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BRCA Screening Study Uses Consumer Initiated Model to Enroll Thousands in Ashkenazi Jewish Community

Mar 12, 2018 | Turna Ray

Premium

NEW YORK (GenomeWeb) – Researchers launched a study last week in which they hope to enroll 4,000 men and women of Ashkenazi Jewish ancestry across four US cities and test out a consumer-initiated model that involves healthcare providers and genetics experts to screen for BRCA1 and BRCA2 gene mutations.

The BRCA Founder Outreach (BFOR) study has more than $1 million in philanthropic funding from the Sharon Levine Corzine Foundation and involves Memorial Sloan Kettering Cancer Center in New York, Dana-Farber Cancer Institute and Beth Israel Deaconess Medical Center in Boston, Cedars-Sinai Medical Center in Los Angeles, and the Basser Center for BRCA at the University of Pennsylvania. The project will employ certain strategies used by direct-to-consumer genetic testing companies, such as a digital enrollment and education platform and consumer initiated testing, but will also involve doctors and genetic counselors when study participants receive test results.

In the pilot phase of the project, individuals in New York, Los Angeles, Philadelphia, and Boston who have at least one grandparent of Jewish ancestry can use an online patient engagement platform to watch educational videos about the study and give consent for participation. They can then provide a blood sample at a local Quest Diagnostics Patient Service Center for testing, a service that the reference lab is providing for free to BFOR participants.

Quest will test for the three founder mutations — BRCA1 185delAG, BRCA1 5382insC, and BRCA2 6174delT — that show up in one in 40 individuals in the Ashkenazi Jewish population but are exceedingly rare in other ethnic groups. Quest's CLIA-certified lab will test every sample on two next-generation sequencing platforms in parallel to ensure accuracy.

Individuals with these mutations are at significantly higher risk of breast, ovarian, and prostate cancers compared to the general population and they've taken a toll on the Jewish community.

Rosalind Franklin, for example, the Jewish chemist whose x-ray diffraction studies were critical to James Watson and Francis Crick's insights about the structure of DNA, died at age 37 from ovarian cancer.

Historians have suggested that Franklin's early-onset ovarian cancer may have been due to one of the BRCA Ashkenazi founder mutations.

Kenneth Offit, chief of the clinical genetics service at MSK and a principal investigator of the BFOR study, led the team that discovered BRCA2 6174delT in 1996 and has seen descendants of Franklin with the same mutation. It's estimated that 40 percent of ovarian cancers may be prevented in the Ashkenazi Jewish community with increased screening for these founder mutations and preventive surgery. Yet, awareness and access to BRCA testing has lagged.

"If you had asked me 20 years ago where we would be in terms of uptake, I would have thought we'd be further along among individuals of Ashkenazi background," said Offit.

There are more than 5 million individuals of Ashkenazi Jewish descent in the US who are older than 25 years, and around 90 percent haven't been tested for these mutations. "The challenge before us is not one of greater commercialization of genomic testing, but rather the transformation of medical practice to use genomic testing," he said.

BFOR's launch last week aligned with consumer genomics firm 23andMe getting the US Food and Drug Administration's authorization to sell BRCA testing for the three Ashkenazi BRCA mutations directly to consumers, without a doctor's prescription. 23andMe aims to democratize access to genetic testing with its $199 online service that provides reports on ancestry, traits, carrier status, and health risks, including the BRCA test. The firm directs customers to genetic counseling resources, but the price of the test doesn't include counseling.

Offit presented BFOR as an alternative to the commercial DTC model, one where participants can advance research and get free testing with the necessary support from genetics experts and doctors.

After participants join the study online and are tested, they can decide whether they want to see and discuss the results with their own doctors or with genetics experts from MSK, Dana-Farber, Beth Israel, Cedars-Sinai, or Basser. The primary care providers or genetics experts can then offer post-test counseling, additional genetic testing, or recommend risk-reducing surgeries if appropriate.

When patients bring in reports from DTC consumer genetics companies to their doctors, however, the interaction doesn't always go smoothly. A survey of 2,000 customers of DTC genetic testing services, published in in 2016 in the *Annals of Internal Medicine,* found that of the 540 people who actually shared their reports with their doctors, 35 percent said they were very satisfied with the encounter and 18 percent said they weren't satisfied at all. The senior author, Brigham and Women Hospital's Robert Green, suggested in the paper that some patients may be dissatisfied because their belief that this testing is valuable clashes with their doctors' training with respect to how DTC genetic testing results should be integrated into care.

Because Offit and his colleagues are pursuing a strategy similar to the model used by consumer genetics testing firms, they're interested in seeing how many people choose to discuss their results with their own doctors, and how these physicians handle the interaction. "It's not at all clear what people will choose," Offit noted. "Will they have confidence in their doctors or will they pick the experts? And how many of these doctors will accept this responsibility and engage?"

In the week that BFOR has been enrolling patients, around 200 people have joined. So far, participants are evenly distributed in age, suggesting it's not just the young and computer savvy signing up. Approximately one third of the participants have indicated they want to discuss test results with their own doctors. If doctors have questions or need help interpreting results, BFOR experts will provide that support.

However, the 4,000-participant study is just the pilot phase. Offit and his collaborators have ambitions to apply what they learn from the pilot to a larger screening project for the Ashkenazi Jewish population in the US. In the next phase, investigators hope to perform a saliva-based genetic test, so participants can submit a sample from home, and assess mutations in other cancer risk genes unique to the Ashkenazi population. The researchers also envision conducting similar screening efforts in other ethnic communities that are impacted by different BRCA1/2 founder mutations.

Offit and his collaborators are working closely with the Jewish community in conducting BFOR and leaders from a number of Jewish organizations, such as the patient support group Sharsheret, are playing an advisory role. Rochelle Shoretz, a Jewish woman diagnosed with breast cancer in 2001 at the age of 28, founded Sharsheret as a resource for young women in her community who had cancer and were looking for support.

Shoretz passed away in 2015 from complications of breast cancer. "She knew we were going to do this study," said Offit, who is on Sharsheret's medical advisory board.

Through Sharsheret, Shoretz helped her community open up about cancer. The organization partners with synagogues around the country, groups on college campuses, researchers, drug makers, genetic testing companies, and medical centers to raise awareness of the prevalence of BRCA founder mutations and the increased risk for hereditary cancers in the Ashkenazi Jewish community. Sharsheret has a social media campaign, called "Have the Talk," aimed at encouraging college students to have family health history discussions.

Elana Silber, executive director of Sharsheret, didn’t specifically comment on 23andMe’s direct-to-consumer genetic testing model as an avenue for increased access within the Ashkenazi Jewish community, but emphasized the importance of education. "When testing is deemed appropriate, we feel access is so important that there shouldn’t be barriers for people to get tested," said Silber, who is on the community advisory board for the BFOR study. "But we strongly emphasize speaking with your healthcare professional, understanding what the testing means, and we promote genetic counseling." Sharsheret has established support groups around the country and employs a genetic counselor.

23andMe, meanwhile, celebrated FDA authorization of its BRCA test last week as a step in the right direction for increasing consumer access to genomic information, particularly those who don’t know they have Ashkenazi Jewish ancestry. In a blog post, 23andMe CEO Anne Wojcicki highlighted the stories of several women who, based on family history, would not have sought out genetic testing for cancer risk but found out they had one of the BRCA founder mutations through DTC testing.

FDA’s action also sparked a lot of debate as to whether the agency had appropriately balanced the risks and benefits of providing DTC access to 23andMe’s BRCA test, since the authorization came with a long list of caveats. "The use of the test carries significant risks if individuals use the test results without consulting a physician or genetic counselor," the FDA said in statement, adding that test results shouldn’t be used to guide treatment decisions without confirmatory testing.

The agency also cautioned that a negative test result with 23andMe's test doesn't mean that individuals don't have other BRCA1/2 mutations or deleterious alterations in other cancer-linked genes, which is also the case for participants in the BFOR study. In fact, Shoretz did not have any of the thee BRCA founder mutations. However, within BFOR, Offit emphasized that participants would discuss their results with a doctor or genetics expert and the possibility for further testing.

As part of the FDA authorization, 23andMe has to communicate the limitations of its test in many areas of its online service, and the firm has performed studies showing that customers understood those caveats.