Innovations in Genetic Testing to Address Healthcare Disparities and Improve Outcomes Q&A

Retesting back to how many years and for all specialties?

From the day RiskScore debuted in 2017. Any patient who did not receive RiskScore due to their ancestry is eligible for no cost retesting so long as they meet the clinical criteria for inclusion, for all specialties.

For ancestry distribution, where do Native Americans fit in? East Asian?

Yes! Native Americans fit in best with East Asians according to our work as well as published literature. More broadly, there are two important points to mention regarding the reference ancestries. First, the test does not divide individuals into three distinct ancestries. We are happy to discuss this further. Second, the genetic ancestry measurements are only used to help determine the weight (i.e. risk) assigned to the SNP, and also for calibration (which depends on SNP frequencies). Genetic ancestry is essential in order to achieve accurate risks and calibration, and there is no way to do this accurately based on self-reported ancestry. We did not use self-reported ancestry for the development of RiskScore for all ancestries, and we do not take an individual's self-reported ancestry into account in any way in the calculation of an individual's RiskScore. Only for the purpose of performance evaluation did we use self-reported ancestry, and our PRS showed excellent performance overall, and within populations defined by self-reported ancesry obtained on our test requisition form.

When we say that it is largely or majority covers ancestry of women what amount of women are not able to be generalized by these 3 groups?

Ancestry is no longer a barrier to receiving RiskScore. It is important to note that we are specifically determining genetic ancestry based on genetic markers for the purpose of determining breast cancer risk. This is not a test to explain all genetic human diversity, as that level of categorization does not add to the validity of the test. We are also very specifically referring to genetic ancestry, as opposed to self-reported ancestry, ethnicity, race, or other indices of diversity.

What work is Myriad doing or supporting to ensure those not covered by these three ancestral groups get equitable testing/ follow-up?

See above regarding availability of RiskScore for women of all ancestries. Regarding our continued commitment to equity, we will continue to invest in scientific discovery and innovation to serve patients of all ancestries. We are happy to share more detail; please contact us!

How did you determine which labels you would use for each ancestry category?

In order to determine the reference ancestries, the criteria were as follows: First, the reference ancestries combined should represent a significant portion of all human genetic diversity. Second, reference ancestries should be genetically relatively homogeneous. Third, there should be sufficient data in this ancestry to measure the association of common genetic variants with breast cancer.

Is the ancestry being checked genetically or just by self-report?

The contribution of breast cancer SNPs is weighted according to genetic ancestry markers, as opposed to self-reported ancestry.

How does it factor in breast density?

We are working on breast density. We need to make sure we are not double counting risk from the PRS and the breast density, similar to family history.

Given the high diversity of non-European populations, were there any new risk pertinent SNPs identified when looking at at these populations?

Literature was evaluated to incorporate relevant published SNPs across ancestries. For instance, we incorporated a protective Amerindian SNP (i.e. lowers risk) in self-reported Hispanic patients.

You mentioned the need to identify and test high-risk patients. One major barrier is cost. What is Myriad doing to address and potentially eliminate this barrier

RiskScore is included as part of the MyRisk test at no additional cost. Because patients and their families use test results to make life saving medical decisions, Myriad promises to provide affordable access to testing and comprehensive support for ALL appropriate patients and their families. The Myriad Promise is our commitment to provide patients with accurate and affordable genetic results.

Would you please speak to the clinical utility of riskScore? i.e., How do management recommendations based on riskScore differ from those that may be made from other assessments (e.g., family history) when a patient is not identified to have a high-risk mutation?

A good reference is the JCO. Precision Oncology peer-reviewed paper that demonstrated integrating clinical and polygenic factors into a risk model offers more effective risk stratification and supports a personalized approach to breast cancer screening. This paper showed that 18% of women shifted breast cancer risk categories from their v.7.02 Tyrer-Cuzick-based risk model compared with risk estimates by combined risk score. More publications are coming as we explore diverse ancestries and additional SNPs. There is a signficant, growing body of literature on polygenic risk scores for improving risk stratification. In addition to the above reference, a few more include: Wolfson et al. Genet Med 2021. https://pubmed.ncbi.nlm.nih.gov/34230637/ ; Mavaddat et al Am J Hum Genet 2019 https://pubmed.ncbi.nlm.nih.gov/30554720/

Our goal with RiskScore is to provide a personalized and enhanced genetic breast cancer risk assesment tool that can be used at a provider's discretion in their patient's care plan.

Is Myriad considering re-validating the PRS model in the future for women with high risk lesions (ADH, LCIS)?

It is something that may be evaluated in the future.

I had a patient who had testing even though she did not meet criteria for coverage. Myriad somehow got her test covered. Her RiskScore was very high. So, she wanted to know about her sister's risk as her siser also would not meet criteria. How is Myriad handling these situations?

We do not place a barrier to patients accessing genetic testing. However, if a provider attests to medical necessity of the test and it appears the test may have been ordered in error, we have quality assurance checks in place to ensure the correct test was ordered and all pertinent medical information was provided before determining coverage through an insurer.

What research efforts are being dedicated to gain more knowledge about SNPs in populations outside of Europeans?

We are actively collecting more information across all ancestries to improve discriminatory power of the combined residual risk. We are exploring additional SNPs and updated versions of Tyrer-Cuzick. This includes conducting one of the largest GWAS for people of African ancestry in the world.

Does Myriad provide free familial testing following a positive result?

When a familial mutation is identified in a family most, not all, insurance companies typically cover the cost of familial testing. In a situation in which insurance does not cover cost, Myriad has a robust financial assistance program (www.MyriadPromise.com) and will work directly with the patient to their satisfaction.

Other companies offering NIPT have adopted a patient self-pay rate of $100 if the out-of-pocket cost with insurance is higher. What is Myriad doing to make their testing more accessible to patients of low socioeconomic status in terms of billing?

We have a robust financial assistance program in place for all Myriad tests to ensure that patients are able to access affordable genetics insights. We also believe in cost transparency and have expanded our cost estimates process across products. If you have questions about our financial assistance programs and how we are able to help patients with billing, please contact us! We would love to talk more.

Are you checking if the person's self reported ancestry matches the SNP ancestry testing you're doing for the cancer PRS?

We are not taking into account the self-reported ancestry and relying on the SNP-based ancestry classification since it is a more accurate reflecture of their true ancestry.

Could you provide the reference for the stat that 40% of patients either can or cannot accurately report the ancestry of all four grandparents? I didn't catch that. Thank you!

Condit, C., Templeton, A., Bates, B. et al. Attitudinal barriers to delivery of race-targeted pharmacogenomics among informed lay persons. Genet Med 5, 385–392 (2003). https://doi.org/10.1097/01.GIM.0000087990.30961.72

With a high proportion of couples being of mixed ethnicity will Myriad consider changing reports that currently report reproductive risk estimates for affected offspring "assuming a partner of the same ancestry" when a carrier is identified?

We are evaluating changing the assumption to a global population residual risk.

Do you offer a carrier panel with all the tier 3 recommended ACMG genes (only)?

We currently have a panel that includes the genes named to Tier 3 available on our platform. We are currently in the process of completing a panel that includes only the tier 3 recommendations.

How is Myriad working on making their reports and requisition forms more inclusive? In terms of gender and ethnicity. All Hispanic people are not the same genetically. We are all very diverse.

This is precisely why we are measuring ancestry based on genetic markers with RiskScore. Using genetic markers, we can appropriately account for the vast diversity among self-reported Hispanic women, for example.

Sharing variant interpretation data publicly is largely important for DEI efforts, does Myriad plan to contribute to these efforts?

We appreciate the question and continually evaluate the balance of contributing to research while upholding our core values, including protecting patient privacy and complying with existing laws and regulations. Importantly, we do share data and variant classifications routinely through research collaborations and other academic partnerships. We'd love to have a direct conversation about this; contact us!

Myriad genetics

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