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SHORT COMMUNICATION

Uptake of genetic testing for germline *BRCA1/2* pathogenic variants in a predominantly Hispanic population

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Abstract

Genetic counseling is under-utilized in women who meet family history criteria for *BRCA1* and *BRCA2* (*BRCA1/2*) testing, particularly among racial/ethnic minorities. We evaluated the uptake of *BRCA1/2* genetic testing among women presenting for screening mammography in a predominantly Hispanic, low-income population of Washington Heights in New York City.

We administered the Six-Point Scale (SPS) to women presenting for screening mammography at Columbia University Irving Medical Center (CUIMC) in the Washington Heights neighborhood of New York, NY. The SPS is a family history screener to determine eligibility for *BRCA1/2* genetic testing based upon U.S. Preventive Services Task Force (USPSTF) guidelines that has been validated in low-income, multiethnic populations.

Among women who underwent screening mammography at CUIMC between November 2014 and June 2016, 3,055 completed the SPS family history screener. Participants were predominantly Hispanic (76.7%), and 12% met family history criteria for *BRCA1/2* testing, of whom <5% had previously undergone testing.

In a multiethnic population, a significant proportion met family history criteria for *BRCA1/2* testing, but uptake of genetic testing was low. Such underutilization of *BRCA1/2* genetic testing among minorities further underscores the need to develop programs to engage high-risk women from underrepresented populations in genetic testing services.

Keywords Family history, Hereditary breast and ovarian cancer, *BRCA1/BRCA2* genetic testing, Racial/ethnic minorities.

Introduction

The majority of hereditary breast and ovarian cancers (HBOC) result from pathogenic variants in the *BRCA1* and *BRCA2* genes. Women with germline *BRCA1/2* mutations have estimated risks of 40–87% and 18–88% for breast cancer, respectively [1]. The U.S. Preventive Services Task Force (USPSTF) recommends that women whose family history may be associated with an increased risk of *BRCA1/2* pathogenic variants undergo genetic counseling and/or testing [2]. However, uptake of genetic counseling for women at high risk for HBOC remains low, even among women with breast cancer [3]. Barriers to genetic counseling include patients' lack of knowledge of personal medical history and cancer risk, inaccuracies and inconsistencies in documentation of family history of cancer [4–7], and failure of primary care providers and cancer specialists to obtain adequate family cancer histories in order to refer patients at risk for hereditary cancer to genetic counselors [8–10].

Minority populations are even less likely to undergo genetic counseling/testing for HBOC. Among women diagnosed with breast cancer or with a family history of breast and/or ovarian cancer, Hispanic and black women are less likely than white

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Table 1 Baseline characteristics of women who completed the Six-Point Scale (SPS) family history screener, stratified by eligibility for *BRCA1/2* genetic counseling and/or testing.

Characteristic	Eligible ($n=369$)	Ineligible ($n=2686$)	Total ($n=3055$)
Median age, years (range)	58 (29–91)	59 (33–99)	59 (29–99)
Race/Ethnicity, *N* (%)			
Hispanic	249 (67.5)	2093 (77.9)	2342 (76.7)
White, Non-Hispanic	74 (20.1)	245 (9.1)	319 (10.4)
Black, Non-Hispanic	33 (8.9)	257 (9.6)	290 (9.5)
Asian	7 (1.9)	48 (1.8)	55 (1.8)
Other	6 (1.6)	43 (1.6)	49 (1.6)
Ashkenazi Jewish descent, *N* (%)	42 (11.4)	44 (1.6)	86 (2.8)
Highest level of education, *N* (%)			
High school diploma, GED, or less	185 (50.1)	1666 (62.0)	1851 (60.6)
Vocational, technical, or military	5 (1.4)	38 (1.4)	43 (1.4)
Some college or university	56 (15.2)	342 (12.7)	398 (13.0)
Associate's or bachelor's degree	56 (15.2)	390 (14.5)	446 (14.6)
Graduate or professional degree	67 (18.2)	247 (9.2)	314 (10.3)
Unknown		3 (0.1)	3 (0.1)
Family history of breast cancer, *N* (%)	292 (79.1)	527 (19.6)	819 (26.8)
Family history of ovarian cancer, *N* (%)	149 (40.4)	141 (5.2)	290 (9.5)
Reported prior *BRCA1/2* testing, *N* (%)	17 (4.6)	14 (0.5)	31 (1.0)
Negative genetic test result	13 (3.5)	11 (0.4)	12 (0.4)
Pathogenic variant in *BRCA1/2*	2 (0.5)	0 (0.0)	1 (0.0)
Unknown result	2 (0.5)	3 (0.1)	4 (0.1)

women to undergo testing for *BRCA1/2* pathogenic variants, with odds ratios as low as 0.22 [11–13]. Factors that contribute to lower utilization of genetic counseling among minorities include poor understanding of genetic testing, low perception of personal cancer risk, and decreased frequency of reporting of family history compared to whites [14–17]. Despite these limitations, when provided with information about hereditary cancer, Hispanic women express high levels of interest in undergoing genetic counseling/testing, and when offered *BRCA1/2* testing based on eligibility, high proportions complete testing [14,18].

We evaluated the uptake of *BRCA1/2* genetic testing among women presenting for screening mammography in a predominantly Hispanic, low-income population of Washington Heights in New York City.

Materials and methods

We conducted a prospective study called the Know Your Risk: Assessment at Screening (KYRAS) [19]. Women were approached for enrollment during routine screening mammography at the Avon Breast Imaging Center at Columbia University Irving Medical Center (CUIMC) in the Washington Heights neighborhood of New York, NY, and provided written informed consent to complete a baseline survey and to allow access to their electronic health record (EHR). The inclusion criteria included: (1) women age $\geq$18 years, (2) English or Spanish-speaking, (3) no previous diagnosis of breast cancer. The study was approved by the Institutional Review Board at CUIMC.

We administered a questionnaire collecting information about sociodemographic characteristics, breast cancer risk factors, and prior *BRCA1/2* genetic testing. The Gail model was used to estimate 5-year risk of invasive breast cancer [20]. The questionnaire included the Six-Point Scale (SPS), a family history screener to determine eligibility for *BRCA1/2* genetic testing based upon USPSTF guidelines that has been validated in populations of low income, multiethnic women [21,22]. The SPS is a simplified questionnaire that can be administered in a low-cost, efficient manner, consisting of ten questions that assess eligibility for HBOC genetic testing based upon USPSTF guidelines. The SPS includes questions regarding personal history of breast or ovarian cancer, as well as Jewish ancestry, family history of male breast cancer or ovarian cancer, and history of breast cancer among first- and second-degree female relatives. A score of six or higher on this scale indicates eligibility for HBOC genetic counseling and/or testing.

Results

Of 18,502 women who underwent screening mammography at CUIMC between November 2014 and June 2016, 3558 (19.2%) were approached for participation, 3055 (85.9% of total approached) completed the SPS family history screener, and 503 (14.1% of total approached) refused participation (Fig. 1). The baseline characteristics of women eligible for genetic testing are presented in Table 1. The median age was 58 years (range 29–91). Over two-thirds ($N=253$) were Hispanic, approximately 11% ($N=39$) reported being of Ashkenazi Jewish descent, and about half ($N=190$) had a high school education or less. These demographic characteristics were similar to those among the 9514 of the 18,502 women for whom ethnicity data was available by questionnaire or by EHR data, as published previously [23]. Over 75% of women reported a family history of breast cancer and over 40% a family history of ovarian cancer. About 12% ($N=369$) women were eligible for genetic testing by the SPS, but only 4.6% ($N=17$)

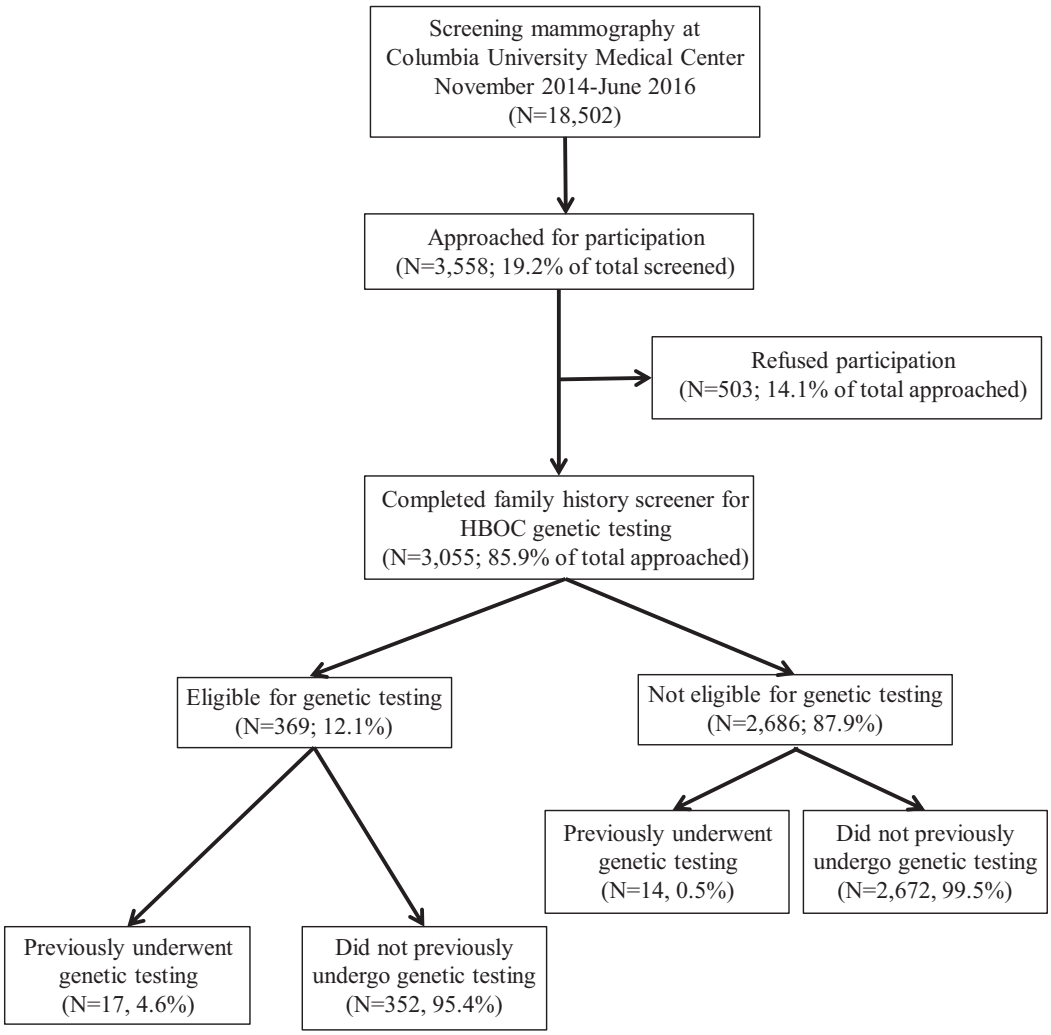

Fig. 1 Flow diagram for the population approached at screening mammography for participation and completion of questionnaire, with responses to questions regarding previous testing for *BRCA1/2* pathogenic variants.

of eligible women had previously undergone *BRCA1/2* genetic testing based upon self-report and EHR review. Fourteen women not eligible for genetic testing by the SPS had undergone genetic testing.

Discussion

We found that in our multiethnic, predominantly Hispanic population presenting for screening mammography, genetic testing for HBOC was significantly underutilized. While 12% of the women who completed the SPS family history screener were eligible for HBOC genetic counseling/testing, less than 5% of those eligible reported previous testing for *BRCA1/2* pathogenic variants. This finding of underutilization of HBOC genetic testing among minorities is in agreement with previous studies [11–13].

Such underutilization of HBOC genetic testing among minorities further underscores the need to develop programs to effectively engage high-risk women from underrepresented populations in genetic testing services. Efforts to increase education about and uptake of HBOC genetic counseling/testing have increasingly focused on the use of computer-based decision aids (DAs) for both patients and providers, including online family pedigree tools such as *iPrevent, Pedigree Assessment Tool (PAT), OPERA*, and *Cancer in the Family* [24–27]. A recent systematic review of decision aids for cancer care decisions, including genetic testing, found that the use of decision aids resulted in improved patient knowledge and accuracy of risk perception, decreased decisional conflict, reduced clinician-directed decision making, and fewer patients being indecisive [28]. Our research group has developed a web-based decision aid for patients and an EHR-embedded breast cancer risk navigation tool for primary care providers. We are currently evaluating their effectiveness in increasing appropriate uptake of *BRCA1/2* genetic counseling in a randomized controlled trial [29]. Our goals are to better integrate HBOC risk assessment into primary care and expand access to *BRCA1/2* testing to a broader population of high-risk women.

Another challenge to expanding access to genetic testing and counseling for hereditary breast and ovarian cancer is that current guidelines for eligibility have the potential to miss women with pathogenic variants, including in *BRCA1/2*.

Recently, an analysis of nearly 1000 women with a diagnosis of breast cancer who had not previously undergone single- or multigene testing found that approximately half of the women did not meet National Comprehensive Cancer Network (NCCN) guidelines for genetic testing; however, when these women subsequently underwent multigene panel testing, the percentage who were found to have pathogenic or likely pathogenic variants was similar between the groups of women meeting and not meeting NCCN guidelines (9.4% vs. 7.9%, respectively, with $p = 0.4241$) [30]. These findings highlight the limitations of current family history guidelines in identifying women who would benefit from genetic counseling and testing services for HBOC, even among patients already diagnosed with breast cancer. There has been discussion not only about modifying current guidelines to refer all women diagnosed with breast cancer for genetic testing regardless of family history, but also about implementing universal screening in the general population. A decision-analytic model evaluating the cost-effectiveness of family history-based *BRCA1/2* testing compared to population-based multigene panel testing for *BRCA1/2* and other moderate- risk pathogenic variants associated with HBOC in the U.S. and U.K. found that population-based testing was more cost-effective and was projected to prevent 1.86% of breast cancers in the U.K. and 1.91% in the U.S. [31]. However, the penetrance of breast and ovarian cancer in carriers of non-*BRCA1/2* pathogenic variants is less well-defined, and variants of unknown significance (VUS) can be discovered as part of a multi-gene analysis, leading to potential clinical confusion and unnecessary testing, procedures, anxiety, and costs. As such, the challenge going forward in adopting broader screening guidelines for HBOC is to balance the benefits of identifying women with pathogenic variants who might benefit from additional screening and cancer prevention with the potential harms of over-testing.

The strengths of our study are the multiethnic, predominantly Hispanic population, which is underrepresented in research on HBOC genetic testing. Potential limitations include the recruitment of participants from a single institution at an urban academic medical center and from a population already actively engaged in screening mammography and potentially more likely to have access to the medical system.

In summary, our study identified significant underutilization of genetic counseling/testing for hereditary breast and ovarian cancer in a multiethnic, predominantly Hispanic and less-educated population. Further efforts should be made to develop programs to effectively engage high-risk women from underrepresented populations in genetic testing services, as well as to explore potential limitations to current guidelines for HBOC screening that might further contribute to poor uptake of these services.

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Declarations of interest

None.

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