# Study improves accuracy of breast cancer test for Ashkenazi Jewish women

July 3 2023

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Manchester researchers have developed a way to improve the accuracy of breast cancer genetic testing for women from Ashkenazi Jewish backgrounds.

New forms of genetic tests can tell women their personal risk of developing breast cancer. However, previous research has shown they are not accurate for many Black, Asian or Ashkenazi Jewish women, or women with a mixed ethnic background.

A new study by researchers in the U.K. and Israel has investigated how to improve breast cancer genetic tests for Ashkenazi Jewish women. This research is part of a wider Manchester-based project which aims to develop accurate tests for women of different ethnicities and reduce inequalities in testing.

The tests look for tiny genetic variations all humans carry—called Single Nucleotide Polymorphisms (SNPs)—which, depending on the unique combination of them, can increase or decrease the risk of breast cancer.

This information is used to produce a Polygenic Risk Score (PRS), which can inform women whether they are at low, average, or high risk of developing breast cancer in the next 10 years. PRS are becoming more widely available through commercial companies and research studies on the NHS breast screening program.

Current PRS were developed from large-scale genome studies which predominantly collected genetic data from mainstream white European populations. As a result, the accuracy of a PRS for an individual will depend on how closely their genetic material resemble those of the people whose data was used to develop the risk score.

This means that while commercially available PRS can accurately predict breast cancer risk for mainstream white European women, they often exaggerate this risk for Black, Asian or Ashkenazi Jewish women, or women with a mixed ethnic background.

In this new study, researchers from Manchester University NHS

Foundation Trust (MFT) and The University of Manchester compared two available PRS based on two SNPs—SNP142 and the commercial SNP78—and analyzed their accuracy for women of Ashkenazi Jewish ancestry.

The findings, published in *Genetics in Medicine*, showed that these PRS tests inaccurately predicted Ashkenazi Jewish women to be at higher risk of developing breast cancer.

After adjusting the test for Ashkenazi Jewish ancestry, the researchers were able to generate a more accurate prediction of breast cancer risk for these women.

The research team used genetic information from Ashkenazi Jewish women in both Manchester and Israel, with data from the Predicting the Risk of Cancer at Screening (PROCAS) study conducted in Greater Manchester, a Manchester regional genetics database, and the Breast Cancer in Northern Israel (BCINIS) study.

This research was led by Professor Gareth Evans, a leading expert in breast cancer genetics and SNPs testing and NIHR Manchester BRC Cancer Prevention and Early Detection Theme Lead.

Professor Evans, who is also a Consultant in Medical Genetics and Cancer Epidemiology at MFT, Consultant at The Christie NHS Foundation Trust and Professor in Medical Genetics and Cancer Epidemiology at The University of Manchester, said, "Polygenic Risk Scores (PRS) are a major component of accurate breast cancer risk prediction and have great potential to improve personalized screening methods. However, it is clear from our findings that you cannot simply apply current PRS developed using genetic data from individuals of white European ancestry to those from Ashkenazi Jewish backgrounds.

"A test result which exaggerates a woman's risk of the disease could lead to undue stress or concern and unnecessary screening and preventative measures that they don't need. Future PRS for Ashkenazi Jewish women should be based on their genetic data to provide a more accurate risk prediction.

"This study is an important step forward in our continued research into breast cancer genetic testing for people of different ethnic backgrounds to improve equity. More accurate and personalized PRS are required to avoid further increasing health inequalities and so patients can receive high-quality screening, care, and treatments."

Vicky Lee, 56, from Manchester, grew up with a strong family history of female cancers and lost her mum to ovarian cancer aged just 47. As genetic sequencing became available, she tested positive for the presence of the BRCA gene and opted for a preventative hysterectomy and later a bilateral mastectomy. Vicky has been a patient at Saint Mary's, Withington and Wythenshawe Hospitals, which are part of MFT.

Vicky, who is Jewish, said, "Before I was tested I had already decided that I would have preventative surgery if I was a BRCA carrier. I'd watched my mum and other members of my family go through ovarian cancers and I knew I had to do everything in my power to prevent my own daughters from watching me fight the same disease.

"The ability to accurately test for gene fragments that might be the cause of family cancers is so important for allowing women to make informed choices about their future health. One size never fits all in medicine and medical advancements that allow women in specific communities to understand their own health picture properly are massively important.

"Preventative surgeries are significant procedures that no woman would undergo lightly. Accurate testing gives women the confidence to make

these decisions based on precise insight and, conversely, allows other women to know with confidence that their risk score is low giving them freedom to go and live their lives."

**More information:** Eleanor Roberts et al, Breast cancer polygenic risk scores derived in White European populations are not calibrated for women of Ashkenazi Jewish descent, *Genetics in Medicine* (2023). DOI: 10.1016/j.gim.2023.100846

Provided by University of Manchester