

# Population carrier screening for fragile X syndrome

## Attitudes and experiences of women undergoing screening

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# Arguments for population screening for FXS<sup>1</sup>

- Most common known cause of inherited intellectual disability
- Significant impact on people with FXS and their families
- Molecular testing is accurate, rapid and inexpensive
- Options for prevention and interventions available

<sup>1</sup>Hill, M.K., Archibald, A.D., Cohen, J., Metcalfe, S.A. 2010.

# Carrier screening for FXS

- **Reproductive risk for female carriers**
  - 50% risk of passing expanded allele to child
  - Risk of expansion from PM to FM varies
- **Health concerns for PM carriers**
  - Primary ovarian insufficiency (FXPOI)
    - Fertility problems
    - 20% risk of early menopause (before 40 yrs)

# Carrier screening - current recommendations

- **Guidelines<sup>1,2,3</sup>**
    - **Carrier testing for:**
      - Family history of FXS or undiagnosed intellectual disability
      - Reproductive or fertility problems
      - Late onset tremor or cerebellar ataxia of unknown origin
  - **Limitations of family history based approach**
    - Dissemination of genetic risk information in families<sup>4</sup>
    - Relies on diagnosis of affected relative
    - Many people do not have a family history of FXS or related conditions
  - **ACOG recommendations (2010)<sup>5</sup>: offer to any woman who requests FXS carrier testing regardless of family history**
- >>> Is population screening for female carriers an option?**

<sup>1</sup>Sherman et al, 2005; <sup>2</sup>McConkie-Rosell et al, 2005; <sup>3</sup>HGSA, 2003;

<sup>4</sup>van Rijn, 1997, <sup>5</sup>ACOG, 2010

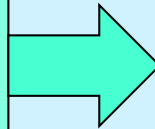
# Population carrier screening for FXS

- **Support for population carrier screening for FXS<sup>1</sup>**
- **Women offered screening may be unprepared for a carrier result <sup>2,3</sup> ( NB No preparation time )**
- **Families support offering carrier screening for FXS<sup>4</sup>**
- **Development of screening programs requires the consideration of:**
  - Community views about screening
  - Practicalities of offering screening

# Our research to date

## 1. Pilot study<sup>1,2</sup>

- Offered FXS carrier screening to non-pregnant women
- Study setting: a sexual and reproductive health clinic

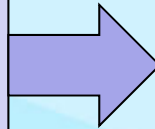


### FINDINGS:

- Interested in screening
- Good knowledge
- Few participants regretted their decision
- Uptake of testing dependent on:
  - reproductive stage of life
  - practicalities of having the test

## 2. Needs assessment<sup>3</sup>

- Explored views of key stakeholders
  - General population
  - Health professionals
  - Families impacted by FXS



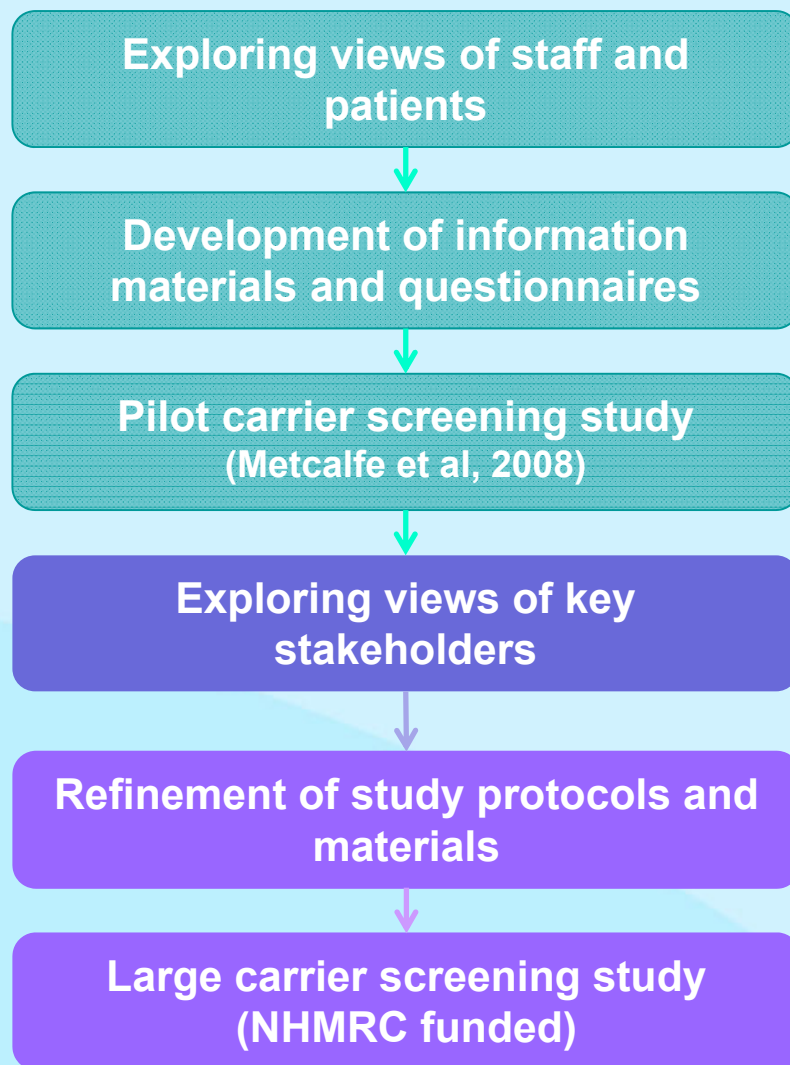
### FINDINGS:

- Lack of awareness about FXS and the implications of genetic screening
- Important to offer all women the *choice* to have screening
- Screening should ideally offered to non-pregnant women
- Screening should be offered in primary healthcare settings
- Women should be supported to make an informed decision

<sup>1</sup>Metcalf et al, 2008; <sup>2</sup>Archibald et al, 2009,

<sup>3</sup>Archibald et al, 2012 – *in press*

# Developing our screening protocol



# Current project

- Carrier screening generally perceived to be acceptable
- Need to support women to make informed decisions
- Need to determine how best to offer screening with impact
- Stages of life at which screening could be offered:

Before pregnancy	Pregnancy
Time for decision-making	Less time for decision-making
More reproductive options	Limited reproductive options
More difficult to access target population	Easy to access target population



# The fragile X syndrome carrier screening study

NHMRC 3yr multi-site attitudinal survey

## Aims:

1. To compare **informed decision-making** by pregnant and non-pregnant women offered carrier screening for FXS
2. To compare **uptake** and **predictors of uptake** in pregnant and non-pregnant women offered carrier screening for FXS
3. To undertake an **economic appraisal** involving: (i) a trial-based cost-effectiveness analysis linking costs with trial outcomes; and (ii) an assessment of the value placed on the information provided using Willingness-To-Pay methods

# Screening offered in primary healthcare settings

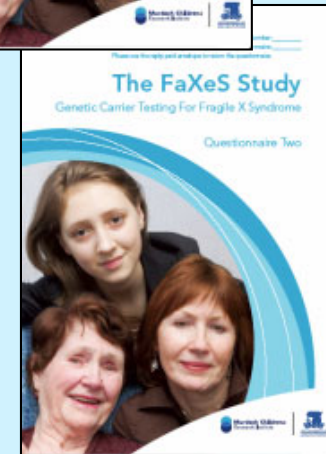
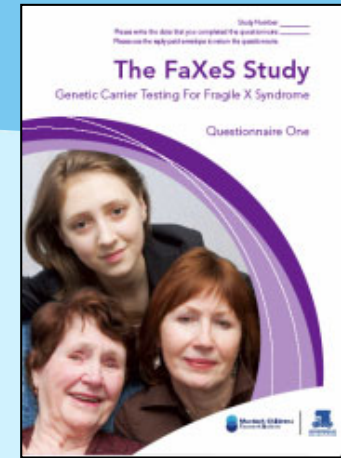
- Victoria and Western Australia
- non-pregnant women in GP clinics
- early pregnancy in obstetric/ultrasound clinics
- take-home information pack, buccal sample, new screening test
- brochure, website (videos), questionnaires

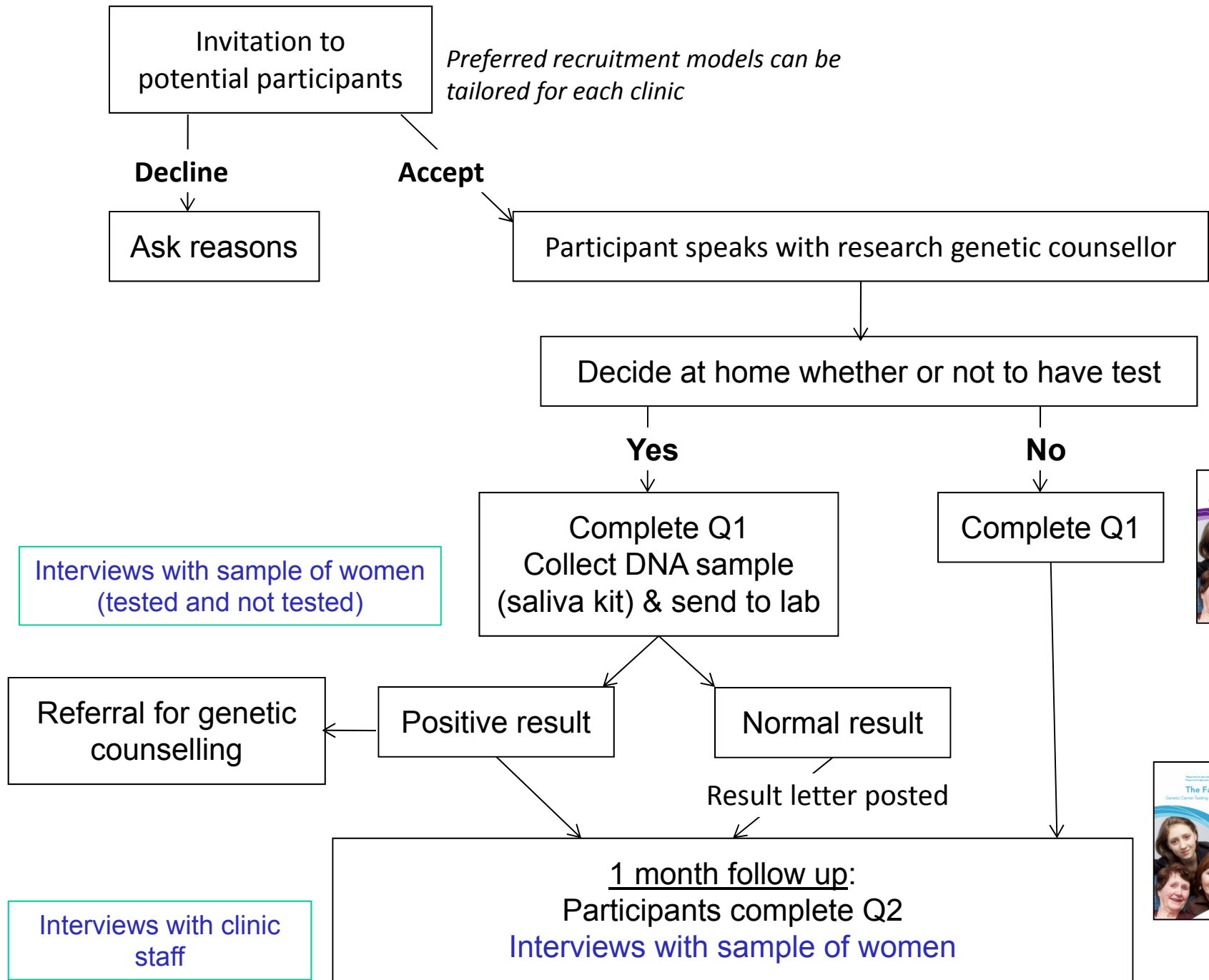
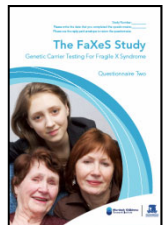
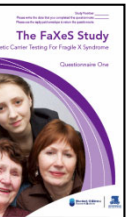
# Providing information

- Healthcare staff upskilled
- Genetic counsellor on site and per telephone
- Brochures - validated
- [www.fragilexscreening.net.au](http://www.fragilexscreening.net.au)
- Time to prepare between info and test
- Follow up interviews

# Data collection

- Questionnaires
  - Socio-demographic
  - Informed decision-making (knowledge, attitudes, deliberation, health beliefs, decision-making process)
  - DASS (depression, anxiety, stress); STAI
  - Willingness-to-pay
  - Decision satisfaction/ regret
- Interviews
  - Informed decision-making (as above)
  - Factors influencing decision
  - Experience of program (women and clinic staff)





Data at end May 2012

**Recruited**  
**n = 803**  
**(690 non-pregnant;**  
**113 pregnant)**

**Awaiting return of**  
**study packs**  
**n = 20**  
**(all pregnant)**

**Made decision**  
**n = 625**  
**(540 non-pregnant;**  
**85 pregnant)**

**Actively withdrawn**  
**n = 52**  
**(49 non-pregnant;**  
**3 pregnant)**

**Q1 never returned**  
**n = 106**  
**(101 non-pregnant;**  
**5 pregnant)**

**Accepted test**  
**n = 523 ~70%**  
**(449 non-pregnant: 70%;**  
**74 pregnant)**

**Not tested**  
**n = 102 actively declined**  
**(91 non-pregnant;**  
**11 pregnant)**

+

**Normal**  
**n = 505**

**Grey Zone**  
**n = 10**

**Premutation**  
**n = 2**

**Awaiting test result**  
**n = 6**

# Considerations for population carrier screening for FXS

- Most women offered screening will have limited/no knowledge or experience of FXS
  - Providing appropriate information is essential
  - Emphasise family history not necessary to be a carrier
- Women may need support in making a decision about screening
  - Providing pre-test genetic counselling is important
- Women may be unprepared for a carrier result
  - Allow appropriate time between info and test
  - Genetic counselling essential if carrier test positive
- Molecular test
  - Traditional PCR  $\pm$  Southern blot
  - New screening test

# Considerations for population carrier screening for FXS

- Offering carrier screening in primary healthcare settings is feasible provided:
  - Appropriate information/training for health professionals
  - Clinic staff are well informed (including practice manager)
  - There is good communication between the coordinators of the screening program and the clinics
- Challenges of carrier screening in pregnancy include:
  - Ensuring prompt test turnaround time
  - Managing anxiety
  - Limited reproductive choices



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## **Needs assessment study**

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## **Pilot study**

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