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Nationwide trends and determinants of germline *BRCA1/2* testing in patients with breast and ovarian cancer

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Abstract

Background: Germline *BRCA1/2* testing (GT) is instrumental in identifying patients with breast (BC) and ovarian cancer (OC) who are eligible for PARP inhibitors (PARPi). Little is known about recent trends and determinants of GT since PARPi were approved for these patients.

Patients and Methods: We performed a retrospective cohort study of patients in a nationwide EHR-derived oncology-specific database with the following GT eligibility criteria: BC diagnosed ≥ 45 years, triple negative BC diagnosed ≥ 60 years, male BC, or OC. GT within one year of diagnosis was assessed and stratified by tumor type. Multivariable log-binomial regressions estimated adjusted relative risks (RR) of GT by patient and tumor characteristics.

Results: Among 2,982 eligible patients with BC, 56.4% of patients underwent GT between 1/2011-3/2020, with a significant increase in GT over time (RR 1.08, 95% CI 1.05-1.11 for each year), independent of when PARPi were approved for *BRCA1/2*-mutated metastatic BC in 1/2018. In multivariable analyses, older age (RR 0.93, 95% CI 0.90-0.96 for every 5 years) and Medicare coverage (RR 0.69, 95% CI 0.49-0.96 versus commercial insurance) were associated with less GT. Among 5,563 eligible patients with OC, 35.4% of patients underwent GT between 1/2011-3/2020, with a significant increase in GT over time (RR 1.11, 95% CI 1.07-1.14 for each year) which accelerated after PARPi were approved for *BRCA1/2*-mutated chemotherapy-refractory OC in

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12/2014 (RR 1.42, 95% CI 1.19-1.70). Older age (RR 0.95, 95% CI 0.93-0.97 for every 5 years) and Black race (RR 0.80, 95% CI 0.65-0.98 versus white race) were associated with less GT.

Discussion: GT remains underutilized nationwide among patients with breast and ovarian cancer. Although GT has increased over time, significant disparities by age, race and insurance status persist.

Conclusion: Additional work is needed to design, implement, and evaluate strategies to ensure that all eligible patients receive GT.

INTRODUCTION

Germline genetic testing (GT) is instrumental in identifying patients with cancer predisposition syndromes who may benefit from additional screenings, risk-reducing and therapeutic interventions, and cascade testing of family members. *BRCA1* and *BRCA2* are cancer susceptibility genes that when mutated, confer an increased risk for breast (*BRCA1*: 65-79%; *BRCA2*: 61-77%) and ovarian (*BRCA1*: 36-53%; *BRCA2*: 11-25%) cancers¹. The National Comprehensive Cancer Network (NCCN) recommends GT for *BRCA1/2* and other high-penetrance cancer susceptibility genes for a subset of patients with breast cancer (e.g.; based on tumor characteristics, age at diagnosis, ancestry, and family history) and all patients diagnosed with ovarian cancer². Despite these recommendations, prior studies have shown suboptimal rates of GT and disparities by age, race, and insurance status³⁻¹⁰.

Since 2014, GT has taken on added significance as poly ADP ribose polymerase inhibitors (PARPi) have introduced biomarker-driven interventions for breast and ovarian cancer patients with germline alterations in *BRCA1/2*^{7,8,11,12}. As the role for GT expands in clinical practice, there is a critical need to understand more recent trends and determinants of its uptake. We performed a retrospective cohort study to characterize nationwide trends and determinants of germline *BRCA1/2* testing in patients diagnosed with breast and ovarian cancer between 2011 and 2020. We hypothesized that GT has increased but that sociodemographic disparities have persisted since PARPi were approved.

METHODS

Data source

This study used the Flatiron Health database, a nationwide, longitudinal, electronic health record (EHR)-derived database comprised of de-identified patient-level structured and unstructured data, curated via technology-enabled abstraction¹³. The database included data from approximately 280 community and academic cancer clinics (~800 sites of care) during the study period. Demographic variables for patients in the Flatiron Health database are similar with respect to age, sex, and geographic distribution to the 18-registry grouping from the Surveillance, Epidemiology, and End Results (SEER) program and data from the National Program of Cancer Registries (NPCR)¹⁴. Centralized abstraction protocols, duplicate chart abstraction, logic checks, and formal adjudication are used to ensure quality control¹⁵.

Patient population

The study included adult patients who met one of the following GT eligibility criteria between January 1, 2011 and March 31, 2020: 1) breast cancer diagnosed ≥ 45 years; 2) triple negative breast cancer (TNBC) diagnosed ≥ 60 years; 3) male breast cancer; or 4) ovarian cancer. The TNBC criterion was applied after April 7, 2011 to reflect the date when NCCN guidelines were updated to include this additional patient population. Patients were required to have both an ICD-9/10 code and pathology consistent with breast or ovarian cancer, as well as at least two encounters on different days and structured EHR activity within 90 days of diagnosis. Follow-up data were included until March 31, 2021.

Outcomes

The primary outcome was GT within one year of diagnosis, defined as *BRCA1/2* testing performed on a blood or saliva specimen to distinguish it from somatic tumor testing. Patients with evidence of GT prior to diagnosis were excluded from the analysis. To explore potential misclassification of this outcome, we reviewed the medical records of a subset of patients with early-stage breast cancer at the University of Pennsylvania to determine the positive (PPV) and negative predictive value (NPV) of Flatiron Health's ascertainment of GT.

A secondary outcome of somatic next-generation sequencing (NGS) within one year of diagnosis was evaluated in an exploratory analysis evaluating the agreement between GT and NGS testing. Patients with evidence of somatic NGS testing prior to diagnosis were excluded from this analysis.

Determinants

Demographic, clinical, and tumor characteristics measured closest to and within 90 days of each patient's diagnosis were evaluated as potential determinants of GT. These variables included age, race, ethnicity, insurance status, Charlson comorbidity index (calculated using ICD-9/10 codes, excluding any cancer), stage at diagnosis, and diagnosis date. Patient sex and TNBC status were also evaluated as potential determinants in the analysis of patients with breast cancer. To evaluate the potential association between PARPi approvals and GT, we defined diagnosis date epochs using the PARPi approval dates of January 12, 2018 for breast cancer (olaparib approval date for *BRCA1/2*-mutated metastatic breast cancer⁷) and December 19, 2014 for ovarian cancer (olaparib approval date for *BRCA1/2*-mutated chemotherapy-refractory ovarian cancer¹¹).

Statistical analysis

Time from diagnosis to GT was evaluated using kernel density plots for both the breast and ovarian cancer cohorts. Baseline characteristics were evaluated using standard descriptive statistics. We evaluated the nature and degree of missingness for variables with missing data and found that they were not missing completely at random. As such, we conducted multiple imputation by chained equations to impute the missing values^{16,17}. We generated 25 imputed datasets, performed our analyses using these datasets, and used Rubin's rules to generate combined effect estimates and variances¹⁸. All analyses utilized the multiply imputed datasets except where noted.

Spline regression was used to estimate the annual prevalence of GT over time and to assess for nonlinearity in the association between GT and patient age for both the breast and ovarian cancer cohorts. We found that the relationship between GT and diagnosis date generally followed a linear pattern and as such, included diagnosis year as a continuous variable in subsequent regression analyses. Univariable log-binomial regressions were used to estimate the relative risk (RR) of GT for the determinants described above. Variables with $p < 0.1$ on univariable models were retained in final multivariable models to estimate the adjusted RR of GT by patient and tumor characteristics. Generalized estimating equations were used to account for clustering by practice site. All analyses were stratified by tumor type. Tests of statistical significance were two-sided, and significance was defined as $p < 0.05$. All analyses were performed using STATA version 17.

Sensitivity analyses

Multiple sensitivity analyses were performed to evaluate the robustness of our results. First, we limited our analyses to the post-PARPi approval period to evaluate more recent determinants of GT. Second, we restricted our analyses to community oncology practices on Flatiron Health's OncoEMR platform to assess the impact of potential misclassification due to chart abstraction from the more heterogeneous set of EHRs used in academic oncology practices. Third, we limited our analyses to patients who remained alive one year after diagnosis to evaluate the impact of potential survival bias. Finally, we used the non-imputed data set to assess the impact of potential bias introduced during the multiple imputation procedure.

Exploratory analysis

We calculated kappa statistics to evaluate the agreement between GT and somatic NGS testing within one year of diagnosis for patients with metastatic breast and any-stage ovarian cancer.

Approval was obtained from the University of Pennsylvania and the Copernicus Group Institutional Review Boards and included waiver of informed consent.

RESULTS

Patient population

We reviewed 12,074 records in the Flatiron Health database that met eligibility criteria, of which 3,529 (29.2%) were excluded due to duplicate records, lack of structured EHR activity, or evidence of GT prior to diagnosis (Supplemental Figure 1). Among 2,982 patients with breast cancer, most patients (64.3%) were eligible for GT due to a diagnosis under age 45 (Table 1). The median age in the breast cancer cohort was 43.0 years; most patients were white (60.1%), not Hispanic or Latino (89.4%), and commercially insured (63.9%). Among 5,563 eligible patients with ovarian cancer, the median age was 65.9 years, 78.0% of patients were white, 92.8% of patients were not Hispanic or Latino, and 59.0% were commercially insured. These baseline characteristics followed a comparable distribution in the multiply imputed datasets (Supplemental Table 1).

Prevalence of germline BRCA1/2 testing over time

Among patients with breast cancer, the prevalence of GT within one year of diagnosis increased from 37.0% in 2011 to 67.9% in 2020 (Figure 1). Over the entire study period, 56.4% of patients were tested within one year of diagnosis, 7.1% were tested after one year, and 36.5% had no documentation of testing. Median time to GT was 42 days (Figure 2). In the ovarian cancer cohort, GT within one year of diagnosis increased from 23.0% in 2011 to 52.9% in 2020 (Figure 1), with 35.4% of patients tested within one year of diagnosis, 8.8% tested after one year, and 55.8% with no documentation of testing over the entire study period. Median time to GT was 101 days (Figure 2).

We evaluated for potential misclassification of GT by reviewing the medical records of 48 patients with early-stage breast cancer at the University of Pennsylvania and calculated a PPV of 96% and NPV of 61% in Flatiron Health's ascertainment of GT. These discrepancies were due to GT results that had been scanned into the EHR but not available to Flatiron Health for abstraction.

Determinants of germline BRCA1/2 testing

Among patients with breast cancer, there were no appreciable differences in GT within one year of diagnosis by sex, race, ethnicity. There was a significant increase in GT over time (RR 1.08, 95% CI 1.05-1.11 for each year after 2011), independent of when PARPi were approved for *BRCA1/2*-mutated metastatic breast cancer in January 2018 (RR 0.98, 95% CI 0.83-1.16 for the post- versus pre-PARPi approval period, p-value for interaction term = 0.465) (Figure 3A, Supplemental Table 2). Compared to patients diagnosed with early-stage disease, patients diagnosed with metastatic disease were less likely to undergo GT (RR 0.76, 95% CI 0.64-0.90 versus stage I disease). There was a negative linear relationship between GT and age (RR 0.93, 95% CI 0.90-0.96 for every 5 years) (Supplemental Figure 2A). After adjusting for age, patients with Medicare were less likely to undergo GT (RR 0.69, 95% CI 0.49-0.96 versus commercial insurance), though the number of patients with Medicare was small (n = 87, 2.9%). Results remained similar in all pre-planned sensitivity analyses except in the analysis limiting to the post-PARPi approval period, where the effect estimates for disease stage, age, and insurance status remained similar in direction and magnitude but were no longer statistically significant (Supplemental Table 2).

In the ovarian cancer cohort, there was a significant increase in GT over time (RR 1.11, 95% CI 1.07-1.14 for each year after 2011) which accelerated after PARPi were approved in December 2014 for *BRCA1/2*-mutated chemotherapy-refractory ovarian cancer (RR 1.42, 95% CI 1.19-1.70 versus the pre-PARPi approval period, p-value for interaction term = 0.003) (Figure 3B, Supplemental Table 3). Patients diagnosed with more advanced disease were more likely to undergo GT compared to those with stage I disease (RR 1.42, 95% CI 1.18-1.70; RR 1.51, 95% CI 1.32-1.73; and RR 1.28, 95% CI 1.10-1.48 for stages II, III, and IV, respectively). Older age (RR 0.95, 95% CI 0.93-0.97 for every 5 years) (Supplemental Figure 2B) and Black race (RR 0.80, 95% CI 0.65-0.98 versus white race) were associated with a lower likelihood of GT, as was healthcare coverage other than a commercial health plan, Medicare, or Medicaid (RR 0.81, 95% CI 0.69-0.95 versus commercial health insurance). Results remained similar in all pre-planned sensitivity analyses.

Exploratory analysis of somatic NGS testing

In an exploratory analysis of 2,005 patients with metastatic breast cancer, 125 (6.2%) completed both GT and somatic NGS testing within one year of diagnosis, 948 (47.3%) completed GT alone, 41 (2.0%) completed somatic NGS testing alone, and 891 (44.4%) had no documentation of either GT or somatic NGS testing. After accounting for the expected cooccurrence of GT and somatic NGS testing due to chance alone, we observed poor agreement in the completion of both tests in any given individual ($\kappa = 0.068$, $p < 0.001$).

Among 5,557 patients with ovarian cancer of any stage, 394 (7.1%) completed both GT and somatic NGS testing, 1,573 (28.3%) completed GT alone, 281 (5.1%) completed somatic NGS testing alone, and 3,309 (59.5%) completed neither. Agreement between somatic NGS testing and GT in this population was also poor ($\kappa = 0.143$, $p < 0.001$).

DISCUSSION

In this nationwide study of patients with breast and ovarian cancer, we demonstrated ongoing underutilization of GT through 2020, with over 40% of patients with breast cancer and 60% of patients with ovarian cancer with no documentation of GT within one year of diagnosis. Although GT has increased over time, significant disparities by age, race, and insurance status persist.

Multiple studies have demonstrated underutilization and sociodemographic disparities in GT, with rates ranging between 52-56% among eligible patients with breast cancer³⁻⁵ and 30-40% among patients with ovarian cancer^{9,19-21}. Increasing age^{3,4,19}, Black race^{5,9,10,19,21,22}, and lack of commercial insurance coverage^{9,10} also have been identified as negative determinants of GT for both tumor types. However, these studies have been limited to single-institution investigations, claims-based analyses among commercially insured individuals, and registry-based studies in select states. In this study, we used a nationwide database comprised predominantly of community oncology practices to corroborate these previous findings while concurrently shedding light on other determinants of GT. Specifically, we observed a negative association between advanced tumor stage and GT for patients with breast cancer but a positive association for patients with ovarian cancer. We hypothesize that the higher prevalence of GT in patients with early-stage breast cancer may have been driven by decisions around risk-reducing surgery rather than PARPi candidacy, as this relationship persisted in our sensitivity analysis of the post-PARPi approval period. In contrast, patients with stage I ovarian cancer may have been less likely to undergo GT due to a perceived lack of therapeutic actionability, as PARPi have only been approved for more advanced disease. This contrasting relationship warrants further study, as it may inform a more tailored approach to improving the uptake of GT in these populations.

An additional strength of our study was the recency of the Flatiron Health database, which enabled us to evaluate recent trends in GT. A prior analysis of the Kaiser Permanente Washington integrated health system between 2005 and 2015 did not identify secular trends in GT among women with breast and ovarian cancer despite universal insurance coverage and access to specialized genetic services²³. A subsequent study using the Georgia and California SEER registries demonstrated an annual 2% increase in GT between 2013 and

2017 among women with breast and ovarian cancer²⁰. Our study spanning up to 2020 suggests that the prevalence of GT may be increasing further, likely due to a combination of PARPi approvals as well as rapidly advancing sequencing technologies²⁴, novel “point-of-care” genetic testing models²⁵⁻²⁸, and the 2013 Supreme Court decision challenging the patentability of the *BRCA1/2* genes²⁹ which have collectively expanded access to and lowered costs for GT. Going forward, additional work is needed to ensure that all eligible patients receive GT, for instance by addressing patient-level barriers to GT; implementing default GT mechanisms into clinician workflows; raising awareness about existing insurance coverage and financial assistance programs for guideline-recommended GT; and simplifying GT guidelines (as was done with the NCCN’s 2022 update recommending GT for all patients with TNBC, regardless of age³⁰).

The role of GT in therapeutic decision-making raises questions about when it should be offered in relation to a patient’s diagnosis and treatment. We demonstrated that time to GT followed a skewed distribution such that fewer than 15% of patients who had not undergone GT within one year of diagnosis received it later in their disease course. These patterns reinforce the importance of obtaining GT results early so that they can be used to determine candidacy not only for PARPi therapy but also for surgical interventions such as risk-reducing bilateral mastectomy and oophorectomy³¹⁻³³. However, offering GT at the time of diagnosis may conflict with the provision of patient-centered care. In a qualitative study of patients with gynecologic malignancies who were eligible for GT, participants requested that GT follow active treatment so as not to overwhelm them at the time of initial diagnosis³⁴. This preference for later GT may be due to difficulty discerning between the preventive versus therapeutic roles of GT, an observation that has been made among both breast and ovarian cancer patients³⁵. Additional research is needed to identify more patient-centered approaches to offering GT while still ensuring that its timing facilitates its use in the delivery of personalized cancer care.

In addition to demonstrating underutilization of GT, this study highlighted a low prevalence of somatic NGS testing among patients with no documented GT, as well as poor agreement between somatic NGS testing and GT among patients with metastatic breast and any-stage ovarian cancer. These real-world practice patterns suggest that somatic NGS testing is not being used as a replacement for germline genetic risk assessment, although we recognize that this study was conducted prior to widespread incorporation of somatic NGS testing into NCCN guidelines. Given that somatic NGS testing is not perfectly substitutive for GT³⁶⁻³⁸, efforts should be made to ensure that all eligible patients are concomitantly evaluated for both germline and somatic genetic variation.

This study has several limitations. First, there are missing data for some of our study variables. We conducted multiple imputations on the missing variables and demonstrated comparable distributions between the non-imputed and multiply imputed data sets. We also conducted a sensitivity analysis using the non-imputed data set and observed findings that were similar to those of our primary analysis. Second, missing documentation of GT performed outside the Flatiron Health network may have led to misclassification of our primary outcome of interest. Indeed, our review of 48 patients with early-stage breast cancer at the University of Pennsylvania revealed a NPV of 61% due to Flatiron Health’s limited

access to scanned records in Penn's EHR. This limitation does not apply to the community oncology practices on Flatiron Health's OncoEMR platform; as such, we conducted a sensitivity analysis restricting to community oncology practices and observed minimal variation in our study results. Finally, we were not able to ascertain specific reasons for why GT was not documented for some patients. Additional research is needed to identify other patient-, clinician-, and system-level determinants of GT.

In conclusion, this study demonstrates ongoing underutilization and sociodemographic disparities in GT among a nationwide cohort of patients with breast and ovarian cancer. Although GT has increased over time, additional work is needed to design, implement, and evaluate strategies to ensure that all eligible patients receive GT.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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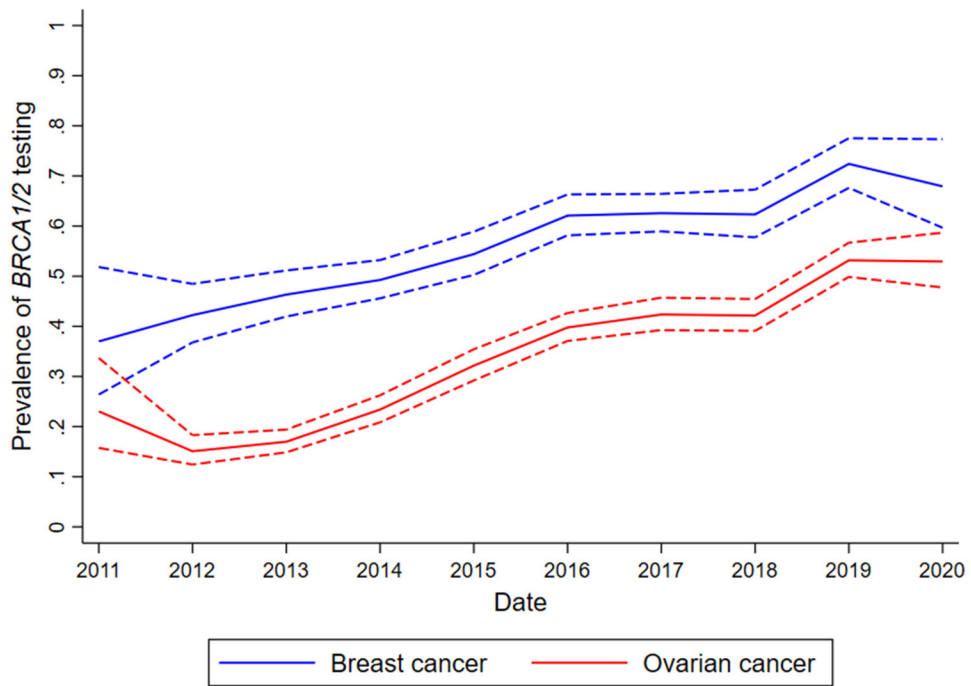


Figure 1. Prevalence of germline *BRCA1/2* testing over time, estimated using spline regressions among patients with breast cancer (blue) and ovarian cancer (red). Germline *BRCA1/2* testing was defined as occurring within one year of diagnosis. Dashed lines indicate 95% confidence intervals.

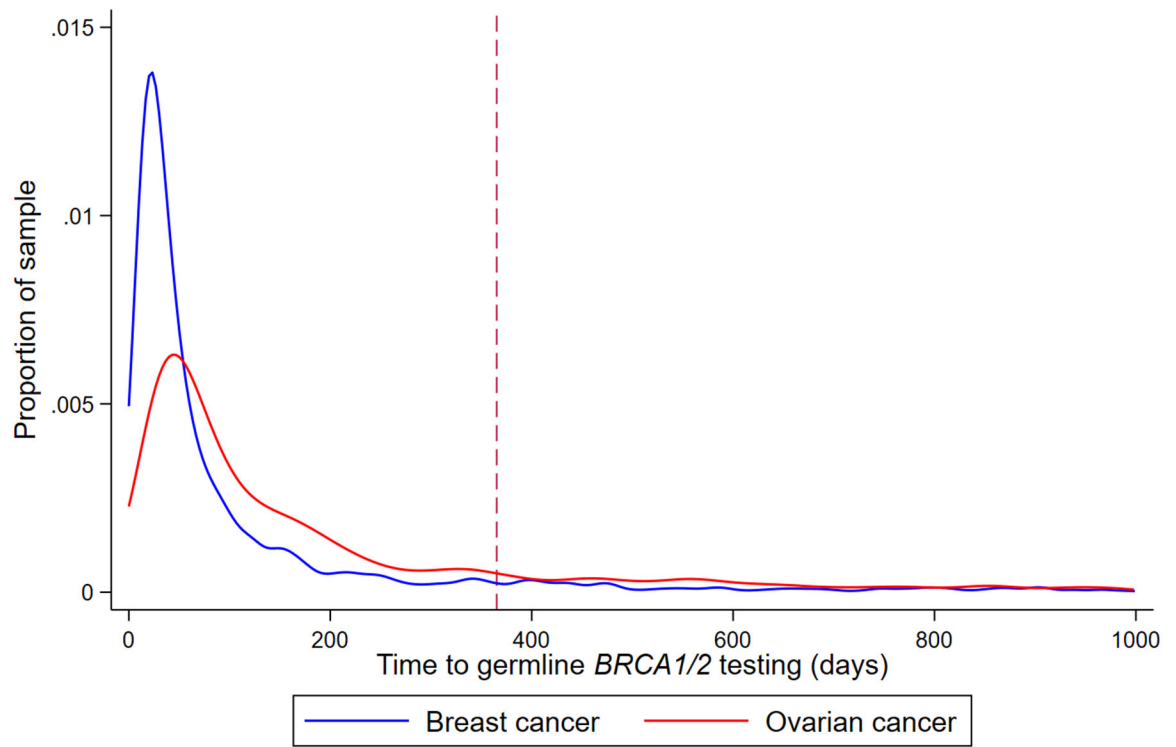
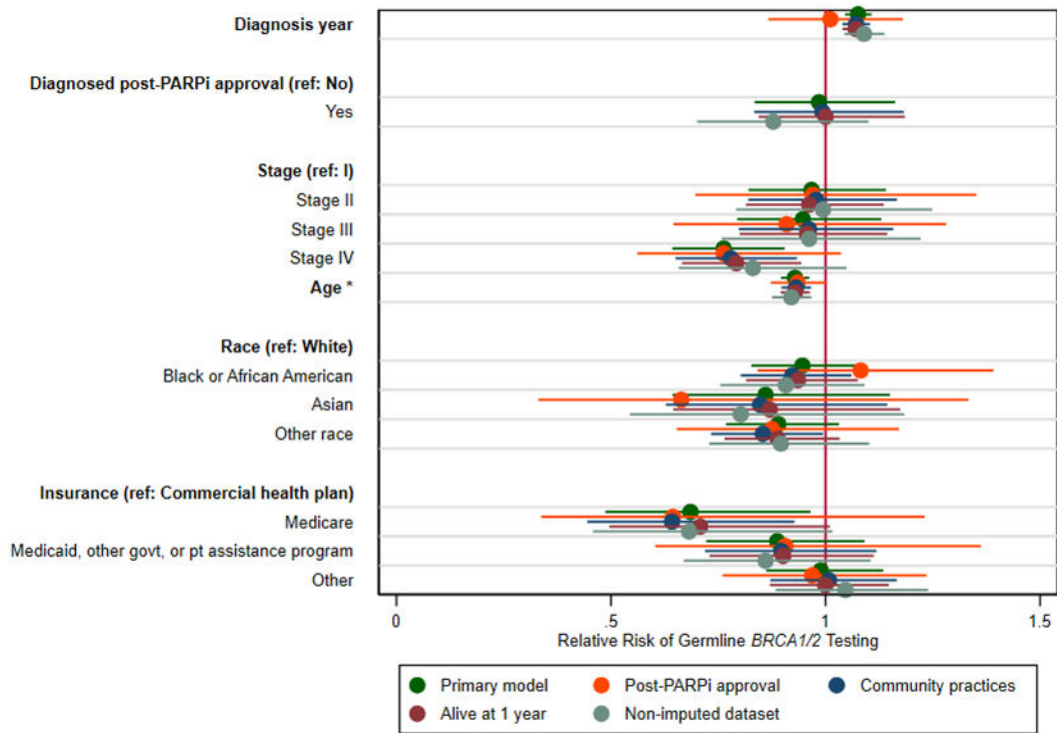
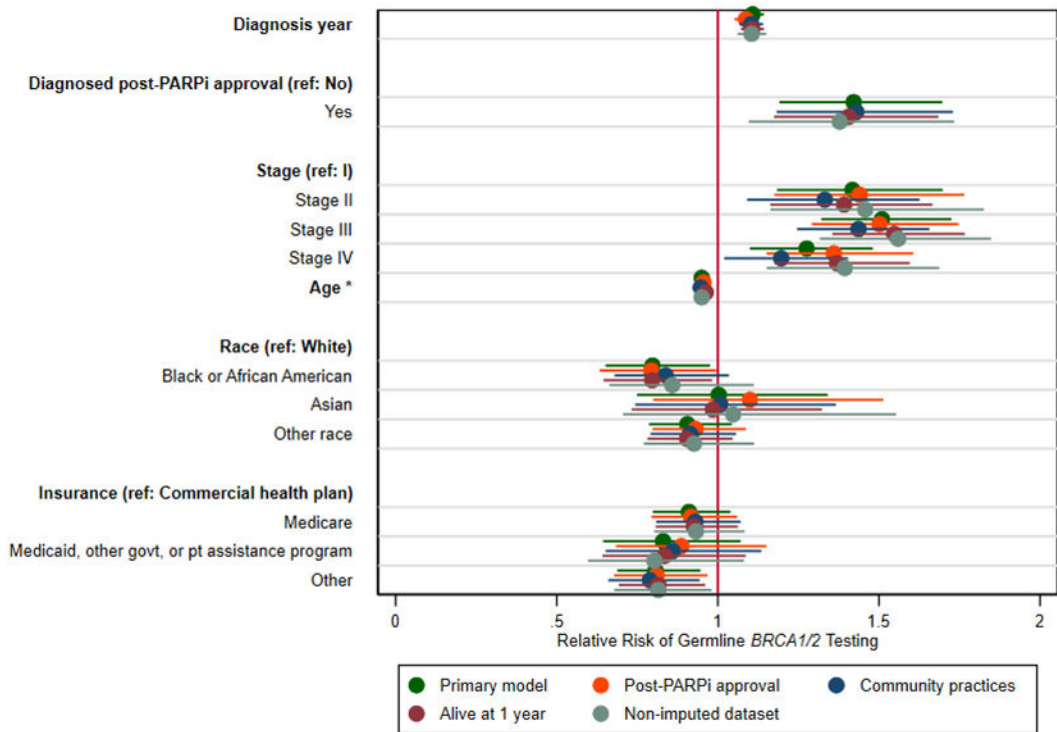


Figure 2. Kernel density plot of time from diagnosis to *BRCA1/2* test result among patients with breast cancer (blue) and ovarian cancer (red). The dashed red line indicates a threshold of 365 days that was used in subsequent analyses.



* Reported in 5-year increments



* Reported in 5-year increments

Figure 3.

Determinants of germline *BRCA1/2* testing within one year of diagnosis among patients with A) breast cancer and B) ovarian cancer. Adjusted relative risks were estimated using log-binomial regressions using the multiply imputed datasets (primary analysis) and in sensitivity analyses limiting to the post-PARP inhibitor approval period, restricting to community oncology practices, limiting to patients who remained alive one year after diagnosis, and using the non-imputed dataset. Generalized estimating equations were used to account for clustering by practice site.

Table 1.

Baseline characteristics

	Breast cancer (n = 2,982)		Ovarian cancer (n = 5,563)	
	Germline BRCA1/2 testing ¹ (n = 1,682)	No germline BRCA1/2 testing ¹ (n = 1,300)	Germline BRCA1/2 testing ¹ (n = 1,968)	No germline BRCA1/2 testing ¹ (n = 3,595)
Diagnosis year				
2011	105 (6.2%)	153 (11.8%)	72 (3.7%)	335 (9.3%)
2012	135 (8.0%)	175 (13.5%)	86 (4.4%)	459 (12.8%)
2013	159 (9.5%)	180 (13.8%)	107 (5.4%)	459 (12.8%)
2014	200 (11.9%)	174 (13.4%)	184 (9.3%)	452 (12.6%)
2015	215 (12.8%)	173 (13.3%)	211 (10.7%)	375 (10.4%)
2016	236 (14.0%)	131 (10.1%)	300 (15.2%)	408 (11.3%)
2017	211 (12.5%)	131 (10.1%)	265 (13.5%)	395 (11.0%)
2018	182 (10.8%)	86 (6.6%)	309 (15.7%)	362 (10.1%)
2019	204 (12.1%)	80 (6.2%)	348 (17.7%)	261 (7.3%)
2020	35 (2.1%)	17 (1.3%)	86 (4.4%)	89 (2.5%)
Diagnosed post-PARPi approval				
No	1265 (75.2%)	1125 (86.5%)	443 (22.5%)	1697 (47.2%)
Yes	417 (24.8%)	175 (13.5%)	1525 (77.5%)	1898 (52.8%)
Eligibility criterion			-- ²	--
Breast cancer <=45	1165 (69.3%)	741 (57.0%)	--	--
TNBC <=60	425 (25.3%)	447 (34.4%)	--	--
Male breast cancer	92 (5.5%)	112 (8.6%)	--	--
Stage				
Stage I	185 (11.0%)	103 (7.9%)	294 (14.9%)	738 (20.5%)
Stage II	460 (27.3%)	282 (21.7%)	180 (9.1%)	283 (7.9%)
Stage III	379 (22.5%)	267 (20.5%)	912 (46.3%)	1337 (37.2%)
Stage IV	418 (24.9%)	390 (30.0%)	430 (21.8%)	787 (21.9%)
Unknown	240 (14.3%)	258 (19.8%)	152 (7.7%)	450 (12.5%)
Age, median (IQR ³)	42.3 (37.6, 48.4)	44.0 (39.8, 53.4)	64.9 (55.7, 72.8)	66.5 (56.9, 75.2)

	Breast cancer (n = 2,982)		Ovarian cancer (n = 5,563)	
	Germline <i>BRCA1/2</i> testing ¹ (n = 1,682)	No germline <i>BRCA1/2</i> testing ¹ (n = 1,300)	Germline <i>BRCA1/2</i> testing ¹ (n = 1,968)	No germline <i>BRCA1/2</i> testing ¹ (n = 3,595)
Race				
Asian	48 (2.9%)	47 (3.6%)	48 (2.4%)	84 (2.3%)
Black or African American	295 (17.5%)	255 (19.6%)	108 (5.5%)	221 (6.1%)
White	957 (56.9%)	668 (51.4%)	1412 (71.7%)	2580 (71.8%)
Other race ⁴	230 (13.7%)	202 (15.5%)	244 (12.4%)	418 (11.6%)
Unknown	152 (9.0%)	128 (9.8%)	156 (7.9%)	292 (8.1%)
Ethnicity				
Not Hispanic or Latino	1511 (89.8%)	1156 (88.9%)	1828 (92.9%)	3334 (92.7%)
Hispanic or Latino	171 (10.2%)	144 (11.1%)	140 (7.1%)	261 (7.3%)
Insurance status				
Commercial health plan	687 (40.8%)	430 (33.1%)	880 (44.7%)	1338 (37.2%)
Medicare	33 (2.0%)	54 (4.2%)	291 (14.8%)	594 (16.5%)
Medicaid, other govt program, or pt assistance program	82 (4.9%)	75 (5.8%)	54 (2.7%)	106 (2.9%)
Other	228 (13.6%)	159 (12.2%)	143 (7.3%)	354 (9.8%)
Unknown	652 (38.8%)	582 (44.8%)	600 (30.5%)	1203 (33.5%)
Charlson comorbidity index				
0	711 (42.3%)	586 (45.1%)	939 (47.7%)	1573 (43.8%)
1+	20 (1.2%)	19 (1.5%)	68 (3.5%)	135 (3.8%)
Unknown	951 (56.5%)	695 (53.5%)	961 (48.8%)	1887 (52.5%)

¹ Germline *BRCA1/2* testing was ascertained within one year of diagnosis

² Listed eligibility criteria do not apply to patients with ovarian cancer

³ IQR = interquartile range

⁴ Includes American Indian or Alaska Native, Hawaiian or Pacific Islander, and race descriptions that fall in multiple race categories