OUTCOMES OF MULTI-GENE TESTING FOR INHERITED CANCER RISK IN PATIENTS OF VARIED ANCESTRIES

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HYPOTHESIS / PURPOSE

- Genetic testing utilization and outcomes can vary by ancestry due to founder mutations, disparities in access to services, varied biological/environmental risk factors, and the knowledge base available to inform variant classification.
- We investigated the impact of an individual's ancestry on utilization and results from clinical testing with a 25-gene panel for assessment of inherited cancer risk for breast, ovarian, colorectal, endometrial, gastric, pancreatic, prostate cancer, and melanoma.

METHODS

- Results are from 102,281 women and 3,412 men tested clinically with the 25-gene hereditary cancer panel (Myriad myRisk™). Since the tested population is heavily biased towards women, male data are not included in most of the analyses.
- Only results from individuals having full panel testing as their original test order are reported.
- Clinical information was obtained from test request forms (TRFs) completed by ordering healthcare providers.
- Pathogenic variants (PVs) are those classified as Deleterious or Suspected Deleterious.
- Ashkenazi Jewish individuals with PVs were considered separately from other individuals of White/Caucasian ancestry.
- The common *CHEK2* 1100del PV was considered separately from other *CHEK2* PVs.
- Test utilization according to ancestry was approximated using the 2010 US Census data, available at census.gov.
- Exact 95% confidence intervals were calculated to identify statistical differences in the proportion of mutations within a gene by ancestry.

RESULTS

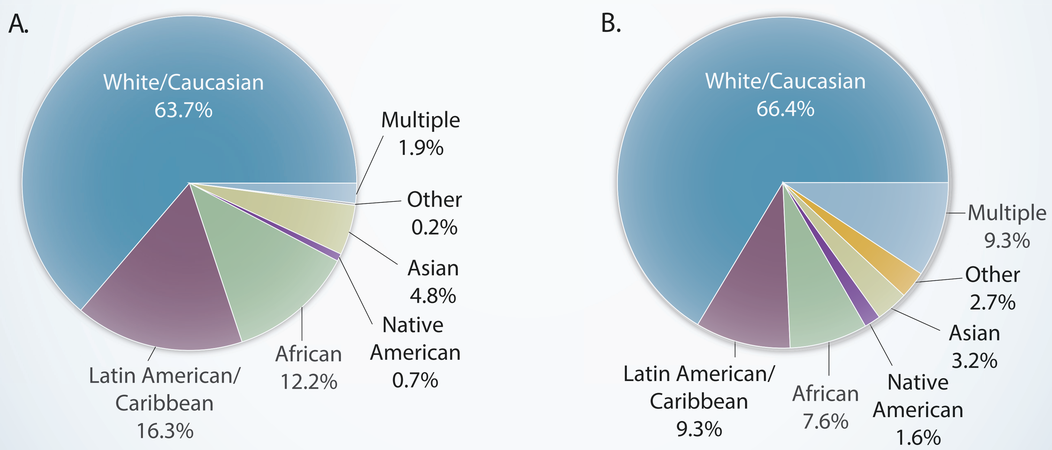
- About 50% of the female sample reported White/Caucasian ancestry (Table 1).
- Excluding women with no specified ancestry (21.0%), or multiple reported ancestries (7.4%), the next three largest groups were Latin American/Caribbean (7.4%), African (6.1%), and Asian (2.5%) (Table 1).
- The positive rate in the four most common ancestries for one or more PVs in women was 7.4% (White/Caucasian), 7.0% (Latin American/Caribbean), 6.5% (African) and 7.7% (Asian) (Table 1).

TABLE 1. POSITIVE RATE ACCORDING TO ANCESTRY

	Female				Male			
	N	% of Tested Patients	Patients with PVs Identified	% of Patients with a PV	N	% of Tested Patients	Patients with PVs Identified	% of Patients with a PV
TOTAL	102,281	96.8%	7158	7.0%	3412	3.2%	492	14.4%
Ancestry								
White / Caucasian	53,573	52.4%	3977	7.4%	1916	56.2%	278	14.5%
Latin American/ Caribbean	7537	7.4%	530	7.0%	238	7.0%	36	15.1%
African	6196	6.1%	402	6.5%	163	4.8%	19	11.7%
Asian	2557	2.5%	197	7.7%	89	2.6%	13	14.6%
Ashkenazi	1326	1.3%	100	7.5%	109	3.2%	18	16.5%
Native American	1307	1.3%	83	6.4%	21	0.6%	4	19.0%
Near East / Middle East	743	0.7%	60	8.1%	43	1.3%	11	25.6%
Multiple	7550	7.4%	470	6.2%	205	6.0%	25	12.2%
Not Specified	21492	21.0%	1339	6.2%	628	18.4%	88	14.0%

FIGURE 1. ANCESTRY PROFILE FOR (A) THE US POPULATION AND (B) THE TESTED POPULATION

US population data **(A)** is based on 2010 US Census Data. The ancestry profile for the tested population **(B)** does not include those patients for which an ancestry was unspecified. These charts include data for both male and female individuals.

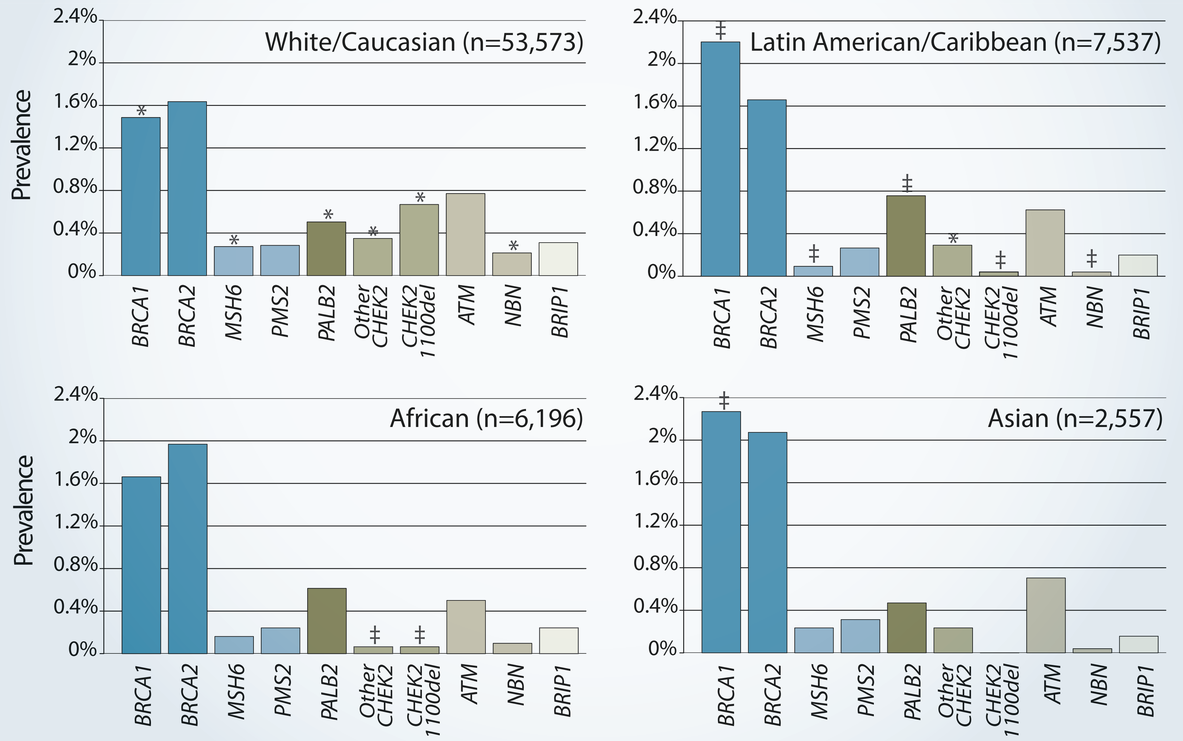


- The distribution of ancestries in the tested population compared to the US population suggests that testing may be under-utilized in individuals of non-European ancestry (Figure 1).
  - The difference in the proportion of individuals reporting multiple ancestries in the US Census data relative to the TRF prevents a quantitative comparison.
- Although there were differences in the prevalence of PVs in different genes by ancestry, the highest numbers of PVs in all groups were in *BRCA1* and *BRCA2*, followed by the moderate penetrance breast cancer genes, *ATM*, *CHEK2*, and *PALB2* (Figure 2).
- *CHEK2* PVs were notably more common in women reporting White/Caucasian ancestry, largely due to the 1100del European founder PV (Figure 2).

FIGURE 2. MUTATION PREVALENCE IN WOMEN ACCORDING TO ANCESTRY

Data is displayed for women with the 4 most common reported ancestries, for the 10 genes in which PVs were most frequently detected.

Statistically significant differences between gene prevalence according to ancestry are noted. Genes marked by * are statistically different than those marked with ‡ in another ancestry. Unmarked genes in an ancestry do not have a statistically different prevalence relative to the other ancestries shown.



CONCLUSION

- Among the women tested, the positive rate for detection of one or more PVs was not strikingly different in any ancestry, and although there were differences in the distribution by gene, there is no evidence to suggest that the benefits of the panel approach are ancestry-specific.

REFERENCES

2010 Census Data (http://factfinder.census.gov/faces/tableservices/jsf/pages/productview.xhtml?pid=DEC_10_DP_DPDP1&src=pt)

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