Using Genomics to Understand an Individual’s Risk for Common Diseases

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For any common disease, we now know hundreds of common genetic variants across the genome which each individually have a small effect on risk.

Information from these can be combined to give a “polygenic risk score” – a numerical summary of an individual’s genetic predisposition to that disease.

Across a population, there will be a distribution of these risk scores. Individuals with high values of the scores can be at significant (and clinically actionable) increased risk.
Coronary Artery Disease (men only)

Genetic risk:
- Top 3% risk
- 40–60% risk
- Top 3% protected

Percentage of the population diagnosed vs. Age (years)
Prostate Cancer (men only)

Genetic risk:
- Top 3% risk
- 40–60% risk
- Top 3% protected

Percentage of the population diagnosed with prostate cancer over age.

- Red line: Top 3% risk
- Blue line: 40–60% risk
- Green line: Top 3% protected
PRS and Non-Genetic Risk Factors

PRS performance stratified by QRisk risk group (ages 40-55)
PRS and family history

PRS performance stratified by family history (1st degree relatives)

- **No family history of heart attack**
- **Family history of heart attack**

**Genetic risk:**
- Top 5% risk
- 40−60% risk
- Top 5% protected

**Percentage of the population diagnosed with CAD**

**Years since assessment**
QRISK alone or with PRS

Consider 13M UK adults aged 40-55, using QRISK > 10%  

<table>
<thead>
<tr>
<th></th>
<th>QRISK only</th>
<th>QRISK + PRS</th>
<th>CAD Diagnoses in group at 8yrs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Above Absolute risk</td>
<td>1,040K</td>
<td>1,326K</td>
<td>798K</td>
</tr>
<tr>
<td>for statins</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Below absolute risk</td>
<td>11,960K</td>
<td>11,674K</td>
<td>528K</td>
</tr>
<tr>
<td>for statins</td>
<td></td>
<td></td>
<td>14.7K</td>
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<td></td>
<td>11,432K</td>
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</tbody>
</table>
Non-European Ancestries are challenging

Coronary artery disease (men only)

European descent  Non-European descent

Genetic risk:

- Top 3% risk
- 40–60% risk
- Top 3% protected

Coronary artery disease (men only)
Non-European Ancestries are challenging

Breast cancer (women only)

European descent

Non-European descent

Genetic risk:
- Top 3% risk
- 40–60% risk
- Top 3% protected

Breast cancer (women only)
GENOMICS plc