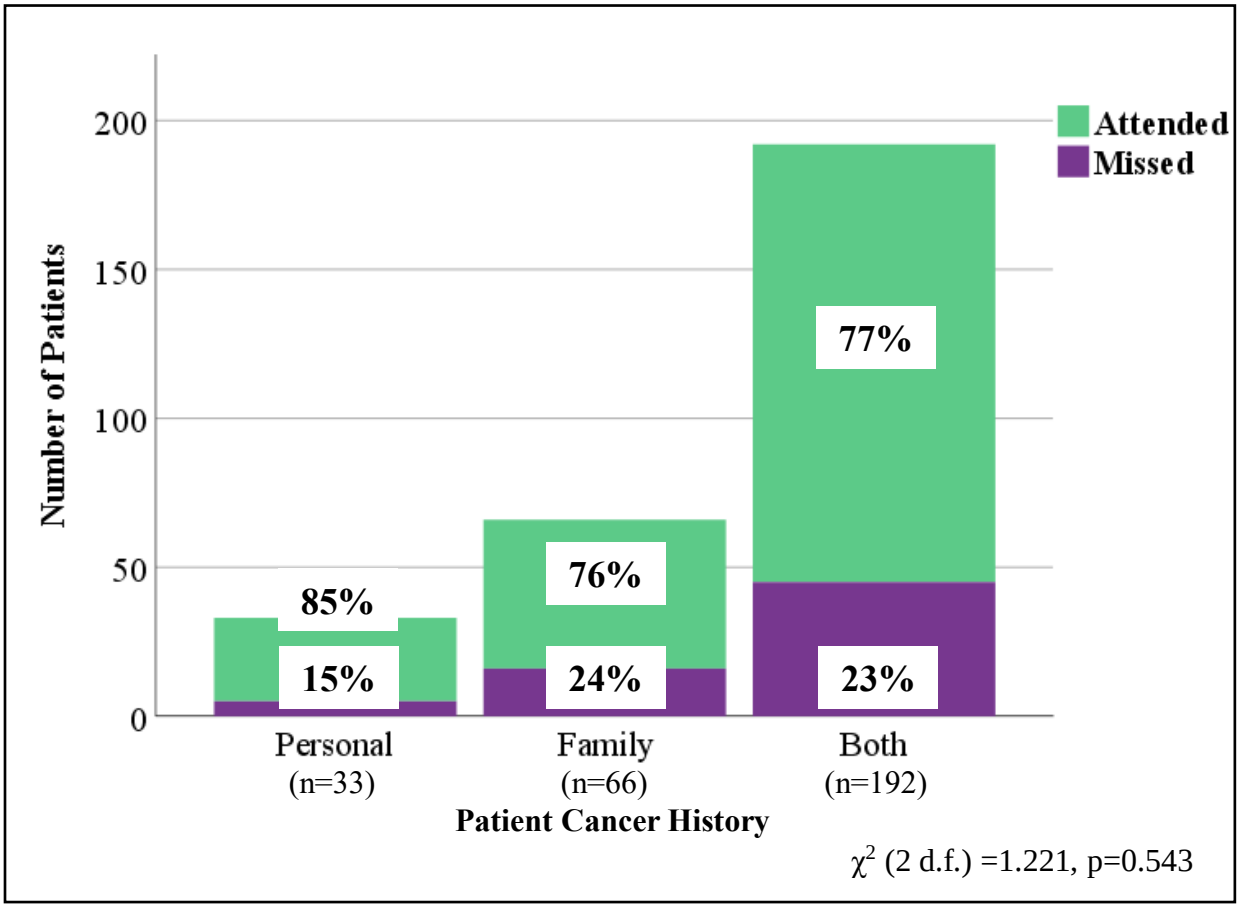
χ^2 (1 d.f.) =0.052, p=0.820

* ”Targeted” testing includes both single gene testing and site-specific mutation testing.

9A) Results Disclosure Visit Attendance by Patient Cancer History



9B) Results Disclosure Visit Attendance by Referral Indication



9C) Results Disclosure Visit Attendance by Genetic Testing Type

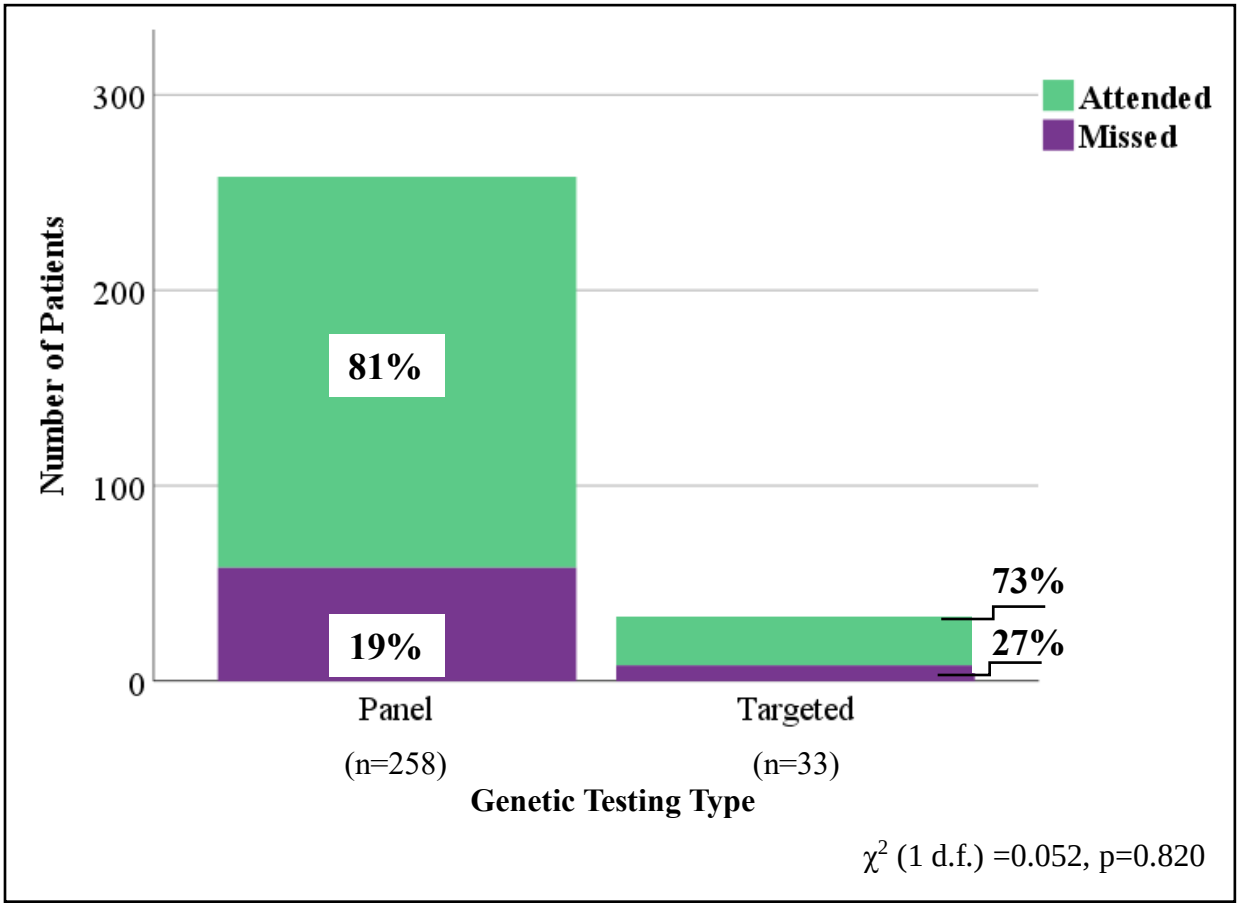


Figure 9: Comparisons of patient personal cancer history, referral indication, and type of genetic testing for patients who missed and who attended their results disclosure visit 9A) Chi-square analysis showed that the attendance rates for patients who had a current cancer diagnosis, a previous diagnosis, or had never had cancer did not differ. **9B)** Referral indication for the initial cancer genetic counseling visit did not influence results disclosure visit attendance rate according to chi-square analysis. **9C)** There was no difference in attendance rate for individuals who had targeted testing compared to those who had gene panel testing, defined as testing of two or more genes concurrently. Targeted testing in this analysis includes both individuals who had single gene testing and those with targeted familial mutation testing.

The potential genetic risk to a patient's children led to the hypothesis that cancer genetic counseling patients who are parents were more likely to have attended their results disclosure visit. Chi-square analysis revealed that patients who have children were more likely to attend their results disclosure visit than patients who do not have children (χ^2 (1 d.f.) =6.896, p=0.009)

(Table 6 and Figure 10A). When parent-status was analyzed separately by sex, mothers were more likely to attend their results disclosure visit than women who did not have children ($p=0.01$). There was no statistically significant difference in the likelihood for fathers to attend their appointment, in comparison to men who did not have children (Fisher's Exact $p = 0.442$). However, the direction of this relationship is in the same direction as for mothers (Table 6 and Figure 10B-C); because of the sample size, there was limited power to investigate this relationship in the male sample.

Table 6: Frequencies of parents and individuals without children who attended and who missed results their results disclosure visit

Results Disclosure Attendance for Patients by Parent-Status

		Results Disclosure Visit Attendance		
		Attended	Percent	Total
Parent-Status	No Children	52	67	78
	Has Children	173	81	213
Total (n)		225		291

χ^2 (1 d.f.) =6.896, p=0.009

Results Disclosure Attendance for Female Patients by Parent-Status

		Results Disclosure Visit Attendance		
		Attended	Percent	Total
Parent-Status	No Children	42	66	64
	Has Children	144	81	178
Total (n)		186		242

χ^2 (1 d.f.) =6.175, p=0.013

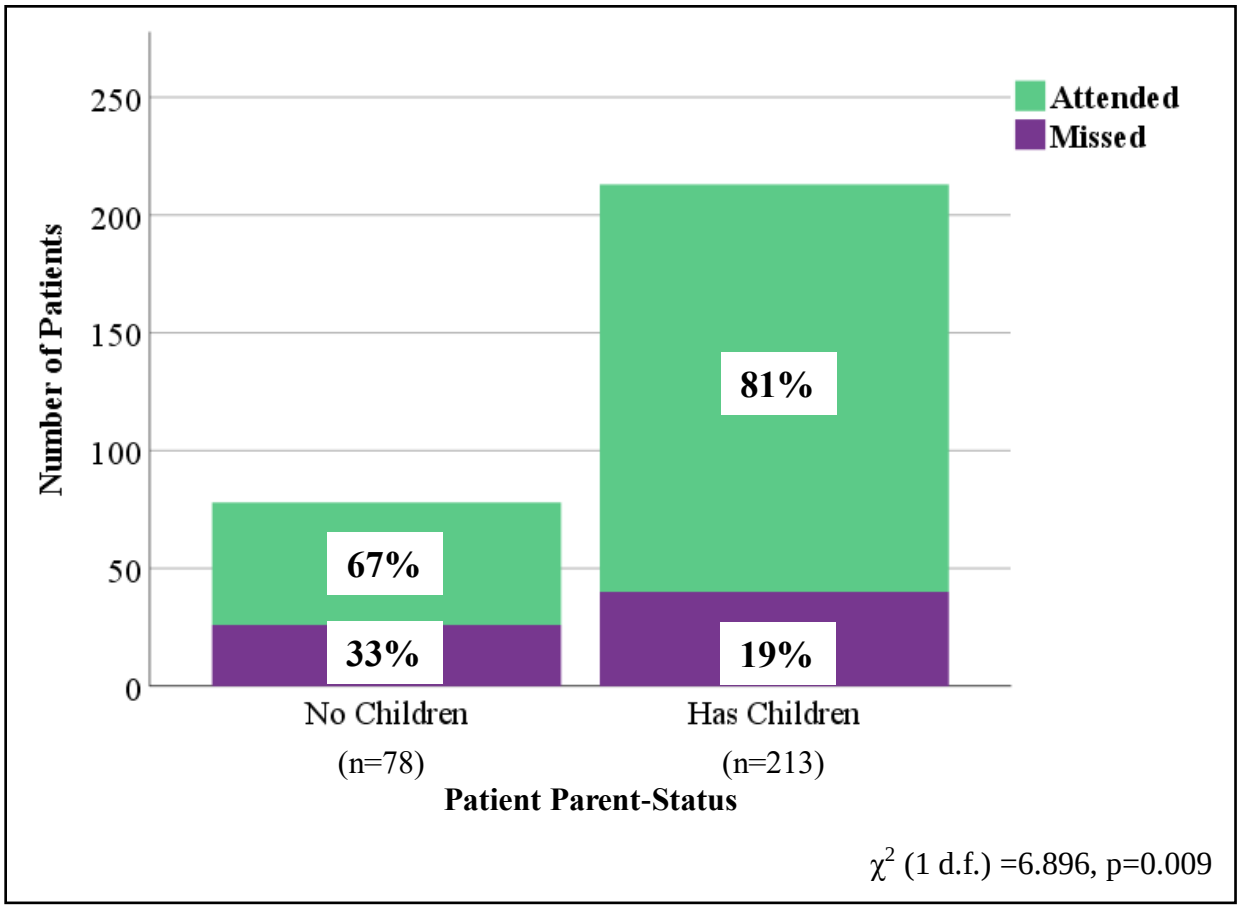
Results Disclosure Attendance for Male Patients by Parent-Status

		Results Disclosure Visit Attendance		
		Attended	Percent	Total
Parent-Status	No Children*	10	71	14
	Has Children	29	83	35
Total (n)		39		49

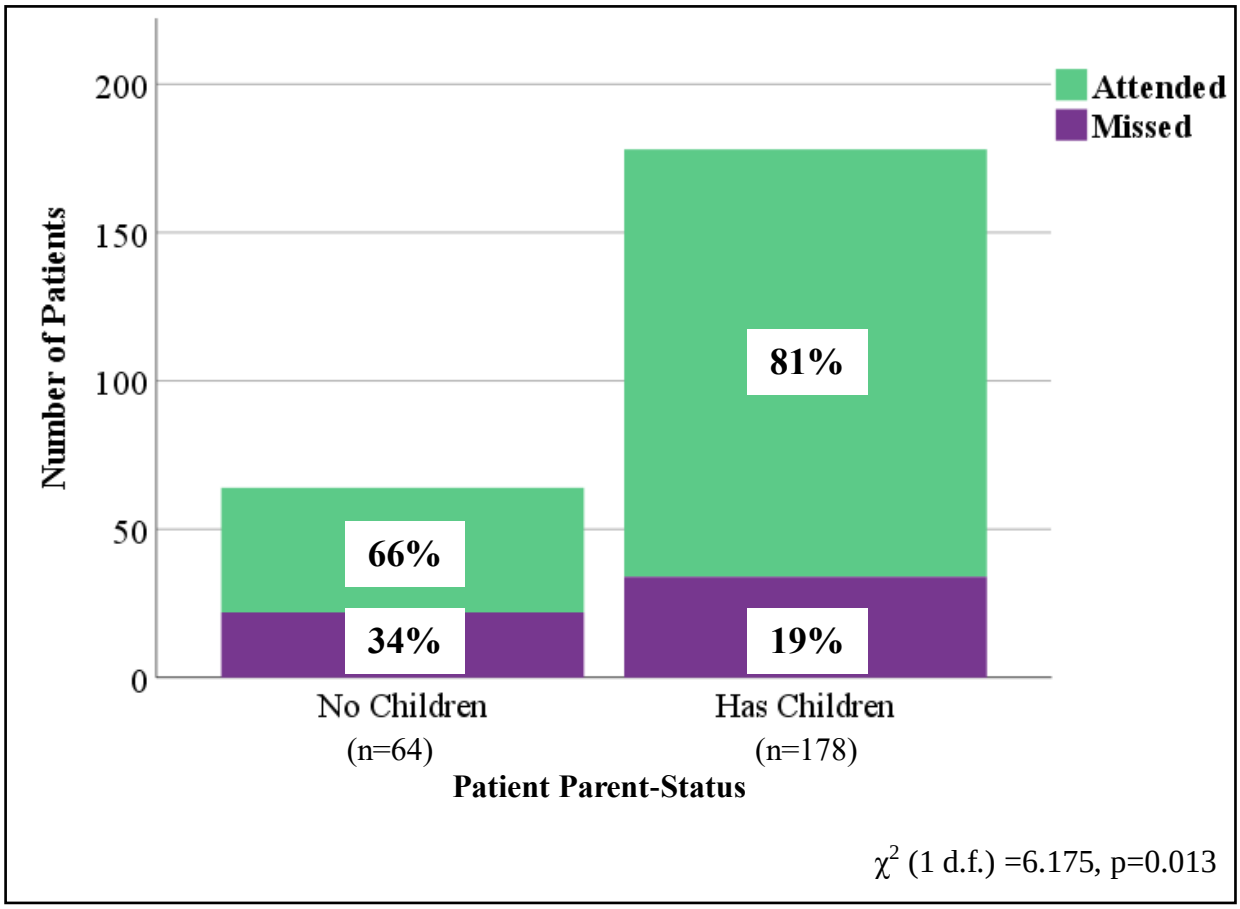
Fisher's Exact p=0.442

*One cell had an expected count less than 5 for statistical analysis. The minimum expected count was 2.86.

10A) Results Disclosure Visit Attendance by Parent-status



10B) Results Disclosure Visit Attendance for Female Patients by Parent-status



10C) Results Disclosure Visit Attendance for Male Patients by Parent-status

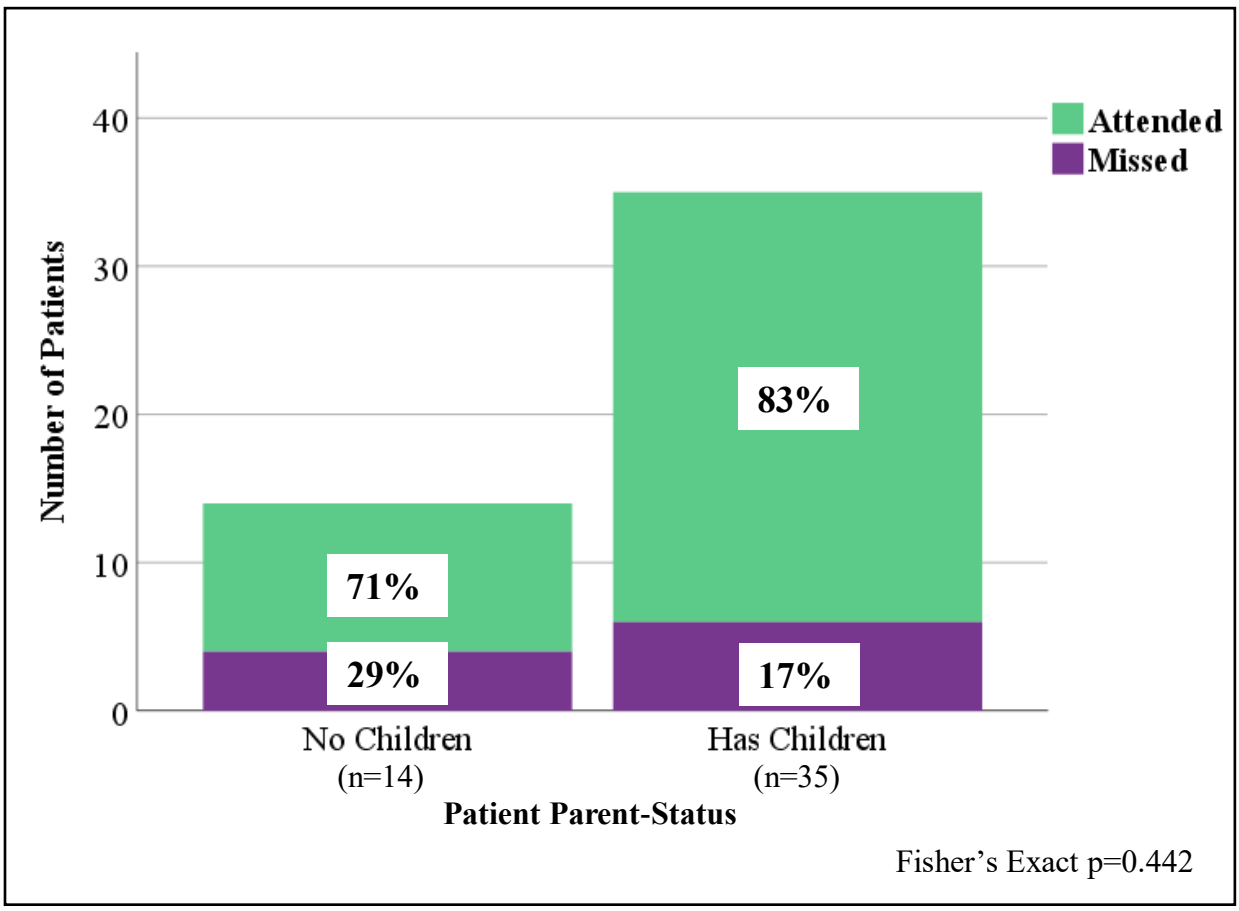


Figure 10: Comparisons between patients who attended and missed their results disclosure visit by whether they have children 10A) Chi-square analysis revealed that patients who are biological parents were more likely to attend their results disclosure appointment than expected **10B)** Chi-square analysis showed that the higher-than-expected attendance rate was upheld in female parents. **10C)** Fathers were more likely than men without biological children to attend their results disclosure, but this result is not statistically significant.

Because a strong family history of cancer increases a patient's risk to have a hereditary cancer syndrome, it was hypothesized that patients who had a greater number and greater proportion of closely related relatives with cancer history would be more likely to attend their results-disclosure visit. The mean total number of first-degree relatives for each patient was approximately 6 relatives, with a minimum of 1 relative and maximum of 19. The mean number

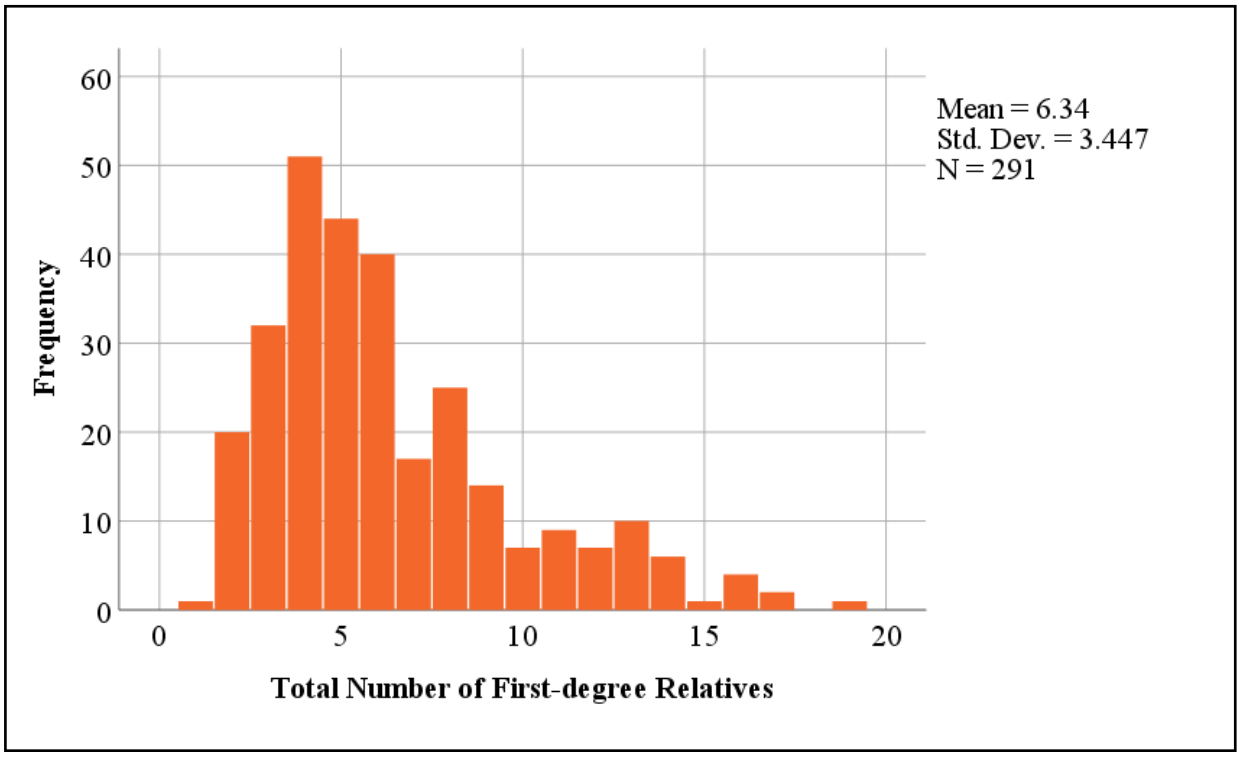
of affected first-degree relatives for patients who attended their appointment was 1.3 relatives compared to 1.5 relatives for those missed their appointment. The mean number of affected first-degree relatives was not significantly different between patients who attended and patients who missed their results disclosure appointment (t(289 d.f.) =-0.991, p=0.332) (Table 7 and Figure 11A). The mean total number of second-degree relatives was approximately 13 people, with a minimum of 0 relatives and maximum of 40 relatives. The average number of affected second-degree relatives for patients who attended their appointment was 1.9 relatives, and 2.2 second-degree relatives for patients who missed their appointment which is not significantly different (t(289 d.f.) =-1.077, p=0.283) (Table 7 and Figure 11B). Additionally, the mean proportion of affected first-degree relatives and of affected second-degree relatives did not differ between patients who attended and patients who missed their results-disclosure visit (t(289 d.f.) =-1.153, p=0.250 for first-degree relatives, t(88.8 d.f.) =-1.598, p=0.114 for second-degree relatives) (Table 8 and Figure 12). These data suggest the number of and proportion of first and second-degree relatives who had a reported cancer history did not significantly impact the results disclosure attendance rate.

Table 7: **Mean number of first and second-degree relatives of the patient that reportedly have had cancer**

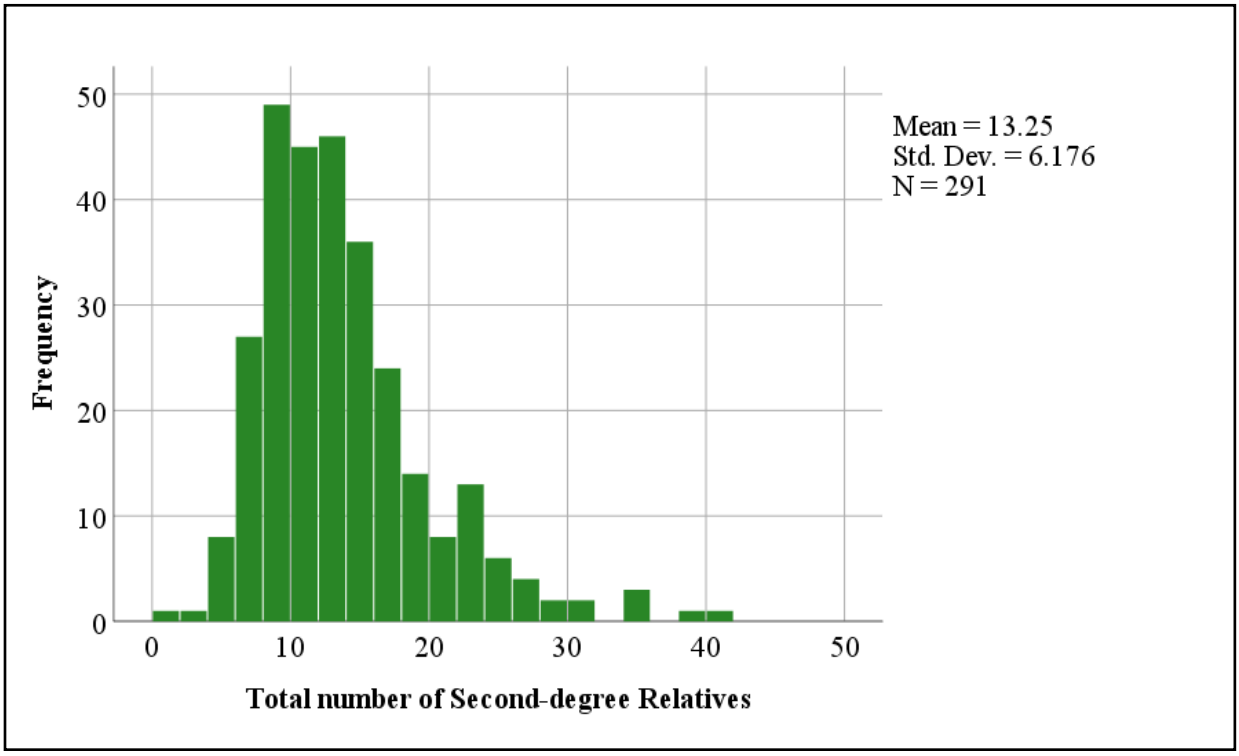
	Second Visit Attendance	N	Mean
Number First-degree Relatives Affected	Attended	225	1.3
	Missed	66	1.5
Number Second-degree Relatives Affected	Attended	225	1.9
	Missed	66	2.2

First-degree relatives: t(289 d.f.) =-0.991, p=0.332
Second-degree relatives: t(289 d.f.) =-1.077, p=0.283

11A) Number of First-degree Relatives in Each Patient's Family



11B) Number of Second-degree Relatives in Each Patient's Family



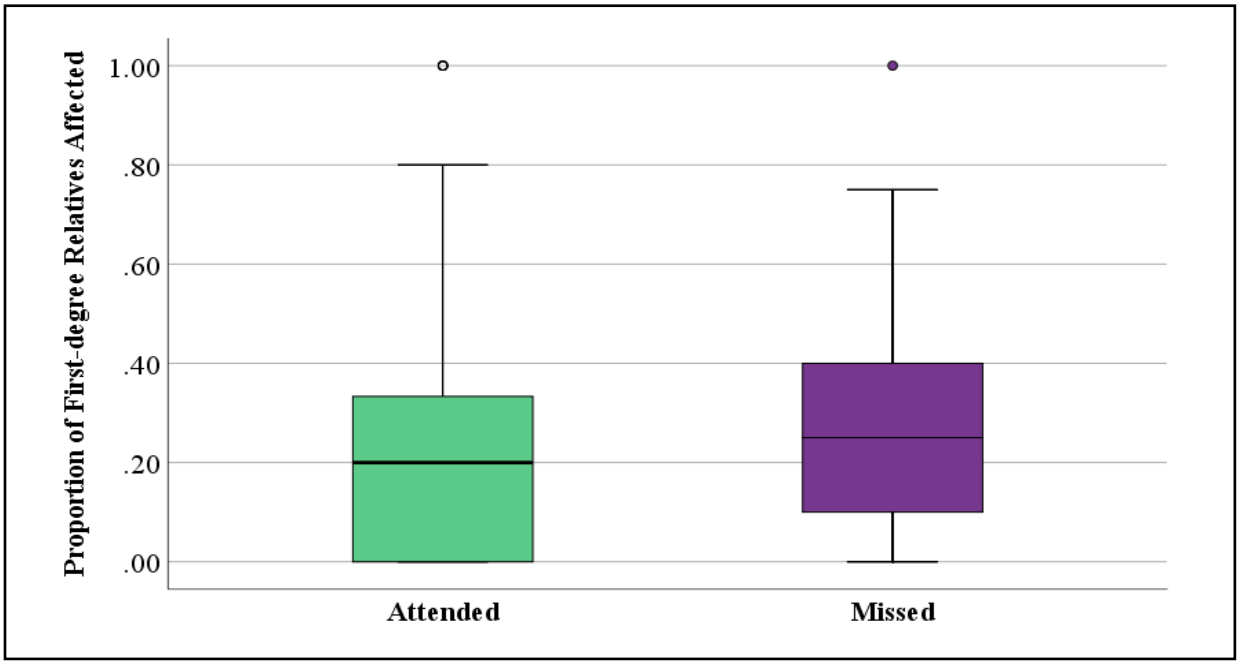
<u>Figure 11</u>: The number of first and second-degree relatives in each patient's family. 11A) The mean total number of first-degree relatives reported by patients at the initial cancer genetic counseling appointment. **11B)** The mean total number of second-degree relatives reported by patients at the initial cancer genetic counseling appointment.

<u>Table 8</u>: Mean proportion of first and second-degree relatives of the patient that reportedly have had cancer

	Second Visit Attendance	N	Mean
Proportion First-degree Relatives Affected	Attended	225	0.24
	Missed	66	0.27
Proportion Second-degree Relatives Affected	Attended	225	0.16
	Missed	65	0.20

First-degree relatives: t(289 d.f.) =-1.153, p=0.250
Second-degree relatives: t(88.8 d.f.) =-1.598, p=0.114

12A) Distribution of Proportion of Affected First-degree Relatives by Results Disclosure Visit Attendance



12B) Distribution of Proportion of Affected Second-degree Relatives by Results Disclosure Visit Attendance

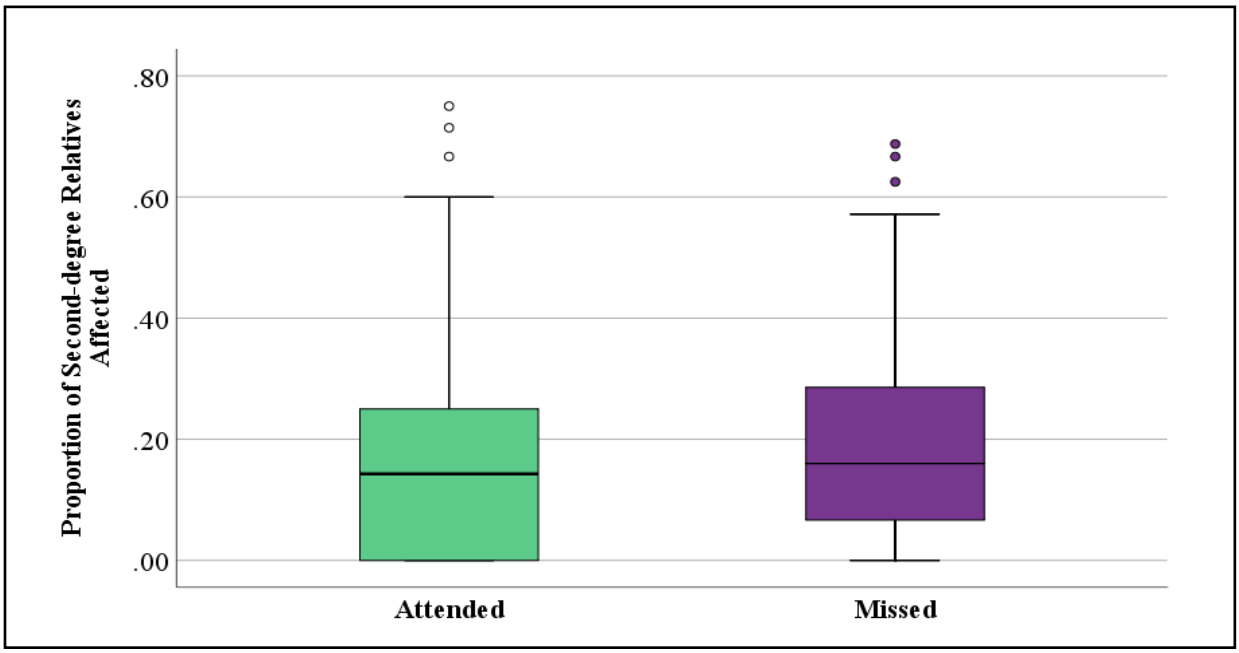


Figure 12: The proportion of first and second-degree relatives affected with cancer. 12A) The distribution of reported first-degree relatives with cancer history. **12B)** The distribution of reported first-degree relatives with cancer history. Black lines represent the median proportions, and the boxes signify the 25th to 75th percentiles for proportion of affected relatives. The bars represent the minimum and maximum values, except for outliers (dots), which are values 1.5 box lengths from the median.

IV. DISCUSSION

Medical providers often interact with their patients across multiple visits rather than simply a first visit to clinic. In the context of cancer genetic counseling, follow-up visits may involve genetic testing results disclosure, discussion of how a patient's medical management should change based on testing results, recommendations for cancer screening and prevention, and coordinating genetic testing for at-risk family members. However, with each scheduled follow-up appointment for a patient, there is a possibility that the patient does not attend that visit and as a result loses the opportunity to discuss critical personal and family health recommendations. The aim of this retrospective chart review was to identify the attendance rate of cancer genetic counseling follow-up visits from patients at UCI that had an initial visit in 2016 or 2017, and to identify factors that differed between patients who attend and patients who miss these visits. Understanding which patients are more likely to miss their follow-up visits can help genetics providers identify at-risk patients who may require a different method or timeline in communicating critical health information.

4.1 Cancer genetic counseling follow-up visit attendance rates

This study recorded visit attendance for patients who had an initial cancer genetic counseling visit between January 1st, 2016, and December 31st, 2017. All patients saw the same genetic counselor. Of the 356 patients who qualified for this study, 291 had genetic testing ordered during their initial cancer genetic counseling visit and were scheduled for a follow-up visit to receive the test results and discuss the personal and family medical implications. This study found that 225 of these patients attended their results disclosure visit (77%), and 66 patients missed their appointment (23%) (Figure 4 and Figure 5). Of the 225 patients who

attended their results disclosure visit, 82 were recommended to have another follow-up visit 6-12 months later typically to discuss whether there were updated medical management guidelines for the patient's positive genetic testing result or to check for updates in the classification status of a variant of uncertain significance identified on genetic testing. Of these 82 patients, 14 attended their follow-up visit (17%), which was a surprisingly low percentage. This subset of patients was not large enough to perform statistical analyses to compare the predictors of those who missed and those who attended their follow-up visit. However, all of these patients had either a positive result on genetic testing, meaning they had detectable mutation in a gene that increases their risk for cancer, and/or a variant of uncertain significance, meaning a genetic variant was detected, but data at the time of the test report was insufficient to classify it as cancer-predisposing or harmless variation. Each of these patients had a clinical indication to return for follow-up as determined by their cancer genetic counselor (Figure 5). It is likely that a proportion of these patients received medical management updates from a non-genetics provider they routinely see, however this study did not calculate how many patients fit this description and did not record what was discussed at relevant appointments with non-genetics providers.

Current literature supports the need to inform patients of reclassification of their variants of uncertain significance on genetic testing. Variants of uncertain significance are common, and the likelihood of a variant of uncertain significance result depends on the number of genes tested, how well-established in scientific literature a gene is, the ethnicity of the patient (Easton et al. 2007; Nanda et al. 2005; Ricker et al. 2016), and the variant classification methodology used by the testing laboratory. A recent study that reviewed cancer genetic testing results from 2006-2016 for over 1.5 million patients through one genetic testing laboratory showed that 18.7% of multigene panels were negative but had at least one reported variant of uncertain significance

(Mersch et al. 2018). Within the time period, 25% of the reported variants of uncertain significance were reclassified to either pathogenic or benign. While most of these variants of uncertain significance were reclassified as benign (91%), 9% were reclassified to pathogenic (Mersch et al. 2018), which is a rate consistent with previous literature (Macklin et al. 2018). For some patients, particularly those with less education, a variant of uncertain significance in a cancer predisposing gene causes anxiety or frustration, (Hallowell et al. 2002; Lumish et al. 2017; O'Neill et al. 2009; Richter et al. 2013) which could be alleviated by being informed that it has been reclassified as benign. For cases in which a variant of uncertain significance is reclassified to pathogenic, the impact is more obvious; medical management is often altered in order to prevent or detect cancer at an early stage when a patient has a known cancer-predisposing mutation. At-risk family members can pursue genetic testing for the known mutation and have a similarly personalized cancer screening course based on their targeted test result. While the benefits of informing patients of reclassified variants of uncertain significance are clear, there is disagreement on who has the responsibility to inform the patient as it may take years for a variant to be reclassified (Hoffman-Andrews 2017; Murray et al. 2011; Otten et al. 2015). In that time, a patient may have changed their phone number, address, and/or primary care physician, making it difficult for the original genetics providers or genetic testing lab to reconnect with the patient. A scheduled in-person follow-up visit with the genetic counselor to discuss any potential updates in variant status may be one strategy to better maintain open lines of communication. Yet, the results of this study showed that a large proportion of individuals scheduled for these types of follow-up visits did not attend their appointment, and the few who did attend their appointment had no change in variant status at the time of the follow-up visit.

Emerging alternate models of genetic counseling may be a reasonable way for some clinics to bypass the barriers specific to in-person follow-up visits. For example, telegenetic counseling uses videoconferencing to connect a genetic counselor and a patient, and genetic counseling by telephone is becoming increasingly common (Bradbury et al. 2011; Peshkin et al. 2016). The National Society of Genetic Counselors has practice guidelines for cancer genetic counselors that include what should be addressed during genetic testing results disclosure. The guidelines acknowledge that some genetic counselors routinely disclose result in-person and others do so by telephone, but do not expressly recommend one method over the other (Riley et al. 2012). A few studies have compared patients who had cancer genetic counseling via telephone to those who had in-person sessions found that patients in these two groups did not differ in their anxiety, cancer-specific psychological distress, or decisional regret and overall satisfaction, but fewer patients elected genetic testing after telephone genetic testing compared to in-person visits for unknown reasons (Kinney et al. 2014; Peshkin et al. 2016). Unsurprisingly, cancer genetic testing patients reported that telephone counseling was more convenient than in-person sessions (Peshkin et al. 2016). In-person initial cancer genetic counseling visits with an option for follow-up appointments via telephone may be one way to maintain genetic testing uptake while also providing a more convenient way for patients and providers to discuss follow-up concerns such as updated medical management, family member testing, and variant of uncertain significance updates. However, this may not a realistic strategy for all genetic counselors because some insurance companies do not cover telegenetic or telephone counseling, and there may be specific limitations depending on the medical institution.

4.2 Factors influencing genetic testing results disclosure visit attendance

One of the aims of this study was to compare demographic traits, personal medical history, and family cancer history of patients who attended and patients who missed their genetic testing results disclosure cancer genetic counseling visit. A better understanding of how these groups of patients differ may help cancer genetic counselors predict who is at higher risk to not attend their follow-up visit, and thus miss crucial information related to their health. In our study population, the patient's sex, ethnicity, age, personal cancer history, initial visit referral indication, type of genetic testing ordered, and number and proportion of first and second-degree relatives affected with cancer did not make it more or less likely that a patient would attend their results disclosure visit. We had expected overlap between the factors we identified and barriers to initial an initial cancer genetic counseling visit or genetic testing previously identified in the literature. Non-White patients tend to have lower awareness of genetic testing and are more likely to have a type of insurance that does not cover or fully cover genetics services (Suther and Kiros 2009). Our study focuses on follow-up visits rather than initial visits, meaning the gap in initial visit uptake between White and non-White patients is bypassed. This study did not find a difference in genetic testing disclosure attendance rate between Asian, Hispanic, and White patients, suggesting that our population does not have ethnicity-based disparities in follow-up visit compliance. Other studies have also shown that men are underrepresented in the cancer genetic counseling clinic (Fraser et al. 2003). This disparity was also reflected in the low frequency of men in the current sample (16% of eligible patients were male, 84% female). However our study found no difference in results disclosure attendance rates based on sex of the patient. Similar to the finding for ethnicity, this may indicate that once a patient has overcome the barriers to a referral or initial visit to cancer genetic counseling, there is no difference or gap in follow-up visit compliance for men in comparison to women. Our study also did not find

attendance differences based on the patient's age. Additionally, whether a person was self-referred or physician-referred, had a personal history of cancer, or a stronger family history of cancer, were not predictors of follow-up visit attendance.

One study surveyed 162 patients about their motivation for pursuing cancer genetic risk evaluation and found that individuals who had a personal history of cancer and higher perceived risk were more likely to seek cancer genetics services, however this was due to concern for their children rather than themselves; patients who did not have children did not have the same level of motivation as those who did even if they had cancer themselves (Fraser et al. 2003). This result is consistent with this study's finding that patients who were parents were more likely than expected to attend their results disclosure appointments, but personal history of cancer did not have an independent impact on attendance. One study of women with breast cancer who were referred for genetic counseling found that having daughters was a predictor of initial genetic counseling appointment attendance and genetic testing uptake (Ayme et al. 2014). This study did not analyze the return visit attendance based on the sex of each patient's children. While many of the patients in this study were referred due to potential increased risks for breast, ovarian, and uterine cancer, there were also patients who were referred because of a personal or family history of cancers that are not as sex-limited, such as colon, pancreatic, or skin cancer.

A hypothesis of this study was that patients who were personally affected by cancer and/or had a higher proportion of family members who had had cancer would be more likely to attend their results disclosure visit, possibly out of a perceived higher personal risk for a positive genetic test. For patients currently undergoing cancer treatment, it is possible that the physical and psychological stress of treatment may cause some patients to defer genetic testing or receiving genetic testing results. On the other hand, for patients who are regularly coming to the

cancer center for treatment it might be more convenient to attend a cancer genetic counseling appointment in the same building or area compared to an unaffected or previously affect patient who would otherwise have no other reason to come to clinic. This study did not assay patient motivation for attending follow-up visits, but a future study should address these concerns.

4.3 Limitations of this study

While many of the conclusions in this study are generalizable to broader cancer genetic counseling practice, a limitation of this retrospective chart review is that the data were collected from one cancer genetic counseling clinic. Genetic counseling clinics can widely differ in their practice strategies and protocols, and it is likely that some are very different in characteristics of the patient population such as socioeconomic status and demographic traits. Our patient population was reflective of the area local to the clinic (Table 9) (U.S. Census Bureau 2017) and was majority White, Hispanic, and Asian, with an underrepresentation of Black, Indian, Middle Eastern, and other ethnicities. As such, this study may be influenced by ethnicity-based disparities in genetics literacy and access to genetics providers (Christensen et al. 2010; Kaphingst et al. 2015; Pagán et al. 2009; Singer et al. 2004), in addition to not being representative of patient populations in other parts of the United States. The focus on one individual cancer genetic counseling clinic is this study was beneficial in ensuring our patients underwent a fairly uniform experience, but likely differs from other cancer genetic counseling clinics that may utilize different timelines of follow-up contact or different methods of communication (i.e. in-person, over the phone, written material, or a combination of different modes).

Table 9: Race and Hispanic-origin estimates of Orange County, CA residents for 2018 as reported by the United States Census Bureau.

Race and Hispanic Origin	Percentage
Non-Hispanic White	40.5%
Black	2.1%
American Indian and Alaska Native	1.0%
Asian	21.0%
Hispanic or Latino	34.2%
Native Hawaiian and Other Pacific Islander	0.4%
Two or more races	3.5%

Note: These percentages were reported by the US Census Bureau. They do not add up to 100%.

This study identified attendance rates for different types of follow-up appointments in the cancer genetic counseling session, and the factors that may influence attendance. Patients who had genetic testing ordered at their first appointment and were scheduled for an in-person follow-up visit for results disclosure were analyzed, but patients who either had genetic testing prior to the initial appointment or did not have genetic testing at the initial appointment had insufficient sample sizes for statistical analysis. It would be interesting to determine whether these two subsets of patients also differed in attendance rate based on whether the patient is a parent, or if there are other factors influencing follow-up visit attendance in these groups.

Another limitation of this study is that it cannot conclude *why* people attended or missed their visits. A survey of patients who both attended and who missed their appointments that examines the patients' motivations and barriers to follow-up appointments is one potential way to address this question that a retrospective chart review cannot. Types of insurance for this study population were collected, but not analyzed, and other socioeconomic factors such as household

income were not collected for this study. Patient concern for cost and insurance coverage of both genetic counseling and genetic testing have been reported by patients as reasons they declined cancer genetics services, and these barriers likely also played a role in the current study (Anderson et al. 2012; Forman and Hall 2009). The results of the current study would be useful in designing a survey targeted to address the reasons patients attended or missed follow-up appointments.

4.4 Conclusions

In summary, this retrospective chart review identified that female patients who have biological children are statistically more likely than expected to attend their genetic testing results disclosure visit. This trend was present for male patients in our study population, but not statistically significant. Independently, the patient's sex, ethnicity, age, personal cancer history, initial visit referral indication, type of genetic testing ordered, and proportion of first and second-degree relatives affected with cancer did not make it more or less likely that a patient would attend their results disclosure visit. We found a surprising drop-off in attendance rates for patients who were asked to return to clinic for another follow-up visit after the results disclosure visit (14/82), and for patients who did not have genetic testing at the initial visit, but were scheduled for follow-up to revisit the option of testing after gathering information from family members if possible (10/33). Awareness of predictors of follow-up visit attendance can help genetic counselors recognize when alternate communication methods should be utilized to best educate and support their patients.

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APPENDIX A

The genes and associated disorders tested in patients who had targeted testing for a specific familial mutation

Gene tested for familial mutation	Associated disorders	Number of patients
APC	Familial adenomatous polyposis (FAP) and attenuated FAP	1
ATM	Predisposition for breast cancer, potential increased risk for ovarian, pancreatic, and prostate cancer	1
BRCA1	Hereditary breast and ovarian cancer (HBOC)	4
BRCA2	Hereditary breast and ovarian cancer (HBOC)	10
MEN1	Multiple endocrine neoplasia type 2 (MEN1)	1
MLH1	Hereditary non-polyposis colon cancer (HNPCC, Lynch syndrome)	3
MSH2	Hereditary non-polyposis colon cancer (HNPCC; Lynch syndrome)	1
MSH6	Hereditary non-polyposis colon cancer (HNPCC; Lynch syndrome)	1
PALB2	Predisposition for breast and pancreatic cancer	1
PMS2	Hereditary non-polyposis colon cancer (HNPCC; Lynch syndrome)	2
		Total: 25

APPENDIX B

The genes and associated disorders tested in patients who had single gene testing

Gene tested	Associated disorders	Number of patients
APC	Familial adenomatous polyposis (FAP) and attenuated FAP	2
MEN1	Multiple endocrine neoplasia type 2 (MEN1)	2
PTCH1	Nevoid basal cell carcinoma syndrome (Gorlin syndrome)	1
NF2	Neurofibromatosis type 2	1
PRKAR1A	Carney complex	1
RB1	Heritable retinoblastoma	1
RET	Multiple endocrine neoplasia type 2 (MEN2) and familial medullary thyroid cancer (FMTC)	3
		Total: 11