Cystic Fibrosis Carrier Screening

A/Prof David Amor, Director, Victorian Clinical Genetics Services and Dr Liane Ioannou, Honorary Research Officer, Murdoch Childrens Research Institute
History of genetic screening in Australia

Until now, the single gene conditions for which pre-pregnancy genetic carrier screening is undertaken are:

- Haemoglobinopathies (thalassaemia)
- Autosomal recessive diseases more common in the Ashkenazi Jewish community including Tay-Sachs disease
- Cystic fibrosis
Population carrier screening for CF

- Cystic fibrosis (CF) is the most common inherited life shortening condition affecting Australian children, with a carrier frequency of 1 in 25.

- Most children with CF (94%) have no family history of the condition.

- The Human Genetics Society of Australasia (2010) recommends that couples planning or in the early stages of pregnancy be made aware of the availability of CF carrier screening.
Program Development

- **2005**: Working group
- **2006**: Pre-pilot
- **2007**: Pilot: private practice
- **2013**: State-wide: shared care
  - General practice
  - Expanded program:
    - more mutations
    - more conditions
How the CF screening program worked

- Pre-pregnancy or prenatal screening offered by obstetrician or GP
- Pre-test information
  - Obstetrician/GP
  - Brochure in test pack
  - Website
- Testing by cheek brush
  - Self-administered
  - 12 CFTR mutations
- Posted to laboratory
- Cost: $200 per test
Individual/couple offered CF carrier screening

Accept

Cheek brush sample provided

Lab performs CF carrier test

Carrier result

Result to referring practitioner & GC

Low risk result

Result to referring practitioner

Genetic counselling offered
The first 7 years experience (MJA 2014)

- Number screened: 10,489
  - Approx 90% females
- Number carriers: 320 (3.05%; 1 in 33)
  - 83% deltaF508 mutation
- Number carrier couples: 15
  - 11 pregnant at time of screening
    - 9 chose prenatal diagnosis
    - 3 affected pregnancies
    - All carrier couples chose prenatal diagnosis or preimplantation genetic diagnosis in subsequent pregnancies
- 1 false negative result (missed case)
  - parents screened as low risk – child with CF due to paternal uniparental disomy of chromosome 7
The ‘long tail’ of recessive genetic disease
VCGS approach

VCGS Reproductive screen
- CF
- SMA
- Fragile X

These disorders are
- Common
- Severe
- Tests relatively sensitive and specific
- Mature technology

Cost to patient AU$385
Diseases screened

**Cystic fibrosis**
CF is an inherited condition affecting breathing and digestion. CF causes thick mucus which traps bacteria, resulting in recurrent infections that damage the lungs. Until recently, many children with CF died in early childhood but now many live to be 30, 40 or more. There is no cure for CF but better treatments are under research and development.

**Fragile X syndrome**
FXS is the most common cause of inherited intellectual disability. People with FXS can have developmental delay, learning difficulties, anxiety, autism and epilepsy. The features of FXS vary from mild to severe with males more likely to be severely affected than females. There is no cure for FXS although some interventions can improve outcomes for people with FXS. Some females who are carriers of FXS may have early menopause.

**Spinal muscular atrophy**
SMA is a condition that affects nerves in the spinal cord and causes muscles to get weaker. There are four types of SMA. SMA type 1 is the most severe. Babies with SMA type 1 have weak muscles from birth and usually do not live past 2 years of age. SMA types 2 and 3 progress more slowly than type 1. There is no cure for SMA, however there are treatments and interventions available aimed at managing symptoms and improving quality of life.
What is the chance that I could be a carrier?

<table>
<thead>
<tr>
<th>Condition</th>
<th>Number of People with the Condition</th>
<th>Number of People Who Are Carriers of the Condition</th>
</tr>
</thead>
<tbody>
<tr>
<td>CF</td>
<td>1 in 2500</td>
<td>1 in 25</td>
</tr>
<tr>
<td>FXS</td>
<td>1 in 4000</td>
<td>1 in 150</td>
</tr>
<tr>
<td>SMA</td>
<td>1 in 6000 – 1 in 10,000</td>
<td>1 in 40</td>
</tr>
</tbody>
</table>
The future

- We are all carriers of 5-10 autosomal recessive mutations
- Theoretically it should be possible to screen all couples prior to pregnancy to identify these mutations
- Offer prenatal diagnosis/PGD to couples who both carry a mutation in the same gene

- Current obstacles =
  - Cost
  - Interpretation
Acknowledgements

Current CF carrier screening team
• Desiree du Sart
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• Kate Scarff

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carrier testing for Cystic Fibrosis
Research Objective

To explore the attitudes and outcomes of population-based CF carrier screening through the evaluation of the VCGS CF carrier screening program
Research Aims

- To identify barriers and facilitators to population-based carrier screening for cystic fibrosis in Australia.
- This was achieved by ascertaining the views and experiences of individuals who:
  1. **Accepted** CF carrier screening (including carriers, non-carriers and carrier couples)
  2. **Declined** CF carrier screening
  3. **Not offered** CF carrier screening (public sector)
Methodology

• Questionnaire-based studies exploring:
  1. Demographics
  2. Knowledge of CF and screening
  3. Factors Influencing the decision to have screening
  4. Attitude towards carrier screening for CF
  5. Outcomes of screening (screened only)
## 1. Demographics

<table>
<thead>
<tr>
<th>Demographic</th>
<th>Categories</th>
<th>No. of Participants (%)</th>
<th>Significance ($\chi^2$)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Offered n=166</td>
<td>Not Offered n=101</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Accepted</td>
<td>Declined</td>
</tr>
<tr>
<td>Gender</td>
<td>Male</td>
<td>3 (2.7)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>109 (97.3)</td>
<td>54 (100.0)</td>
</tr>
<tr>
<td>Age (in years)</td>
<td>&lt;24</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td></td>
<td>25-29</td>
<td>9 (8.2)</td>
<td>5 (9.3)</td>
</tr>
<tr>
<td></td>
<td>30-34</td>
<td>32 (29.1)</td>
<td>29 (53.7)</td>
</tr>
<tr>
<td></td>
<td>35-39</td>
<td>54 (49.1)</td>
<td>19 (35.2)</td>
</tr>
<tr>
<td></td>
<td>40+</td>
<td>14 (12.7)</td>
<td>1 (1.9)</td>
</tr>
<tr>
<td>Highest completed level of education</td>
<td>Secondary school</td>
<td>10 (9.3)</td>
<td>3 (5.7)</td>
</tr>
<tr>
<td></td>
<td>Trade/Apprenticeship/College</td>
<td>20 (18.7)</td>
<td>9 (16.7)</td>
</tr>
<tr>
<td></td>
<td>University degree</td>
<td>75 (70.1)</td>
<td>41 (75.9)</td>
</tr>
<tr>
<td></td>
<td>Other</td>
<td>2 (1.9)</td>
<td>1 (1.9)</td>
</tr>
<tr>
<td>Household Income (in AUD $1000s)</td>
<td>20-40</td>
<td>3 (2.9)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td></td>
<td>41-60</td>
<td>7 (6.7)</td>
<td>1 (1.9)</td>
</tr>
<tr>
<td></td>
<td>61-80</td>
<td>10 (9.6)</td>
<td>4 (7.5)</td>
</tr>
<tr>
<td></td>
<td>81-100</td>
<td>14 (13.5)</td>
<td>8 (15.1)</td>
</tr>
<tr>
<td></td>
<td>&gt;100</td>
<td>70 (67.3)</td>
<td>40 (75.5)</td>
</tr>
<tr>
<td>Ethnicity</td>
<td>Australia</td>
<td>62 (56.9)</td>
<td>26 (50.0)</td>
</tr>
<tr>
<td></td>
<td>America</td>
<td>1 (0.6)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td></td>
<td>Europe</td>
<td>41 (37.6)</td>
<td>23 (44.2)</td>
</tr>
<tr>
<td></td>
<td>Asian</td>
<td>4 (3.7)</td>
<td>1 (1.9)</td>
</tr>
<tr>
<td></td>
<td>New Zealand/Islander</td>
<td>1 (1.9)</td>
<td>2 (3.8)</td>
</tr>
<tr>
<td></td>
<td>Africa</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
</tr>
</tbody>
</table>
2. Knowledge

- CF is a life shortening condition (T)
- CF affects more males than females (F)
- CF affects the lungs (T)
- CF is an inherited condition (T)
- A person with CF inherits gene from both parents (T)
- Carriers of CF usually have a family history (F)
- A carrier couple can have a child who does not have CF (T)
- Carriers show signs of the disease (F)
- If a person has one mutation they are a carrier (T)
- One parent is a carrier still a chance of having child with CF (T)
- CF test can identify all CF carriers (F)
- Need to screen for CF carrier status every pregnancy (F)
- Partner determines risk as a couple (T)
- A negative result means risk of being a carrier is greatly reduced (T)
- If no gene change is found they cannot be a carrier (F)
- Need to screen for CF carrier status every pregnancy (F)

![Bar chart showing percentage correct answers for knowledge questions.](chart.png)
3. Factors Influencing Decision

- Doctor's recommendation
- Partner's opinion
- Family history of condition screened for
- Family history of other genetic conditions
- Perceived susceptibility
- TOP

Percentage influenced (%)

- Accepted
- Declined
- Not Offered
4. Attitudes towards screening for CF

- Screening should be offered prior to pregnancy
- Screening for should be made available to those who wish to have it
- Screening should be available in the public health sector as well as the private
- Less than $50 would be a reasonable price to pay
5. Outcomes of screening

Carriers and Non-Carriers

- All carriers correctly recalled their carrier status and their risk of having a child with CF
- 5% of non-carriers were unsure of their carrier status
- 22% incorrectly recalled their residual risk
Carrier Couples

- Couples experienced surprise on learning their result.
- All couples who were pregnant chose to have prenatal diagnosis.
- Two couples who had an affected pregnancy reported feelings of devastation and grief upon receiving their prenatal diagnosis result and terminated the pregnancy.
- All carrier couples were offered free genetic counseling, with only one couple declining the offer.
- As a result of screening couples either had no further children or utilised prenatal diagnosis or preimplantation genetic diagnosis for subsequent pregnancies.
Overall Conclusions

• CF carrier screening should be available
• CF carrier screening should be offered in the public health system
• All the carrier couples changed their reproductive behavior as a result of their carrier status
• Lack of knowledge is a barrier to accepting screening
• Cost potential barrier in the public health system
Future Directions

• Inform and educate potential participants
  – Implementation of program increases baseline knowledge
  – Health professionals

• Equity of Access
  – Public Health system
  – Cost
  – Accessibility
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