10525 **Poster Session**

Closing the gap: Trends in inconclusive rates on hereditary cancer testing across racial/ethnic groups.

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Background: Several groups have described disparities in genetic test results for inherited breast cancer predisposition, with a disproportionate number of variants of unknown significance (VUS) reported in non-Caucasian individuals. These disparities are due in part to the underrepresentation of non-Caucasians in reference databases and clinical genetic testing cohorts. Over the past few years, diversification efforts have been made however, little data exists on how ethnicity- and gene-specific VUS rates have changed over time and whether such disparities have improved or worsened. **Methods:** We retrospectively reviewed demographic information and test results for individuals who underwent hereditary cancer multigene panel testing between March 2012 and September 2020 at a single laboratory. Individuals who self-reported as African American, Asian, Caucasian, or Hispanic on the test requisition form and whose testing included *ATM, BRCA1, BRCA2, CHEK2* and *PALB2* (five commonly tested breast cancer predisposition genes with management guidelines) were included in the study (n = 284,130). The frequency of germline variants of unknown significance (VUS) in the five geneswas assessed in September 2015 and September 2020. **Results:** Amongst patients tested between March 2012 and September 2015, 82.8% of the study cohort self-reported as Caucasian and 17.2% were not Caucasian (6.5% African American, 6.0% Hispanic, and 4.6% Asian). The proportion of non-Caucasian individuals in the study cohort increased slightly by September 2020 to 22.8% (77.2% Caucasian, 9.2% African American, 8.4% Hispanic, and 5.3% Asian). Consistent with previous reports, Caucasians had the lowest VUS rate overall in both 2015 and 2020. This was also true at the individual gene level, with the exception of *CHEK2*. Over time, we observed a relative decrease in VUS rates across all ethnicities. Between 2015 and 2020, the overall VUS rate for the five included genes in non-Caucasian individuals was reduced by 32.0% in non-Caucasians compared to 23.6% in Caucasians. The absolute difference in VUS rate between non-Caucasians and Caucasians decreased from 7.9% in 2015 to 4.5% in 2020. **Conclusions:** While VUS rates for commonly tested breast cancer predisposition genes remain higher in non-Caucasians relative to Caucasians, our results demonstrate that this gap has been reduced over a five-year time period. These findings may be indicative of efforts by clinicians and laboratories to reduce these disparities. Further studies are necessary to improve the clinical utility of genetic testing in under-represented populations. Research Sponsor: Ambry Genetics.

	ATM		*BRCA1*		*BRCA2*		*CHEK2*		*PALB2*	
	2015	2020	2015	2020	2015	2020	2015	2020	2015	2020
African American	10.2%	5.2%	1.5%	1.6%	4.2%	2.8%	1.1%	0.8%	2.0%	1.3%
Asian	6.3%	5.1%	3.2%	2.3%	5.0%	4.2%	2.5%	2.5%	5.8%	2.2%
Caucasian	4.1%	3.2%	0.9%	0.8%	2.0%	1.5%	1.9%	1.5%	1.5%	1.1%
Hispanic	6.1%	4.2%	1.3%	1.0%	2.6%	2.5%	2.8%	2.1%	1.6%	1.2%