

Launch of first polygenic breast cancer risk assessment score validated for women of all ancestries

Main ideas

- A study of more than 275,000 women (ASCO abstract and presentation, *Journal of Clinical Oncology*, May 28, 2021) described development and validation of a new method for polygenic breast cancer risk assessments in women of all ancestries.
- Myriad Genetics has expanded access to genetic testing by launching the first polygenic breast cancer risk assessment score calibrated for women of all ancestries.
- The Myriad MyRisk® Hereditary Cancer test with RiskScore® provides a precise breast cancer risk assessment for women not previously diagnosed with breast cancer, regardless of ancestry.
- MyRisk with RiskScore is an important step to address racial and ethnic disparities in the healthcare system.

Background

Breast cancer risk can be accurately estimated using single-nucleotide polymorphisms (SNPs) with small effects aggregated into polygenic risk scores (PRSs). To date, PRSs have primarily been developed and validated for populations of European descent.

“The polygenic risk score is one of the most powerful risk prediction tools in the field of breast cancer, and until now a validated model has not been available to assess women of all ancestries,” said Holly Pederson, M.D., director of Medical Breast Services at Cleveland Clinic and presenter of the data published in the *Journal of Clinical Oncology*.

Study goal

To make a PRS available for all women, Myriad Genetics – in collaboration with a team of genetic researchers – developed and conducted a study to validate a novel PRS that utilized individual ancestral genetic composition.

The study’s goal was to define a PRS for all ancestries that combines ancestry-specific SNPs with breast cancer risk SNPs. An additional goal was to achieve a high level of accuracy for all women in terms of good risk discrimination and accurate risk calibration.

Challenges

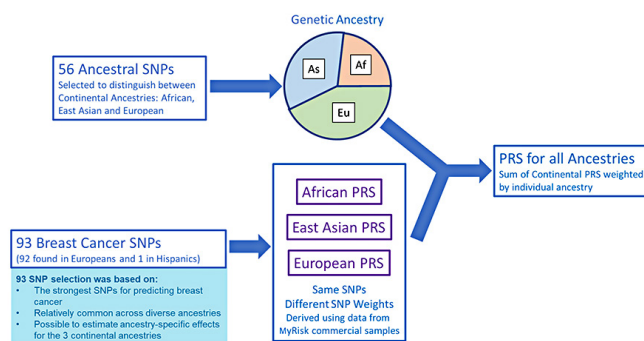
A challenge of using PRS across ancestries is that SNP frequencies and associations between SNPs and breast cancer differ by ancestry.

Study methods

Ancestry-specific PRSs corresponding to three major US source population continental ancestries were developed from 149 SNPs. The three continental ancestries were: an African PRS; an East Asian PRS; and a European PRS.

For each patient, ancestry-informative SNPs were used to calculate the fractional ancestry attributable to each of the three continents. The PRS was the sum of 93 breast cancer risk SNPs weighted according to genetic ancestral composition and ancestry-specific breast cancer risks.

Figure 1: PRS is informed by genetic ancestry

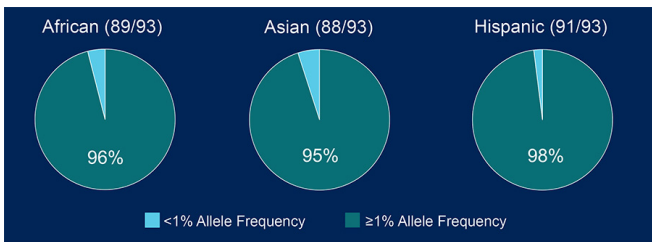


The PRS was then validated in an independent cohort. There were more than 189,000 women in the development set and more than 89,000 in the independent validation set. In both sets, about 23% of women had a personal history of breast cancer and about 30% had first a degree relative with breast cancer. The two groups were similar in terms of self-reported ethnicity.

Results

European-derived breast cancer SNPs were found to be common to all ancestries. At least 95% of breast cancer SNPs had a ≥ 1% frequency of risk alleles within each of the self-reported patient populations.

Figure 2: Frequency of risk alleles in each population



Also, within each validation sub-cohort, defined by self-reported ancestry, the data showed meaningful risk discrimination. Women in the top percentile of the PRS had risk estimates 2-3-fold higher than typical women. For women in the top decile, risk was approximately doubled compared to a typical woman with the exception of self-reported Black/African women where the risk increased by 44%.

As intended, the PRS for all ancestries is centered around zero (Figure 3) for unaffected patients, except for self-reported Hispanic patients where there is a slight shift due to a protective Amerindian SNP.

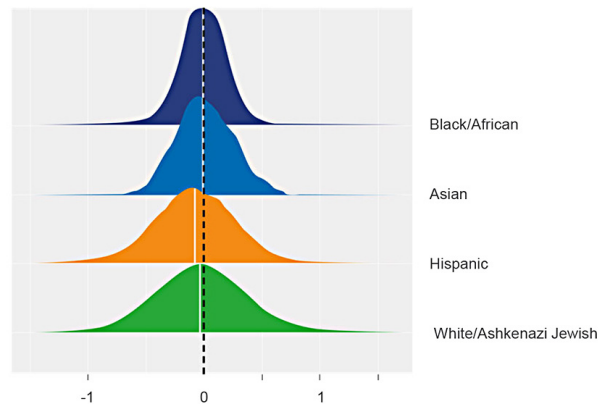
Summary

The collaboration between Myriad Genetics and academic researchers resulted in development of a PRS that is accurate for women of all ancestries and can be adapted as additional data become available. This clinically validated PRS provides calibrated genomic risk identification for all women.

About Myriad Genetics

Myriad Genetics is a leading genetic testing and precision medicine company dedicated to advancing health and wellbeing for all, empowering individuals with vital genetic insights and enabling healthcare providers to better detect, treat and prevent disease. Myriad discovers and commercializes genetic tests that determine the risk of developing disease, accurately diagnose disease, assess the risk of disease progression, and guide treatment decisions across medical specialties where critical genetic insights can significantly improve patient care and lower healthcare costs. For more information, visit the Company’s website: www.myriad.com.

Figure 3: PRS for all ancestries



“Our data now provide a framework for a PRS that delivers a personalized genomic breast cancer risk assessment to any and all interested women. The updated PRS, validated and well-calibrated, may be the most exciting clinical development in risk stratification since multi-gene panel testing,” said Dr. Pederson.

From research to application

Following the validation and calibration of the PRS for women of all ancestries, Myriad Genetics has launched a new version of its market-leading MyRisk Hereditary Cancer Test. For the first time, women of all ancestries can now receive a personalized polygenic breast cancer risk assessment together with the market’s most accurate hereditary cancer test.

MyRisk with RiskScore offers a breast cancer risk assessment designed to improve patient outcomes and help minimize healthcare disparities. RiskScore results are informed by a combination of genetic markers, clinical and biological variables, personal and family history, and ancestry-specific data. RiskScore is available at no additional cost to women who take the MyRisk test.

With traditional hereditary cancer tests, approximately 90-95% of women will test negative for high-risk gene mutations, but still have additional breast cancer risks that need to be managed. The RiskScore component of MyRisk helps women and their physicians assess those added risk factors. An estimated 56% of patients who undergo MyRisk testing and receive a RiskScore result qualify for medical management changes such as increased cancer surveillance or intervention.