Abstract #858

Ancestry-Specific Prevalence of Pathogenic Variants Among Patients with Breast Cancer Who Do Not Meet Guidelines for Genetic Testing

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Background

- Patients with breast cancer (BC) who harbor germline pathogenic variants (PVs) in hereditary cancer-associated genes have improved survival when their surgical and other treatment decisions are tailored to their specific genetic alterations.
- Additionally, the identification of germline PVs is crucial for family members, as it allows for interventions that can decrease cancer-related morbidity and mortality.
- Commonly utilized guidelines recommend genetic testing only under specific conditions:
  - if cancer is diagnosed at a young age, typically ≤ 50 yrs
  - if there is a strong family history (FH) of cancer
  - or if there are specific tumor characteristics.
- Several studies have demonstrated that many patients who do not meet these criteria unknowingly carry PVs and may, therefore, be receiving suboptimal care.
- In the United States, Black and Hispanic women face disproportionately high rates of BC mortality, highlighting the importance of genetic testing in these populations.
- It is unclear whether guideline-based restrictions differentially impact women of certain ancestral backgrounds.
- We explored this question by estimating PV prevalence among BC patients of Asian, Black/African, Hispanic, Multiple, and White/non-Hispanic ancestries who do not meet guidelines for genetic testing.

Methods

- Multivariable logistic regression models were constructed to analyze trends in the prevalence of PVs based on age, personal/family history, and ancestry in a consecutive cohort of patients referred for hereditary cancer testing with a multigene panel.
- We report age- and ancestry-specific model-based estimates of prevalence for patients diagnosed with BC with no FH and no prior personal history of cancer of any type.
- Prevalence is summarized overall for 25-48 hereditary cancer genes with guideline-based medical management recommendations, as well as for the genes most frequently implicated in BC.

Results

- Among 245,669 female patients with BC, 8,025 (3.3%) were Asian, 25,900 (10.5%) were Black/African, 20,022 (8.1%) were Hispanic, 141,279 (57.5%) were White/non-Hispanic, and 16,689 (6.8%) were patients with multiple self-reported ancestries (**Table 1**).
- Overall prevalence estimates of any PV were 6.3% for those diagnosed at age 50 and 3.6% among those diagnosed at age 80 (**Figure 1 and Supplementary Table 1**).
- Estimates of PV prevalence for a patient with BC with no FH and no prior personal history of cancer of any type were similar across ancestries, with the highest prevalence among Hispanic women (**Figures 1 and 2, Supplementary Table 1**).

Table 1. Age of breast cancer diagnosis and PV status by ancestry

Ancestry	N (%)	Age BC Diagnosis Mean (SD)	Any PV (%)	BC Gene PV* (%)	*BRCA1/2* PV (%)
All Patients	245,669	52 (**11.9**)	23,771 (**9.7%**)	18,423 (**7.5%**)	10,345 (**4.2%**)
Asian	8,025 (**3.3%**)	48.6 (**10.5**)	704 (**8.8%**)	549 (**6.8%**)	413 (**5.1%**)
Black/African	25,900 (**10.5%**)	50.8 (**11.9**)	2,458 (**9.5%**)	1,903 (**7.3%**)	1,347 (**5.2%**)
Hispanic	20,022 (**8.1%**)	48.6 (**11.1**)	2,217 (**11.1%**)	1,907 (**9.5%**)	1,230 (**6.1%**)
Multiple	16,689 (**6.8%**)	49.7 (**11.4**)	1,646 (**9.9%**)	1,327 (**8.0%**)	809 (**4.8%**)
White/Non-Hispanic	141,279 (**57.5%**)	53.2 (**11.9**)	13,487 (**9.5%**)	10,158 (**7.2%**)	5,089 (**3.6%**)

*BC Gene PV refers to *BRCA1, BRCA2, CHEK2, ATM,* and *PALB2.*

Figure 1. Model-Based Estimates of PV Prevalence in All Patients

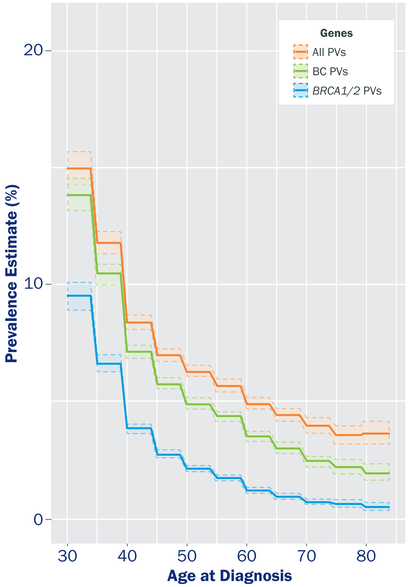
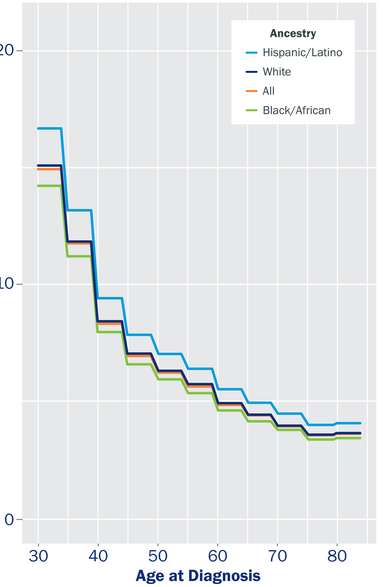


Figure 2. Model-Based Estimates of PV Prevalence by Ancestry



Please see **Supplementary Table 1** for full prevalence estimate data:

Conclusions

- Among patients with BC from diverse ancestries, a substantial fraction of patients who do not meet guidelines for genetic testing may unknowingly carry PVs.
- Removing age-based restrictions on genetic testing could improve the survival of patients with BC and identify family members appropriate for genetic testing.

Female = sex at birth **Disclosures:** All authors were employees of Myriad Genetics, Inc. at the time of this study and received salaries and stock as compensation. **Email for questions: rbernhis@myriad.com**