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Canadian BRCA Screening Project Aims to Demonstrate Public Health Benefits of Universal Testing Program

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Premium

NEW YORK (GenomeWeb) – A Canadian project trying to expand access to BRCA1 and BRCA2 genetic screening has tested more than 500 people and identified cancer risk mutations in individuals who wouldn't have qualified for such assessments according to existing guidelines.

Hereditary cancer genetics experts Mohammad Akbari and Steven Narod at the Women's College Hospital in Toronto, launched The Screen Project earlier this year in collaboration with Boston-based Veritas Genetics. Those leading the project hope to ultimately demonstrate that a program providing BRCA screening to women starting age 30 can be implemented in a cost-effective manner and benefit public health by preventing cancer.

Since March, 515 individuals have gotten tested, and researchers have reported results to more than 330 participants. Eight patients have mutations in BRCA1/2, conferring significantly heightened risk compared to the general population for breast, ovarian, and prostate cancer.

However, only half of these patients meet testing criteria set forth by the Ontario provincial government dictating who can receive covered testing. The other four "wouldn't have been caught at all," according to existing guidelines, said Veritas Chief Commercial Officer Doug Flood.

Like US insurers, Canadian provinces generally pay for BRCA testing when individuals meet strict criteria around their personal and family history of cancer. Studies have now shown that these guidelines are insufficient in that they fail to identify 50 percent of individuals who have deleterious BRCA1/2 genetic mutations but lack family history for cancer.

Although one in 200 people in Canada have deleterious mutations in BRCA genes, because of screening criteria dictating who can receive covered testing, many of these individuals may not find out they have a risk mutation or find out only after they get cancer, too late to take preventive action through surgery.

Individuals interested in The Screen Project can enroll online, order testing from Vertias for US$165, and submit a saliva sample for analysis using a collection kit mailed to their homes. Veritas' business model is to price its genetic testing products so that consumers can pay out of pocket for them. "We don't seek reimbursement," said Flood. "We try to keep a very low price so more people can access it. So, the idea of a population study was very attractive to us."

Once the genetic analysis is complete, WCH's Familial Breast Cancer Research Unit contacts those with cancer risk mutations to disclose their results and refers them for further genetic counseling through

WCH's in-house counselors or through local counselors.

There isn't ready access to genetic counseling in all parts of Canada, which is a further hindrance to testing even for those who meet testing criteria, Akbari noted. As such, the aim of The Screen Project, he said, is to not only open up testing access throughout Canada, but to provide counseling support to help those with deleterious mutations understand what the results mean for their health and for their families.

Individuals with negative results can reach out to WCH if they have questions or concerns. If testing detects variants of unknown significance — variants with insufficient evidence to determine if they are definitively linked to cancer or benign — Veritas reports them to researchers at WCH, who then get in touch with individuals to explain the findings. So far, out of the 300 individuals with test results, 11 have a VUS.

When project participants learn they have a deleterious mutation, they can feel concerned, Akbari said, but with counseling they are able to handle the results. Similarly, those with VUS are given the support to understand the results. "For that reason, I call this guided direct-to-consumer testing," Akbari said. "People will not be left on their own to decide what to do with the test results."

The Screen Project has been an ambition of Akbari and his colleagues at WCH's Familial Breast Cancer Research Unit for around a decade. After two decades of research on BRCA1 and BRCA2, he believes these genes are ready to be offered through a universal screening program because deleterious mutations are common enough in the population and the knowledge of having a mutation is actionable from a cancer prevention standpoint.

Furthermore, although these two genes are highly variable, there is a substantial body of research to rely on when it comes to classifying VUS. "After 20 years of working on these genes, now we have enough knowledge to interpret many of the missense variants we see," he said.

However, Akbari's earlier attempts to launch a universal BRCA screening program were met with resistance. In the summer of 2014, he made an appeal at the annual Clinical Genome Conference for universally screening women for pathogenic mutations in BRCA1/2 starting age 30. His idea didn't sit well with the audience, recalled Akbari, a renowned hereditary cancer researcher who discovered RECQL as a breast cancer susceptibility gene. "I actually got comments after my talk where people essentially thought I was out of my mind."

By the time he made this pitch, however, Akbari had already gathered substantial data that existing testing criteria resulted in many at-risk individuals not being tested. He began noticing this as early as 2007, when WCH's Canadian and US research collaborators would send samples to be retested for BRCA mutations.

At the time in the US, only Myriad Genetics held the patent rights to commercially perform BRCA1/2 genetic testing. So, when researchers at other labs identified a deleterious mutation in a study participant and the participant wanted to know her status, they couldn't communicate the result without infringing Myriad's IP. US researchers collaborating with WCH would send the samples to be reanalyzed for free in Canada, so that it could be legally reported to individuals who wanted to know their BRCA status. (In Canada, the provincial government authorities decided not to allow Myriad to enforce its gene patents.)

In retesting these samples, however, "we noticed we were getting lots of positives in patients that didn't meet testing criteria," Akbari recalled. "We felt something was going wrong here, and that we really needed a population-based genetic testing program for BRCA1 and BRCA2 for every individual at a certain age."

In 2008, WCH launched a study offering free testing to all Jewish women living in Ontario for three BRCA1/2 mutations that show up in the Ashkenazi population. Of the 6,000 women who registered for this study, 1 percent carried one of these BRCA gene mutations. "This was the proof of principle for us that we're missing a lot of carriers with these testing criteria," Akbari said, noting that around two-thirds of the

women with deleterious mutations wouldn't have met testing requirements set forth by the provincial government.

Based on this experience, WCH wanted to push ahead and offer BRCA genetic screening more broadly beyond the Jewish population, but in order to do so, the test would have to sequence the two genes entirely, which was a more expensive proposition than gauging specific mutations. In 2013, WCH collaborated with genomics technology firm WaferGen Bio-systems to develop a next-generation sequencing BRCA test using its SmartChip PCR system at a price per patient of around $200, including the cost of recruitment, DNA analysis, and reporting results.

However, when WCH began offering this tool to genetics labs around Ontario, they weren't interested. "Unfortunately, we couldn't convince any labs to start doing this," Akbari said. He estimated that when the Canadian health system pays for BRCA testing it costs somewhere in the range of $1,200 to $1,500. But because BRCA testing is free for qualifying patients through the health system, commercial labs were skeptical that the public would want to pay out-of-pocket for this test, even at a substantially lower price.

It wouldn't be until Veritas launched its consumer-friendly priced BRCA1/2 testing service in 2015 that Akbari finally saw an avenue for launching a universal BRCA screening project. "That was an 'A-ha!' moment for us," he said. "We really didn't need to establish a laboratory ourselves because we are interested in the screening, not the laboratory part of it."

A year before Veritas launched its low-priced testing service, another breast cancer research pioneer, University of Washington's Mary-Claire King, had published a study of 8,000 healthy Ashkenazi men in Israel, and reported that half of those with BRCA mutations came from families without a strong history of breast and ovarian cancers. Based on this finding, King began advocating for screening women at age 30 for BRCA mutations, regardless of their personal or family history of cancer.

King's recommendation has its share of skeptics, but her advocacy has also spurred free BRCA screening programs and inspired low-cost genetic testing companies like Color to partner with employers to offer subsidized testing within wellness programs. Now, Akbari is no longer alone in his push for universal BRCA screening. He joked that one of the people who blew off his appeal for universal screening in 2014 wrote to him after King started advocating for the same, and conceded that "Okay, maybe you're right. And I said, 'Thank God!'"

As The Screen Project tests more people, and the findings more starkly demonstrate the insufficiency of existing testing guidelines, Veritas' Flood expects there will be more viral support and backing from the cancer community for universal BRCA screening. The project has been advertised, featured in pamphlets in doctors' offices, and there are plans to host webinars for doctors around Canada. "We're proud of what we've accomplished with a pretty small budget," he said.

The goal within the project is to test 10,000 individuals to identify 50 BRCA1/2 mutation carriers. But based on the mutation frequency so far, Akbari estimated that many carriers will be identified after testing 2,500 individuals. He hopes this will provide enough data to convince the Canadian health system that universal BRCA screening for women starting at age 30 is something that can be done cost effectively and with the necessary counseling support, and that this should be done from a public health standpoint.

Moreover, counter to naysayers, the experience within the The Screen Project already suggests Canadians are interested in learning their cancer risk information. "In fact, they are so interested that they are ready to pay out-of-pocket for it," he said. "So, imagine the response if this was available to them for free."

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