original contributions

CARE DELIVERY ReCAP

Utilization, Timing, and Outcomes of BRCA Genetic Testing Among Women With Newly Diagnosed Breast Cancer From a National Commercially Insured Population: The ABOARD Study

Joanne Armstrong, MD, MPH[1]; Kristian Lynch, PhD[2]; Katherine S. Virgo, MBA, PhD, FASCO[3]; Marc D. Schwartz, PhD[4]; Sue Friedman, DVM[5]; Marleah Dean, PhD[6]; James E. Andrews, PhD[7]; Elizabeth Bourquardez Clark, MPH[2]; Joanna Clasen, MPH[2]; Jessica Conaty, MPH[2]; Olivia Parrillo, BS[2]; and Rebecca Sutphen, MD[2]

QUESTION ASKED: Among women with newly diagnosed breast cancer whose providers plan germline genetic testing, what is the timing of testing and results delivery relative to definitive surgical treatment (DST) and what is the impact on the type of surgery chosen?

SUMMARY ANSWER: Nearly half of patients with newly diagnosed breast cancer (PNDBC) for whom genetic testing was appropriate did not receive results in time to use them for surgical decision making. Women who were aware of their results presurgery, whether positive or negative for a mutation, were more likely to undergo a surgery type appropriate for their level of risk based on the results and relevant family history; women older than 50 who knew they were negative were much less likely to undergo unnecessary bilateral mastectomy (BLM).

WHAT WE DID: All PNDBC for whom BRCA germline testing was ordered within 1 year of diagnosis through a large commercial health insurer (Aetna) between March 2014 and June 2015 were prospectively ascertained at the time of test ordering and mailed study questionnaires. Data capture included sociodemographics, personal and family cancer history, timing of both test results delivery and DST, and test results. Provider-reported data included the patient's relevant personal and family cancer history and timing of test submission obtained from test request or submission forms. The analysis focused on both the timing of genetic testing and receipt of the results relative to DST (ie, *before v after*) and choice of DST (ie, BLM *v* lumpectomy or unilateral mastectomy).

WHAT WE FOUND: Only 54% of PNDBC undergoing BRCA germline testing were aware of their results before DST; approximately 23% were tested before surgery, but proceeded with surgery before receiving the results; 22% were not tested until after surgery. Women who were aware of their results presurgery, whether positive or negative for a mutation, were more likely to undergo a surgery type appropriate for their level of risk based on the results and relevant family history; women older than 50 who knew they were negative were much less likely to undergo unnecessary BLM.

BIAS, CONFOUNDING FACTOR(S), REAL-LIFE IMPLICATIONS: Increasingly, physicians caring for patients with newly diagnosed cancer are identifying those for whom genetic counseling and hereditary cancer genetic testing is appropriate. Timing of these services is critical for enhancing outcomes. The study found great variability in the timing of genetic testing and results delivery, with nearly half of the women not receiving the results until after their surgery was completed. Women who tested positive were significantly less likely to undergo BLM if they were unaware of their positive results before surgery. Among women older than 50 with negative or normal results, those who knew before surgery that they tested negative for a mutation were significantly less likely to undergo unnecessary BLM. A limitation of this study is the lack of patient or provider data regarding the reasons for delaying testing or results delivery until after surgery—so it is unknown how many women or providers might have made informed decisions to delay. Nevertheless, these findings have important implications for enhancing patient care and reducing unnecessary healthcare costs. Specifically, given the high likelihood of negative results for most tested patients, especially among women older than 50, the study has potential implications for reducing the number of unnecessary, potentially harmful, and costly bilateral mastectomies.

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Utilization, Timing, and Outcomes of BRCA Genetic Testing Among Women With Newly Diagnosed Breast Cancer From a National Commercially Insured Population: The ABOARD Study

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abstract

PURPOSE To evaluate timing and outcomes of BRCA testing and definitive surgical treatment among patients with newly diagnosed breast cancer.

METHODS Patient-reported (n = 1,381) and deidentified health-plan (n = 2,369) data were analyzed from a consecutive national series of 3,750 women whose healthcare providers ordered BRCA testing between March 2014 and June 2015, within 1 year following breast cancer diagnosis.

RESULTS Among 1,209 respondents, 54.4% received the genetic test results presurgery, 23.2% tested presurgery but received the results postsurgery, and 22.3% tested postsurgery. Patients aware of mutation-positive results presurgery were more likely to choose bilateral mastectomy (BLM) (n = 32/37) compared with patients who learned of positive results postsurgery (n = 14/32), (odds ratio [OR] = 8.23, 95% CI = 2.55 to 26.59, $P <$ .001). When compared with women tested postsurgery, only women unaware of negative results presurgery had higher BLM rates (adjusted OR = 1.70, 95% CI = 1.07 to 2.69, P = .02). Among women > 50 tested presurgery, those unaware of negative results presurgery were more likely to choose BLM (n = 28/81) compared with those aware of negative results (n = 32/168) (OR = 2.25, 95% CI = 1.23 to 4.08, negative results awareness × age interaction, and P = .007).

CONCLUSION Nearly half of participants did not receive BRCA results presurgery, which limited their ability to make fully informed surgical treatment decisions. This may represent suboptimal care for unaware mutation-positive patients compared with those who were aware presurgery. Women > 50 who test negative are significantly less likely to choose BLM, a costly surgery that does not confer survival advantage, if they are aware of negative results presurgery. These results have important implications for quality of care and costs in the US health system.

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INTRODUCTION

Approximately 5%-10% of patients with newly diagnosed breast cancer (PNDBC) are at high risk for second primary breast cancers and ovarian cancer because of hereditary breast and ovarian cancer (HBOC) syndrome, most commonly because of an inherited mutation in *BRCA1* or *BRCA2*.[1-6] Patients with breast cancer who are BRCA mutation carriers have a 25%-65% risk for developing a second primary breast cancer[1,3,7-11] and a 10%-45% lifetime ovarian cancer risk.[2,3,11] Such high cancer risks and availability of effective preventive strategies to manage them make it critical to identify patients at increased hereditary risk, refer them for genetic counseling and testing, and present them with personalized risk-appropriate management options. National guidelines specify which patients warrant referral for genetic assessment based on personal and family history factors that indicate HBOC risk.[12]

To maximize genetic testing benefits, appropriate and timely risk management must be initiated. Among PNDBC a crucial related factor is *timing* of genetic testing (ie, *before v after* definitive surgical treatment [DST]). The time required for genetic testing and receipt of the results is short enough that PNDBC can undergo genetic counseling, testing, and results disclosure before DST. Germline mutations can identify patients for whom bilateral mastectomy (BLM) is likely beneficial.[13-16] Recent studies demonstrate that BLM substantially reduces contralateral breast cancer

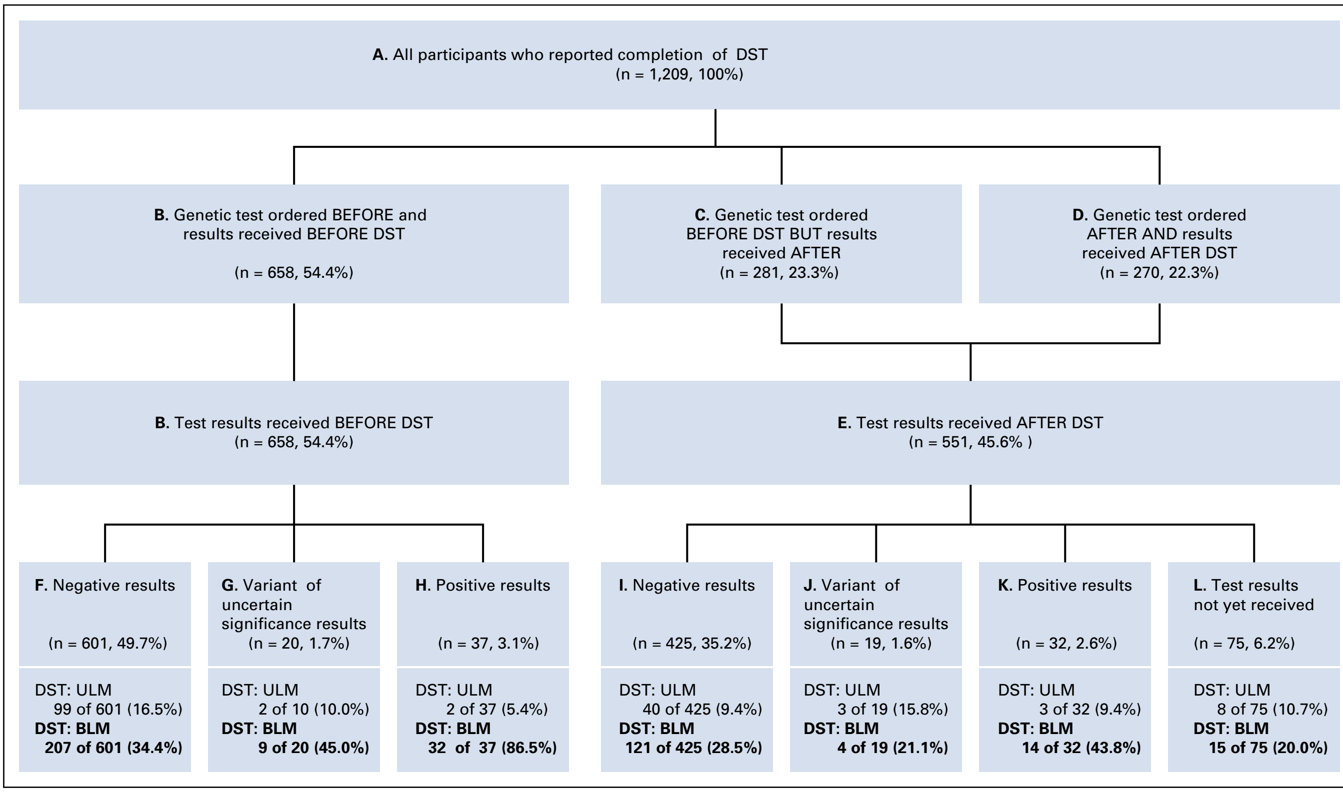

FIG 1. Timing of BRCA testing and results relative to definitive surgical treatment. BLM, bilateral mastectomy; DST, definitive surgical treatment; ULM, unilateral mastectomy.

risk.[17-21] PNDBC aware of increased risk before DST may choose BLM rather than lumpectomy or unilateral mastectomy (UM).[14,22,23] Beyond the benefit of decreased risk for second primary breast cancer, women choosing BLM as DST may also avoid radiotherapy and additional surgery after primary treatment and have better reconstruction options.[3,14,24,25] Thus, *presurgical* identification of PNDBC with HBOC permits more personalized and informed surgical decision making and improves outcomes.

Unfortunately, in the United States, available data are limited regarding genetic testing of PNDBC at HBOC risk with regard to timing of testing relative to surgical treatment, surgical decision making, and treatment outcomes. These data are primarily from small academic or clinical center studies[14,16,23,26-30] and/or did not specifically examine timing of test ordering.[31] However, in a retrospective population–based study, among 522 PNDBC with stages 0-II tested postdiagnosis, 72.4% reported genetic testing presurgery versus 27.6% postsurgery; among those tested presurgery, the proportion receiving results presurgery versus postsurgery was not reported.[32] Among the 393 PNDBC who reportedly met national guidelines for genetic testing,[33] 80% of those with a mutation, 43% with a variant of uncertain significance (VUS), and 34% with negative results had BLM.

The American BRCA Outcomes Among the Recently Diagnosed Study is a collaborative, prospective study of women undergoing BRCA testing through a large commercial health insurer (Aetna) within 1 year postdiagnosis of primary breast cancer. This ongoing investigation collects baseline and longitudinal patient-reported, provider-reported, and health claims data on a consecutive national series of PNDBC at high HBOC risk undergoing genetic testing to evaluate medical decisions and outcomes. This report highlights the timing of patients' genetic testing and receipt of results relative to DST (ie, *before v after*) and choice of DST (ie, BLM *v* lumpectomy or UM).

METHODS

Aetna's[34] commercially insured members are demographically reflective of the larger US commercially insured population. Since the majority of patients with breast cancer undergoing genetic testing in the United States are commercially insured, the study population is inferred to be generally representative of the US BRCA testing population of age 64 and younger.[33,35,36] Genetic testing requests are preapproved by Aetna based on national testing guidelines.[12]

The University of South Florida Institutional Review Board approved this study. Study materials (informed consent form and questionnaire), in English and Spanish, were mailed to all women diagnosed with breast cancer within the previous year, 6 weeks after Aetna received their BRCA test request form (TRF). Participants could return these materials via postage-paid return envelope to University of South Florida study investigators or complete online. Aetna provided the ordering provider's TRF and insurance approval data. The TRF identified the patient's specific test with indication, demographics, and relevant personal and family cancer history.

Study methodology approximated the ABOUT Study (described elsewhere[37,38]). Per a modified Dillman method, prepaid $5 in US dollars (USD) cash incentives, $20 (USD) gift cards for questionnaire completion, and nonrespondent reminders were provided, which enhanced response rate.[39]

Study Sample

Materials were mailed nationwide to 3,750 PNDBC consecutively ascertained through TRFs submitted between March 2014 and June 2015; 37% (n = 1,381) completed and returned the informed consent form and baseline questionnaire. Based on provider-reported data, respondents were similar to the overall group's age at diagnosis and relevant personal or family cancer history. Individuals with stage IV cancer (n = 23) were excluded. There were differences by race or ethnicity: Asians, African-Americans, and Hispanics were less likely to respond (−5.1%, 95% CI = −7.0 to −3.3).

Measures

Participants were sorted into three timing groups: results received pre-DST, results received post-DST but testing conducted pre-DST, or tested post-DST. These groups were determined by TRF submission and patient-reported DST and results-received dates. Participants with missing or inaccurate dates were excluded (n = 149/1,358). Data from 1,209 respondents were analyzable.

Sociodemographics included age at diagnosis (presented in quintiles), race or ethnicity, education, household income, and marital status. Patients reported their stage at breast cancer diagnosis, hormone receptor status, and family history of relevant HBOCs: breast, ovarian, melanoma, and/or pancreatic. See Table 1 for categorical descriptors.

DST options included three categories: excisional biopsy or lumpectomy, UM, and BLM. Participants reported the month or year of DST. For patients reporting excisional biopsy plus lumpectomy, UM, or BLM within a 3-month timespan, the most extensive surgery was classified as DST. Participants indicated personal versus doctor involvement in DST decision making on a 5-item scale (Table 1).[40,41] Participants' genetic test results were collapsed to mutation-negative, mutation-positive, or VUS.

Statistical Analyses

Sociodemographics and personal or family cancer history were compared among participants undergoing genetic testing and receiving results pre- versus post-DST and those undergoing BLM versus other DST. Chi-square or Fisher exact tests detected differences in proportions between groups. Linear trend in proportions across ordinal groups was examined using Cochran-Armitage tests.[42] Univariate and multivariate logistic regression models were fitted. First, we characterized the receipt of test results timing relative to DST and performed stratified analyses based on the genetic results. Additional analyses examined if patient characteristics modified the association between testing or results timing and DST choice. Statistical significance was set at $P < .05$. The a priori statistical plan included stratification by BRCA-positive or BRCA-negative results to test for differences or interactions between patient characteristics and downstream outcomes (ie, BLM rates). Analyses were performed using SPSS[43] and SAS.[44]

RESULTS

Timing of Genetic Testing, Results Receipt, and DST

Among 1,209 participants undergoing DST, 54.4% received genetic test results pre-DST (Fig 1). Of those receiving results post-DST (45.6%), approximately half had testing ordered presurgery (n = 281/551). Overall, for *BRCA 1/2*, 5.7% tested mutation-positive; 3.2% had a VUS, 84.9% were mutation-negative, and 6.2% reported not receiving results (most not meeting medical necessity criteria). The genetic results distribution did not differ between patients receiving results pre- versus postsurgery (Fig 1).

Patients who learned of their mutation-positive results presurgery were significantly more likely to obtain BLM (86.5%) versus patients who learned that they were mutation-positive post-DST (43.8%; odds ratio [OR] = 8.23, 95% CI = 2.55 to 26.59, $P < .001$). Furthermore, women aware of their mutation before DST had increased odds of BLM compared with mutation-positive women tested presurgery but received the results postsurgery (55.0%, n = 11/20; OR = 5.24, 95% CI = 1.44 to 19.03, $P = .01$) and even higher odds compared with those tested postsurgery (25.0%, n = 3/12; OR = 19.20, 95% CI = 3.83 to 96.16, $P < .001$).

Among women with mutation-negative results, participants aware of their results pre- (34.4%) versus postsurgery (28.5%) were more likely to choose BLM (OR = 1.32, 95% CI = 1.01 to 1.73, $P = .04$). The percentage choosing BLM after receiving negative results was similar among patients who were tested presurgery but received the results postsurgery (35.3%, n = 73/207; OR = 0.96, 95% CI = 0.69 to 1.34, $P = .83$), but was significantly higher than patients tested postsurgery (22.0%, n = 48/218; OR = 1.86, 95% CI = 1.30 to 2.62, $P = .001$).

Among the few with the VUS results, BLM rates were not significantly different across timing groups.

TABLE 1. Characteristics of Respondents (n = 1,209) and Distribution by Timing of Results Receipt Relative to DST

				Timing of Receipt of Results in Relation to DST								
					After DST		OR (95% CI)[a]					
					Testing Ordered							
	Total		Mutation-Positive	Before DST	Pre-DST	Post-DST	Univariate Regression (n = 1,209)			Multivariate Regression (n = 1,182)[b]		
Characteristic	**N**	**%**	**%**	**%**	**%**	**%**	**OR**	**95% CI**	***P***	**OR**	**95% CI**	***P***
All respondents	1,209	100.0	5.7	54.4	23.2	22.3	—	—	—	—	—	—
Genetic test results[c]												
Mutation-positive	69	5.7	100.0	53.6	29.0	17.4	0.82	0.50 to 1.33				
Mutation-negative	1,026	84.9	0.0	58.6	20.2	21.2	1.00	Reference				
VUS	39	3.2	0.0	51.3	15.4	33.3	0.74	0.39 to 1.41	.71			
Age at diagnosis												
≤ 40 years (first quintile)	218	18.0	8.7	73.4	17.0	9.6	3.96	2.67 to 5.87		4.36	2.81 to 6.76	
41-45 years (second quintile)	277	22.9	4.0	64.6	20.6	14.8	2.62	1.84 to 3.74		3.00	2.02 to 4.45	
46-50 years (third quintile)	261	21.6	6.1	51.0	23.7	25.3	1.49	1.05 to 2.12		1.54	1.05 to 2.26	
51-56 years (fourth quintile)	207	17.1	5.8	41.1	25.6	33.3	1.00	0.69 to 1.46		1.04	0.70 to 1.57	
> 56 years (fifth quintile)	246	20.3	4.5	41.0	29.3	29.7	1.00	Reference	< .001	1.00	Reference	< .001
Family history of breast, ovarian, melanoma, or pancreatic cancer												
No	421	34.8	5.0	54.6	23.5	21.9	1.00	Reference		1.00	Reference	
Second-degree relative only	450	37.2	5.3	54.9	21.6	23.5	1.01	0.77 to 1.32		1.26	0.93 to 1.69	
First-degree relative	338	28.0	7.1	53.6	25.1	21.3	0.96	0.72 to 1.28	.93	1.57	1.13 to 2.18	.03
Race or ethnicity												
Black or African American	86	7.1	1.2	68.6	17.4	14.0	1.94	1.21 to 3.11		2.06	1.20 to 3.52	
American Indian or Alaska Native, Middle Eastern or North African, and Native Hawaiian or other Pacific Islander	72	6.0	2.8	52.8	30.5	16.7	0.99	0.61 to 1.60		0.80	0.47 to 1.36	
White, non-Hispanic, and non-Ashkenazi Jewish	881	72.9	6.0	53.0	22.6	24.4	1.00	Reference		1.00	Reference	
Ashkenazi Jewish[d]	97	8.0	9.3	56.7	23.7	19.6	1.16	0.76 to 1.77		1.48	0.92 to 2.38	
Hispanic[e]	73	6.0	5.5	53.4	30.1	16.5	1.02	0.63 to 1.64	.10	1.02	0.60 to 1.74	.04
Tumor hormone receptor status												
Estrogen or progesterone receptor–positive	809	66.9	4.4	53.9	24.2	21.9	1.00	Reference		1.00	Reference	
Triple-negative	188	15.6	14.9	66.0	17.0	17.0	1.66	1.19 to 2.31		1.88	1.30 to 2.72	
Estrogen and progesterone receptor–negative	67	5.5	1.5	47.7	26.9	25.4	0.78	0.48 to 1.29		0.77	0.45 to 1.31	
Do not know or others	145	12.0	2.8	45.5	24.1	30.4	0.72	0.50 to 1.02	.001	0.90	0.60 to 1.36	.003
Cancer stage												
Stage 0	263	21.8	3.4	49.4	25.1	25.5	1.00	Reference		1.00	Reference	
Stage I	452	37.4	4.9	51.1	26.1	22.8	1.07	0.79 to 1.45		1.12	0.80 to 1.56	
Stage II	362	29.9	7.2	63.0	17.7	19.3	1.74	1.26 to 2.40		1.71	1.20 to 2.44	
Stage III	125	10.3	9.6	53.6	24.0	22.4	1.18	0.77 to 1.81	.002	1.02	0.64 to 1.62	.008
Education												
No college	164	13.6	6.7	48.8	23.8	27.4	0.69	0.50 to 0.97		0.83	0.56 to 1.24	
Some college	214	17.7	4.7	45.3	25.7	29.0	0.60	0.45 to 0.82		0.62	0.44 to 0.88	
College degree	822	68.0	5.7	57.9	22.6	19.5	1.00	Reference	.001	1.00	Reference	.03
Household income, US dollars												
< 50K	223	18.4	6.7	53.8	26.5	19.7	1.00	Reference		1.00	Reference	
50-100K	370	30.6	5.4	55.4	19.5	25.1	1.07	0.76 to 1.49		0.97	0.66 to 1.42	
> 100K	539	44.6	5.9	55.8	23.6	20.4	1.09	0.79 to 1.49		0.86	0.58 to 1.29	
No information provided	77	6.4	2.6	41.5	28.6	29.9	0.61	0.36 to 1.03	.13	0.75	0.41 to 1.36	.72

(continued on following page)

TABLE 1. Characteristics of Respondents (n = 1,209) and Distribution by Timing of Results Receipt Relative to DST (continued)

	Total		Mutation-Positive	Before DST	After DST: Testing Ordered Pre-DST	After DST: Testing Ordered Post-DST	Univariate Regression (n = 1,209) OR (95% CI)[a]			Multivariate Regression (n = 1,182)[b]		
Characteristic	**N**	**%**	**%**	**%**	**%**	**%**	**OR**	**95% CI**	***P***	**OR**	**95% CI**	***P***
Marital status												
Married or living with partner	935	77.3	5.9	55.2	22.1	22.7	1.00	Reference		1.00	Reference	
Divorced or separated	136	11.2	5.9	44.9	33.8	21.3	0.66	0.46 to 0.95		0.68	0.45 to 1.02	
Single, never married, or widow	124	10.3	4.0	58.1	20.1	21.8	1.12	0.77 to 1.64	.05	0.84	0.54 to 1.29	.15
Patients' involvement in deciding surgical treatment												
Doctor primarily decided alone	83	6.9	4.8	39.8	25.3	34.9	1.00	Reference		1.00	Reference	
Doctor primarily decided but considered patient's opinion	77	6.4	5.2	44.1	27.3	28.6	1.20	0.64 to 2.25		1.19	0.61 to 2.33	
Patient and doctor shared responsibility in making decision	462	38.2	4.1	53.2	22.5	24.3	1.73	1.07 to 2.78		1.90	1.14 to 3.17	
Patient primarily decided but considered doctor's opinion	477	39.5	6.7	60.2	22.6	17.2	2.29	1.42 to 3.69		2.15	1.29 to 3.59	
Patient primarily decided alone	103	8.5	9.7	55.3	24.3	20.4	1.88	1.04 to 3.38	.002	1.51	0.80 to 2.84	.01

(Column group "Timing of Receipt of Results in Relation to DST" spans Before DST through Multivariate Regression.)

Abbreviations: DST, definitive surgical treatment; OR, odds ratio; VUS, variant of uncertain significance.

[a]An OR > 1 indicates the chance of more likely receiving genetic test results before versus after definitive surgical treatment.

[b]Multiple logistic regression excluded 27 patients with missing information on cancer stage (n = 7), education (n = 9), marital status (n = 14), or patient's involvement in deciding surgical treatment (n = 7); additionally, the multivariate model also included these covariates in the table, as applicable: age, family history, race or ethnicity, tumor hormone receptor status, and household income.

[c]There were 75 participants (about 6.2%) who had reported that they did not receive the results, of which 64% had testing ordered pre-DST and 36% were tested post-DST.

[d]Of the Ashkenazi Jewish patients, one also self-described as Hispanic and four as Black or African American; all Others were White.

[e]Of the Hispanic patients, three also self-described as non-White other than Black or African American; all Others were White.

Association of Patient Characteristics With Timing of Genetic Testing

Most respondents were White, non-Hispanic (72.9%), college graduates (68%), and married or living in a marriage-like relationship (77.3%) with household incomes of $50,000 (USD) or more (75.2%); only 8% were Ashkenazi Jewish (Table 1). A positive genetic test result was more likely among patients with later-stage cancer (ie, stages II and III, $P = .005$) and triple-negative disease (14.9%, $P < .001$).

Univariate logistic regressions identified the factors associated with increased odds of undergoing testing and receiving the results presurgery: age < 50 ($P < .001$), college education ($P = .001$), stage II disease ($P = .002$), triple-negative disease ($P = .001$), and greater involvement in surgical decision making ($P = .002$), which multivariate logistic regression confirmed. When treated as effect modifiers, relevant family cancer history ($P = .03$) and race or ethnicity ($P = .04$) also increased odds of receiving the results pre-DST. African Americans and participants with stronger family history (ie, first-degree relative with related cancer) were more likely to receive the results presurgery. In multivariate regressions, equal proportioning was observed across most demographic subgroups, except for older participants (less likely to have testing ordered presurgery, $P = .02$) and Hispanics and non-White participants (more likely to have testing ordered presurgery than White non-Hispanics, $P = .02$).

Patient Characteristics, Timing of Genetic Test Results, and Surgical Treatment Choice

Among mutation-positive women, older women (> 56 years) were less likely to have BLM as DST (27.3%) compared with younger women (74.1%; $P = .005$; Fig 2A), with no other significant personal factors associated. The significantly higher rates of BLM among all women aware of their mutation presurgery (n = 32/37) versus women who were not (n = 14/32) (OR = 8.23, 95% CI = 2.55 to 26.6, $P < .001$) were not explained by age at diagnosis (age-adjusted OR = 6.12, 95% CI = 1.79 to 20.9, $P = .004$). No interaction was observed between mutation results awareness and age among women tested presurgery.

Among mutation-negative women, factors associated with choosing BLM as DST included age < 50 at diagnosis (OR = 1.86, 95% CI = 1.37 to 2.53, $P < .001$), stage II versus stage 0 or I (OR = 1.42, 95% CI = 1.04 to 1.93, $P = .03$), stage III versus stage 0 or I (OR = 2.84, 95% CI = 1.80 to 4.50, $P < .001$), and greater involvement in surgical decision making (OR = 1.91, 95% CI = 1.62 to 2.62, $P < .001$). Compared with women whose test was ordered

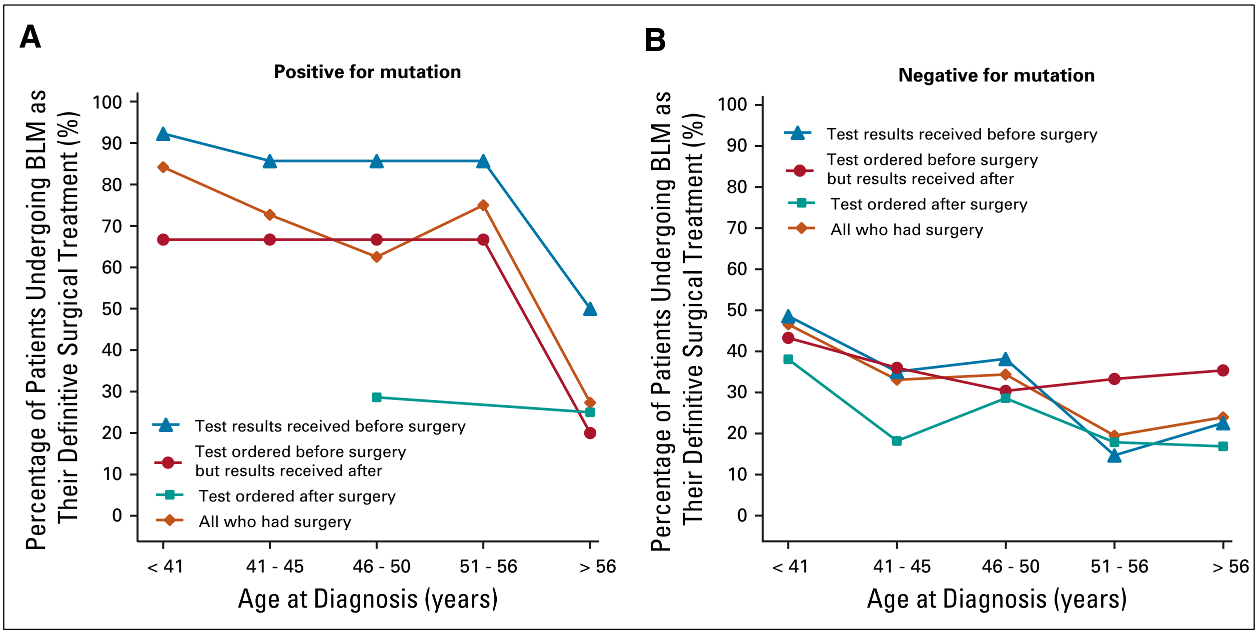

FIG 2. Timing of BRCA testing and results relative to BLM and age, stratified by mutation status. Timing of BRCA testing and results by age among patients with newly diagnosed cancer who underwent BLM as definitive surgical treatment, stratified by (A) positive versus (B) negative results. BLM, bilateral mastectomy.

postsurgery, women whose test was ordered presurgery had higher BLM rates, regardless of result awareness presurgery (OR = 1.86, 95% CI = 1.30 to 2.67, P = .001) or postsurgery (OR = 1.93, 95% CI = 1.26 to 2.96, P = .003). Age at diagnosis, cancer stage, and patient involvement in decision making were associated with different BLM rates between women aware of negative results presurgery and women tested postsurgery (adjusted OR = 1.37, 95% CI = 0.092 to 2.02, P = .12). When adjusting for factors associated with BLM, the BLM rate remained significantly higher only among patients who were unaware of negative results (adjusted OR = 1.70, 95% CI = 1.07 to 2.69, P = .02). Therefore, among mutation-negative women tested presurgery, awareness of negative results presurgery resulted in lower BLM rates. Thus, we examined whether patient characteristics modified the impact of negative results awareness on BLM rates.

A significant interaction existed between negative results awareness and age among women tested presurgery (interaction, P = .007). Among women older than 50 who were tested presurgery, those unaware of negative results were far more likely to choose BLM compared with women aware of negative results presurgery (OR = 2.25, 95% CI = 1.23 to 4.08, P = .008). This was not observed for those diagnosed at age 50 or younger (Fig 2B).

DISCUSSION

This study examined the timing of genetic testing and results disclosure with respect to surgical treatment decisions in a large national sample of commercially insured patients with breast cancer whose genetic testing was requested by a healthcare provider within 1 year postdiagnosis. Timing of testing and results delivery relative to surgical treatment were highly variable. Approximately 22% of patients remained untested until after DST; 23% were tested before DST, but proceeded with surgery before receiving the results; and 54% were tested and aware of the results presurgery. Delaying testing until postsurgery or undergoing surgery before the test results become available may represent suboptimal care.

Consider a woman who undergoes breast-conserving surgery and subsequent radiation therapy. Months later, she learns about and pursues genetic testing, discovers she is a mutation carrier, and then chooses BLM. Thus, the patient undergoes an additional surgical procedure and radiation therapy, both avoidable if she initially had results presurgery. In addition, her reconstructive options are now more limited and radiation effects on tissue may contribute to suboptimal reconstructive results. For example, autologous reconstructions can be performed only once in a lifetime. If a woman initially chooses UM and transverse rectus abdominis myocutaneous flap reconstruction and later opts for contralateral prophylactic mastectomy, contralateral surgery would require a different reconstructive procedure, likely with less symmetric cosmetic results and possibly inferior psychosocial outcomes.[27,45] Thus, in addition to substantially reducing risk for contralateral breast cancer, PNDBC who choose BLM as their DST may avoid radiation treatment, the potential need for additional surgery in the future, and have better possibilities for symmetrical reconstruction and improved cosmetic results.[3,14,24,25,46,47]

Factors associated with receiving genetic testing results presurgery included young age at diagnosis, triple-negative disease, stage II disease, college education, African American race, family history of relevant cancers in first-degree relatives, and greater patient involvement in surgical decision making. Previous research suggests that BRCA mutation prevalence among African American patients with breast cancer < 50 years of age is sufficiently high to warrant testing, regardless of family history.[48] It is notable that Ashkenazi Jewish ancestry, associated with higher a priori mutation risk, did not prompt earlier testing that might have affected surgical decision making. A possible explanation is that Ashkenazi ethnicity is not always routinely collected or known by healthcare providers.

Overall, rates of BLM were 21.5% among patients tested postsurgery, 34.2% if testing occurred presurgery but the results were received postsurgery, and 37.7% among patients aware of the results presurgery. The lower BLM rate among patients tested postsurgery, who were potentially unaware of hereditary mutation risk presurgery, compared with those tested presurgery but results received postsurgery, suggests that the testing process itself, in the absence of results, may lead to higher BLM rates. This is concerning because a large proportion of US-based testing is for patients who do not meet testing guidelines, that is, average-risk patients, who may proceed with BLM, although BLM offers no survival advantage.[33]

For approximately 23% of patients tested presurgery, physicians proceeded with surgery without test results, consistent with other recent findings,[33] which potentially represents suboptimal care. In a survey of surgeons ordering genetic testing for PNDBC approximately 30% would never delay surgery 1-3 weeks to await genetic results,[33] although most laboratories can expedite results in 1-2 weeks for patients facing imminent treatment. Our findings indicate that results timing affects BLM rates both among women with positive and negative results. The odds that a woman who ultimately tests mutation-positive would undergo BLM as DST were eight times greater if her mutation status was known presurgery. More women with positive results might choose this approach and experience the potential benefits of personalized, timely information if they are aware of their results presurgery. Importantly, the analysis also suggests that more women older than 50 who tested negative would likely not choose BLM if they are aware of their negative results presurgery. As the majority of patients with breast cancer will test negative, the potential impact of ensuring testing and results disclosure presurgery is large with respect to reducing the number and costs of more extensive surgeries lacking survival advantage. In some cases, however, it is possible that the surgical plan was unalterable regardless of results, because of clinical factors or patient and/or physician preferences. Since the analysis did not include data regarding patient and physician reasons for timing of testing and results delivery or for pursuing definitive surgery before obtaining testing and/or results, it is not possible to assess how outcomes might have differed if all patients had been aware of the results before DST. It is likely that some patients did not wish to be tested and/or learn the results before surgery or did not wish to base the decision regarding DST on the results.

One of this study's strengths is its basis on real-world experiences of a national, community-based sample of patients undergoing genetic testing through commercial health insurance. Previous studies were largely limited to a few academic medical centers and/or did not examine timing of ordering and results disclosure pre- versus postsurgery. To our knowledge, no studies with a similar scope have been reported. This study also combines both provider-reported and patient-reported data to ensure more comprehensive analyses. This study is limited in that it did not collect provider perspectives regarding decision making. Additionally, study inclusion criteria limited the testing timeframe to include only women tested within 1 year following diagnosis; therefore, we might have missed some patients who had genetic testing ordered more than a year postdiagnosis. If so, then an even higher proportion of patients appropriate for genetic counseling and testing are receiving services too late to optimize outcomes. In an effort to disseminate these important findings in a timely manner, we were unable to conduct all desired analyses. This ongoing longitudinal investigation will further explore decision making, associated motivators, genetic counseling, and satisfaction with decisions.

Clearly, physicians caring for PNDBC are uniquely positioned to deliver high-quality precision medicine and enhance outcomes. NCCN guidelines have long recommended that genetic counseling is performed as part of the presurgical workup of PNDBC.[12] However, we find that high-risk, PNDBC identification and provision of genetic services before surgery are highly variable. Only 54% received timely genetic testing and results to inform DST selection. Such practice variability affects surgical choice and downstream health outcomes, with attendant health and financial costs.

Many physicians self-report discomfort in ordering and interpreting genetic tests, yet many patients report no referral to a genetic counselor.[33,38,49] A primary reason patients do not pursue genetic counseling and testing is lack of physician recommendation.[38,49] Our results and other recent data[50] also suggest that physicians may not be routinely assessing essential risk factors, such as Ashkenazi Jewish ethnicity. Most health plans (including Aetna) cover referral to a genetic counselor, even facilitating patient access and availability by telephone; a randomized controlled trial documented this method of delivery as timely, efficient, cost-effective, and satisfactory to patients.[51,52] Currently, genetic counseling services are dramatically underutilized.[38] Systematic approaches are needed so that all patients meeting national genetic counseling and testing guidelines are identified and offered services, ideally, before surgical treatment so that personal genomic data critical to decision making are available in time to inform life-altering decisions.[16,53]

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DISCLAIMER

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AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

Utilization, Timing, and Outcomes of BRCA Genetic Testing Among Women With Newly Diagnosed Breast Cancer From a National Commercially Insured Population: The ABOARD Study

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