Post-mortem Genetic and Polygenic Profiling: Informing Risk to Living Relatives

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Utility of Genetics in the Dead

Causes of Death
Molecular Autopsy for Sudden Unexpected Death
DNA Confirms Here Lieth Richard III,
Undertaker Ton Peeling Lies
Utility of “Molecular Autopsy” to the Living

Medical examiner says job is about both life and death

What about genetic risk for early “normal” death?

* e.g. Coronary artery disease related death before 50 years of age

<table>
<thead>
<tr>
<th>Early Heart Attack Heritability</th>
</tr>
</thead>
<tbody>
<tr>
<td>Table 12-1. OR for Combinations of Parental Heart Attack History</td>
</tr>
<tr>
<td>Parental Heart Attack History</td>
</tr>
<tr>
<td>No family history</td>
</tr>
<tr>
<td>One parent with heart attack at ≥50 y of age</td>
</tr>
<tr>
<td>One parent with heart attack at &lt;50 y of age</td>
</tr>
<tr>
<td>Both parents with heart attack at ≥50 y of age</td>
</tr>
<tr>
<td>Both parents with heart attack, 1 at ≤50 y of age</td>
</tr>
<tr>
<td>Both parents with heart attack, both at &lt;50 y of age</td>
</tr>
</tbody>
</table>

*OR indicates odds ratio; CI, confidence interval. Data derived from Chen et al.*
Inheritance of Genetic Risk

- **Monogenic Risk**: <10% of genetic risk
  - 20% known

- **Polygenic Risk**: >90% of genetic risk

Polygenic Risk Score

**ATTENTION!**
Genetic Risk is Unmodifiable but Probabilistic

PRSs Identify Groups of People at Elevated risk for CAD

Polygenic Risk is Actionable

Polygenic Molecular Autopsy

Early Heart Attack
Polygenic risk in deceased
Clarify risk in the living
The Rise of Personal Genetic Testing Services

~17 million tests sold
Polygenic risk possible but unavailable

MyGeneRank

Current Requirements
- iOS Device
- 23andMe Data

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