***BRCA* sequencing and large rearrangement testing in young Black women with breast cancer**

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Abstract Young Black women in the United States are disproportionately afflicted with breast cancer, a proportion of which may be due to *BRCA1* and *BRCA2* (*BRCA*) gene mutations. In a cancer registry-based sample of young Black women with breast cancer, we evaluated: (1) the prevalence of *BRCA* mutations detected through full gene sequencing and large rearrangements testing and (2) proportions that accessed genetic services pre-dating study enrollment. Black women diagnosed with invasive breast cancer $\leq$ age 50 years in 2009–2012 were recruited through the Florida Cancer Registry. Participants completed genetic counseling, a study questionnaire, and consent for medical record release. Saliva specimens were collected for *BRCA* testing. Overall, 13 participants (9 %) had *BRCA* mutations detected (including 11 through full gene sequencing and two through large rearrangements testing). One of these large rearrangements, *BRCA1* (delExon8), was identified in a participant who had previously tested negative on clinical comprehensive BRCAnalysis that was performed prior to undergoing a lumpectomy. Although all 144 participants met national criteria for referral for cancer genetic risk assessment, 61 (42 %) were referred for genetic counseling and/or had genetic testing preceding study enrollment, and only 20 (14 %) received genetic counseling. Our findings emphasize

the importance of large rearrangements testing to increase detection of deleterious *BRCA* mutations in young Black women with breast cancer. The registry-based design of our study increase the generalizability of findings compared with efforts focused on clinic-based populations. Furthermore, results suggest efforts are needed to improve access to genetic counseling and testing.

Keywords *BRCA* testing · Genetic counseling · Black women · Breast cancer · Cancer registry

Introduction

Young Black women bear a disproportionate burden associated with breast cancer incidence and mortality compared with their White counterparts (American Cancer Society 2011). Given that early onset breast cancer is a hallmark feature of germline mutations in the inherited breast cancer susceptibility genes, *BRCA1* and *BRCA2* (*BRCA*), a portion of these breast cancers may be attributed to mutations in these genes. Identifying *BRCA* mutations can profoundly influence health outcomes. Mutations in the *BRCA* genes confer a lifetime risk of breast cancer in the range of 60–70 % (Antoniou et al. 2003; Chen and Parmigiani 2007; Litton et al. 2011), as well as a much higher risk of a second primary breast cancer than non-carriers, particularly for those diagnosed at a younger age (Graeser et al. 2009; Malone et al. 2010). Those identified with mutations may avail themselves to the latest cancer risk management strategies including increased surveillance and preventive surgeries to improve their outcomes (Narod and Offit 2005).

Studies conducted in primarily White populations indicate that an estimated 5 % of all breast cancers are due to mutations in the *BRCA* genes (Malone et al. 2006). However, the prevalence estimates in Black women remain uncertain, mostly due to their reported low uptake of *BRCA* testing and bias inherent

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in clinic-based samples (Newman 2005). Additionally, minority-serving physicians have been found to be less likely to have ever ordered a genetic test for breast cancer or to have referred a patient for genetic testing compared with those serving a smaller proportion of minorities (Shields et al. 2008). Despite these concerns about disparities, the overall proportion of young Black women with breast cancer who access genetic counseling and *BRCA* testing remains uncertain due to under-representation of Black women in the only population-based study of young women with breast cancer we are aware of that reported on access to genetic services (Anderson et al. 2012).

The majority of *BRCA* gene mutations are detected through full gene sequencing; however, an additional 10 % of all mutations are estimated to be large rearrangements, which cannot be detected through sequencing. Detection of a large rearrangement requires additional testing through different technologies such as multiplex ligation-dependent probe amplification (MLPA) (Kang et al. 2010; Palma et al. 2008; Roa et al. 2011). Until recently within the United States, clinical testing for *BRCA* mutations was mainly available through Myriad Genetics (Myriad), the company that used to own the patent on these genes (Myriad Genetics Laboratories and Pharmaceuticals). However, this is no longer the case since the ruling in June 2013 by the U.S. Supreme Court that genes are not patentable because they are products of nature. Prior to the beginning of 2013, when clinical *BRCA* testing was ordered through Myriad, the standard test was called “Comprehensive BRACAnalysis,” which included *BRCA* sequencing and testing for five rearrangements in *BRCA1* (which was added in 2003) (Shannon et al. 2011). However, this test is estimated to miss up to 10 % of all mutations (Kang et al. 2010; Palma et al. 2008; Roa et al. 2011). Testing for additional large rearrangements has been available through Myriad since 2006 (referred to as “BRACAnalysis Rearrangement Testing” or “BART”), yet it had to be ordered separately. Rearrangement testing has very recently become automatically included as part of Myriad’s new standard test that is referred to as “integrated BRACAnalysis.” However, rearrangement testing continues to be billed to insurers as a separate cost of \$700, and this cost is not yet covered by all insurers even when women meet insurers’ criteria for *BRCA* testing. Furthermore, the longstanding uncoupling of BART testing from comprehensive BRACAnalysis has resulted in an out-of-pocket expense, even among many of those who had health insurance coverage for *BRCA* testing at the time they were tested. Fortunately for some patients, the cost of BART has and continues to be covered through Myriad when a patient lacks coverage for it through their health insurance, and the lab is provided with information from the healthcare provider that the patient is at ≥ 30 % risk of having a *BRCA* mutation or the patient meets internal laboratory criteria (NCCN Guidelines Updated to Include BRACAnalysis® Large Rearrangement

Test (BART™)). Despite the option for some patients to receive free BART testing, there have been challenges at the provider level to identify those who qualified for this option, as demonstrated in our Florida-wide survey of providers who order *BRCA* testing (Pal et al. 2013b).

Based on published data through Myriad Genetics, the frequency of mutations detected through large rearrangements testing may differ by ethnic background (Judkins et al. 2012). However, there have been very limited studies of *BRCA* mutations among population-based samples of young Black women with breast cancer, and none of these have included large rearrangements testing (Pal et al. 2013a; John et al. 2007; Malone et al. 2006; Newman et al. 1998). Through a population-based sample of Black women with early onset breast cancer recruited through the Florida state cancer registry, the objective of the current study was to assess: (1) the prevalence of *BRCA* mutations detected through full gene sequencing and large rearrangement testing and (2) proportion of women who accessed genetic services pre-dating study enrollment.

Materials and methods

Eligible patients were self-identified Black women diagnosed with invasive breast cancer at or below age 50 years between the years 2009 and 2012 who were living in Florida at the time of diagnosis and alive at time of contact. Upon approval of the institutional review boards of the University of South Florida and the Florida Department of Health (DOH), registry-based recruitment was initiated. The Florida State Cancer Registry released patient contact information and available clinical (i.e., age at diagnosis, stage of diagnosis, histologic subtype) and demographic (i.e., county of residence, marital status, primary payor at diagnosis) information on all 913 eligible participants that together constitute the population of interest.

Participants were recruited using previously described state-mandated recruitment methods (Pal et al. 2010). A sample of 481 eligible women were successfully contacted and asked to: (1) provide verbal and written informed consent, including medical records release; (2) complete a study questionnaire, which included sociodemographic, epidemiologic, and lifestyle factors as well as information about referral for genetic counseling and/or testing predating study enrollment; (3) receive telephone genetic counseling to discuss inherited breast cancer with a certified genetic counselor, during which a three-generation pedigree was generated (for participants who reported prior clinical *BRCA* testing, results were obtained through signed medical releases and used during the pre-test genetic counseling session); and (4) provide a mailed saliva sample for DNA testing.

BRCA testing was performed on participants through DNA extracted from the saliva specimen. Testing included full gene

sequencing and comprehensive rearrangement testing through MLPA of the *BRCA1* and *BRCA2* genes, as previously described (Zhang et al. 2011). Demographic and clinical characteristics of all young Black women eligible to participate, as well as the subset of 144 participants for whom genetic testing was completed, were summarized using descriptive statistics, including means, standard deviations, and frequencies. Comparisons were made using large sample *z*-tests and chi-square goodness-of-fit tests to assess whether this subset differed from the overall population for demographic and clinical characteristics available from the cancer registry. All statistical tests were two-sided and considered statistically significant at a level of $p \leq 0.05$. Mutation prevalence and proportions of those who accessed genetic counseling and/or testing services were calculated along with 95 % confidence intervals.

Results

Demographic and clinical information on the 144 participants who completed genetic counseling and testing are similar to demographic and clinical characteristics of all 913 individuals that comprise the entire population, as shown in Table 1. The majority of participants had private insurance. Mean age of participants at breast cancer diagnosis was 43 years, with approximately half with stage 1 disease. Approximately 43 % of participants were married (including common law), and over one third had an annual household income below \$50,000.

The number of family members with breast and/or ovarian cancers are compared in Table 2 according to whether participants received genetic testing prior to the study and also according to *BRCA* carrier status. A total of 13 mutations in the *BRCA* genes were detected in the 144 participants (i.e., 9.0 %; 95 % Confidence Interval (CI) 4.9 % to 14.9 %), including 11 detected through gene sequencing and two detected through large rearrangement testing (Table 3). Of the women in whom we identified mutations, six had previously undergone clinical *BRCA* testing prior to study enrollment, and all but one of these women had a mutation detected on clinical testing. In this patient, who had undergone prior comprehensive BRACAnalysis, a *BRCA1* mutation (*BRCA1* del exon 8) was identified in our study through large rearrangements testing. Review of this participant's medical records indicated that she was 34 years at diagnosis and had testing performed in the pre-surgical setting, prior to definitive surgical treatment. Following receipt of her clinical genetic test result, she had a lumpectomy as part of her breast cancer treatment. Review of her family history indicated multiple first-, third-, and fourth-degree relatives with breast cancer (as illustrated in Fig. 1). Based on the Myriad risk assessment model, she had an a priori risk of

21.2 % for having a *BRCA* mutation. The other mutation detected through large rearrangements testing (*BRCA1* in exon 13) is one of the five *BRCA1* rearrangements included as part of comprehensive BRACAnalysis, in a woman who was 45 years at diagnosis who had not received prior genetic testing.

Among the 144 participants, all met current National Comprehensive Cancer Network (NCCN) guidelines for referral for cancer risk assessment (Genetic/Familial High-risk Assessment: Breast and Ovarian 2012). Slightly less than half ($n=61$; 42 %; 95 % CI 34 %–51 %) were referred by a healthcare provider for genetic counseling and/or underwent genetic testing prior to study enrollment. However, of the subset of 43 women who were referred for genetic counseling, only 20 (14 % of all participants; 95 % CI 9 %–21 %) reported meeting with a genetic counselor to learn about their risk for breast or ovarian cancer (as illustrated in Fig. 2). Based on our review of prior *BRCA* test results from the commercial laboratory following signed release by the participants, we determined that 16 (11 %) had both counseling and testing, four (3 %) had genetic counseling but no testing, and 25 (17 %) had *BRCA* testing but no genetic counseling. An additional four participants reported having had genetic testing; however, the commercial laboratory had no record indicating they were tested. In total, 41 (28 %; 95 % CI 21 %–37 %) participants were tested through comprehensive BRACAnalysis prior to our study, of whom 12 also received BART testing.

Discussion

Our efforts, to the best of our knowledge, are the first to focus on a population-based sample of young Black women with breast cancer, in which the main objective was investigation of *BRCA* mutation prevalence through both sequencing and large rearrangement testing of both *BRCA1* and *BRCA2*. In contrast, two of three prior studies in which *BRCA* testing was conducted in population-based samples with relatively large numbers of Black women included *BRCA1* but not *BRCA2* sequencing (John et al. 2007; Newman et al. 1998). This is particularly problematic because in the third population-based study, Malone et al. (2006) reported that *BRCA1* mutations were significantly less common among their 483 Black cases (1.4 %) compared with 1,145 White cases (2.4 %), and *BRCA2* mutations were slightly more common among Black cases (2.6 % versus 2.1 %). Two thirds of the cases in the study by Malone et al. (2006) were age 45 years and above at diagnosis, and large rearrangement testing was not performed. Our study is unique because we only included Black women age 50 years and below, and we also tested all participants for large rearrangements. Due to these differences between the studies, it is not surprising that our overall prevalence of *BRCA* mutations was more than twice as high as the Malone

Table 1 Clinical and demographic variables

	Participants <i>N</i> =144	All potential participants in registry, <i>N</i> =913	<i>P</i> value
Age at diagnosis (mean (SD))	42.8 (5.5)	42.6 (6.2)	.33
Stage at Diagnosis (<i>n</i> (%))			
1	76 (52.8)	441 (48.4)	0.26
2	3 (2.1)	24 (2.6)	
3	49 (34.0)	281 (30.8)	
4	4 (2.8)	39 (4.3)	
Other (distant/unknown/unstaged)	12 (8.3)	128 (14.0)	
Histologic subtype (<i>n</i> (%))			
Ductal	109 (75.7)	711 (77.9)	0.19
Lobular	8 (5.6)	42 (4.6)	
Mixed	14 (9.7)	54 (5.9)	
Other	13 (9.0)	106 (11.6)	
Marital status at diagnosis (<i>n</i> (%))			
Married (including common law)	60 (41.7)	391 (42.8)	0.78
Other	84 (58.3)	522 (57.2)	
Insurance status at diagnosis (<i>n</i> (%))			
Not insured	14 (9.7)	79 (8.7)	0.35
Private insurance	76 (52.8)	527 (57.7)	
Medicaid	23 (16.0)	160 (17.5)	
Medicare	11 (7.6)	40 (4.4)	
Other (NOS, military insurance)	17 (11.8)	96 (10.5)	
No answer or prefer not to answer	3 (2.1)	11 (1.2)	
Total household income (<i>n</i> (%))			
<\$25,000	55 (38.2)	ND	N/A
\$25,000–\$49,000	36 (25.0)		
\$50,000+	46 (31.9)		
No answer or prefer not to answer	7 (4.9)		
Education (<i>n</i> (%))			
≤12th grade/GED	38 (26.4)	ND	N/A
Vocational school/some college	48 (33.3)		
≥College graduate	56 (38.9)		
No answer or prefer not to answer	2 (1.4)		

NOS insurance was not otherwise specified, ND no registry data were available for income or education, N/A not applicable

et al. 2010 study (9 % compared with 4 %). Our findings, along with findings of prior studies, indicate similar prevalence estimates of *BRCA* mutations in Blacks and Whites (Haffty et al. 2009; Hall et al. 2009; Malone et al. 2006), despite the higher prevalence of triple negative breast cancers (Carey et al. 2006; Lund et al. 2008), disproportionate numbers with early onset disease (American Cancer Society 2011; 2009), and higher mortality rates (American Cancer Society 2011; 2009) in Black women.

Data on the prevalence of *BRCA* large rearrangements in different ethnic groups, including African Americans, have been published through Myriad Genetics. In this report, patients were subdivided into a “high-risk” group (which was comprised of patients who met specific eligibility criteria developed by the

testing laboratory which qualified them to have additional large rearrangements testing at no charge) as well as an “elective” group (which comprised individuals who pursued additional large rearrangements testing but did not meet testing laboratory eligibility criteria for free testing) (Judkins et al. 2012). In African American women within the high-risk group, mutations were detected through comprehensive BRACAnalysis (which includes full gene sequencing and testing for five *BRCA1* large rearrangements) and large rearrangements testing (called “BART” by the testing laboratory) in 26.9 % and 2.4 % of all samples tested, respectively. This can be contrasted with the elective group, in which mutations were detected in 11.4 % and 0.1 %, respectively. Thus, large rearrangements accounted for a small proportion of overall mutations detected in the Myriad

Table 2 Family history of cancers and Myriad risk assessment stratified by carrier status and receipt of testing prior to study enrollment ($n = 144$)

		Carrier status		Prior testing	
		Yes $n = 13$	No $n = 131$	Yes $n = 41$	No $n = 103$
No. of first- to third-degree relatives with cancer					
Breast cancer	0	6 (46)	66 (50)	18 (44)	54 (52)
	1	3 (23)	35 (27)	10 (24)	28 (27)
	2	2 (15)	22 (16)	7 (17)	17 (17)
	≥3	2 (15)	8 (6)	6 (15)	4 (4)
Ovarian cancer	0	12 (92)	104 (80)	31 (76)	85 (82)
	1	1 (8)	23 (18)	9 (22)	15 (15)
	2	0 (0)	2 (1.5)	1 (2)	1 (1)
	≥3	0 (0)	2 (1.5)	0 (0)	2 (2)
Both breast and ovarian cancer	0	12 (92)	129 (99)	39 (95)	102 (99)
	≥1	1 (8)	2 (1)	2 (5)	1 (1)
Total no. with breast and/or ovarian cancer	0	5 (39)	56 (43)	17 (42)	44 (43)
	1	4 (31)	35 (27)	5 (12)	34 (33)
	2	2 (15)	24 (18)	11 (27)	15 (15)
	3	0 (0)	11 (8)	3 (7)	8 (8)
	≥4	2 (15)	5 (4)	5 (13)	2 (2)
Myriad risk assessment	0–5 %	9 (69)	90 (69)	28 (68)	71 (69)
	6–15 %	2 (15.5)	30 (23)	6 (15)	26 (25)
	≥16	2 (15.5)	11 (8)	7 (17)	6 (6)

study. In contrast, a clinic-based study identified large rearrangements, which would not have been detected with BRACAnalysis, in seven of 136 (5 %) non-Ashkenazi Jewish individuals, and these seven mutations constituted (16 %) of the 44 total mutations detected (Palma et al. 2008). In our study, the overall proportion of participants with a large rearrangement was small. Nevertheless, one out of 13 (7.6 %) mutations we identified would not have been detected through Comprehensive BRACAnalysis. Interestingly, this large rearrangement is one of three that together made up 60.5 % of all large rearrangements detected in African Americans in the Myriad dataset (Judkins et al. 2012). Finally, another chart review study reported on 257 patients in whom BART tests were performed at a single institution over a 3-year period. Results indicated that 40 % of patients in whom mutations were detected through BART did not meet the laboratory criteria for free testing (Shannon et al. 2011). Based on these results, the authors concluded that BART testing should be included when Comprehensive BRACAnalysis is offered. Our study also supports this conclusion in that the participant in whom the *BRCA1* del exon 8 mutation was detected had previously undergone comprehensive BRACAnalysis (with negative results) and did not meet eligibility criteria for free BART testing based on the Myriad risk assessment model. Despite its limitations, the Myriad model is a commonly used method in the U.S. of estimating the chances that a *BRCA*

Table 3 Results of *BRCA* testing, prior clinical testing status of 13 patients in whom mutations were detected

Study results	Prior testing ^a	Results of prior testing	Age at diagnosis	Risk Assessment ^b	Receptor status (ER/PR/HER2)
BRCA1 deletion of exon8	BRACAnalysis	No mutation detected	34	21.2 %	ER+/PR–
BRCA2 exon11 5844del5	BRACAnalysis	<i>BRCA2</i> exon11 5844del5	45	4.7 %	ER–/PR–/HER2+
BRCA2 exon11 4699del4	N/A	N/A	47	10.4 %	ER–/PR–/Her2–
BRCA2 exon11 3908delTG	BRACAnalysis	<i>BRCA2</i> exon11 3908delTG	40	4.7 %	ER–/PR–
BRCA1 exon19 5296del4	BRACAnalysis	<i>BRCA1</i> exon19 5296del4	31	4.7 %	ER–/PR–/Her2–
BRCA2 exon3 343delG	N/A	N/A	44	4.7% ^c	ER+/PR+
BRCA1 exon19 5296del4	N/A ^d	N/A	47	10.4 %	ER–/PR–
BRCA1 exon13 c.4357+1G>A	N/A	N/A	48	4.7 %	ER–/PR–
BRCA2 exon 11 6365C>A	N/A	N/A	43	4.7 %	ER–/PR–
BRCA2 exon11 4699del4	BRACAnalysis	<i>BRCA2</i> exon11 4699del4	45	4.7 %	ER+/PR–
BRCA1 exon11 2190delA	BRACAnalysis+BART	<i>BRCA1</i> exon11 2190delA	46	13.3 %	ER+/PR+/Her2–
BRCA1 duplication13	N/A	N/A	45	10.3 %	ER+/PR+
BRCA1 exon16 IVS16+6 T>C	BRACAnalysis	<i>BRCA1</i> exon16 IVS16+6 T>C	33 ^e	4.7 %	ER–/PR–/Her2–

^a Clinical testing prior to study enrollment^b Risk assessment using the Myriad risk assessment model^c Participant's uncle diagnosed with breast cancer at age 70 years not included in risk assessment^d Participant was diagnosed with bilateral breast cancer and also had blood drawn for BRCA testing but never tested because insurance did not cover^e Participant was diagnosed with another primary breast cancer diagnosis at age 28 years, prior to enrollment

Abbreviations: Br: breast cancer; d.: age at death. Black shaded circles: reflect individuals diagnosed with breast cancer; those with diagonal line: reflect that individual deceased

Fig. 1 Pedigree of participant with no prior mutation on BRACAnalysis who has a large gene rearrangement

Fig. 2 Venn diagram showing the number of participants referred for genetic counseling (+refer), number who attended genetic counseling (+attend), and number who received *BRCA* testing (+test) prior to study enrollment. The minus sign indicates the absence of a referral, attendance, or testing

mutation will be identified. Nevertheless, our participant's family history is very striking, and assessment with the Manchester scoring system (which is less commonly used in the U.S., but has been demonstrated to be more accurate than the Myriad risk model in a U.K. study) would have given her a >50 % chance of a *BRCA* mutation (Evans et al. 2004, 2005).

Ultimately, our results and those from prior studies suggest that the uncoupling of Comprehensive BRACAnalysis and BART has lead to incomplete *BRCA* testing in patients. This has been formally recognized in the 2012 NCCN practice guidelines (Genetic/Familial High-risk Assessment: Breast and Ovarian 2012), which were updated to recommend that large rearrangements testing should be considered part of standard *BRCA* testing for any patient in whom testing is indicated. Our study highlights the importance of these guidelines. Additionally, the recent ability for other labs to offer *BRCA* testing in the U.S. and recent changes by Myriad so that sequencing and large rearrangement testing are automatically ordered together are important steps to increase access to

testing and help ensure that testing is complete. Additionally, more insurers are covering the cost of large rearrangement testing. Specifically, Medicare guidelines were revised as of 01 October 2012, to include large rearrangements testing in any patient who qualified for comprehensive BRACAnalysis, and other insurers such as Tricare and United Health have followed suit. Thus, at a policy level, insurance coverage for this testing continues to expand, yet this fails to address large rearrangements testing for patients who have previously had Comprehensive BRACAnalysis. Furthermore, the historic lack of insurance coverage for large rearrangements testing and prior requirement to order these tests separately means that some women with hereditary breast and ovarian cancer who were previously tested (and their affected family members) remain unidentified. Although no standard clinical guidelines exist for these patients, follow-up mechanisms through treating healthcare providers to re-contact them about the updated testing recommendation by NCCN may be appropriate, when feasible (Rubinstein 2008).

Our findings regarding referral and clinical access to genetic counseling and/or testing demonstrate an opportunity to enhance adherence to NCCN guidelines for referral for cancer risk assessment services. All 144 of our study participants met NCCN referral guidelines based on their personal history of breast cancer at or below age 50 years. Of these, only 45 (31 %) had genetic counseling and/or testing, although an additional 16 (11 %) were referred but did not follow through with genetic counseling or testing (as illustrated in Fig. 2). These findings provide a population-based estimate of young Black women with breast cancer who are referred to and access genetic services and also highlight the need to improve awareness about identifying appropriate patients for *BRCA* risk assessment at the provider level. A recently published study of 125 Black women at high risk for *BRCA* mutations found that physicians had recommended genetic counseling in over two thirds of the sample, but the likelihood of recommendation was significantly lower among participants who were recruited through the community (Thompson et al. 2012). Prior population-based efforts using a state cancer registry to determine patient referral and access to genetic services in young women with breast cancer is limited to a single survey of women with breast cancer diagnosed below age 50 years throughout the state of Michigan. Of all 289 respondents, 42.2 % reported receiving genetic counseling. Blacks represented only 8.3 % of respondents, yet comprised 21.3 % of non-respondents (Anderson et al. 2012). Nevertheless, among the 24 Black participants, only five (21 %) reported having received genetic counseling, which is higher than the proportion who reported having received genetic counseling in our study (i.e., 14 %). The difference in these rates may simply be due to sampling error given the small number of Black participants in the Michigan study.

However, it is also possible that the Michigan results reflect rates higher than national averages due to the policy work conducted through Michigan DOH to enhance access to *BRCA*-related counseling and testing (Duquette et al. 2012). Our results are also subject to state-specific factors. In particular, the low numbers of genetic professionals in Florida (Pal et al. 2013b) coupled with Myriad Genetics' direct-to-consumer marketing campaigns in Florida (Matloff and Caplan 2008) are some factors that could have contributed to large testing volume by non-genetics professionals. This may have resulted in the higher than expected number of individuals (i.e., 28 %) who underwent clinical *BRCA* testing preceding study enrollment, yet low number who reported having genetic counseling (i.e., 14 %). Although the proportion of Black women who accessed clinical *BRCA* testing is encouraging, several guidelines recommend genetic counseling when performing genetic testing (Genetic/Familial High-risk Assessment: Breast and Ovarian 2012; American Society of Clinical Oncology policy statement update: genetic testing for cancer susceptibility 2003; Robson et al. 2010; Cancer-related Genetic Testing and Counseling: Workshop Proceedings 2007; Berliner and Fay 2007; ACOG Practice Bulletin No. 103: Hereditary breast and ovarian cancer syndrome 2009; Role of the Oncology Nurse in Cancer Genetic Counseling 2009; Force 2005; National Accreditation Program for Breast Centers 2012). In fact, the 2005 U.S. Preventive Services Task Force made a grade B recommendation that women at increased risk for *BRCA* mutations should be referred for genetic counseling and evaluation for *BRCA* testing (Force 2005). Furthermore, the 2012 Commission on Cancer standards through the American College of Surgeons also indicates that "Cancer risk assessment, genetic counseling, and testing services are provided to patients either on-site or by referral, by a qualified genetics professional" (2012 Breast Center Standards Manual through the National Accreditation Program for Breast Centers (NAPBC) 2012). These recommendations for genetic counseling in the context of testing has been reflected in both NCCN practice guidelines (Genetic/Familial High-risk Assessment: Breast and Ovarian 2012) and the American Society of Clinical Oncology policy statements (American Society of Clinical Oncology policy statement update: genetic testing for cancer susceptibility 2003; Robson et al. 2010). The lack of adherence to existing national guidelines for performing genetic counseling prior to clinical *BRCA* testing suggests there remain tremendous opportunities for education and outreach at the provider level.

There were several strengths in our study, including our registry-based design, which enabled recruitment of a population-based sample that was not significantly different than the entire population of interest in terms of several key clinical and demographic variables available through the State Cancer Registry. This suggests that our participants are

likely to be a representative sample of our population of interest and thereby enhances the generalizability of our findings. Nevertheless, other unmeasured differences between our sample and the population of interest could exist and the possibility of bias cannot be eliminated entirely. Furthermore, our sample size limits our ability to draw firm conclusions about the prevalence of *BRCA* mutations in unselected young Black women with breast cancer. However, our 95 % confidence interval indicates the mutation prevalence among this understudied population probably falls between 5.4 % and 14.8 %. Interestingly, the mutation prevalence among the group of women who were tested prior to the study was higher than among the women who were not previously tested. This could simply be due to chance, as we are underpowered to detect statistically significant differences between these subgroups. However, we believe that another possible explanation for the differences could be that individuals at higher risk to have a mutation are more likely to have been tested. Table 2 suggests a potential trend for more women with very strong family histories of cancer (i.e., women in the highest Myriad risk classification and women with four or more close relatives with breast and/or ovarian cancer) to have received testing prior to the study. Nevertheless, caution is necessary when drawing any conclusions given the small number of women who fall into these categories.

An added strength is that we collected information on pretest counseling and clinical *BRCA* testing prior to study enrollment, which has not been done in other population-based studies that have reported on *BRCA* prevalence (John et al. 2007; Malone et al. 2006; Newman et al. 1998). This allowed us to estimate a population-based prevalence of pretest counseling and *BRCA* testing among young Black women, thereby adding to the limited literature available on this topic (Anderson et al. 2012). In both our study and the Michigan study, receipt of genetic counseling was self-reported and subject to bias. We also do not know what type of health care providers counseled the participants. Nevertheless, taken together, results from these two studies suggest the presence of a gap in access to genetic counseling among Black women. Finally, unlike the Michigan study, we took a more comprehensive approach to data collection, which resulted in our ability to also report on the prevalence of *BRCA* testing, and this estimate is less subject to recall bias because we obtained copies of prior *BRCA* test results to verify self-reported genetic testing.

In summary, results from our study suggest that large rearrangements testing in young Black women with breast cancer increases the yield of *BRCA* testing and reiterates the importance of offering this to all high-risk patients in whom comprehensive BRACAnalysis was performed. Furthermore, there remain additional opportunities to increase awareness about cancer risk assessment services among providers to promote adherence to existing best practices guidelines.

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