Asian
Hispanic
INDEPENDENT CRS EVALUATION
● A Combined Risk Score (CRS), incorporating the 149-SNP PRS with version 7 of the clinical and family history-based Tyrer-Cuzick (TC) model.

We recently developed and validated a 149-SNP PRS for women of diverse backgrounds who were negative for pathogenic variants in breast cancer (BC) susceptibility genes. The 149-SNP PRS incorporates ancestry informative variants with 93 BC-associated variants. It was significantly associated with BC risk after accounting for reported ancestry.

Figure 3. Risk Reclassification

Table 2. Risk Reclassification by Ancestry

- Family history was highly significant, but weakly correlated with the 149-SNP PRS (r=0.08; p=6.3x10^{-95}). After adjusting for multiple testing, no other TC factors were associated with the 149-SNP PRS.

RESULTS

- Adding PRS to TC significantly altered breast cancer risks for all ancestries, with 17.3% of patients classified differently by CRS vs TC alone (Table 2, Figure 3).

- Among patients who were classified as high-risk by TC, 29.1% were downgraded by CRS.

- Combining the 149-SNP PRS with TC substantially improved risk stratification over TC alone (Figure 2).

- This is the first breast cancer risk model based on a polygenic score, the 149-SNP PRS, which incorporates genetically determined ancestral composition and is validated for diversity.

- By combining the 149-SNP PRS with TC substantially improved risk stratification over TC alone and may therefore lead to enhanced breast cancer risk reduction strategies such as increased surveillance and use of preventive medications.

CONCLUSIONS

REFERENCES