Pan-Cancer Panel Testing: Variation in Testing and Results by Ancestry

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BACKGROUND

- Multi-gene pan-cancer panel tests and reduced testing costs have allowed for greater access to hereditary cancer genetic testing
- Several studies[1-3] have demonstrated that a substantial number of patients with clinically actionable variants are missed by current testing criteria that is largely based on age at diagnosis, family history, and ancestry
- Here we assess ancestry-based differences in testing practices for individuals with and without a personal and/or family cancer history

METHODS

- Clinical information was obtained from provider-completed test request forms for women who had pan-cancer panel testing from 2013 to 2018 (N=427,864)
- The pan-cancer panel test included: *APC*, *ATM*, *BARD1*, *BMPR1A*, *BRCA1*, *BRCA2*, *BRIP1*, *CDH1*, *CDK4*, *CDKN2A*, *CHEK2*, *EPCAM*, *GREM1*, *MLH1*, *MSH2*, *MSH6*, *MUTYH*, *NBN*, *PALB2*, *PMS2*, *POLD1*, *POLE*, *PTEN*, *RAD51C*, *RAD51D*, *SMAD4*, *STK11*, and *TP53*
- The proportion of patients with a pathogenic variant (PV), family cancer history (FHx), and age at testing were evaluated for the four most common ancestries in this cohort (White/Non-Hispanic, Black/African, Hispanic/Latino American, Asian)
- Analyses were performed separately based on personal cancer history (affected, unaffected)

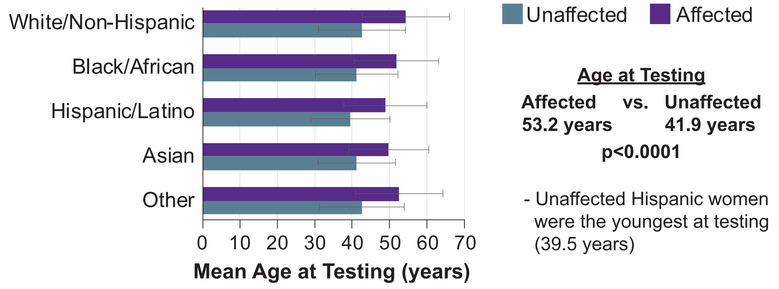
RESULTS

Table 1. Distribution of Affected Status by Ancestry

Ancestry	Total N	Affected N (%)	Unaffected N (%)
White/Non-Hispanic	231,555	82,996 (35.8)	148,559 (64.2)
Black/African	34,631	11,913 (34.4)	22,718 (65.6)
Hispanic/Latino	33,092	10,773 (32.6)	22,319 (67.4)
Asian	10,244	4,636 (45.3)	5,608 (54.7)
Other*	2,333	861 (36.9)	1,472 (63.1)
Total**	427,864	147,501 (34.5)	280,363 (65.5)

*Other includes Native American, Ashkenazi, Middle Eastern, Pacific Islander, and all other single ancestries **Total also includes individuals with multiple ancestries and no ancestry indicated

Figure 1. Age at Testing by Ancestry and Affected Status



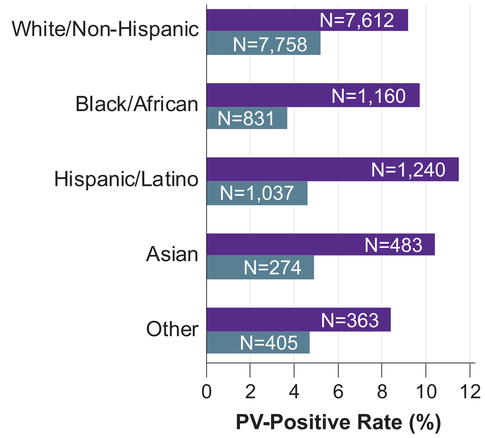
Age at Testing

Affected 53.2 years vs. Unaffected 41.9 years

p<0.0001

- Unaffected Hispanic women were the youngest at testing (39.5 years)

Figure 2. PV-Positive Rate by Ancestry and Affected Status

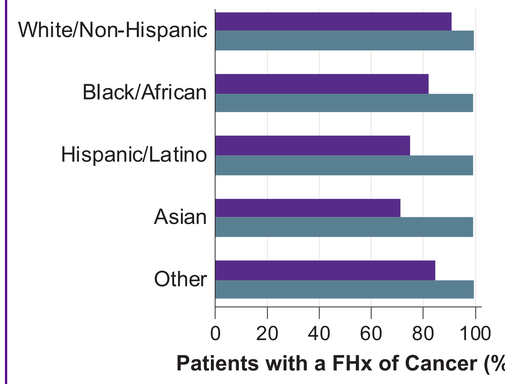


- A substantial proportion of unaffected patients had a PV (4.9%)

- White: 5.2%
- Black: 3.7%
- Hispanic: 4.6%
- Asian: 4.9%

- Positive rates were higher among affected patients (9.4%)

Figure 3. FHx by Ancestry and Affected Status



- Unaffected individuals reported a higher rate of FHx of cancer than affected individuals

- Total: 99.3% vs. 87.4%
- White: 99.4% vs. 91.0%
- Black: 99.1% vs. 82.0%
- Hispanic: 99.2% vs. 75.0%
- Asian: 99.0% vs. 71.2%

CONCLUSIONS

- Obtaining an accurate family cancer history is of critical importance in identifying unaffected women at increased risk of carrying a PV, regardless of ancestry
- The older age of affected women at testing and high rate of FHx suggests a missed opportunity
  - Patients could be tested earlier and receive risk-reducing intervention(s)
  - Women of reproductive age could undergo preconception counseling and consider preimplantation genetic diagnosis

REFERENCES

1. Li J, et al. Prevalence of *BRCA1* and *BRCA2* pathogenic variants in a large, unselected breast cancer cohort. *Int J Cancer*. 2019;144(5):1195-1204
2. Knerr S, et al. Trends in *BRCA* Test Utilization in an Integrated Health System, 2005-2015 *J Natl Cancer Inst*. 2019 Feb 8. [Epub ahead of print]
3. Beitsch PD, et al. Underdiagnosis of Hereditary Breast Cancer: Are Genetic Testing Guidelines a Tool or an Obstacle? *J Clin Oncol*. 2019;37(6):453-460

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