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Editorial

USPSTF Recommendations for *BRCA1* and *BRCA2* Testing in the Context of a Transformative National Cancer Control Plan

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In the August 20, 2019, issue of *JAMA*, the US Preventive Services Task Force (USPSTF)[1] offers updated recommendations for risk assessment, counseling, and genetic testing for the *BRCA1* and *BRCA2* genes. As in 2013, the USPSTF recommends risk assessment for women with family histories of breast, ovarian, tubal, or peritoneal cancers using risk stratification tools and offering those with positive results genetic counseling and possible testing (Grade B recommendation). The USPSTF continues to recommend against large-scale population risk assessment (Grade D recommendation). The 2019 recommendations explicitly add ethnicities and ancestries associated with pathogenic *BRCA1* or *BRCA2* gene variants (eg, Ashkenazi Jewish) as an indicator for risk assessment, dramatically expanding the number of testable patients in the primary care setting from the 2013 recommendations. Importantly, the USPSTF emphasizes that "Genetic counseling…should be done by trained health professionals, including trained primary care providers." With the increase in women eligible for genetic counseling and testing under these recommendations and the explicit directive for primary care practitioners (PCPs) to consider clinical genetics training per the 2019 USPSTF recommendations, the oncology community should welcome the opportunity to better integrate comprehensive cancer risk assessment and genetic testing for *BRCA1* and *BRCA2* into routine preventive medicine.

The 2019 updates bring the USPSTF recommendations in line with those of the National Comprehensive Cancer Network, American College of Medical Genetics and Genomics, and American College of Obstetricians and Gynecologists. Population-based risk assessment may increase insurance coverage and clinician-directed access to cancer genetic testing for up to 50% more women in the primary care setting than family history–based risk assessment alone.[2] As described in the 2019 consensus report by the National Academies of Sciences, Engineering, and Medicine, *Guiding Cancer Control: A Path to Transformation,* cancer control in the United States fundamentally depends on improving the availability of preventive interventions.[3]

We note, however, that researchers are actively reporting higher *BRCA1* and *BRCA2* mutation frequencies across diverse populations than previously realized. Germline *BRCA1* and *BRCA2* mutations have been identified in 12% to 18% of African American patients with breast cancer.[4,5] Hispanic high-risk patients living in the US Southwest with a personal or family history of breast or ovarian cancer were found to have *BRCA1* and *BRCA2* mutation rates as high as 25%, with 6% associated with a Mexican founder mutation.[6] Our team has also documented 11% germline *BRCA1* and *BRCA2* mutations in a cohort of Nigerian patients with breast cancer, and mutation rates as high as 25% are reported in patients with breast and ovarian cancer in India.[7,8] These rates are comparable to the *BRCA1* and *BRCA2* mutation rates initially characterized in patients of Ashkenazi ancestry with breast cancer. Large biobanking studies of unselected general populations are also finding higher frequencies of *BRCA1* and *BRCA2* mutations than expected. Geisinger Health System sequenced more than 50 000 patients and reported pathogenic *BRCA1* and *BRCA2* mutations in 0.5% of patients relative to the commonly quoted 0.0025% in the US general population.[9] With next-generation sequencing, cancer interception and prevention through genetics no longer need to be limited to the specific founder populations previously required to identify disease-associated genes.

Although preventive cancer genetics incorporated in the primary care setting instead of a specialty setting should improve accessibility and equitable distribution of resources, it is also easy to

envision the specification of ethnicity or ancestry leading PCPs to inadvertently exacerbate inequality. Racial/ethnic disparities in *BRCA1* and *BRCA2* testing are well documented, with African American and Hispanic women undergoing testing at reduced rates compared with white women. Reasons include less awareness of genetic testing, distrust of the medical system, and lower education levels, but also physician communication and referral patterns.[10] The cost of testing, now at $250 out of pocket if not covered by third-party payers, continues to remain an understandable point of concern for patients and the health care system, but can be consciously addressed to reduce disparities in testing.[11] The updated USPSTF recommendations do not mention specific ethnic groups or communities, but they are notably silent on the costs of testing or ensuring accessibility in limited-resource settings. These recommendations must continue to evolve and advocate for best practices in prevention for patients but avoid exacerbating already unequal access to counseling and testing.

BRCA1 and *BRCA2* have nearly 2 decades of evidence for counseling, testing, and intervention, as the USPSTF notes. Expanding access to genetic counseling and testing across the medical spectrum of care to primary care is not only appropriate, but also critical. Because there are fewer than 700 cancer-specific genetic counselors in the United States relative to the nation's more than 300 000 PCPs, opportunities to expand cancer genetics education in an interdisciplinary and interprofessional curriculum for health professionals need to be explored.[12,13] The benefits of early cancer detection and interception afforded with these genes cannot be realized without health care professionals at all levels participating to some extent in the counseling and testing process.

Germline testing for *BRCA1* and *BRCA2* remains woefully underused in the United States. As of 2015, only 20% to 30% of patients eligible for *BRCA1* and *BRCA2* testing based on personal breast or ovarian cancer history actually discussed testing with a clinician,[14] although this will likely increase as *BRCA1* and *BRCA2* transitions to a predictive biomarker in oncology care. Among unaffected women with a positive family history screen, less than 10% of patients reported discussing genetic testing with a health care professional.[15] Primary care practitioners face challenges such as infrequent experience, lack of updated knowledge, and lack of familiarity with advanced genetics services that can create discomfort with discussions about personalized medicine and genetic testing.

Even beyond preventive oncology and *BRCA1* and *BRCA2* testing, clinical genetics is advancing rapidly in ways relevant to primary care. Preventive cardiology previously focused on specific hereditary cardiac disorders but now involves complex genetic concepts such as clonal hematopoiesis for the traditional primary care domain of hyperlipidemia.[16] The *MIT Technology Review*[17] estimates that 26 million consumers have taken direct-to-consumer genetic tests, including the Health Predispositions testing from 23andMe. Basic genetic literacy for PCPs will only become more crucial as subspecialties further integrate precision medicine and direct-to-consumer tests become more popular.

Support for PCPs to build genetic literacy requires systems-level effort from the ground up. In 2015, Vassy et al[18] proposed an educational framework that can be used to assess genomic medicine competency in trainees. Even brief experiences shadowing in a clinical cancer genetics clinic during clinical training can reduce the barrier to a counseling discussion. We also advocate for leveraging technology to support both patients and health care professionals. Alternative service models, such as telemedicine counseling or online education, generally find positive patient outcomes, although long-term understanding and uptake of interventions still need to be studied.[19] Point-of-care educational support can be provided to patients at clinic visits before or during already-scheduled counseling or testing appointments, limiting barriers in teaching and allowing for assessment of understanding in real time.[20] Cancer genomics education programs designed for health care professionals (such as those by The Jackson Laboratory or City of Hope) can offer PCPs Continuing Medical Education credit with online modules of varying intensity. Standardized genetics education upfront for both PCPs and patients allows board-certified genetic counselors and other genetics specialists to then focus on complex cases and families who need more extensive workup. Forms of

the USPSTF guidelines have been in place for more than a decade, but PCPs need adequate tools to participate fully in preventive oncology.

As a way to expand access to genetic counseling and testing without excessive burden to already overwhelmed PCPs, it is appropriate for USPSTF recommendations to be conservative from a cancer genetics counseling perspective. Testing all patients with breast cancer to improve prevention in at-risk healthy family members is being debated because of emerging data that family history of breast and ovarian cancer may not be an optimal marker for cancer risk.[21] Moreover, pancreatic cancer, prostate cancer, and melanoma are considered relevant cancers for *BRCA1* and *BRCA2* family histories, and the USPSTF guidelines did not review data on men regarding genetic counseling and testing. Comprehensive cancer risk assessment and prevention programs use tools well beyond family history and *BRCA1* and *BRCA2* mutation status, including multigene panels and complex risk calculators that incorporate genetic test results and lifestyle factors. Polygenic risk scores, which incorporate many genetic changes with small contributions to risk in unaffected women, are also being explored clinically.[22] Although management is not discussed by USPSTF, preventive oncology's importance at every level becomes concrete when we consider promising prevention options such as low-dose tamoxifen for preinvasive breast lesions[23] or magnetic resonance imaging to improve risk assessment for *BRCA1* and *BRCA2* carriers.[24] The USPSTF recommendations are designed to promote primary prevention of cancers associated with *BRCA1* and *BRCA2*. Narrow guidelines make sense to encourage health care professionals in whom familiarity with genetics is not guaranteed, but so does awareness of what cancer prevention options are available to patients after the genetic counseling and testing process.

Genetic counseling and testing in the context of advanced cancer loses sight of the failure of prevention and early detection that occurred for each of these patients. The 2019 USPSTF recommendations on *BRCA1* and *BRCA2* take a necessary step toward mainstreaming genetics to accelerate the control of cancer through prevention. As more patients will be eligible for counseling and testing, we can only gain the full benefit of preventive oncology by expanding the number of practitioners capable of engaging with these patients. Building the infrastructure to do so now, without further exacerbation of disparities, on behalf of individuals harboring inherited pathogenic mutations in *BRCA1* and *BRCA2* genes will equip our health care system to take on the rapid evolution of medicine in the genomic era.

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