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Germline Genetic Testing After Cancer Diagnosis

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IMPORTANCE Germline genetic testing is recommended by practice guidelines for patients diagnosed with cancer to enable genetically targeted treatment and identify relatives who may benefit from personalized cancer screening and prevention.

OBJECTIVE To describe the prevalence of germline genetic testing among patients diagnosed with cancer in California and Georgia between 2013 and 2019.

DESIGN, SETTING, AND PARTICIPANTS Observational study including patients aged 20 years or older who had been diagnosed with any type of cancer between January 1, 2013, and March 31, 2019, that was reported to statewide Surveillance, Epidemiology, and End Results registries in California and Georgia. These patients were linked to genetic testing results from 4 laboratories that performed most germline testing for California and Georgia.

MAIN OUTCOMES AND MEASURES The primary outcome was germline genetic testing within 2 years of a cancer diagnosis. Testing trends were analyzed with logistic regression modeling. The results of sequencing each gene, including variants associated with increased cancer risk (pathogenic results) and variants whose cancer risk association was unknown (uncertain results), were evaluated. The genes were categorized according to their primary cancer association, including breast or ovarian, gastrointestinal, and other, and whether practice guidelines recommended germline testing.

RESULTS Among 1 369 602 patients diagnosed with cancer between 2013 and 2019 in California and Georgia, 93 052 (6.8%) underwent germline testing through March 31, 2021. The proportion of patients tested varied by cancer type: male breast (50%), ovarian (38.6%), female breast (26%), multiple (7.5%), endometrial (6.4%), pancreatic (5.6%), colorectal (5.6%), prostate (1.1%), and lung (0.3%). In a logistic regression model, compared with the 31% (95% CI, 30%-31%) of non-Hispanic White patients with male breast cancer, female breast cancer, or ovarian cancer who underwent testing, patients of other races and ethnicities underwent testing less often: 22% (95% CI, 21%-22%) of Asian patients, 25% (95% CI, 24%-25%) of Black patients, and 23% (95% CI, 23%-23%) of Hispanic patients ($P < .001$ using the χ^2 test). Of all pathogenic results, 67.5% to 94.9% of variants were identified in genes for which practice guidelines recommend testing and 68.3% to 83.8% of variants were identified in genes associated with the diagnosed cancer type.

CONCLUSIONS AND RELEVANCE Among patients diagnosed with cancer in California and Georgia between 2013 and 2019, only 6.8% underwent germline genetic testing. Compared with non-Hispanic White patients, rates of testing were lower among Asian, Black, and Hispanic patients.

Editorial

Supplemental content

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Genetic testing for inherited cancer risk can improve survival for patients diagnosed with cancer by enabling genetically targeted therapies such as poly(adenosine diphosphate–ribose) polymerase inhibitors.[1,2] Genetic testing can also improve outcomes for relatives of patients with cancer by modifying cancer screening and preventive therapies.[3,4] Germline testing, in which inherited DNA is sequenced, is recommended by practice guidelines for patients with several cancer types, including breast, ovarian, pancreatic, colorectal, and prostate.[5-7] With advances in sequencing technology, the number of genes tested has increased and costs have declined.

However, little is known about germline genetic testing or results in patients diagnosed with cancer. The rates and results of germline genetic testing were analyzed in patients diagnosed with cancer in California and Georgia between 2013 and 2019 according to the statewide Surveillance, Epidemiology, and End Results (SEER) registries.

Key Points

Question Among patients in the Surveillance, Epidemiology, and End Results registries diagnosed with cancer between 2013 and 2019, what was the prevalence of germline genetic testing?

Findings In this observational study that included 1 369 602 patients diagnosed with cancer in California and Georgia, germline genetic testing after cancer diagnosis was low (6.8%; n = 93 052). Testing was highest in males with breast cancer (50%) and in patients with ovarian cancer (38.6%).

Meaning Few patients diagnosed with cancer between 2013 and 2019 in California and Georgia underwent germline testing.

Methods

Patient Cohort

Patients aged 20 years or older who had been diagnosed with any type of cancer from January 1, 2013, through March 31, 2019, and were reported to SEER registries as part of statewide surveillance in California and Georgia were identified. These patients were linked to germline genetic testing results from the 4 laboratories (Ambry Genetics, GeneDx, Invitae, and Myriad Genetics) that performed the majority of testing for patients in these states.[8,9] The exclusion criteria were (1) cancer diagnosis only on death certificate or autopsy, (2) younger than 20 years of age, (3) sex coded as other, and (4) genetic testing before cancer diagnosis, which could be ascertained beginning January 1, 2012 (eFigure 1 in Supplement 1).

The analytic data set contained linked SEER registry variables and the test results from the laboratories, but omitted all personal identifiable information.[10] Participant consent was waived. The institutional review boards overseeing the SEER registries approved the research.

Testing Results

Three of 4 laboratories submitted results for all germline cancer genetic tests performed in the US from January 1, 2013, through March 31, 2021, which helped to identify results for patients who had cancer and then moved out of state. The fourth laboratory, which contributed 1% of tests in this data set, submitted results from tests performed in California and Georgia only. Laboratories submitted gene-level interpretations provided to the ordering clinician according to criteria from the American College of Medical Genetics and Genomics.[11]

The laboratory results were categorized as pathogenic (defined as variants associated with an increased risk of cancer), benign (defined as variants not associated with an increased risk of cancer), and uncertain (defined as variants for which the associated risk of cancer was unknown). Patients with both pathogenic and uncertain results in different genes were categorized as having pathogenic results, whereas patients with only uncertain results were categorized as having uncertain results. The results from all 4 laboratories were combined for the analysis, comprising 107 tested genes. Additional details appear in the eMethods in Supplement 1.

Outcome Measures

The primary outcome was germline genetic testing within 2 years of the cancer diagnosis. Tests performed later are less consistently related to the index cancer. The SEER variables included sex (male, female, other, unknown), cancer stage, age at cancer diagnosis, race and ethnicity (patients who are Asian [including Pacific Islanders], Black, Hispanic, non-Hispanic White [hereafter, White], or Other [Native American, unknown, and Other]), poverty assessed at the US Census tract level (<10%, 10%-19%, ≥20%), whether the patient lived in an urban or rural zip code as classified by SEER, and state (California and Georgia).[12] Race and ethnicity data were collected because they are social determinants of health and to identify disparities by race and ethnicity in testing. Race and ethnicity were abstracted from medical records by trained staff at the state tumor registries and the categories were based on definitions from the US Census Bureau.

We evaluated testing for all cancer types in the SEER site recode variable. The analyses focused on 8 cancer types, of which 6 had established germline genetic testing indications: these were breast; colorectal; endometrial; epithelial ovarian, fallopian, and peritoneal (hereafter, ovarian); pancreatic; and prostate.[5-7] Lung cancer was included because of its recently discovered association with pathogenic results in various genes.[13] Patients with multiple primary tumor types were included because prior studies showed frequent pathogenic results in patients with multiple cancer types.[14] Patients with 1 or more cancer diagnosis (either before their index cancer or ≤2 years afterward) were included in the category of multiple cancer types.

Genes were grouped by associated cancer types or syndromes and by those recommended for testing by practice guidelines. All genes recommended for testing by practice guidelines from the National Comprehensive Cancer Network,[5-7] the American College of Medical Genetics and

Genomics[11] (n = 62; eTable 1 in Supplement 1), or both were categorized as follows: breast or ovarian cancer-associated genes including *BRCA1* and *BRCA2* (*BRCA1/2*); gastrointestinal cancer-associated genes not previously included in the breast or ovarian category, including Lynch syndrome genes; and other hereditary cancer syndrome genes. The genes not recommended for testing after a cancer diagnosis were categorized as non-guideline-recommended genes.

Statistical Analysis

The individual patient was the unit of analysis. We evaluated the presence and results of genetic testing according to age, race and ethnicity, and cancer type using SEER data. Testing trends were analyzed with logistic regression modeling, controlling for age, cancer type, and diagnosis year. In a separate logistic regression model, we assessed whether testing varied across race and ethnicity among the 3 cancer types (male breast, female breast, and ovarian[5,15]) with the highest testing rates overall, which were recommended for testing by practice guidelines throughout the study period, and by year, holding age constant and allowing testing trends and racial and ethnic differences to vary by year.

We examined the results by the categories defined above as breast and ovarian cancer-associated genes, gastrointestinal cancer-associated genes, other hereditary cancer syndrome genes, and non-guideline-recommended genes across selected cancer types. Additional details appear in the eMethods in Supplement 1. The statistical analyses were performed using SAS version 9.4 (SAS Institute Inc).

Results

Testing Use

From January 1, 2013, through March 31, 2019, there were 1 369 602 patients diagnosed with cancer who met the inclusion criteria (eFigure 1 in Supplement 1) and 93 052 (6.8%; 95% CI, 6.8%-6.8%) underwent germline genetic testing through March 31, 2021 (**Table 1** and **Table 2**). The proportion of patients tested varied by cancer type: male breast (50%), ovarian (38.6%), female breast (26%), multiple (7.5%), endometrial (6.4%), pancreatic (5.6%), colorectal (5.6%), prostate (1.1%), and lung (0.3%). Genetic testing for all other cancer types appears in eTable 2 in Supplement 1. The rates of testing increased over time, particularly for patients with pancreatic cancer (from 1.2% in 2013 to 18.6% in 2019). Testing remained low in patients with lung cancer (from 0.1% in 2013 to 0.8% in 2019; eTable 3 in Supplement 1).

Multivariable Model of Testing

In a logistic regression model, rates of testing were lower in older patients. Eighteen percent were tested at 40 years of age compared with 2% for patients diagnosed at 80 years of age, adjusting for year and type of cancer. Testing probability was highest at 51% (95% CI, 48%-53%) for male breast cancer, 36% (95% CI, 36%-36%) for ovarian cancer, and 22% (95% CI, 22%-22%) for female breast cancer, adjusting for year and age. The modeled probability of testing increased over time for all cancer types, but testing rates exceeded 50% for male breast cancer only (**Figure 1** and eTable 4 in Supplement 1).

A second multivariable regression model for testing included race and ethnicity. Controlling for age, cancer type, and year, testing probability differed between racial and ethnic groups overall (χ^2 = 2341, P < .001) and was lower for Asian patients (6%; 95% CI, 6%-6%), Black patients (6%; 95% CI, 6%-6%), Hispanic patients (6%; 95% CI, 6%-6%), and Other patients (5%; 95% CI, 5%-5%) compared with White patients (8%; 95% CI, 8%-8%). The racial and ethnic disparities for testing were largest among patients with male breast cancer, female breast cancer, or ovarian cancer (22% [95% CI, 21%-22%] for Asian patients, 25% [95% CI, 24%-25%] for Black patients, 23% [95% CI, 23%-23%] for Hispanic patients, and 31% [95% CI, 30%-31%] for White patients; P < .001 using the χ^2 test).

The modeled probability of genetic testing by year and race and ethnicity among patients with male breast, female breast, and ovarian cancer types vs other cancer types appears in **Figure 2**. A race and ethnicity × diagnosis year interaction term showed no improvement in racial and ethnic differences over time. Compared with White patients, the odds of testing by year decreased for Hispanic patients (odds ratio [OR], 0.98 [95% CI, 0.97-0.99]) and were unchanged for Asian patients (OR, 1.00 [95% CI, 0.98-1.01]), Black patients (OR, 0.99 [95% CI, 0.98-1.01]), and Other patients (OR, 0.99 [95% CI, 0.95-1.03]); the comparisons yielded statistically significant results (likelihood ratio χ^2_4 = 9.76, P = .045; eTable 5 in Supplement 1).

Pathogenic and Uncertain Results by Race, Ethnicity, and Cancer Type

The median number of genes tested increased by year from 2 in 2013 to 34 in 2019. The frequency of pathogenic results was similar across cancer types (10%-30%) and stable over time (eTable 6 in Supplement 1). Uncertain results increased at a greater rate in races and ethnicities other than White (40.0% in Asian patients in 2019 vs 12.2% in 2013, 39.0% in Black patients in 2019 vs 7.5% in 2013, 29.3% in Hispanic patients in 2019 vs 8.6% in 2013, 24.9% in White patients in 2019 vs 6.3% in 2013, and 34.6% in Other patients in 2019 vs 3.8% in 2013; χ^2 = 1808, P < .001; eTable 7 in Supplement 1). The ratio of uncertain to pathogenic results varied by race and ethnicity: White patients diagnosed in 2019 were 1.73 (95% CI, 1.56-1.92) times more likely to receive uncertain results (24.9%) than pathogenic results (14.4%), whereas Asian and Black patients diagnosed in 2019 were 3.74 (95% CI, 3.13-4.46) times more likely to receive uncertain results (40.0% for Asian patients and 39.0% for Black patients) than pathogenic results (10.2% for Asian patients and 11.0% for Black patients) (eTable 7 in Supplement 1).

Genes With Pathogenic Results by Cancer Type

Of all pathogenic results, 67.5% to 94.9% of variants were identified in genes for which practice guidelines recommend testing and 68.3% to 83.8% of variants were identified in genes associated with the diagnosed cancer type.

Table 1. Characteristics of Patients Diagnosed With Cancer in California and Georgia and Reported to Surveillance, Epidemiology, and End Results (SEER) Registries From 2013 to 2019 by Germline Genetic Testing Status[a]

	Breast (female)		Breast (male)		Colorectal		Endometrial		Lung		Ovarian		Pancreatic		Prostate		Multiple cancer types		All other cancer types	
	No.	Tested, %	No.	Tested, %	No.	Tested, %	No.	Tested, %	No.	Tested, %	No.	Tested, %	No.	Tested, %	No.	Tested, %	No.	Tested, %	No.	Tested, %
Overall	203 575	26.0	1344	50.0	93 562	5.6	38 324	6.4	103 139	0.3	16 444	38.6	30 595	5.6	140 810	1.1	231 261	7.5	510 548	0.9
State																				
California	159 165	24.7	984	49.1	72 281	5.6	30 728	6.1	74 026	0.3	13 347	37.5	24 047	5.9	104 471	1.2	180 456	7.4	400 579	0.9
Georgia	44 410	30.6	360	52.5	21 281	5.9	7596	7.3	29 113	0.2	3097	43.1	6548	4.5	36 339	0.8	50 805	7.6	109 969	0.8
Sex[b]																				
Female	203 575	26.0	NA	NA	44 460	6.2	38 324	6.4	50 274	0.5	16 444	38.6	15 039	5.8	NA	NA	119 761	13.0	223 276	1.4
Male	NA	NA	1344	50.0	49 102	5.1	NA	NA	52 865	0.2	NA	NA	15 556	5.4	140 810	1.1	111 500	1.5	287 272	0.6
Age group at diagnosis, y																				
20-39	10 569	69.5	36	55.6	4014	28.8	1719	14.7	833	2.8	946	39.4	509	16.7	67	6.0	2980	19.3	49 721	2.2
40-49	34 645	56.7	117	55.6	9160	19.4	3622	10.8	2828	1.8	1871	45.9	1478	12.6	3035	2.9	8527	26.8	51 496	2.0
50-59	50 867	25.0	284	47.5	22 419	5.1	10 462	6.8	15 329	0.5	3832	44.1	5017	7.6	27 877	1.4	26 876	15.1	100 773	1.0
60-69	56 394	15.7	398	55.3	24 948	2.9	13 680	5.6	31 660	0.3	4564	41.6	9087	6.5	60 888	1.0	59 743	9.1	134 498	0.7
70-79	35 037	10.3	310	49.4	18 326	2.0	6473	4.2	32 439	0.2	3370	36.1	8334	4.6	37 263	0.9	73 545	5.0	103 458	0.4
≥80	16 063	4.4	199	39.7	14 695	0.8	2368	2.0	20 050	0	1861	16.7	6170	1.5	11 680	0.6	59 590	2.0	70 602	0.1
Race and ethnicity[c]																				
Asian	26 749	23.4	117	44.4	11 828	4.6	4602	6.3	11 695	0.4	2084	36.5	3476	5.9	9369	1.1	15 271	10.5	44 184	0.9
Black	23 957	26.0	212	44.8	11 528	4.4	4384	4.4	12 580	0.2	1390	29.4	3848	3.3	24 007	0.7	20 278	7.7	41 730	0.7
Hispanic	37 294	26.8	153	43.1	18 350	6.5	8116	6.0	10 532	0.3	3396	34.3	5572	4.8	21 360	0.7	24 266	9.1	91 939	1.1
Non-Hispanic White	112 660	26.5	844	53.7	50 356	5.9	20 705	7.0	67 657	0.3	9438	41.9	17 525	6.3	78 893	1.3	169 841	6.9	313 091	0.9
Other[d]	2915	20.6	18	33.3	1500	4.0	517	4.4	675	0.1	136	40.4	174	5.2	7181	0.6	1605	5.2	19 604	0.7

Abbreviation: NA, not applicable.

[a] Includes genetic tests performed after and within 2 years of diagnosis from January 1, 2013, through March 31, 2021.

[b] Those coded as other (n = 328) were excluded (eFigure 1 in Supplement 1).

[c] Race and ethnicity data were collected by self-report and the categories are mutually exclusive. The categories were based on definitions from the US Census Bureau. Race was derived from the SEER race1 variable (North American Association of Central Cancer Registries [NAACCR] variable 160). Ethnicity (Hispanic ethnicity) was obtained from NAACCR Hispanic identification algorithm–derived Hispanic origin (NAACCR variable 191). All patients identified as Hispanic were coded as Hispanic regardless of race.

[d] Includes patients with SEER race1 variable coded as Native American, unknown, and Other.

Table 2. Additional Characteristics of Patients Diagnosed With Cancer in California and Georgia and Reported to Surveillance, Epidemiology, and End Results (SEER) Registries From 2013 to 2019 by Germline Genetic Testing Status[a]

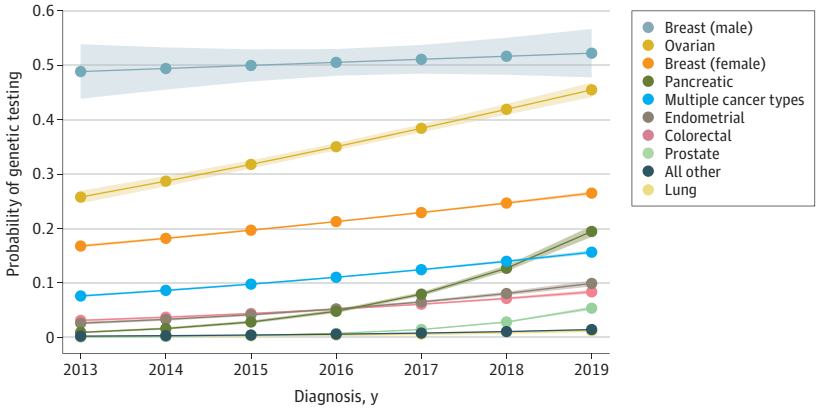
	Breast (female)		Breast (male)		Colorectal		Endometrial		Lung		Ovarian		Pancreatic		Prostate		Multiple cancer types		All other cancer types	
	No.	Tested, %	No.	Tested, %	No.	Tested, %	No.	Tested, %	No.	Tested, %	No.	Tested, %	No.	Tested, %	No.	Tested, %	No.	Tested, %	No.	Tested, %
Overall	203 575	26.0	1344	50.0	93 562	5.6	38 324	6.4	103 139	0.3	16 444	38.6	30 595	5.6	140 810	1.1	231 261	7.5	510 548	0.9
Poverty assessed at the US Census tract level																				
Low (<10%)	106 118	27.9	710	54.1	42 010	6.5	18 226	7.0	43 766	0.4	8241	43.0	14 827	7.4	72 408	1.4	125 222	8.1	255 603	1.0
Medium (10%-19%)	62 000	24.4	400	47.5	30 956	5.3	12 559	6.1	34 546	0.3	5149	35.9	9458	4.3	42 555	0.8	68 738	6.9	158 704	0.8
High (≥20%)	35 457	22.9	234	41.9	20 596	4.4	7539	5.2	24 827	0.2	3054	31.2	6310	3.3	25 847	0.6	37 301	6.3	96 241	0.7
Zip code classified by SEER																				
Urban	190 340	26.1	1245	50.1	85 984	5.7	35 673	6.4	92 393	0.3	15 351	38.6	28 264	5.7	129 858	1.1	213 129	7.6	471 730	0.9
Rural	13 235	24.2	99	48.5	7578	4.9	2651	5.2	10 746	0.2	1093	38.0	2331	4.4	10 952	0.9	18 132	6.3	38 818	0.7
Cancer stage[b]																				
0	35 224	20.3	138	46.4	4640	2.5	142	2.1	289	0.7	38	28.9	223	1.3			NA	NA	NA	NA
I	82 431	25.7	399	54.1	19 152	4.6	26 416	6.0	18 694	0.5	3080	34.7	3503	6.0	29 557	0.5	NA	NA	NA	NA
II	50 216	30.6	433	54.7	19 325	6.3	1700	5.1	6953	0.2	1235	44.0	6045	6.2	62 491	0.6	NA	NA	NA	NA
III	17 030	32.2	180	49.4	22 690	7.4	4552	8.6	18 195	0.3	5970	45.1	2892	9.8	16 696	1.8	NA	NA	NA	NA
IV	9398	19.7	115	40.0	19 685	6.1	3255	9.0	52 395	0.3	5156	36.1	15 285	5.0	15 620	3.7	NA	NA	NA	NA

Abbreviation: NA, not applicable.

[a] Includes genetic tests performed after and within 2 years of diagnosis from January 1, 2013, through March 31, 2021.

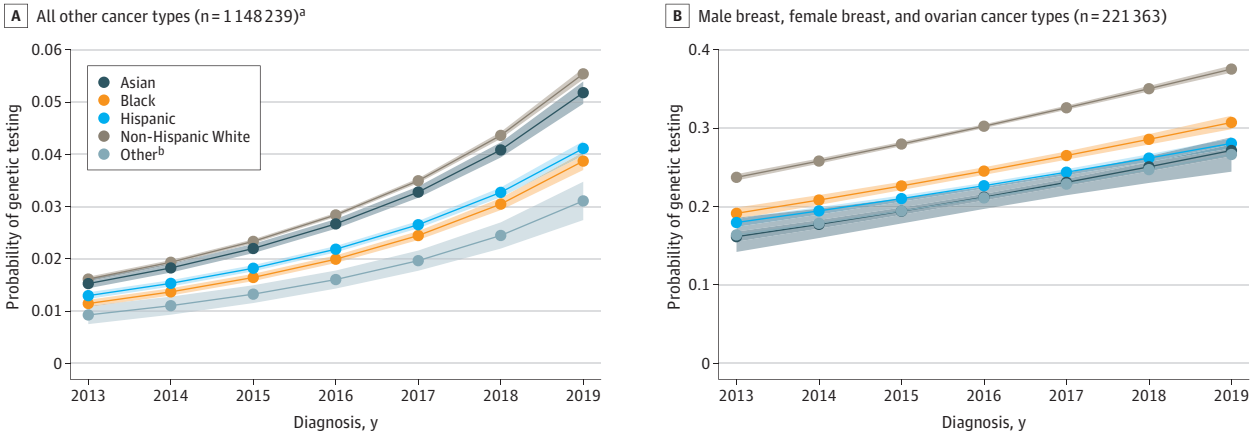
[b] Stage was obtained from SEER-derived American Joint Committee on Cancer 7 stage group (North American Association of Central Cancer Registries [NAACCR] variable 3430) for cases diagnosed before 2018 and SEER-derived extent of disease 2018 stage group (NAACCR variable 818) for cases diagnosed during or after 2018. Stage was omitted for categories including more than 1 cancer type (eg, multiple cancer types and all other cancer types).

Figure 1. Modeled Probability of Genetic Testing Over Time in the Most Common Cancer Types Diagnosed From 2013 to 2019



The probabilities were predicted from a logistic regression model that included variables for age, cancer type, diagnosis year (2013-2019), and a diagnosis year × cancer type interaction, averaging across a constant age distribution for all years and cancer types. The shading around the curves represents 95% CIs.

Figure 2. Modeled Probability of Genetic Testing Over Time Across Racial and Ethnic Groups



The probabilities were predicted from a logistic regression model that included age, cancer type, diagnosis year (2013-2019), an indicator for the 3 cancer types (male breast, female breast, and ovarian) with the highest testing rates that had testing guidelines throughout the study period, and 3 interactions: (1) cancer type and age, (2) racial and ethnic group and year, and (3) the 3 cancer types (male breast, female breast, and ovarian) with the highest testing rates and racial and ethnic group. The estimates were averaged across constant age and cancer type distributions within each of (1) other cancer types (excluded male breast, female breast, and ovarian) and (2) only male breast, female breast, and ovarian cancer types. The racial and ethnic categories were mutually exclusive. The shading around the curves represents 95% CIs.

[a] Includes all cancer types not included in panel B.

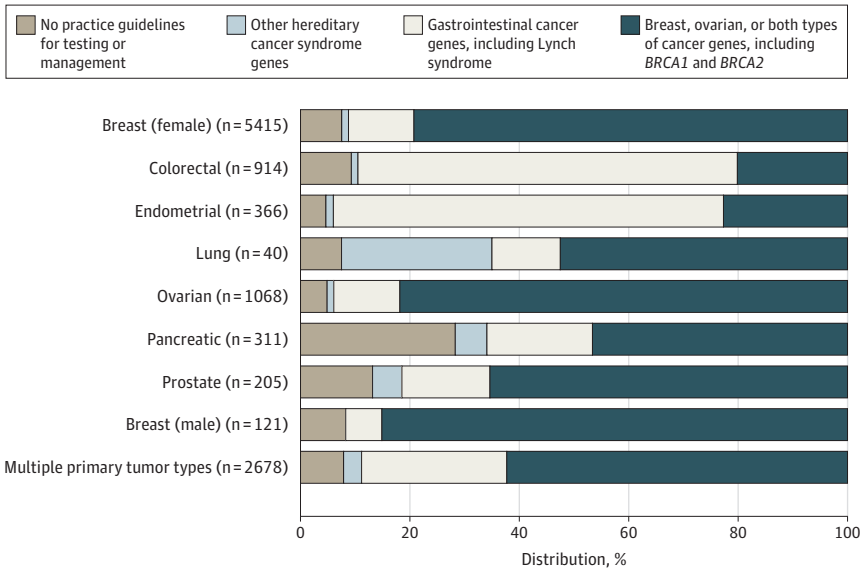
[b] Includes patients with Surveillance, Epidemiology, and End Results race1 variable coded as Native American, unknown, and Other.

The distribution of genes for individuals with pathogenic results (by cancer-associated gene categories) appear in **Figure 3**. Gastrointestinal cancer-associated genes represented 68.3% of pathogenic results in colorectal cancer and 71.8% of pathogenic results in endometrial cancer. Breast and ovarian cancer-associated genes represented 79.5% of pathogenic results in female breast cancer, 83.8% in male breast cancer, and 82.0% in ovarian cancer. Non-guideline-recommended genes represented between 5.1% of pathogenic results in endometrial cancer to 28.1% of pathogenic results in pancreatic cancer. In a sensitivity analysis, *MUTYH* was recoded as a non-guideline-recommended gene, and the non-guideline-recommended genes increased to 10.4% of pathogenic results in endometrial cancer and 32.5% in pancreatic cancer (eFigure 2 in Supplement 1).

Discussion

In this population-based study conducted in California and Georgia between 2013 and 2021, use of germline genetic testing was only 6.8% after a cancer diagnosis. Genetic testing rates increased over time, but even in 2021 were far lower than 100% for specific cancer types, such as ovarian, male breast, and pancreatic, recommended by practice guidelines. Because clinical trials have demonstrated that

Figure 3. Distribution of Genes for Patients With Pathogenic Results



The results are grouped by associated cancer types or hereditary syndromes and by practice guideline indications for testing across selected cancer types (additional details appear in eTable 1 in Supplement 1).

germline-directed cancer screening, preventive surgery, and targeted therapies can improve survival,[1-4] low rates of germline genetic testing may contribute to higher rates of cancer mortality.

The racial and ethnic disparities of lower rates of testing in Asian, Black, and Hispanic patients compared with White patients were largest for the 3 cancer types that had the highest testing rates overall and that had established recommendations from practice guidelines throughout the study period[5,15]: male breast, female breast, and ovarian. This finding is consistent with prior studies.[9,16,17] Racial and ethnic differences in testing persisted through 2021. Although there are many possible explanations (including individual preferences and insurance coverage), strategies such as education of clinicians, incorporating genetic counselors into oncology practices, telemedicine, and electronic health record reminders warrant study to address testing gaps affecting patients who are Asian, Black, or Hispanic.[18,19]

Testing rates were heterogeneous between syndromes with higher rates of testing in primarily *BRCA1/2*-associated (26.0% for breast cancer and 38.6% for ovarian cancer) than Lynch syndrome–associated cancer types (5.6% for colorectal cancer and 6.4% for endometrial cancer). Persistent undertesting of Lynch syndrome–associated cancer types represents a target for improvement because population frequencies of pathogenic results in Lynch syndrome genes and *BRCA1/2* are similar.[20,21] Germline genetic testing rates did not differ by cancer stage; this appears inconsistent with previous reports that sequencing advanced cancer types often identifies results warranting confirmatory germline testing.[22] The lack of association between cancer stage and germline genetic testing may reflect insufficient confirmatory testing of patients with advanced cancer and failure to offer testing to patients' relatives.[23,24]

Although testing failed to meet practice guidelines, it increased substantially over time. This might be explained by the growing evidence demonstrating benefits of treatment with poly(ADP-ribose) polymerase inhibitors. These drugs were approved for *BRCA1/2*-associated ovarian cancer in 2014, breast cancer in 2018, pancreatic cancer in 2019, and prostate cancer in 2020.[2,25-27]

Pathogenic results were most common in genes with management guidelines, such as prophylactic salpingo-oophorectomy or frequent screening colonoscopy.[5,6] This suggests that most pathogenic results may facilitate personalized, risk-adapted care. Pathogenic results often occurred in diagnosis-concordant genes (eg, breast cancer– and ovarian cancer–associated genes in patients with breast cancer),[5,6] but were also observed in diagnosis-discordant categories. These results offer support for panel testing of multiple genes across cancer types with appropriate counseling.

By contrast, higher rates of uncertain results, particularly in Asian and Black patients, have the potential to result in suboptimal care because some studies reported mismanagement of uncertain results with preventive surgeries.[28,29] Prior studies have shown that uncertain results are more frequent among patients from racial and ethnic groups that have had less access to genetic testing.[18,30] Even though germline genetic testing costs have declined and insurance coverage has increased, out-of-pocket costs in the range of $100 to $250 may present a barrier to testing. Increased access to both clinical testing and genetics research is needed for underrepresented groups.

Limitations

This study has several limitations. First, germline genetic testing from laboratories other than the 4 laboratories selected for this study, or from direct-to-consumer laboratories, was not ascertained; however, evidence suggested that

these 4 participating laboratories were the primary genetic testing laboratories.[8,9]

Second, SEER lacks data about family history or tumor sequencing. Third, insurance information was incomplete. Fourth, data were not available about why germline genetic testing did not occur, such as when testing was declined by patients. Fifth, data were limited to California and Georgia and may not apply to other states in the US.

Conclusions

Among patients diagnosed with cancer in California and Georgia between 2013 and 2019, only 6.8% underwent germline genetic testing. Compared with non-Hispanic White patients, rates of testing were lower among Asian, Black, and Hispanic patients.

ARTICLE INFORMATION

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