Improving a Polygenic Risk Score (PRS) for Breast Cancer (BC) Risk Assessment in Diverse Ancestries

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Table 1. Characteristics of women included in the validation cohort

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>European</th>
<th>Black/African</th>
<th>Mixed Ancestry</th>
<th>East Asian</th>
<th>South Asian</th>
<th>White</th>
<th>All</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at diagnosis (y)</td>
<td>50.9 (14.6)</td>
<td>47.9 (12.9)</td>
<td>45.4 (13.3)</td>
<td>50.4 (13.3)</td>
<td>42.0 (13.0)</td>
<td>51.4 (14.6)</td>
<td>49.1 (14.6)</td>
</tr>
<tr>
<td>Odds ratio (OR) from multivariable regression model*</td>
<td>1.51 (1.40, 1.63)</td>
<td>2.13 (1.98, 2.29)</td>
<td>1.39 (1.19, 1.61)</td>
<td>1.42 (1.33, 1.52)</td>
<td>1.40 (1.27, 1.54)</td>
<td>1.56 (1.43, 1.70)</td>
<td>1.53 (1.41, 1.67)</td>
</tr>
<tr>
<td>Association with BC risk model</td>
<td>2.16 (1.90, 2.45)</td>
<td>2.73 (2.42, 3.07)</td>
<td>1.92 (1.63, 2.25)</td>
<td>2.03 (1.84, 2.25)</td>
<td>2.12 (1.85, 2.49)</td>
<td>2.29 (2.10, 2.50)</td>
<td>2.18 (2.00, 2.37)</td>
</tr>
</tbody>
</table>

*OR adjusted for age at diagnosis.

Results

• Characteristics of the validation cohort are detailed in Table 1.

• For each ancestry, MA-385 improved on clinical factors and outperformed MA-149 (Figure 2).

• In non-Europeans, MA-385 was a better BC risk predictor (OR, 1.47; 95% CI, 1.43–1.52) than MA-149 (OR, 1.40; 95% CI, 1.35–1.45).

• Associations were strongest in Ashkenazi Jewish and Hispanic women.

• MA-385 identified more women at >2-fold higher BC risk than MA-149 (6.3% vs 2.0%, respectively).

• For each ancestry, MA-385 improved on clinical factors and outperformed MA-149.

Conclusions

• MA-385 was well-calibrated, improved upon clinical factors, and outperformed existing PRS in all tested ancestries.

• Incorporation of MA-385 into risk assessment could improve the early detection and prevention of BC.

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References: