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Adherence patterns to National Comprehensive Cancer Network (NCCN) guidelines for referral to cancer genetic professionals

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Abstract

Objective—Genetic predisposition is responsible for 5–10% of breast cancer, 10% of ovarian cancer and 2–5% of uterine cancer. The study objective was to compare genetic counseling and testing referral rates among women with breast cancer that met NCCN referral guidelines to the referral rates among women with gynecologic cancers and determine predictors of referral.

Methods—Utilizing an institutional tumor registry database, patients from an academic women's oncology program were identified who met a subset of NCCN guidelines for genetic referral between 2004 and 2010. Patients diagnosed with ovarian cancer, breast cancer ≤50 years of age, or uterine cancer <50 years of age were included. A retrospective electronic chart review was conducted to evaluate for a genetic referral and uptake of genetic testing.

Results—820 women were included (216 uterine, 314 breast, and 290 ovarian cancer). The overall genetic referral rate was 21.7%. 34% of eligible breast cancer patients were referred compared to 13.4% of uterine cancer and 14.5% ofovarian cancer patients ($p < 0.0001$). Younger age, breast cancer diagnosis, family history and earlier stage were all significant referral predictors. The odds of being referred increased with the number of affected family members. 70.8% of referred patients, consulted with genetics. Among those who consulted with genetics, 95.2% underwent testing.

Conclusions—Although increasing, genetic counseling remains underutilized across cancer diagnosis. Women with breast cancer are more likely to be referred than women with gynecologic cancers. Younger age, earlier stage and positive family history appear to be predictive of referral for genetic evaluation.

Keywords

Hereditary cancer; Genetic counseling; Practice patterns

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1. Introduction

Over the past two decades, with the completion of the human genome project, the ability to offer patients genetic testing to identify cancer predisposition has become an accessible and valuable tool in cancer risk assessments. Currently more than 100 genes have been identified that confer an increased risk of cancer [1] and over 50 hereditary cancer syndromes have been described [2]. More recently the introduction of next generation sequencing has reduced the cost and increased the efficiency of genetic testing while allowing for the assessment of gene panels [1].

Women harboring a deleterious BRCA 1 or 2 mutation have a 40–65% lifetime risk of developing breast cancer and a 11–40% risk of developing ovarian cancer [3]. Approximately 5–10% of breast cancer patients [4] and 13–16% [5–7] of ovarian cancer patients harbor a germline BRCA 1 or 2 mutation. These rates are even higher in women with high-grade serous ovarian cancer and fallopian tube cancer [7,8].

Lynch syndrome, known for its contribution to hereditary colon cancer, is responsible for 10% of endometrial cancer in women younger than 50 years old, which often presents as the sentinel cancer [9]. The cumulative lifetime risk of endometrial cancer among women with Lynch syndrome is up to 71% [10,11]. In addition, women diagnosed with Lynch syndrome are at an increase risk for developing ovarian cancer compared to the general population (3-14% vs 1.4%) [11].

The National Comprehensive Cancer Network (NCCN), an alliance of leading cancer centers, has developed a comprehensive set of clinical practice guidelines to assist practitioners in the management of care for oncology patients. In 1998, guidelines to identify women at risk for hereditary breast and ovarian syndrome as well as Lynch syndrome were incorporated into the larger body of practice guidelines. These recommendations specify that any women diagnosed with epithelial ovarian/fallopian tube/primary peritoneal cancer, breast cancer diagnosed at or before the age of 50, or endometrial cancer diagnosed before the age of 50 should be referred for a genetic risk assessment [12,13].

Genetic counseling and testing offers a number of benefits, for both patients and their families. Genetic counseling assists women in making informed decisions about their health and treatment, improves knowledge of cancer genetics, modifies cancer risk perceptions, and reduces cancer associated anxiety [14,15]. BRCA mutation carriers may benefit from prophylactic surgery, utilization of chemoprevention, as well as increased surveillance. For example, risk-reducing salpingo-oophorectomy was associated with an 80% reduction in ovarian and fallopian tube cancer risk and a 50% reduction in breast cancer risk. Prophylactic mastectomy decreased breast cancer risk by 90-95% pending ovarian status [16,17]. In studies of women with BRCA1 or 2 mutations who underwent risk reduction salpingo-oophorectomy, occult gynecological carcinomas were identified in up to 9% of cases [18,19]. In addition, adherence to patient surveillance guidelines improves after genetic counseling and testing [20]. Family members of mutation carriers may have the opportunity to seek testing prior to the onset of disease and choose to take prophylactic actions.

Unfortunately, referral to genetic counseling is often low and has been reported to be lower among women with ovarian cancer compared to women with breast cancer [21]. Despite ovarian cancer being the most lethal of gynecologic malignancies, public awareness is much greater for breast cancer. Higher rates of breast cancer and greater media attention given to breast cancer may offer an explanation to this discrepancy.

The purpose of this study was to investigate genetic counseling referral rates for women with breast cancer compared to women with gynecologic cancers. Our secondary aim was to determine predictors of referral to genetic counseling.

2. Methods

An institutional tumor registry database was queried to identify women with breast carcinoma (“infiltrative ductal carcinoma”, “infiltrative lobular carcinoma”, “ductal carcinoma in situ”, “lobular carcinoma in situ”) epithelial ovarian/fallopian tube/primary peritoneal carcinoma (“serous carcinoma”, “clear cell carcinoma”, “endometrioid carcinoma”, “mucinous adenocarcinoma”) and endometrial carcinoma (“endometrioid carcinoma”, “papillary serous carcinoma”, “mixed cell adenocarcinoma”, “clear cell carcinoma”, “carcinosarcoma”, “leiomyosarcoma”, “endometrial stroma sarcoma”) treated at The Program in Women's Oncology, Women and Infants Hospital, Brown University from 2004 to 2010. From this sample, eligible women were selected who met designated National Comprehensive Cancer Network (NCCN) hereditary breast and ovarian cancer and Lynch syndrome guidelines for referral to genetics. The eligibility criteria for inclusion included: a personal endometrial cancer diagnosis less than 50 years of age, breast cancer diagnosis at or before 50 years of age, or a personal history of epithelial ovarian, fallopian tube, or primary peritoneal cancer at any age [12,13]. Women with synchronous or metachronous primaries meeting the respective age inclusion criteria, were analyzed under both cancer diagnoses as each new diagnoses represented a trigger for referral. Women excluded from this study were known mutation carriers or had already undergone genetic counseling and testing prior to the first encounter at our institution, lacked documentation of follow-up provider encounters at our institution besides operative or pathology reports in the electronic medical record, cancer diagnosis outside of the study age criteria, women less than 18 years of age, and women with non-epithelial ovarian cancer histology. This project was approved by the hospital Institutional Review Board (IRB).

We conducted a retrospective electronic chart review of women meeting the inclusion criteria. All notes, which included letters from tumor board, office notes, inpatient progress notes and consultation notes were reviewed to assess for documentation of referral to cancer genetics. A patient was considered “referred for genetic counseling” if a discussion was documented between the physician and patient discussing referral or if a consultation note was generated from a genetic counselor. A patient was considered referred but not counseled if the conversation was documented between the physician and the patient however no consultation or genetic notes were found. Those patients who received genetic testing were identified by a positive or negative mutation test result noted in the electronic chart.

Data collected included: age at diagnosis, year of diagnosis, race, tumor histology and stage, treatment, documented family history, insurance type, treating provider, parity, AshkenaziJewish heritage, referral to genetics, timing of referral, acceptance of genetic testing and identification of a mutation.

Data analysis was performed with SAS version 9.2 (Cary, NC). Categorical variables were compared with chi-square of Fisher's exact test. Continuous variables were compared using ANOVA. An alpha level of 0.05 was used for statistically significance. Logistic regression was used to calculate odds ratio and 95% confidence intervals; 95% CIs for odds ratio excluding 1.0 were statistically significant.

3. Results

A total of 3032 women with breast cancer, 837 women with ovarian, fallopian tube or primary peritoneal cancer and 1689 women with endometrial cancer received treatment at Women and Infants Hospital between 2004 and 2010. Among the total cancer cases, 216 women with uterine cancer (12.8%), 901 women with breast cancer (29.7%) and 622 women with ovarian cancer (74.3%) were found to meet the inclusion criteria for this study. Based on a priori power calculation, to detect a 15% genetic testing referral difference between cancer diagnosis groups, 422 breast cancer, 234 ovarian cancer and 117 endometrial cancer charts meeting criteria for referral for genetics were needed. An interim analysis demonstrated statistical significance of the study and data entry was terminated with 100% of the eligible uterine cases (216), 34.9% of the eligible breast cancer patients (314) and 46.6% of the eligible ovarian cancer patients (290) entered.

Table 1 demonstrates the distribution of the patients categorized by the cancer diagnosis. Women with both uterine and breast cancer were diagnosed at an earlier stage (stages 0-2) than women with ovarian cancer (stages 3-4) ($p < 0.001$). More than 85% of women in each group identified as Caucasian. A reported family history of cancer was seen in 48.6-60.7% of the patients included in this study, with breast cancer patients having the highest percentage (60.7%, $p = 0.03$).

The overall genetic referral rate was 21.7%. As depicted in Table 2, the rate of referral was highest for breast cancer (34.1%) while the referral rates for ovarian cancer and endometrial cancer were 14.5% and 13.4% respectively ($p < 0.001$). Among women referred, 77.6% of breast cancer patients, 62.1% of uterine cancer patients and 59.5% of ovarian cancer patients followed up for genetic counseling ($p < 0.05$). Overall, 70.8% of women referred for genetic counseling were compliant with the recommended referral and received counseling. Among those women who received genetic counseling, 95.2% of women proceeded with genetic testing. This rate did not vary significantly by the type of cancer diagnosis. A genetic mutation was detected in 46.7% of the uterine cancer patients, 44% of the ovarian cancer patients and 16.5% of the breast cancer patients.

Table 3 compares the characteristics of the women referred for counseling and testing to those who were not referred. As a group, women referred for genetic testing were younger (median age 44) at the timeofdiagnosis comparedtothose who were not referred (median age

48, p < 0.0001), with an adjusted OR of 0.94 (CI: 0.92–0.96), Table 4. Among women referred for counseling and testing, women diagnosed with advanced stage cancer (stages 3 and 4) were less likely to be referred than early stage (stages 0–2) (21.9% vs. 78.1%, p < 0.0003). Lastly, as expected, women referred for counseling were more likely to have a positive family history (76.2% vs. 23.8%, p < 0.0001).

Patients with a positive family history were 4.39 times (CI: 2.76–6.98) more likely to be referred (Table 4). This odds ratio is noted to increase with increasing numbers of affected family members (1 member; 2.75 (CI: 1.74–4.35), 3 members; 10.2 (CI: 5.53–18.9)). Women with uterine cancer are 0.30 (CI: 0.19–0.47) times less likely than those with breast cancer to be referred to genetics which remains consistent when controlling for age and family history (Tables 4, 5). Women with ovarian cancer are 0.33 (CI: 0.22–0.49) times less likely than those with breast cancer to be referred for counseling and testing (Table 4), which becomes non-significant when controlling for age and family history (Table 5).

Overall, from 2006 to 2010 the referral rates to genetic counseling increased from 10% to 41.5% (Fig. 1). In 2007, a sharp increase is noted in each cancer diagnosis, with an overall doubling of referrals (15.2% to 30.7%).

4. Discussion

Referrals for genetic counseling and testing have been endorsed by The Society of Gynecologic Oncology (SGO), National Comprehensive Cancer Network (NCCN), and the American College of Obstetricians and Gynecologists (ACOG) highlighting the need for cancer risk assessments to be an integral part of office visits [22,23]. While evidence-based genetic counseling and testing guidelines for hereditary breast & ovarian cancer and Lynch syndrome have been published and updated since 1994 even among oncologists, implementation of these practice guidelines appears to be lagging as genetic counseling services remain underutilized. This underutilization has persisted despite advances in genetic testing and increased access. In this study, we achieved an overall 27.1% referral rate, which collaborates with the literature for practicing oncologists (19–48% referral rate) [24–27].

The purpose of this study was to go beyond reporting a referral rate, and explore characteristics that are associated with the likelihood of physician initiated genetic counseling and testing referrals. First, we observed a difference in referral patterns based on cancer diagnosis. Women with breast cancer were more likely than women with ovarian or endometrial cancer, to be referred for genetic counseling, based on crude odds ratios, echoing the findings from Powell et al., where 21% of women with ovarian cancer and 59% women with breast cancer were referred [19]. However, in our study when controlling for age and family history, there was no significant difference in referral patterns between women with breast cancer and those with ovarian cancer. This may suggest that age and family history are more powerful drivers of genetic referrals rather than cancer diagnosis. It is interesting to note, the same pattern does not hold true comparing referrals for women with uterine cancer to those with breast cancer, as women with uterine cancer were still less likely to be referred even when family history and age are controlled for (Table 4). One explanation for the pattern seen is that women with ovarian cancer often present with larger

disease burden, multiple comorbidities and face treatment complexities thereby crowding the opportunity to offer genetic counseling. The timing of referral is different based on cancer diagnosis (Table 2). 45% of women with breast cancer are referred at diagnosis or before treatment compared to 21% of women with uterine cancer. 69% of women with ovarian cancer were referred to genetics during or after treatment influencing the observed drop in the 2010 referral rate to 16.7% as these women were not captured in the study period (Fig. 1). Given this timing in conjunction with the disease recurrence rate, and 5-year overall survival for women with ovarian cancer compared to women with uterine or breast cancer, women with ovarian cancer may have died before genetic testing is offered. 45% of eligible women with uterine cancer were referred for counseling and testing in 2010. This high referral rate may be partially accounted for by the number of eligible new diagnosis (n = 10) in 2010 was smaller than previous years in, resulting in a larger percent increase with each additional referral.

As demonstrated in Fig. 1, referral patterns are increasing over time. Public awareness for genetic testing has greatly increased likely due to marketing campaigns, greater provider awareness, enhanced provider education and patient discussions. The NCCN inclusion criteria for genetic testing referrals have broadened while testing has become more available and accessible. Given that breast cancer is the most common cancer among women and the number of new ovarian and endometrial cancer does not even equal that of breast cancer, it is reasonable that public awareness of the genetic contribution to breast cancer is more salient [19,28]. Breast cancer awareness campaigns and advocacy groups have vested much effort in raising public attention. For example, in 2012, the Susan Komen Foundation raised $130 million while the Ovarian Cancer Research Fund raised $2.9 million [29]. In 2003 Myriad genetics began marketing genetic testing with the well-known BRCA Analysis campaign. CDC investigations found that campaigns increased awareness among providers and increased ordering of genetic testing among providers. In more recent years, direct to consumer marketing has been employed to increase utilization of genetic testing as well [30].

Since 1996 ASCO affirms the oncologist's role in collecting and documenting a cancer family as part of preventative oncology [31] in light of 10–30% of patients having a personal or family health history suggesting hereditary or familial cancer susceptibility [23,32,33]. In this study, we found that a positive family history correlated with a greater likelihood of being referred and this relationship got stronger as the number of affected family members increased from 1 to 3. Interestingly, we found that 16.3% of women with a known cancer diagnosis did not have a documented family history in their electronic medical record. Prior studies have demonstrated that providers often fail to collect a complete family history, and Wood et al. even noted a difference among oncologist in collecting family histories from breast (32.9%), and colon cancer (22%) patients [27,34].

We found stage at presentation to be associated with referral; with women who presented at an earlier stage more likely to be referred than those who presented with more advanced cancer. This finding may be explained by the fact that women with advanced disease may initially present with multiple complex issues requiring immediate attention and taking priority over genetic counseling. Diagnosis of cancer at a young age is a hallmark of a

hereditary predisposition. We found that younger women are more likely to be referred for genetic counseling which parallels previous studies [23,35]. This trend was seen for the ovarian and breast cancer patients when looked at stratified by cancer diagnosis as well.

In Table 3, private/managed care insurance status was associated with the likelihood of being referred ($p = 0.05$). This observation is primarily reflective of the referral pattern seen in women with ovarian cancer as a statistical difference in referrals for women with breast or uterine cancer stratified by insurance was not seen (unreported data). Approximately 75% of women with breast and uterine cancer in this study had private/managed care (Table 1) limiting the ability to detect the impact of insurance status. However extrapolating from the ovarian data, which is more evenly distributed, we see that private/managed care insurance is associated with a greater likelihood of being referred. The passage of GINA (The Genetic Information Nondiscrimination Act) of 2008 prohibiting insurers from denying or canceling coverage based on genetic information is one example of reducing barriers that may impact motivation for counseling and testing. The rollout of the Affordable Care Act represents an opportunity for advocacy to ensure that genetic testing is universally covered using criteria set forth by the NCCN.

Understanding their children's risk was reported as motivation for genetic testing[35,36,38] however we did notfind anassociation of parity with genetic testing and this conclusion was not supported by our data. Levy et al. reported on racial difference in genetic testing, with Hispanics and African Americans testing less frequently than non-Jewish white women [40], however due to the homogenous sample size a difference was not replicated in this study.

Many women lack knowledge or carry misperceptions regarding cancer genetics and their risk highlighting the role of physicians as educators and drivers of genetic referrals [34,38]. Fifty-five percent of women diagnosed with ovarian cancer are unaware of the availability of genetic testing [38]. Studies have shown that physician recommendation is a powerful predicator of a patient's decision to undergo testing with Schwartz et al. showing that patients were three times more likely to undergo genetic testing if referred by a provider [39]. After genetic counseling, women report less anxiety. Lacour et al. in 2008 found that 87–89% of women diagnosed with ovarian cancer would be willing to have genetic testing [38]. Similarly, we found that among referred women 70.7% met with a genetic counselor.

A unique aspect of this study is the focus on women with a personal cancer diagnosis, not just an at-risk population. Pal et al. suggested that greater than 30% of BRCA-associated ovarian carcinoma would be missed by relying on family history alone [6]. Although, Aslop et al. found 44% ofwomen with aBRCA mutation did not have a positive family history in our study, 82% of the women with uterine cancer, 71% of women with breast cancer and 86% of women with ovarian cancer had a positive family history [5]. A survey by Bruno et al. found that 84% of women with a breast cancer diagnosis compared to 57% with a positive family history would definitely or probably accept genetic testing [36]. Ultimately by testing the proband, false negative rates are reduced and if a specific mutation is identified, the scope of testing recommended for family members is narrowed. Identifying BRCA positive ovarian cancer tumors has treatment management and prognosis significance. Poly ADP ribose polymerase (PARP) inhibitors are now FDA approved for

treatment of BRCA positive ovarian cancer and studies have shown these tumors respond differently to chemotherapy and exhibit sensitivity to platinum [37].

The single institution, retrospective nature of this study serves as limitations. In addition, all information was gathered from a review of electronic medical records, which suffered from incomplete or missing data in some cases. Although our women's oncology program is the largest gynecologic oncology treatment institution in southern New England, genetic testing is also done in the community, and referrals outside of our system may not have been captured. It is also quite possible that discussion regarding counseling and testing occurred but documentation was lacking. Lack of ethnic diversity in our sample serves as a limitation in this study and testing rates may not be representative of other institutions. Literature demonstrates that African Americans are less likely to be referred for genetic counseling and rates in communities with a larger percentage of African Americans may actually be even lower than reported in this study. [40].

The 2012 version of the NCCN guidelines were applied to determine adherence in this study. During the study period from 2004to2010, the guidelines remained consistent referring women less than 50 years of age with breast cancer for genetic counseling. For ovarian cancer, the guidelines before 2009 were more stringent requesting not only a personal diagnosis but also an affected family member. This was also seen in the screening recommendations for Lynch syndrome, with guidelines prior to 2009 requiring either a personal diagnosis of multiple primary cancers or an affected family member. This variation in guidelines serves as a limitation to this project, but also provides insight into the trends seen in Fig. 1 [12,13].

The results from this study have generated ideas to improve upon the referral rate. The genetic program, with a catchment area of Rhode Island, Connecticut and Southern Massachusetts, has become seamlessly integrated into the Program in Women's Oncology. Patient access to genetic counseling is simplified. Counseling is housed on the same floor with the oncology clinic and efforts are directed towards coordination of appointments. Genetic counselors have weekly conference reviewing new and follow-up cases. They routinely participate in weekly tumor board meetings to capture new potential patients and serve as a safety net for existing patients. Their input is incorporated into the official recommendations sent to the oncologic and referring physician. Over the last few years, there has been an increase in genetic counseling presence in several arenas; department didactic programs, direct education and community outreach, and increased interaction with fellows. As a result of these efforts, there has been an overall increase in the number of new referrals from 480 in 2011 to 625 in 2014.

Integrating key genetic questions and demographics into the electronic record which alerts providers of patients meeting criteria for referral has been recommended. Gathering information regarding the providers' perspective as to the barriers to integrating genetic counseling and testing into routine practice may increase referral rates. In addition, routine IHC testing of all uterine specimens from women with endometrial cancer to detect microsatellite instability (MSI) is being performed at our institution and at many institutions throughout the country.

In summary, genetic counseling and testing recommendations have not been fully integrated into clinical practice despite women's interest. The significantly larger percentage of breast cancer patients referred for genetic testing compared to ovarian and uterine cancer patients may represent a greater awareness among providers of BRCA testing for breast cancer, increased consumer marketing or may be associated with the earlier age and stage when they present for care. As gynecologist oncologists, providing a complete spectrum of care for patients, serving to coordinate patient care in alliance with practice guideline is among our primary responsibilities. Genetic testing has the potential to reduce the morbidity and mortality from breast and gynecologic cancers. Development of tools to facilitate comprehensive cancer risk assessments and seamless referrals are essential to ensure affected and high risk women are receiving appropriate services.

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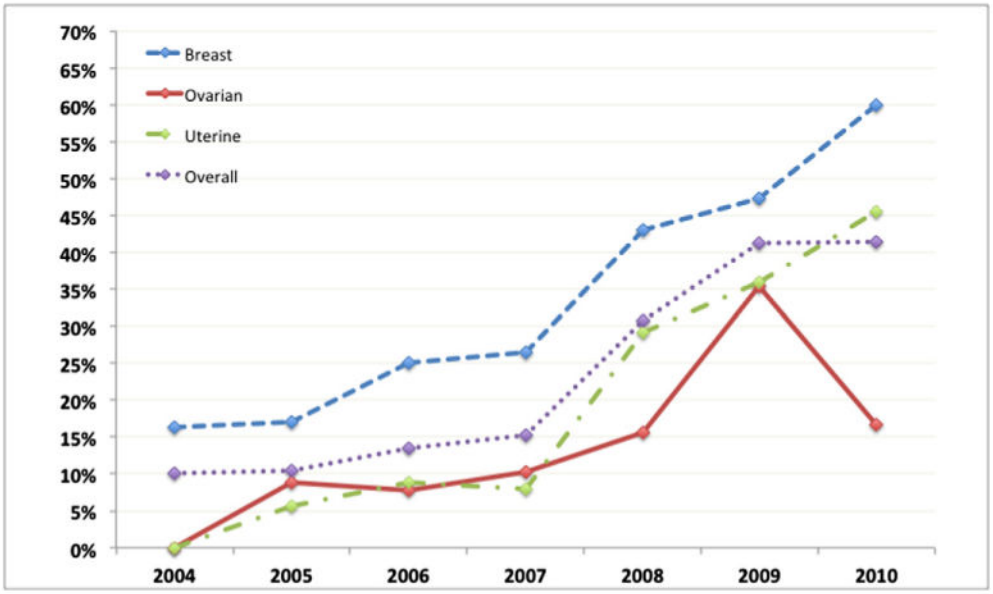
Highlights

- Genetic counseling and testing is being underutilized.
- Breast cancer patients are more likely to be referred for genetic counseling.
- Referred patients are likely to follow up with counseling and testing.



	2004	2005	2006	2007	2008	2009	2010
Breast	16.3%	17.1%	25.0%	26.5%	43.1%	47.3%	60.0%
Ovarian	0.0%	8.9%	7.7%	10.3%	15.6%	35.3%	16.7%
Uterine	0.0%	5.7%	8.8%	7.9%	29.2%	36.0%	45.5%
Overall	10.0%	10.4%	13.5%	15.2%	30.7%	41.2%	41.5%

Fig. 1. Genetic referrals, by year and cancer diagnosis

Table 1
Demographics, stratified by cancer diagnosis

	Uterine n (col %)	Breast n (col %)	Ovarian n (col %)	p-Value overall
Total	216	314	290	
Age at diagnosis	(n = 216)	(n = 314)	(n = 290)	
Mean (SD)	43.9 (5.6)	43.6 (5.1)	62.0 (12.6)	<0.0001[a]
Median (min–max)	46 (24–50)	45 (22–52)	63.0 (23–89)	
Stage at diagnosis	(n = 213)	(n = 313)	(n = 286)	
0–II	175 (82.2)	280 (89.5)	87 (30.4)	<0.0001[b]
III–IV	38 (17.8)	33 (10.5)	199 (69.6)	
Race/ethnicity	(n = 195)	(n = 288)	(n = 279)	
Caucasian	180 (92.3)	254 (88.2)	265 (95.0)	
African American	6 (3.1)	10 (3.5)	8 (2.9)	0.01[c]
Hispanic	7 (3.6)	21 (7.3)	3 (1.1)	
American Indian/Eskimo	1 (0.5)	0	1 (0.4)	
Asian	1 (0.5)	3 (1.0)	2 (0.7)	
Insurance	(n = 207)	(n = 269)	(n = 286)	
Private/managed care	160 (77.3)	210 (78.1)	163 (57.0)	<0.0001[b]
Medicaid/Medicare	37 (17.9)	50 (18.6)	115 (40.2)	
Uninsured	10 (4.8)	9 (3.3)	8 (2.8)	
Family history of cancer	(n = 144)	(n = 242)	(n = 245)	
Yes	70 (48.6)	147 (60.7)	125 (51.0)	0.03[b]
No	74 (51.4)	95 (39.3)	120 (49.0)	
Parity	(n = 194)	(n = 228)	(n = 270)	
Nuliparous	86 (44.3)	43 (18.9)	61 (22.6)	<0.0001[b]
Parous	108 (55.7)	185 (81.1)	209 (77.4)	

[a] ANOVA.

[b] Chi-square.

[c] Fisher's exact test.

Table 2
Genetic referral rate stratified by cancer diagnosis

	Uterine n (col %)	Breast n (col %)	Ovarian n (col %)	P-value overall
Total	216	314	290	
Referred to genetics	29 (13.4)	107 (34.1)	42 (14.5)	<0.0001[a]
If referred, when	(n = 29)	(n = 107)	(n = 42)	
At diagnosis	2 (6.9)	44 (41.1)	11 (26.2)	
Before treatment	4 (13.8)	4 (3.7)	2 (4.8)	<0.0001[a]
During treatment	7 (24.1)	41 (38.3)	13 (30.9)	
After treatment	16 (55.2)	18 (16.8)	16 (38.1)	
If referred:	(n = 29)	(n = 107)	(n = 42)	
Patient saw genetics	18 (62.1)	83 (77.6)	25 (59.5)	0.05[a]
If referred:	(n = 28)	(n = 102)	(n = 42)	
Positive family history	23 (82.1)	72 (70.6)	36 (85.7)	0.11[a]
If referred, age	(n = 29)	(n = 107)	(n = 42)	
Mean (SD)	42.7 (6.9)	41.7 (5.5)	53.4 (12.0)	<0.0001[b]
Median (min–max)	45 (24–50)	43 (25–50)	53.5 (29–75)	
If referred, parity	(n = 29)	(n = 102)	(n = 42)	
Nuliparous	13 (44.8)	18 (17.6)	8 (19.1)	0.007[a]
Parous	16 (55.2)	84 (82.4)	34 (80.9)	
If pt referred and saw genetics:	(n =18)	(n = 83)	(n = 25)	
Number tested	16 (88.9)	79 (95.2)	25 (100)	0.22[c]
If tested:	(n = 15)	(n = 79)	(n = 25)	
Mutation identified,	7 (46.7)	13 (16.5)	11 (44.0)	0.004[a]
BRCA 1 & 2	0	11 (84.6)	8 (72.7)	
HNPCC/Lynch syndrome	3 (42.8)	0	1 (9.1)	
Unknown significance	1 (14.3)	0	0	
p53	3 (42.8)	1 (7.7)	1 (9.1)	
Missing	0	0	1 (9.1)	
If referred & tested:	(n = 16)	(n = 77)	(n = 25)	
Positive family history	13 (81.3)	53 (68.8)	21 (84.0)	0.25[a]
If referred & tested, age	(n = 16)	(n = 79)	(n = 25)	
Mean (SD)	42.6 (5.7)	41.2 (5.5)	52.8 (11.8)	<0.0001[b]
Median (min–max)	44 (32–50)	42 (25–50)	52 (29–75)	
If referred & tested, parity	(n = 16)	(n = 76)	(n = 25)	
Nuliparous	8 (50)	13 (17.1)	5 (20.0)	0.02[a]
Parous	8 (50)	63 (82.9)	20 (80.0)	

[a] Chi-square.

[b] ANOVA.

[c] Fisher's exact test.

Table 3
Demographics stratified by referral to genetics

	Referred	Not referred	p-Value
Total	178 (21.7%)	642 (78.3%)	
Age at diagnosis	(n = 178)	(n = 642)	
Mean (SD)	44.6 (9.1)	51.7 (12.6)	<0.0001[a]
Median (min–max)	44 (24–75)	48 (22–89)	
Stage at diagnosis	(n = 178)	(n = 634)	
0–II	139 (78.1)	403 (63.6)	0.0003[b]
III–IV	39 (21.9)	231 (36.4)	
Race/ethnicity	(n = 171)	(n = 591)	
Caucasian	153 (89.5)	546 (92.4)	0.08[c]
African American	5 (2.9)	19 (3.2)	
Hispanic	13 (7.6)	18 (3.1)	
American Indian/Eskimo	0 (–)	2 (0.3)	
Asian	0 (–)	6 (1.0)	
Insurance	(n = 162)	(n = 600)	
Private/managed care	126 (77.8)	407 (67.8)	0.05[b]
Medicaid/Medicare	32 (19.7)	170 (28.3)	
Uninsured	4 (2.5)	23 (3.8)	
Family history of cancer	(n = 172)	(n = 459)	
Yes	131 (76.2)	211 (46.0)	<0.0001[b]
No	41 (23.8)	248 (54.0)	
Parity	(n = 173)	(n = 519)	
Nuliparous	39 (22.5)	151 (29.1)	0.09[b]
Parous	134 (77.5)	368 (70.9)	

Besides total numbers, all percents listed are column percents.

[a] ANOVA.

[b] Chi-square.

[c] Fisher's exact test.

Table 4

Odds ratios; referral to genetics

Predictor variable	Referral for genetic testing Crude odds ratio	Referral for genetic testing Age adjusted odds ratio
Age at diagnosis	0.94 (0.92–0.96)	–
(per unit increase in age)		
Stage at diagnosis		
Stages 0–II	2.04 (1.38–3.02)	1.38 (0.78–2.42)
Stages III–IV	Ref	Ref
Cancer diagnosis		
Uterine	0.30 (0.19–0.47)	0.35 (0.21–0.58)
Breast	Ref	Ref
Ovarian	0.33 (0.22–0.49)	0.87 (0.51–1.50)
Parity		
Nuliparous	Ref	Ref
Parous	1.41 (0.94–2.11)	1.65 (0.98–2.77)
Family history		
Positive	3.75 (2.53–5.58)	4.39 (2.76–6.98)
Negative	Ref	Ref
Number of affected family members		
0	Ref	
1	2.75 (1.74–4.35)	–
2	4.40 (2.61–7.41)	
3 or more	10.2 (5.53–18.9)	
Insurance type		
Private/managed care	Ref	Ref
Medicaid/Medicare	0.61 (0.40–0.93)	0.91 (0.53–1.57)
Uninsured	0.56 (0.19–1.65)	0.63 (0.18–2.22)

Table 5

Odds ratios; referral to genetics by cancer diagnosis

Predictor variable	Referral for genetic testing Crude odds ratio	Referral for genetic testing Adjusted for age and family history
Cancer diagnosis		
Uterine	0.30 (0.19–0.47)	0.34 (0.20–0.57)
Breast	Ref	Ref
Cancer diagnosis		
Breast	Ref	Ref.
Ovarian	0.33 (0.22–0.49)	0.92 (0.53–1.60)