Economic evaluation of population-based preconception carrier screening for genetic diseases in Australia

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What is known:

Autosomal recessive

Carrier parent
Carrier parent

Unaffected child
Carrier child
Carrier child
Affected child

GenIMPACT | Faculty of Business and Economics | Department of Economics
What have been done:

- Targeted carrier screening
  - Ashkenazi Jewish ancestry (Tay-Sachs), African (Sickle cell anemia and European ancestries (Cystic fibrosis)
  - Self pay A$720 per person (444 euro)
  - Inequity
Preconception carrier screening

**Aim**
Develop an economic model to evaluate the health and economic impacts of introducing expanded preconception carrier screening in Australia

**Method:**
- Modelling approach: individual level (microsimulation) model
- Base population: 2021 Australian Bureau of Statistics Census
- Disease list: 300 genes (commercially available)
- Parameters: Literature search and expert advice:
  - incidence, costs (direct and indirect)
  - life expectancy, onset of disease
  - quality-adjusted life-years (QALY),
  - reproductive choice e.g.. IVF
Preconception carrier screening

**Perspective:** Healthcare and societal

**Outcomes:**
Cost-effectiveness per (a) life-year gain (b) Quality-adjusted life years (QALY)
Affected births and lifetime costs averted

**Modelling Uncertainty:**
One-way sensitivity
Probability sensitivity analysis (Bootstrapping of estimates)
Schematic overview of the population-wide preconception carrier screening for genetic disease

Figure 1: Schematic flow chart of preconception carrier screening

- Preconception carrier screening (PCS) offered
  - Accept
    - NO
      - Unknown at-risk pregnancy
      - PCS offered to prospective parents
        - Accept
          - YES
            - Carrier screening (see below)
          - NO
            - Unaffected baby
            - Affected baby
Schematic overview of the population-wide preconception carrier screening for genetic disease

- **Reproductive options**
  - IVF and preimplantation genetic diagnosis; or IVF using donated gametes.
  - Decision to not have children
  - Natural conception

- Not pregnant
- Pregnant
  - Unaffected baby
  - Prenatal diagnosis offered (see Figure 1)
- Pregnant
- Not pregnant
Schematic overview of the population-wide preconception carrier screening for genetic disease

Carrier screening

- Low-risk
  - No further testing
    - Unaffected baby
- Carrier
  - Pregnant?
    - YES
      - Reproductive options (see Figure 2)
    - NO
  - Identified affected foetus
- Prenatal diagnosis offered
  - Accept
    - YES
      - Affected baby
    - NO
      - Unaffected baby
  - Termination of pregnancy
## Parameters

<table>
<thead>
<tr>
<th>Model Parameters</th>
<th>Description</th>
<th>Value- Base case</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Base population</td>
<td>Births in 2016</td>
<td>212,200</td>
<td>Australian Census, 2016</td>
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<tr>
<td>Life expectancy,</td>
<td>Life expectancy, years</td>
<td></td>
<td>Australian Life tables, 2019</td>
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<tr>
<td>years</td>
<td></td>
<td></td>
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<tr>
<td>Health-related quality of life</td>
<td>Australian population</td>
<td></td>
<td>McCaffrey N et al, 2016</td>
</tr>
<tr>
<td>Carrier screening</td>
<td>Proportion of couples who take-up PCS</td>
<td>0.5</td>
<td>Loannou L. et al, 2013; van Steijvoort E et al, 2020</td>
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<tr>
<td></td>
<td>Proportion of couples who become pregnant before PCS</td>
<td>0.69</td>
<td>Archibald A et al, 2018</td>
</tr>
<tr>
<td>Intervention</td>
<td>At-risk couples using PGT; donated gametes, natural conception; gave up having children</td>
<td>0.59 (0.53-0.65); 0.07 (0.05-0.12); 0.2 (0.16-0.26); 0.14 (0.04-0.18)</td>
<td>Azimi M, et al, 2016; Snowdon C et al, 1997; van Steijvoort E et al, 2020; Taber K et al, 2019</td>
</tr>
<tr>
<td></td>
<td>at-risk couples who undertake prenatal diagnostic testing</td>
<td>0.9±0.25</td>
<td>Archibald A et al, 2018</td>
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<tr>
<td>Discounting</td>
<td></td>
<td>0.05</td>
<td>Australian Institute Health and Welfare</td>
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</tbody>
</table>
## Results

<table>
<thead>
<tr>
<th></th>
<th>Cost up-front carrier screening &amp; downstream, A$M</th>
<th>Total disease treatment costs, A$M (95%CI)</th>
<th>Total QALY '000 (95%CI)</th>
<th>ICER</th>
</tr>
</thead>
<tbody>
<tr>
<td>No population screening</td>
<td></td>
<td></td>
<td>62.0 (51.0-71.9)</td>
<td></td>
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<tr>
<td>Three genes screening</td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td>Expanded carrier screening</td>
<td>75.1</td>
<td>1132 (959.4-1354)</td>
<td>60.6 (50.1-72.7)</td>
<td></td>
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<td></td>
<td>190.7</td>
<td>978.9 (874.3-1229.3)</td>
<td>68.0 (54.8-83.9)</td>
<td>Dominant (higher QALY, lower costs)</td>
</tr>
</tbody>
</table>

Abbreviation: ICER: Incremental cost-effectiveness ratio; QALY: Quality adjusted life-years; 3 genes: cystic fibrosis, X-linked and spinal muscular atrophy; A$M: Australian dollar in million; 95%CI 95% confidence interval
Based and projected cumulative number of children with recessive disorders, 2016, 2021-2061
Based and projected cumulative lifetime healthcare costs, 2016, 2021-2061

Cost '000 (AUD)

- No population screening
- Three condition screening
- Expanded PCS

Total disease treatment cost (A$M)
Sensitivity analysis – Cost Impact varying uptake rate for expanded screening

Cost (AUD' 000)

- Compared to no screening (ASM)
- Compared to three condition screen (A$M)

Scenarios:

- Scenario 1: 25% uptake
- Scenario 2: 34% uptake
- Scenario 3: 50% uptake
- Scenario 4: 69% uptake
- Scenario 5: 75% uptake
- Scenario 6: 100% uptake
### Sensitivity analysis- varying elective termination of affected pregnancy

<table>
<thead>
<tr>
<th></th>
<th>Total investment A$M</th>
<th>Total disease treatment costs A$M</th>
<th>Total QALY, 000</th>
<th>ICER with expanded PCS (A$)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>No population screen</strong></td>
<td>-</td>
<td>1,460.10</td>
<td>62.0 (51.0 – 71.9)</td>
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<td></td>
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<td>(1,181.1 – 1,736.4)</td>
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<tr>
<td>Expanded PCS (10%)</td>
<td>189.3</td>
<td>1,271.10</td>
<td>76.7 (63.1 – 92.4)</td>
<td>A$5,371 per QALY</td>
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<td></td>
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<td>(1,061.6 – 1,510.9)</td>
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<tr>
<td>Expanded PCS (90%)</td>
<td>191.2</td>
<td>760.8 (638.8 – 908.6)</td>
<td>59.3 (48.5 – 71.7)</td>
<td>Lower QALY, Lower cost</td>
</tr>
<tr>
<td>Three genes screening</td>
<td>75.1</td>
<td>1,132.50</td>
<td>60.6 (50.1 – 72.7)</td>
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<tr>
<td></td>
<td></td>
<td>(959.4 – 1,354.0)</td>
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Abbreviation: ICER: Incremental cost-effectiveness ratio; QALY: Quality adjusted life-years; three genes: Cystic fibrosis, X-linked and spinal muscular atrophy; A$M: Australian dollar in million; 95%CI 95% confidence interval
Limitation

1. Assumptions on key parameters
2. Both members of the couple were tested simultaneously
3. QALY
4. Finally, the model assumed perfect sensitivity and specificity for screened diseases
Conclusion

- Population carrier screening
  = cost-saving compared with no population screening
  = cost-effective compared with three-condition screening

- Annual public investment of A$190.7 m for expanded RCS (0.1% of health budget) public healthcare cost A$632.0 million (= A$3.40 saving for A$1 invested)
THANK YOU

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