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# CME REVIEW ARTICLE 26

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# Disparities in Genetic Management of Breast and Ovarian Cancer Patients

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**Importance:** Hereditary breast and ovarian cancer syndrome (HBOC) is most often caused by pathogenic variants in the *BRCA1* or *BRCA2* genes. Guidelines exist for genetic testing in patients at high risk, yet significant disparities in genetic testing and management remain. These disparities result in missed opportunities for cancer prevention and treatment.

**Objective:** This review details the multiple layers of disparities in genomic knowledge, testing referral, completion, and posttesting risk reduction for at-risk populations.

**Evidence Acquisition:** A comprehensive search of the PubMed database was conducted in September 2023 for studies addressing disparities at all points of HBOC risk assessment and risk reduction.

**Results:** Disparities in genomic knowledge, referral and testing, and in cancer risk reduction exist by race, ethnicity, insurance status, socioeconomic status, age, and care setting in the United States. Many mitigation strategies have been explored with some success.

**Conclusion:** Each component contributes to a "leaky pipe" in *BRCA* testing and management whereby patients eligible for intervention trickle out of the pipe due to inequities at each step. Implementation of proven strategies aimed at disparity reduction in this setting is essential, as well as additional strategy development.

**Relevance:** This review provides clinicians with a comprehensive understanding of disparities in the identification and management of individuals at risk for or diagnosed with HBOC and strategies to reduce disparities in their own practice.

**Target Audience:** Obstetricians and gynecologists, family physicians.

**Learning Objectives:** After participating in this activity, the learners should be better able to discuss disparities in the testing for and risk-reducing management of patients with pathogenic variants of *BRCA1/2*; describe populations in which these disparities are greatest; and explain proven strategies for practice change to mitigate these disparities.

Hereditary breast and ovarian cancer syndrome (HBOC), most commonly caused by pathogenic variants in the *BRCA1* and *BRCA2* genes, is a well-known genetic cancer syndrome that accounts for 10% of all breast cancer cases and up to 20%–25% of ovarian, fallopian tube, and primary peritoneal cancer cases.[1] Breast cancer is the leading cause of cancer in women in the United States, with more than 239,000 new cases diagnosed and more than 40,000 deaths in 2020.[2] Ovarian cancer is the second most prevalent gynecologic cancer and accounts for the most deaths due to gynecologic cancer at a rate of 9.2/100,000 women.[2]

Current National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines) and the American Society of Clinical Oncology recommend germline genetic testing (GGT) for any woman diagnosed with breast cancer

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at 50 years or younger and in individuals of any age when treatment decisions may be impacted, such as when treatment with a poly(ADP-ribose) polymerase (PARP) inhibitor may be considered. The Society for Gynecologic Oncology (SGO), American Society of Clinical Oncology, and NCCN Guidelines recommend genetic testing for any individual with a personal or family history (first-or second-degree relative) of epithelial ovarian cancer (EOC), including fallopian tube and primary peritoneal cancer, at any age, and for patients with high probability of a pathogenic variant based on a validated model.[3–5] Family history of other BRCA-related cancers including prostate and pancreatic cancers, among others, should also prompt testing recommendations (Table 1).

Even with detailed guidelines, implementation can be challenging, and referral rates remain suboptimal.[6–10] A multitude of studies have found significant disparities by race, ethnicity, primary language, insurance status, age, and treatment setting for referral and completion of germline genetic and somatic tumor testing. We review the existing literature on disparities in germline and somatic genetic testing for *BRCA1/2* starting from disparate knowledge about the genetic makeup of diverse populations, to germline and somatic testing referral, risk reduction, and cancer management. We propose a "leaky pipe" framework to describe the cumulative detrimental effect of disparities at each of these critical junctures in the genetic evaluation process (Fig. 1). Although there are other cancers associated with germline *BRCA* mutations, such as prostate and pancreatic cancers, which are similarly affected by significant disparities,[11] we focus our discussion on breast and ovarian (including fallopian tube and primary peritoneal) cancers.

## CURRENT KNOWLEDGE OF GENETICS

The prevalence of *BRCA1/2* pathogenic variants varies among different racial and ethnic populations. Women of Ashkenazi Jewish descent harbor higher rates of *BRCA1/2* mutations due to founder effects.[12,13] However, our current knowledge of existing pathogenic or likely pathogenic variants of *BRCA1/2* is based on work completed in predominantly non-Hispanic White (NHW) populations.[14,15] Underrepresentation of minority populations has led to misestimation of race and ethnicity-based risk,[13,16] which then has implications for the development of guidelines. This adds to existing bias in referral patterns due to lower perceived risk by referring providers. It may also impact how patients perceive their own risk and decrease the likelihood of seeking out or completing genetic testing when referred.

Insufficient data on minority racial and ethnic groups also impact the interpretability of genetic testing. Several studies have shown higher rates of variants of unknown significance in Black patients, with some reporting rates as high as 44.5% in Black patients compared with 23.7% in NHW patients.[17–22] Multiple studies have also identified higher rates of *BRCA1/2* pathogenic variants or new founder mutations in underrepresented racial/ethnic populations.[13,16,20,23,24] Ciuro et al examined 761 patients tested for *BRCA* pathogenic variants, 198 of whom were African American, 466 non-Ashkenazi Jewish White, 54 Ashkenazi Jewish White, and 43 patients categorized as "other," and found that African American patients had a *BRCA1/2* pathogenic mutation rate of 8.1%, near that of Ashkenazi Jewish patients (9.3%), and much higher than the non-Ashkenazi Jewish White population (3.6%).[13] The landscape of pathogenic variants as we know it is predicated on biased and incomplete data. These data inform guidelines and clinical practice inherently biasing the process of genetic testing and management.

## GERMLINE GENETIC TESTING IN AT-RISK, UNAFFECTED INDIVIDUALS

Accurately identifying at-risk individuals unaffected by a *BRCA*-related cancer for GGT based on family history or risk factors alone poses many challenges. Conducting detailed and accurate family histories can be time consuming, and histories can be limited by both patient and provider-driven factors. Guidelines for genetic testing evolve over time, sometimes rapidly, posing challenges to providers across specialties to maintain up-to-date knowledge. The commonly used cascade-testing (testing of family members for a specific variant based on a known-affected individual's positive test result) strategy relies heavily on a patient's willingness to communicate their own test results and risks to family members. Communication rates and quality vary widely despite the use of "family letters" from providers intended to communicate this critical information.[25,26]

There are several studies addressing disparities experienced by at-risk individuals without a personal history of a *BRCA*-associated cancer. Sutton et al studied patients referred for cancer-related genetic counseling (GC) and examined predictors of completing GC services. They found that married individuals and those with insurance had twice the odds of completing GC compared with single individuals and those who were uninsured.[27] However, because of the nature of the

TABLE 1
Genetic Testing Guidelines for Hereditary Breast and Ovarian Cancer (*BRCA1/2*)

| | NCCN* | ASCO† |
|---|---|---|
| General Testing Guidelines (as related to BRCA1/2 testing) | Individuals with any blood relative with a known P/LP variant in a cancer susceptibility gene<br>Individuals meeting the criteria below but who tested negative with previous limited testing (eg, single gene and/or absent deletion duplication analysis) and are interested in pursuing multi-gene testing.<br>- A P/LP variant identified on tumor genomic testing that has clinical implications if also identified in the germline<br>- To aid in systemic therapy and surgical decision-making<br>- For personal or family history of breast, ovarian, pancreatic, prostate, or colorectal cancer.<br>- May be considered for: individuals of Ashkenazi Jewish ancestry without additional risk factors and persons with a personal history of serous endometrial cancer | Individuals newly diagnosed with stage I–III or de novo stage IV/metastatic breast cancer if *any*:<br>- ≤65 y old<br>- Candidates for PARP inhibitor therapy<br>- Triple-negative breast cancer<br>- Personal or family history suggestive<br>- Male sex assigned at birth<br>- Ashkenazi Jewish ancestry or member of a population with an increased prevalence of founder mutations<br>Individuals diagnosed with recurrent breast cancer (for PARP inhibitor candidacy)<br>Individuals diagnosed with a second primary breast cancer (contralateral or ipsilateral breast) |
| Breast Cancer Testing Guidelines<br>Patients with a **personal history of breast cancer** | Personal history of breast cancer with:<br>Age ≤50 y<br>Any age with:<br>- Treatment indications (ie, decisions regarding PARP inhibitors)<br>Pathology/histology:<br>- Triple-negative breast cancer<br>- Multiple primary breast cancers (synchronous or metachronous)<br>- Lobular breast cancer with personal or family history of diffuse gastric cancer<br>Male breast cancer<br>Ashkenazi Jewish ancestry | — |
| Breast Cancer Testing Guidelines<br>By **family history alone** | Family history:<br>≥1 1st-, 2nd, or 3rd-degree relative on same side of family with *any*:<br>- Breast cancer at age ≤50 y<br>- Male breast cancer<br>- Ovarian cancer<br>- Pancreatic cancer<br>- Prostate cancer with metastatic, or high- or very-high-risk group<br>≥3 diagnoses of breast and/or prostate cancer (any grade) on same side of the family including the patient | — |
| Breast Cancer Testing Guidelines<br>**Lower-risk groups to consider** | Testing **may** be considered:<br>- Personal history of breast cancer <60 y old<br>- Personal history of breast cancer dx at any age with ≥1 1st-, 2nd-, or 3rd-degree blood relative with intermediate-risk prostate cancer with intraductal/cribriform histology<br>Individuals unaffected but with a >5% probability of BRCA1/2 P/LP variant based on probability models‡ | — |
| Ovarian Cancer Testing Guidelines<br>**Patients with a personal history of ovarian cancer** | Personal history of EOC at any age | Personal history of EOC at any age |

*Continued next page*

TABLE 1. *(Continued)*

| Ovarian Cancer Testing Guidelines | NCCN* | ASCO† |
|---|---|---|
| **Patients without a personal history of ovarian cancer** | 1st- or 2nd-degree blood relative with EOC at any age<br>Individuals unaffected but with a 2.5%–5% probability of BRCA1/2 P/LP variant based on probability models‡ | 1st- or 2nd-degree blood relative with ovarian cancer with a known germline P/LP variant |

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†Adapted from ASCO "Germline Testing in Patients With Breast Cancer: ASCO-Society of Surgical Oncology Guideline," January 4, 2024, and "Germline and Somatic Tumor Testing in Epithelial Ovarian Cancer." January 27, 2020.

‡ Example probability models include Tyrer-Cuzick, BRCAPro, or CanRisk.

EOC, epithelial ovarian cancer including fallopian tube and primary peritoneal cancers; P/LP, pathogenic/likely pathogenic.

study, they were unable to determine whether patients in need of referral were actually referred. In another study of all patients referred for GGT for *BRCA*, education level and personal history of cancer were associated with completing GGT, but no associations were found between age, race, language, family history, parity, marital status, religion, socioeconomic status, or insurance status and completion of testing. Still, approximately only half of at-risk patients completed testing, indicating that there is significant room for improvement in testing overall.[28] Poor identification of at-risk minority individuals is a missed opportunity for cancer prevention for the patient as well as their family.

## GERMLINE GENETIC TESTING IN INDIVIDUALS WITH *BRCA*-RELATED BREAST AND OVARIAN CANCER

### Breast Cancer

Numerous studies have shown significant disparities in receipt of GC and completion of germline *BRCA* testing among patients diagnosed with breast cancer.[6,19,20,29–35] Despite recommendations for genetic evaluation, there remains a large gap in actual implementation and receipt of genetic testing. In one study of 440 participants with invasive breast cancer diagnosed at 50 years or younger between 2009 and 2012, only 51% of patients were referred for or received GGT.[29] Another study of patients with breast cancer who qualified for genetic testing noted an increase in overall referral rates from 37% to 68%, but there remained a significant proportion of patients who were not being referred or tested.[6]

Disparities in GGT by race/ethnicity, insurance status, income, geography, practice setting (community vs academic), education, and language have been identified in patients with invasive breast cancer. Pace et al, using state-level registry data in Massachusetts, studied 2424 patients 45 years or younger with private insurance or Medicaid to determine factors predicting receipt of *BRCA1/2* testing within 6 months of their cancer diagnosis. Fifty-five percent of patients received testing within 6 months of diagnosis, but non-Hispanic Black women had less than half the odds of receiving testing compared with NHW women. Similar findings were noted for patients with Medicaid compared with private insurance and for patients living in lower-income regions.[31]

Differences in referral and receipt of GGT in patients with breast cancer by race have been particularly well documented.[6,20,30,31,35] For example, Cragun et al concluded that discussion of GC and completion of GGT in patients with breast cancer 50 years or younger were 16

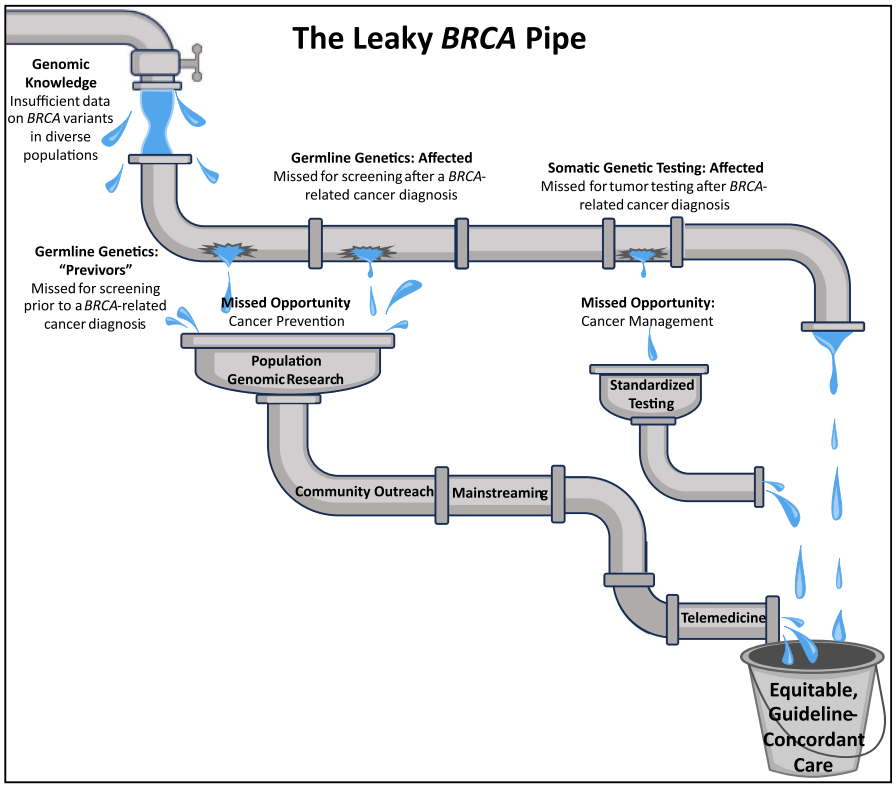


FIG. 1. The leaky *BRCA* pipe. Insufficient knowledge of the genomic landscape of *BRCA* variants across diverse populations impacts guideline development and leaves many at risk. Failure to properly identify and refer at-risk patients, or "previvors," further increases the number of patients missed who could benefit from risk-reduction measures. After diagnosis of a *BRCA*-related cancer, failure to refer patients for GGT limits both the ability to provide secondary prevention (ie, offering RRSO to a patient diagnosed with germline *BRCA*-positive breast cancer for ovarian cancer prevention) and impacts direct cancer management options, such as PARP inhibitor therapy. Missed somatic genetic testing of tumors also has downstream effects on cancer management option. Each step of the way, patients are lost in the process of providing equitable, guideline-concordant care that could improve morbidity and mortality by facilitating highly effective prevention and management strategies. Diversity in population and genomic research, community outreach and education, standardization of testing procedures, mainstreaming of genetic testing, and telemedicine offer opportunities to improve patient capture and increase utilization of guideline-concordant care.

times less likely to occur for Black patients than their NHW counterparts. Only 36.1% of Black patients completed GGT compared with approximately 65% of NHW patients.[30] Various explanations for these disparities include lower awareness regarding genetic testing availability and benefit among minority groups, lower support or perceived support for obtaining GC and testing, resource limitations (ie, access to genetic counselors, insurance status, etc), and perceived negative attitudes toward genetic testing and concerns about discrimination.[20] However, studies have shown that once issues of disparate awareness are addressed, many patients show similar eagerness to pursue genetic testing, suggesting that some barriers that we perceive as cultural may in fact be driven by inequitable distribution of information.[20] Provider referral or discussion of genetic testing presents an opportunity for patient education; it also remains one of the strongest factors associated with completion of GC and GGT.[30]

## Ovarian Cancer

The SGO has also recognized disparities in germline and somatic genetic testing, as well as follow-up risk-reduction utilization in ovarian cancer patients as an important issue facing patients diagnosed with ovarian cancer and the providers who care for them.[5] GGT for *BRCA1/2* pathogenic variants has been recommended for all women diagnosed with EOC, regardless of family history or age at the time of diagnosis. This is driven both by the frequency at which germline genetic mutations are detected and because of possible treatment opportunities with PARP inhibitor. The universal nature of these guidelines has improved overall GGT rates for patients diagnosed with EOC; however, referral rates for ovarian cancer GGT remain suboptimal ranging from 53% to 72%.[7–10]

Similar to patients with breast cancer, racial, socioeconomic, geographic, practice-setting, and insurance-associated disparities are seen in referrals and completion

of GGT for EOC,.[7–10,23,36–38] In 2021, Lin et al completed a comprehensive systematic review and meta-analysis of 35 studies investigating disparities in GGT in ovarian cancer and found lower rates of referrals and testing completion in Black patients (24%) compared with their NHW counterparts (40%). Of those who were referred, even fewer completed testing, with only 26% of Black patients completing GGT compared with 43% of NHWs. They also found significant differences by insurance status, with 39% of privately insured patients, compared with 27% publicly insured, and 24% uninsured patients referred for GGT and respective completion rates of 47%, 26%, and 23%.[37] Another group reported even more strikingly disparate GGT referral rates by race, with 61% of Caucasian patients referred compared with 40%, 38%, and 33% of Asian, Latina, and Black women, respectively. Primary language and insurance status were strongly associated with disparate referral and testing rates.[38]

## SOMATIC TUMOR TESTING IN OVARIAN CANCER

Somatic genetic testing, genetic sequencing of the tumor itself, is another route for genetic testing in EOC and plays a key role in the management of patients with advanced or recurrent EOC. At minimum, this may involve selected testing of tumors for homologous recombination deficiency and BRCA status. More extensive next-generation sequencing can also be completed to evaluate large panels of potential gene variants within a tumor and can inform therapy decision or eligibility for clinical trial participation (often, although not exclusively, in the recurrent setting). Unlike GGT, clear guidelines for who should undergo somatic genetic testing and when in their disease course it should occur are lacking. Undoubtedly, this leads to significant heterogeneity across physician practices and patient populations.

Huepenbecker et al evaluated more than 2500 patients with EOC between 2011 and 2018, 72% of whom were NHW, 67.5% with stage III or IV disease, and 90.5% seen in community practice setting. Seventy-two percent of all patients underwent any type of *BRCA* testing, with 62.5% having germline testing only, 10.6% receiving somatic testing only, and 19.9% completing both germline and somatic testing. Somatic testing was far more common in the recurrent disease setting, with 51.7% of those patients completing somatic testing. They did not find disparities by race/ethnicity but did find that patients treated in an academic setting and younger patients were more likely to complete any type of testing.[8] Gamble et al investigated multiple forms of "precision medicine testing," in ovarian cancer patients, including limited *BRCA* testing, full sequencing/next-generation sequencing for somatic and germline, and ancillary pathology such as immunohistochemistry studies. They found increasing rates of all precision medicine testing over time but noted a significant testing rate gap for publicly insured patients from 7% to 21% between 2011 and 2017. The ability to assess racial disparities across the entire study population was limited by database content, but within the group of patients insured by Medicaid, rates of molecular testing (excluding immunohistochemistry) in Black patients were significantly lower compared with NHW patients.[10] In another study comparing germline and somatic testing rates among patients with EOC based on practice setting, care at safety net hospital and having public insurance were associated with lower rates of both germline and somatic testing completion.[9] More research is needed to further understand disparities in somatic testing for patients with EOC as this may be a significant source of inequity in treatment recommendations and clinical trial enrollment, particularly for racial/ethnic minorities and publicly insured patients.

## POSTTEST MANAGEMENT

### Breast and Ovarian Cancer Risk Reduction

Referral for and completion of GGT is only one piece of the genetic puzzle. Testing gives patients and clinicians valuable and potentially life-altering information, but that information requires appropriate action. Management decisions that arise after a positive test include both risk reduction strategies and, for those with an active *BRCA1/2*-related cancer diagnosis, treatment decisions.

Risk reduction strategies are a critical component of posttest management for those who are diagnosed with a pathogenic *BRCA1/2* variant. Breast cancer risk reduction recommendations include intensive active surveillance with yearly mammography and breast magnetic resonance imaging (MRI) and enrollment in a high-risk breast cancer screening clinics where available. Prophylactic risk-reducing mastectomy (RRM) can also be offered. If diagnosed with a unilateral breast cancer, patients may choose to undergo a contralateral prophylactic mastectomy or may be a candidate for additional prophylactic pharmacotherapy.[3,39–42] Ovarian cancer has no proven reliable screening method, but risk-reducing bilateral salpingo-oophorectomy (RRSO) has been shown to have overall mortality benefit and is recommended between 35 and 40 years old for patients with pathogenic variants of *BRCA*1 and between 40 and 45 years old for those with *BRCA*2 once childbearing is complete.[3,41,43] Combined oral contraceptive pills have also been shown to reduce ovarian cancer risk and can be used as a conservative risk-reduction measure in

those whose families are not yet complete or who decline surgery, although data on possible increased breast cancer risk in the *BRCA1/2* population are conflicting.[41,44,45] Investigation of staged procedures with salpingectomy followed by oophorectomy at a later stage is ongoing but is not recommended outside of the context of a clinical trial (Table 2).

There is a paucity of data regarding posttest management in *BRCA1/2*-positive patients, but available evidence shows significant differences in uptake of several risk management strategies. RRSO rates in NHW populations with germline *BRCA1/2* pathogenic variants have been estimated to be around 70%–80%.[30] Cragun et al found that rates of RRM and RRSO were significantly lower in Black patients with *BRCA1/2* pathogenic variants than in NHW and Hispanic individuals with RRM rates of 95.7%, 68.8%, and 81.8%, respectively, and RRSO rates of 76.6%, 28.1%, and 90.9%, respectively. Disparities were also seen in overall guideline-concordant breast cancer risk reduction (either RRM or active screening) with 100% of NHW, 85.7% of Black, and 100% of Hispanic patients receiving some form of guideline-concordant risk reduction.[30] Another study found that whereas risk-reducing surgery uptake was higher in NHW patients, risk-reducing medication use was more common in participants identifying as Black, Indigenous, or People of Color.[25] RRSO uptake has also been studied in Latina patients, with an uptake rate of 68% in a study of 100 women with *BRCA1/2* pathogenic variants. The vast majority of those who had not yet undergone RRSO were considering the surgery (86%), whereas 13% were unsure or had decided against risk-reducing surgery.[46]

The etiology of these disparities has not been fully explored. Possible contributing factors may include provider-based bias in counseling; differential interpretations of risk and benefit, which may be informed by personal, family, and community experiences with *BRCA* and cancer-related care; cultural and societal differences in acceptability of interventions; and differential access due to geography, socioeconomic status, insurance status, and/or educational attainment. Further research is needed to elucidate the drivers of disparities in the application and uptake of risk-reducing care. This research should be used to guide development of culturally informed active mitigation strategies to ensure maximal benefit can be gleaned from genetic testing results for all patients.

TABLE 2
Risk-Reducing Management Options for Breast and Ovarian Cancer in BRCA1/2-Positive Patients

| Site | Variant | Management |
|---|---|---|
| Breast (female)* | *BRCA1* | Breast awareness starting age 18 y |
| | *BRCA2* | Clinical breast exam, every 6–12 mo, starting at age 25 y |
| | | Breast screening: |
| | | - Age 25–29 y: annual breast MRI screening |
| | | - Age 30–75 y: annual mammogram and breast MRI screening |
| | | - Age >75 y: individualize management |
| | | - Discuss RRM† |
| | | Consider risk reduction agents: |
| | | - Premenopausal: tamoxifen or clinical trial |
| | | - Postmenopausal: tamoxifen, raloxifene, aromatase inhibitors, or clinical trial |
| Ovarian cancer | *BRCA1* | RRBSO‡ at age 35–40 y, once childbearing is complete |
| Ovarian cancer | *BRCA2* | RRBSO‡ at age 40–45 y, once childbearing is complete |

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*Although not endorsed in the current NCCN Guidelines®, contralateral prophylactic mastectomy may be considered in patients with a diagnosed unilateral breast cancer and with a P/LP *BRCA1/2* variant, per the American Society of Breast Surgeons.[43]

†RRM may be with skin-sparing or nipple-areolar complex–sparing removal of bilateral breasts.[41]

‡Principles of RRBSO include thorough visual inspection of the abdomen and pelvis, obtaining pelvic washings at the start of the procedure, division of the infundibulopelvic ligament a minimum of 2 cm distal to visible ovarian tissue to ensure complete ovarian tissue removal, division of the fallopian tube and utero-ovarian ligament as close to the uterus as possible, contained removal of all samples, and serial section of the ovaries and fallopian tubes at the time of pathologic examination.[41]

RRBSO, risk-reducing bilateral salpingo-oophorectomy.

### Cancer Treatment: PARP Inhibitor Use for Ovarian and Breast Cancer

Even less is known about the downstream effects of disparities in both germline and somatic genetic testing on treatment-related decisions in patients with breast and ovarian cancer. PARP inhibitors were approved for use first in ovarian cancer in 2014 and have since radically changed the landscape of EOC management. They have significantly improved progression-free and overall survival in patients with germline *BRCA* pathogenic variants in particular.[47–51] PARP inhibitors have since been approved for use in *BRCA*-related breast cancer and other *BRCA*-related cancers.[52,53]

Studies have previously shown stark disparities in treatment patterns and outcomes by race/ethnicity across gynecologic cancers including ovarian cancer, resulting in lower 5-year overall survival in Black patients compared with NHW patients.[54] Similar findings have been documented in breast cancer, with resultant higher breast cancer–related mortality in Black women.[55] To date, no studies have examined patterns of PARP inhibitor use. Given that PARP inhibitor use is directly related to completion of genetic testing (germline and/or somatic), it may be particularly susceptible to downstream effects of disparities in genetic testing and should be further investigated. Literature examining the makeup of clinical trial populations has shown significant underrepresentation of Black and Hispanic individuals in clinical trials investigating PARP inhibitor use in ovarian cancer.[56] Although clinical trial enrollment may not directly reflect broader practice, lower identification of eligible patients due to lack of genetic testing may have influenced enrollment, among a multitude of other contributing factors, and may in turn influence clinical practice.

## DISCUSSION

### BRCA Evaluation and Management: A Leaky Pipe

Disparities in the evaluation and management of *BRCA1/2*-related breast and ovarian cancer create a leaky pipe that worsens disparities in outcomes at each step of the way. Our skewed pool of knowledge regarding racial and ethnic prevalence of mutations affects guidelines on testing, potentially missing entire high-risk populations based on incomplete data. Failure to properly identify previvors, survivors with predisposition for cancer, for genetic testing based on family history or the complex challenges of completing cascade-testing leads to larger proportions of patients missing opportunities for cancer risk reduction. Those who are diagnosed with a *BRCA1/2*-related cancer but do not receive appropriate germline and/or somatic genetic testing miss both secondary risk reduction strategies and potentially life-prolonging management options of their active disease. Their families are also missing the opportunity for risk reduction. We know that Black women have worse outcomes across gynecologic and breast cancer.[54,55] Disparities in testing in patients with a diagnosed cancer are certainly not limited to women with breast and ovarian cancer and have been seen in lung, pancreatic, and prostate cancer populations,[11,57] highlighting the importance of improving equitable access to genetic testing and management in all patients with cancer.

### Proposed Interventions

Disparities exist along the entire spectrum of HBOC evaluation and management. This results in the perpetuation of disparities in outcomes for both primary and secondary risk reduction as well as active disease management. Identifying these disparities is only the first step. There have been a number of proposed mitigation strategies, particularly focused on disparities in GGT referral and completion.

Mainstreaming, or physician-ordered testing (rather than by a genetic counselor) followed by posttesting referral for GC, and other similar variations of provider-based testing have been investigated with high-quality evidence indicating an increase in both referral and testing completion rates.[7,16,37] Komenaka et al reported their experience with a surgeon-based referral model wherein a breast surgeon underwent the City of Hope Intensive Course in Cancer Risk Counseling to overcome a lack of GC services at a large county hospital. They showed significant improvement in access to genetic services overall but were limited by provider time and clinical space constraints, as well as challenges with health literacy and appointment reliability.[16] Telemedicine or "telegenetics" services have also been proposed as a mechanism to reduce disparities in access, particularly those due to geographic barriers and genetics professional shortages.[36–38] Integrating genetics providers within cancer care clinics, both at larger centers and at satellite clinics associated with large cancer centers, and increasing involvement of counselors in multidisciplinary care teams are suggested to increase identification of at-risk patients.[37,38] Still, these interventions are aimed at patients with existing cancer diagnoses. There have been fewer interventions directed toward improving the identification and referral of previvors. The SGO has also endorsed these strategies as effective for reducing disparities for access to genetic testing in patients' ovarian cancer diagnoses.[5]

Additional strategies for streamlining care have been discussed such as standardized referral forms, electronic

medical record alerts, and defining reflex testing pathways; however, data on their efficacy are lacking.[7,37,38] Some have advocated for universal *BRCA* germline testing of all women 35 years and older to increase detection rates and reduce disparities.[58,59]

To address gaps in *BRCA*-specific knowledge and awareness in communities with lower testing rates and poorer outcomes, complementary strategies geared toward improving health literacy, *BRCA*-specific knowledge, and awareness are critical.[7,20,30,59] Some have suggested community-based public health educational campaigns and have declared the need for a sweeping public health agenda to address disparities in genetic testing and the downstream impacts on patient care.[7,60] Others have developed video series directed toward improving *BRCA*-specific knowledge to be used in conjunction with professional counseling.[61] These campaigns could target both improved understanding of personal risk and *BRCA* awareness and encourage communication about family histories and testing results within communities. Improved awareness and understanding of *BRCA* in underrepresented communities have been shown to increase interest in and acceptability of genetic testing.[20,59]

To better understand the frequency of *BRCA* mutations across racial and ethnic groups, population-based genetic testing studies should be initiated to assess family histories (ie, the proportion of patients who should be referred for genetic testing) and to determine the true prevalence of *BRCA* mutations in different racial and ethnic groups. This will allow identification of, and reclassification of, variants of unknown significance seen more commonly in populations currently underrepresented in *BRCA* germline testing studies.

Additional work is needed to fully evaluate the genomic landscape of more diverse patient populations to better clarify patient-specific risk, inform equitable and accurate guideline development and clinical practice, and to improve interpretability of genetic testing across populations. Further research is also needed to better evaluate disparities in posttesting management uptake both for risk reduction and for active cancer management. Comprehensive data are needed to inform our understanding of the barriers to these stages of care and to develop strategies to ensure equitable access to *BRCA*-related care.

## CONCLUSION

Significant disparities exist in the genetic evaluation of *BRCA*-related HBOC in every step of the process from the genomic data that informs interpretation of results and generation of guidelines, to genetic referral and testing patterns for germline and somatic genetic testing, to subsequent management. Multifaceted interventions are needed to address each of these "leaks" within the genetic evaluation and management pipeline for HBOC to ensure equitable care for all.

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