

# Multigene assessment of genetic risk for multiple primary breast cancers

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#### Disclosures:

JK, DT, KM, KS, KB, EH, SC and TS are employees of Myriad Genetics, Inc.; JS is currently an employee of Guardant Health and owns Myriad Genetics stocks. Other authors have no conflict of interests.



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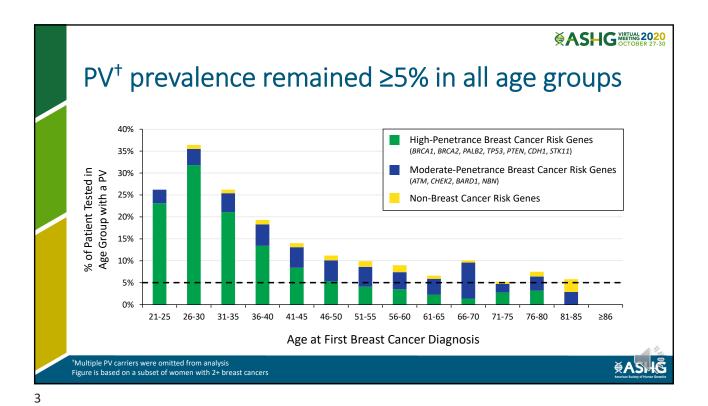
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## Background & Methods

- A better understanding of hereditary cancer risk for ≥2 breast cancers beyond the BRCA1 and BRCA2 genes is needed to improve personalized risk assessment and medical management.
- We assessed the risk of ≥2 breast cancers for all genes included in a multi-gene panel test.

### **♦**ASHG WIRTUAL 2020 OCTOBER 27-30 Women referred for hereditary cancer testing 25-28 gene hereditary cancer panel testing at Myriad Genetics (2013-2018) N=732,338 Women with a personal history of breast cancer Any history of DCIS and/or invasive breast cancer indicated on the TRF N=200,126 Exclude women who meet any of the following: 1. From states that don't allow the use of de-identified genetic data (N=48,889) Previous single-site or founder mutation testing (N=46,790) Pancreatic or ovarian cancer diagnosed before their first breast cancer 4. Only meet the definition for >2 breast cancers based on DCIS and invasive breast cancer at the same age (N=3,217) 5. Pathogenic variant in MUTYH (N=1,635) Women with ≥2 Breast Cancers Women with At least 2 instances of breast cancer indicated 1 Breast Cancer on the TRF at the same age (synchronous) or different ages (metachronous) N=88,759 N=10,220

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Among women with breast cancer, **★ASHG** WIRTUAL 2020 OCTOBER 27-30 7 genes were associated with a significantly increased risk for a 2<sup>nd</sup> breast cancer Gene % of Cohort N % of Cohort Odds Ratio (95% CI) p-value **Breast Cancer Risk Genes** 11.86 7165 8.07 1.54 (1.44, 1.65) <0.001 BRCA1 3.51 2.15 1.74 (1.55, 1.97) <0.001 337 2007 < 0.001 BRCA2 2 26 1.57 (1.39, 1.77) 130 1.27 735 0.83 1.62 (1.34, 1.96) < 0.001 PALB2 TP53 21 0.21 84 0.09 2.56 (1.56, 4.20) <0.001 PTEN 13 0.13 26 0.03 3.80 (1.88, 7.69) < 0.001 CDH1 13 0.13 50 0.06 2.42 (1.30, 4.52) 0.01 STK11 1 0.01 8 0.01 1.22 (0.14, 10.35) 0.86 1.35 (1.15, 1.57) <0.001 CHEK2 186 1.82 1236 1.39 ATM 1.17 (0.95, 1.45) 0.14 BARD1 0.29 212 0.24 1.27 (0.87, 1.87) 0.22 0.20 0.15 1.29 (0.78, 2.12) 0.32 Non-Breast Cancer 1.03 1.10 0.92 (0.75, 1.13) Risk Genes 5 10 Multivariable logistic regression models determined relative risk of multiple breast cancers conferred by pathogenic variants as odds ratios and 95% confidence **♦ASHE** intervals (CIs). All models accounted for age of diagnosis, personal and family cancer history, and ancestry. Multiple PV carriers were omitted from analysis

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### **Conclusions**

- Risk for two or more breast cancers was significantly elevated for several high- and moderate-penetrance breast cancer risk genes, affirming the association of two or more breast cancers with diverse genetic etiologies.
- Our findings suggest no clear decline in pathogenic variants in women with two or more breast cancers after age 50.
- Multigene panel testing should be considered for all women with two or more breast cancers.



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