BRCA1/2 genetic testing recommendations still leave issues unresolved

August 20 2019

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The U.S. Preventive Services Task Force (USPSTF) has released a new Recommendation Statement for *BRCA1/2* evaluation, urging the medical community to widen the parameters used to assess *BRCA1* and *BRCA2*

mutation risks and increase the use of genetic counseling and testing for those with the highest risk. While the changes are beneficial, the recommendations still fail to address many persisting problems in the modern world of genetic testing, according to a new *JAMA* editorial co-authored by Susan Domchek, MD, executive director of the Basser Center for BRCA at the Abramson Cancer Center at the University of Pennsylvania.

"Genetic testing is an area of medicine that is progressing very quickly, which means providers need to be nimble in order to keep up," Domchek says. "The medical community needs to consider what genetic health data is truly helpful to a patient, strive to test those who may be genetically predisposed to an increased risk of cancer, and work to educate patients and providers on how to correctly and effectively use their test results to make better healthcare decisions."

Mutations in *BRCA1* and *BRCA2* have been linked to significantly increased risks of breast, ovarian, prostate, and pancreatic cancers, and there are many commercially available tests that can reliably show whether someone has a *BRCA1* and/or *BRCA2* mutation. Domchek, and co-author Mark Robson, MD, a medical oncologist and chief of Breast Medicine Service at Memorial Sloan Kettering Cancer Center, write that one important point not included in the new recommendations is the link between genetic testing and treatment plans. They note that *BRCA1/2* status can impact surgical decision making for patients newly diagnosed with early stage breast cancer and influence treatment plans for certain advanced cancers, such as metastatic breast cancer. The USPSTF does not include newly diagnosed breast or ovarian cancer patients or advanced cancer patients in its recommendations.

Authors express other concerns, which are not addressed in the new recommendations, specifically relating to large-panel genetic tests that are available. Previous genetic tests analyzed a few specific genes at a

time, but there are now tests that can sequence up to 80 genes at once. While that sounds like invaluable innovation, there are a plethora of genetic mutations with weak, questionable, or no links to cancer at all. Positive results for those types of mutations could create fear or distract from real genetic indicators like changes to *BRCA1/2* genes. Additionally, the direct-to-consumer multi-panel tests one can do at home—such as those offered by companies like 23andMe—further remove people from genetic specialists trained to educate and evaluate how results may be more or less meaningful given an individual's health, history, and family history.

"We should think of genetic testing like the internet," Domchek says. "It's a tool, full of information, but there's nuance in making sense of that information and determining how to act on it."

Although the authors would have liked to see more from the new USPSTF recommendations, they say the two main changes to those recommendations are certainly valuable.

"The statement adds those who have previously been diagnosed with breast or ovarian cancer, but are now cancer free, to the list of those who should undergo careful genetic risk-assessment, which is a positive addition as finding a *BRCA1/2* mutation in these patients could directly impact their medical care and have implications for their relatives. It also more explicitly includes ancestry as a risk factor," Domchek says.

The new recommendation urges more broad ancestry knowledge to be used when considering genetic testing, not just family history of cancer. Certain populations, specifically those with Ashkenazi Jewish heritage, have a higher prevalence of *BRCA1/2* mutations.

While these expansions are positive, Domchek notes that many individuals at the highest risk of having a *BRCA1* or *BRCA2* mutation do

not undergo genetic testing. In addition, racial and socioeconomic disparities in the uptake of genetic testing remain.

"It's the duty of all health care professionals to help our patients effectively employ genetic testing," Domchek says. "These updates are a positive step forward, but we need to continue advancing BRCA-related research and ensure that those at the highest risk have access to testing."

More information: *JAMA* DOI: 10.1001/jama.2019.10987

Provided by Perelman School of Medicine at the University of Pennsylvania