Supplemental Online Content

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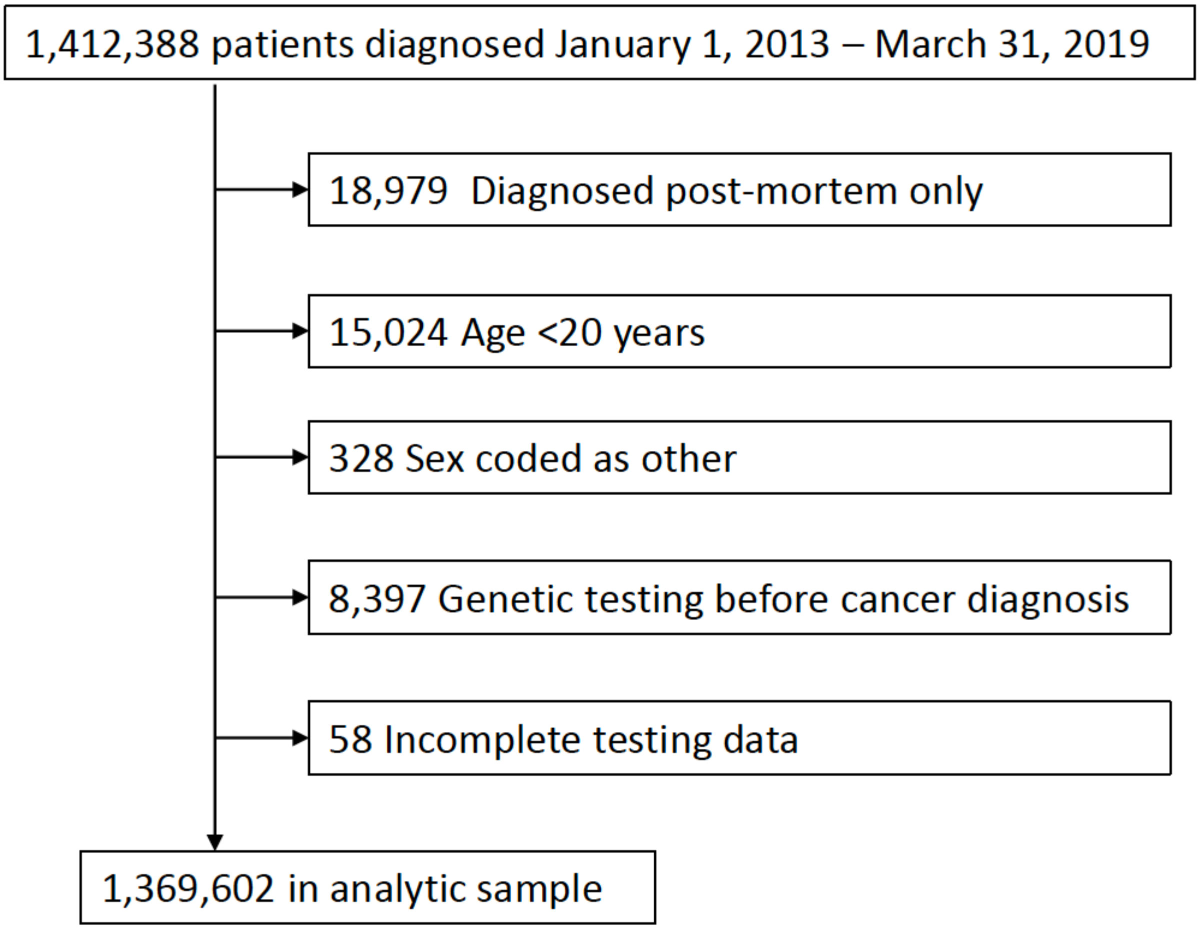
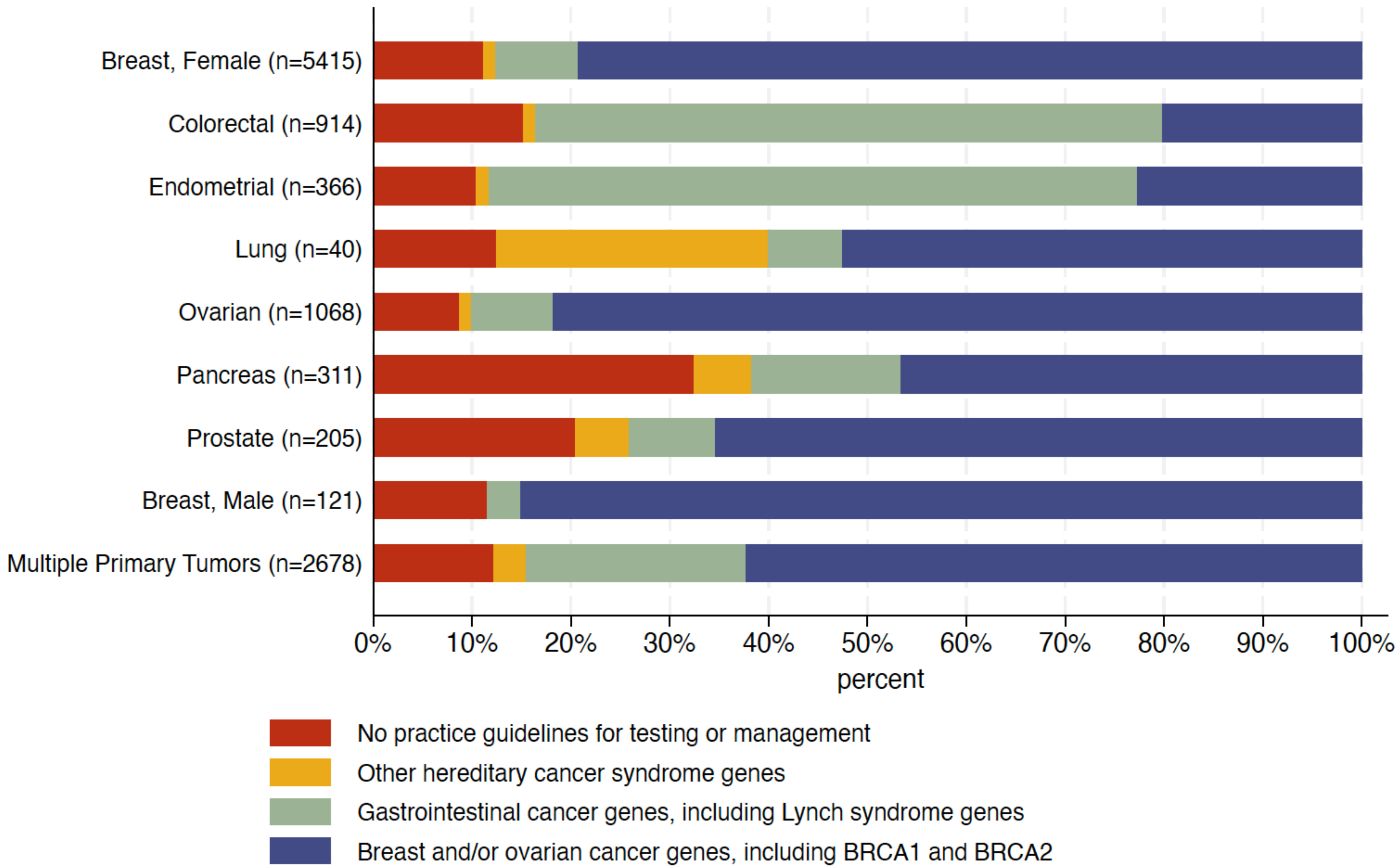
This supplemental material has been provided by the authors to give readers additional information about their work.

eFigure 1. Flow and decay diagram



eFigure 2. Genes with pathogenic results, grouped by associated cancers and/or hereditary syndromes and by practice guideline indications for clinical testing, with *MUTYH* re-categorized as a gene with no practice guidelines for testing.



eMethods

Genetic Testing Results

To protect confidentiality of the four participating laboratories, only those genes that were offered for testing by two or more laboratories (N=107, shown in **eTable 1**) were included for analysis. If a patient received more than one test of a given gene over time, or if the laboratory re-classified results of a tested gene over time (e.g., uncertain to benign), the most recent interpretation provided by the laboratory to the ordering clinician was used for analysis.

Logistic Regression Model Specification and Model Output

Model for Testing Time Trends Across Years of Cancer Diagnosis, 2013-2019

The model for testing from 2013-2019 includes age (in decades, centered at the mean age of the sample, 62 years) and calendar year of cancer diagnosis (2013-2019, centered at 2016). The model also includes fixed effects for 10 cancer types (the 8 most common along with a group representing multiple cancers and a final group for all other cancers), thus estimating the variation in testing rates across cancers. An interaction term of year with cancer type was also included to allow the trends across year to vary across the cancer types. The coefficients for these variables were large with relatively small standard errors. The outputs of this model are shown as predicted probabilities of testing by the year and cancer type variables averaging across age in **Figure 1,** and the odds ratios for each variable in the full model are presented in **eTable 4**.

Model for Differences in Genetic Testing by Racial and Ethnic Groups

For this model, we built on the trend model described above by adding a variable with five racial and ethnic groups (Asian, Black, Hispanic, non-Hispanic White, Other). In addition, we added a variable (breast-ovary) that indicates the three cancers with the highest testing rates that had testing guidelines throughout the study period (male breast, female breast, and ovarian cancer), as these cancers might be expected to have fewer racial and ethnic disparities, given the presence of well-established guidelines for testing.

Thus, the second model added an interaction between the breast-ovary variable and racial and ethnic group to test whether the race and ethnicity effects were different among male breast, female breast, and ovarian cancer versus all other cancers. The improvement in fit was assessed by the magnitude of the interaction coefficients along with the 95% confidence intervals, as well as by a likelihood ratio test comparing the two models. As all of these suggested improved model fit, the interaction term was retained.

In a third model, we added an interaction term between the racial and ethnic groups and year of cancer diagnosis, to assess for changes in the odds of testing between racial and ethnic groups across years of cancer diagnosis as a sign that any disparities are increasing or decreasing. Again, improvement in fit was assessed by the magnitude of the interaction coefficients and the likelihood ratio test comparing the second and third models. In this case, model fit also improved by a smaller amount judging by the relatively small coefficients for the interaction terms; however, with the large sample size, overall model fit still improved using the likelihood ratio test, with a conventional $p<0.05$ value cutoff, so the interaction was retained in the final model. The outputs of this model are shown as predicted probabilities **Figure 2** and tables of odds ratios for all three models, along with the likelihood ratio tests, are in **eTable 5**.

Results of the models are presented as marginal effects or as differences in the probability of the outcome as a predictor changes, holding all the other covariates constant by averaging across the covariate values of all the persons in the sample[1].

eReference

1. Norton EC, Dowd BE, Maciejewski ML. Marginal Effects-Quantifying the Effect of Changes in Risk Factors in Logistic Regression Models. *JAMA*. Apr 2 2019;321(13):1304-1305. doi:10.1001/jama.2019.1954

eTable 1. All tested genes, grouped by cancer type associations and testing guideline recommendations
Breast and/or Ovarian Cancer-Associated Genes[a]
BRCA1
BRCA2
ATM
BARD1
BRIP1
CDH1
CHEK2
DICER1
NF1
PALB2
PTEN
RAD51C
RAD51D
SMARCA4
STK11
TP53
Gastrointestinal Cancer-Associated Genes[a]
Lynch Syndrome genes
EPCAM
MLH1
MSH2
MSH6
PMS2
Other gastrointestinal cancer-associated genes
APC
AXIN2
BMPR1A
CDKN2A
GREM1
MLH3
MSH3
MUTYH[b]
NTHL1
POLD1
POLE
SMAD4
Other Hereditary Cancer Syndrome-Associated Genes[a]
BAP1
CDK4
CEBPA
EGFR
FH
FLCN
KIT
LZTR1
MAX
MEN1
MET

eTable 1. All tested genes, grouped by cancer type associations and testing guideline recommendations
MITF
NF2
POT1
PTCH1
RB1
RET
SDHA
SDHAF2
SDHB
SDHC
SDHD
SMARCB1
SUFU
TMEM127
TSC1
TSC2
VHL
WT1
Genes with No Guidelines for Clinical Testing after a Cancer Diagnosis
AIP
AKT1
ALK
BLM
BUB1B
CASR
CDC73
CDKN1B
CDKN1C
CFTR
CPA1
CTC1
CTNNA1
CTR9
CTRC
DIS3L2
DKC1
EGLN1
FAM175A
FANCC
FANCM
GALNT12
GATA2
HOXB13
KIF1B
MRE11A
NBN
PALLD
PDGFRA
PHOX2B

eTable 1. All tested genes, grouped by cancer type associations and testing guideline recommendations
PRKAR1A
PRSS1
RAD50
RECQL
RINT1
RNF43
RPS20
RTEL1
RUNX1
SMARCE1
SPINK1
SPRED1
TERC
TERT
XRCC2
[a]Practice guidelines of the National Comprehensive Cancer Network and/or American College of Medical Genetics advise testing of these genes for cancer risk assessment and/or cancer treatment, in appropriate clinical circumstances. [b]Given uncertainty as to whether monoallelic *MUTYH* pathogenic results are clinically actionable, *MUTYH* was re-coded as a gene with no testing guidelines in a sensitivity analysis, the results of which are shown in **eFigure 2**.

eTable 2. Genetic testing utilization among individuals with all other cancer types[a], diagnosed 2013-2019		
Anatomic site as coded by SEER	N	Tested, %
Lip	1,699	0.2
Tongue	8,660	0.4
Salivary gland	2,945	0.5
Floor of mouth	878	0.2
Gum and other mouth	3,136	0.4
Nasopharynx	1,839	0.3
Tonsil	5,650	0.3
Oropharynx	1,223	0.0
Hypopharynx	1,083	0.2
Other oral cavity and pharynx	427	0.0
Esophagus	9,143	0.7
Stomach	18,382	3.1
Small intestine	5,051	3.6
Anus, anal canal and anorectum	7,461	0.9
Liver	23,056	0.1
Intrahepatic bile duct	3,217	2.7
Gallbladder	3,262	1.1
Other biliary	5,023	2.6
Retroperitoneum	825	3.0
Peritoneum, omentum and mesentery	168	3.0
Other digestive organs	1,759	1.8
Nose, nasal cavity and middle ear	1,691	0.5
Larynx	5,994	0.2
Pleura	1,238	0.5
Trachea, mediastinum and other respiratory organs	341	0.6
Bones and joints	1,695	1.1
Soft tissue including heart	8,110	1.7
Melanoma of the skin	93,891	0.8
Other non-epithelial skin	5,430	0.9
Cervix uteri	10,642	1.3
Uterus, not otherwise specified	1,271	3.5
Ovary (non-epithelial)	1,611	6.3
Vagina	1,154	1.0
Vulva	6,171	1.1
Other female genital organs	693	11.7
Testis	7,947	0.5
Penis	1,514	0.2
Other male genital organs	351	0.6
Urinary bladder	36,781	0.3
Kidney and renal pelvis	37,548	1.6
Ureter	1,242	0.6
Other urinary organs	776	0.3
Eye and orbit	2,170	1.2
Brain	12,893	1.0
Cranial nerves and other nervous system	754	1.7
Thyroid	33,945	1.3

Other endocrine including thymus	1,593	5.6
Hodgkin, nodal	5,323	0.7
Hodgkin, extranodal	106	0.9
Non-Hodgkin lymphoma, nodal	28,183	0.4
Non-Hodgkin lymphoma, extra-nodal	22,617	0.3
Myeloma	16,860	0.2
Acute lymphocytic leukemia	690	0.7
Chronic lymphocytic leukemia	2,643	0.3
Other lymphocytic leukemia	863	0.3
Acute myeloid leukemia	7,404	0.2
Chronic myeloid leukemia	4,170	0.4
Other myeloid/monocytic leukemia	200	0.5
Acute monocytic leukemia	386	0.0
Other acute leukemia	295	0.3
Aleukemic, subleukemic and not otherwise specified	971	0.2
Mesothelioma	271	0.0
Kaposi sarcoma	423	0.0
Miscellaneous	34,791	0.6
[a]Excludes cancers in Table 1: breast (female), breast (male), colorectal, endometrial, lung, ovarian, pancreatic, prostate and multiple primary tumors		

eTable 3. Genetic testing time trends[a] among individuals diagnosed with cancer in Georgia and California and reported to SEER registries from 2013-2019

	Breast, Female		Breast, Male		Colorectal		Endometrial		Lung		Ovarian		Pancreas		Prostate		Multiple Primary Tumors		All Other Cancers	
	N	T, %	N	T, %	N	T, %	N	T, %	N	T, %	N	T, %	N	T, %	N	T, %	N	T, %	N	T, %
Year of Diagnosis																				
2013	31,438	21.6	188	43.1	14,223	3.2	5,429	2.9	16,457	0.1	2,584	28.2	4,515	1.2	21,520	0.1	42,203	5.2	76,920	0.3
2014	31,526	23.4	214	52.3	14,888	4.2	5,832	4.1	16,465	0.1	2,609	35.3	4,692	2.0	19,780	0.2	38,720	6.2	80,893	0.5
2015	32,808	25.2	216	52.3	15,213	4.9	6,133	5.3	16,759	0.2	2,770	37.8	4,835	2.6	21,611	0.3	35,265	7.1	83,314	0.7
2016	32,741	25.8	222	50.0	15,367	5.7	6,286	6.6	16,719	0.3	2,636	39.9	5,013	4.3	22,716	0.7	33,162	7.4	83,211	0.9
2017	33,282	27.0	205	51.7	15,131	7.0	6,527	7.5	16,743	0.4	2,688	41.2	5,026	6.0	24,647	1.3	32,338	8.4	83,911	1.2
2018	33,351	30.6	232	46.6	14,987	7.9	6,569	9.9	15,907	0.6	2,574	45.6	5,213	13.0	24,262	2.7	39,845	9.8	82,048	1.5
2019[b]	8,429	33.7	67	61.2	3,753	9.1	1,548	10.4	4,089	0.8	583	54.2	1,301	18.6	6,274	3.7	9,728	11.0	20,251	2.0

Abbreviations: N, number; T, Tested

[a]Includes genetic tests performed from January 1, 2013, through first quarter of 2021 (through March 31)

[b]Includes diagnoses only through the first quarter of 2019 (through March 31)

eTable 4. Logistic regression model output for individuals diagnosed with cancer in Georgia and California and reported to SEER registries from 2013-2019, controlling for age and cancer type and allowing for a year by cancer type interaction (odds ratios and 95% confidence interval)

	Odds Ratio	95% CI
Age (decades)	0.51	[0.51,0.52]
Year of diagnosis	1.20	[1.18,1.22]
Cancer type		
Colon	1	[1,1]
Uterine	1.01	[0.95,1.07]
Breast-Female	5.97	[5.78,6.17]
Lung	0.068	[0.059,0.078]
Ovary	13.5	[12.9,14.1]
Pancreas	0.92	[0.85,0.99]
Prostate	0.13	[0.11,0.14]
Breast-Male	28.8	[25.5,32.5]
Multiple	2.46	[2.37,2.54]
All Other	0.10	[0.097,0.11]
Year x Cancer Interaction		
Colon x year	1	[1,1]
Uterine x year	1.07	[1.04,1.10]
Breast-Female x year	0.93	[0.91,0.95]
Lung x year	1.20	[1.12,1.29]
Ovary x year	0.99	[0.96,1.01]
Pancreas x year	1.48	[1.43,1.55]
Prostate x year	1.68	[1.60,1.76]
Breast-Male x year	0.85	[0.80,0.91]
Multiple x year	0.97	[0.95,0.98]
All Other x year	1.13	[1.10,1.15]
N	1369602	

eTable 5. Three logistic regression model outputs regressing genetic testing on SEER racial and ethnic categories controlling for year, age and a variable that indicates three cancers with the highest testing rates that had testing guidelines throughout the study period (male breast, female breast, and ovarian cancer) for cancers diagnosed in Georgia and California from 2013-2019. The base model includes the year cancer-type interaction, the second model includes an interaction between race and ethnicity and the breast-ovarian grouping variable and the third includes an interaction of race and ethnicity and year.

	Base		Cancer type interaction		Year interaction	
	Odds Ratio	95% CI	Odds Ratio	95% CI	Odds Ratio	95% CI
Breast-ovary	61.4	[59.2,63.7]	66.0	[63.5,68.6]	66.2	[63.6,68.8]
Year of diagnosis	1.13	[1.12,1.13]	1.13	[1.12,1.13]	1.13	[1.12,1.14]
Age (decades)	0.50	[0.50,0.50]	0.50	[0.50,0.50]	0.50	[0.50,0.50]
Race-Ethnic group:						
NH White	1	[1,1]	1	[1,1]	1	[1,1]
Black	0.70	[0.68,0.72]	0.67	[0.64,0.70]	0.67	[0.65,0.70]
Asian	0.68	[0.67,0.70]	0.93	[0.89,0.97]	0.93	[0.89,0.97]
Hispanic	0.67	[0.66,0.69]	0.74	[0.71,0.76]	0.75	[0.72,0.77]
Other	0.55	[0.51,0.59]	0.53	[0.47,0.59]	0.53	[0.47,0.60]
Cancer type:						
Colon	10.3	[9.79,10.7]	10.2	[9.72,10.7]	10.2	[9.72,10.7]
Uterine	10.5	[9.86,11.1]	10.3	[9.70,10.9]	10.3	[9.70,10.9]
Breast-Female	1	[1,1]	1	[1,1]	1	[1,1]
Lung	0.67	[0.58,0.78]	0.68	[0.59,0.78]	0.68	[0.59,0.78]
Ovary	2.26	[2.18,2.35]	2.27	[2.19,2.35]	2.27	[2.19,2.35]
Pancreas	9.40	[8.65,10.2]	9.39	[8.65,10.2]	9.39	[8.65,10.2]
Prostate	1.30	[1.17,1.44]	1.33	[1.20,1.47]	1.33	[1.20,1.47]
Breast-Male	4.76	[4.23,5.35]	4.70	[4.18,5.29]	4.70	[4.18,5.29]
Multiple	24.0	[23.1,25.0]	24.4	[23.5,25.4]	24.4	[23.5,25.4]
All Other	1	[1,1]	1	[1,1]	1	[1,1]
Cancer x Year:						
Colon x year	1.08	[1.06,1.09]	1.07	[1.05,1.09]	1.07	[1.05,1.09]
Uterine x year	1.15	[1.12,1.18]	1.15	[1.12,1.18]	1.15	[1.12,1.18]
Breast-Female x year su	1	[1,1]	1	[1,1]	1	[1,1]
Lung x year	1.29	[1.20,1.38]	1.29	[1.20,1.38]	1.28	[1.20,1.38]
Ovary x year	1.06	[1.04,1.08]	1.06	[1.04,1.08]	1.06	[1.04,1.08]
Pancreas x year	1.60	[1.54,1.66]	1.60	[1.54,1.66]	1.60	[1.54,1.66]
Prostate x year	1.80	[1.73,1.88]	1.80	[1.73,1.88]	1.80	[1.73,1.88]
Breast-Male x year	0.92	[0.86,0.98]	0.92	[0.86,0.98]	0.92	[0.86,0.98]
Multiple x year	1.04	[1.03,1.05]	1.04	[1.02,1.05]	1.03	[1.02,1.04]
All Other x year	1.21	[1.19,1.23]	1.21	[1.19,1.23]	1.21	[1.19,1.23]
Breast-ovary x Race-Ethnic:						
Breast-ovary x NH White			1	[1,1]	1	[1,1]
Breast-ovary x Black			1.06	[1.01,1.12]	1.06	[1.01,1.12]
Breast-ovary x Asian			0.62	[0.59,0.65]	0.62	[0.59,0.65]
Breast-ovary x Hispanic			0.86	[0.82,0.90]	0.85	[0.82,0.89]
Breast-ovary x Other			1.08	[0.94,1.25]	1.08	[0.93,1.24]
Race-Ethnic x Year:						
NH White x year					1	[1,1]
Black x year					0.99	[0.98,1.01]
Asian x year					1.00	[0.98,1.01]
Hispanic x year					0.98	[0.97,0.99]
Other x year					0.99	[0.95,1.03]
Likelihood ratio Chi2			380.5		9.76	
Degrees of freedom			4		4	
p-value			4.5e-81		0.045	
N	1369602		1369602		1369602	

eTable 6. Uncertain and pathogenic results[a] and ratio in individuals with selected cancers diagnosed and reported to Georgia and California SEER registries, 2013-2019

	Breast, Female (n=52,893)			Breast, Male (n=672)			Colorectal (n=5,277)			Endometrial (n=2,434)			Lung (n=313)			Ovarian (n=6,345)			Pancreas (n=1,711)			Prostate (n=1,502)			Multiple Primary Tumors (n=17,239)		
Year of Diagnosis	U%	P%	U:P	U%	P%	U:P	U%	P%	U:P	U%	P%	U:P	U%	P%	U:P	U%	P%	U:P	U%	P%	U:P	U%	P%	U:P	U%	P%	U:P
2013	7.2	7.8	0.92	7.4	14.8	0.50	8.3	19.4	0.43	8.8	13.8	0.64	18.8	12.5	1.50	7.8	17.7	0.44	7.6	9.4	0.80	0.0	29.4	0.00	7.6	13.0	0.58
2014	12.0	8.6	1.39	8.0	13.4	0.60	14.7	17.3	0.85	15.9	11.7	1.36	13.0	13.0	1.00	13.0	17.1	0.76	14.9	16.0	0.93	12.1	21.2	0.57	12.0	14.0	0.86
2015	16.9	10.6	1.59	14.2	16.8	0.84	17.4	16.6	1.05	20.0	16.9	1.18	7.4	25.9	0.29	16.4	16.3	1.01	17.2	15.6	1.10	15.4	15.4	1.00	15.0	15.5	0.97
2016	18.5	10.9	1.70	18.9	20.7	0.91	19.2	18.9	1.02	17.7	19.2	0.92	12.7	3.6	3.50	17.7	18.5	0.96	22.0	17.3	1.27	18.5	18.5	1.00	18.8	16.1	1.17
2017	22.8	10.9	2.10	17.9	19.8	0.90	26.4	16.2	1.63	24.4	15.4	1.59	33.3	7.6	4.40	21.9	15.9	1.38	27.8	18.9	1.47	24.0	16.1	1.49	22.4	16.8	1.34
2018	26.4	11.5	2.30	32.4	14.8	2.19	27.9	17.0	1.65	26.8	13.6	1.98	31.6	17.9	1.77	23.1	16.4	1.41	28.0	21.1	1.33	28.4	11.0	2.58	25.2	16.3	1.54
2019[b]	29.2	11.0	2.66	19.5	36.6	0.53	27.4	16.8	1.63	26.1	11.8	2.21	32.3	12.9	2.50	26.9	15.2	1.77	28.5	14.1	2.03	33.6	11.5	2.93	30.4	17.0	1.78

Abbreviations: SEER, Surveillance, Epidemiology and End Results; U, uncertain results only (no pathogenic results); P, pathogenic results; U:P, ratio of uncertain results to pathogenic results

[a]Includes genetic test results from January 1, 2013, through first quarter of 2021 (through March 31); cell percentage is the number of patients with given result divided by number of patients tested for that cancer type and year

[b]Includes cancer diagnoses through the first quarter of 2019 (through March 31)

eTable 7. Uncertain and pathogenic results[a] and ratio in individuals with cancers diagnosed and reported to Georgia and California SEER Registries, 2013-2019, by race and ethnicity

	Asian (n=10,284)			Black (n=9,606)			Hispanic (n=16,538)			Non-Hispanic White (n=55,601)			Other (n=1,023)		
Year of Diagnosis	U%	P%	U:P	U%	P%	U:P	U%	P%	U:P	U%	P%	U:P	U%	P%	U:P
2013	12.2	9.3	1.31	7.5	9.7	0.77	8.6	12.1	0.71	6.3	10.1	0.63	3.8	6.3	0.60
2014	18.4	10.8	1.71	17.4	9.4	1.86	10.7	12.8	0.84	10.9	10.9	1.00	7.4	9.9	0.75
2015	26.0	11.7	2.21	23.0	10.1	2.27	16.2	15.9	1.02	13.9	12.3	1.13	13.5	10.8	1.25
2016	29.0	11.7	2.47	24.3	13.5	1.80	18.3	15.7	1.16	15.6	12.9	1.21	17.6	17.6	1.00
2017	34.1	10.8	3.16	29.9	11.1	2.71	21.3	15.2	1.40	20.1	13.3	1.51	35.0	13.3	2.63
2018	40.1	9.9	4.07	32.8	10.8	3.03	25.9	16.0	1.62	22.2	14.2	1.56	28.2	9.1	3.09
2019[b]	40.0	10.2	3.91	39.0	11.0	3.55	29.3	13.2	2.21	24.9	14.4	1.73	34.6	9.1	3.80

Abbreviations: SEER, Surveillance, Epidemiology and End Results; U, uncertain results only (no pathogenic results); P, pathogenic results; U:P, ratio of uncertain results to pathogenic results

[a]Includes genetic test results from January 1, 2013, through first quarter of 2021 (through March 31); cell percentage is the number of patients with given result divided by number of patients tested for that race or ethnicity and year category

[b]Includes cancer diagnoses through the first quarter of 2019 (through March 31)