Common genetic variants associated with breast cancer risk used in the Athena study to enhance models identifying women for chemoprevention

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Background
The U.S. Preventive Services Task Force recommends that women with a ≥5% five-year risk of developing breast cancer consider taking selective estrogen receptor modifiers (SERMs) or aromatase inhibitors (AIs) to reduce their risk.

The Athena Breast Health Network is a research and care collaboration among the five University of California (UC) Medical Centers and Sanford Health that aims to improve care and includes to date 115,000 women.

Methods
To examine the associations between SNP PRS and known breast cancer risk factors (ethnicity, family history of breast cancer and number of biopsies)
To quantify the likely impact on combining a risk factor based risk models with SNP PRS on women’s five-year risk estimates
Evaluate how this strategy would affect the proportion of women recommended for chemoprevention

Results
PRS is significantly associated with a family history of breast cancer (p=1.796E-5), neither SNP allele count nor PRS associates with previous biopsy status.

By ANOVA, there is a statistically significant association between the number of breast cancer risk alleles and race/ethnicity (p=2E-16).

Applying Tukey post-hoc analysis to identify which pairs of ethnicities/races have significantly different PRS, we find that Black, Asian and Hispanic women have significantly more risk alleles than do White women. Black women also have significantly more risk alleles than Asian and Hispanic women.

Conclusion
• Addition of PRS to breast cancer risk models changes the classification as high risk (≥5% five-year risk estimated for a considerable proportion of women)
• BSCC + PRS: 68% of women change risk stratification (net population impact 28%)
• Gail + PRS: 42% of women change risk stratification (net population impact 14.7%)
• PRS is significantly associated with family history of breast cancer
• Number of breast cancer risk alleles is significantly associated with race/ethnicity.

Next Steps
• Assess impact of combining PRS with BCSC and Gail scores on breast cancer risk in WISDOM Study (opening 3rd quarter 2016)
• Annual vs. risk-based screening in 100,000 women

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