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Preconception Carrier Testing

Researching the ethical and practical issues

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Introduction

PhD student in Clincal Ethics and Law/medical doctor

- CELS, *Clinical Ethics and Law,* in Southampton &
- Clinical Genetics in Groningen, the Netherlands

What I will discuss today

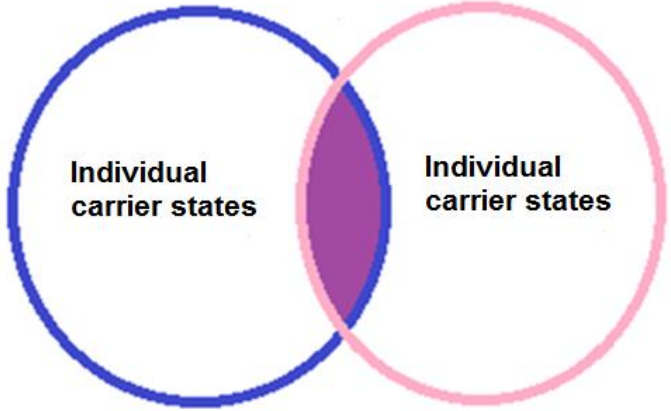
Should we offer genetic testing **before conception** and **to *any* couple planning** a pregnancy?

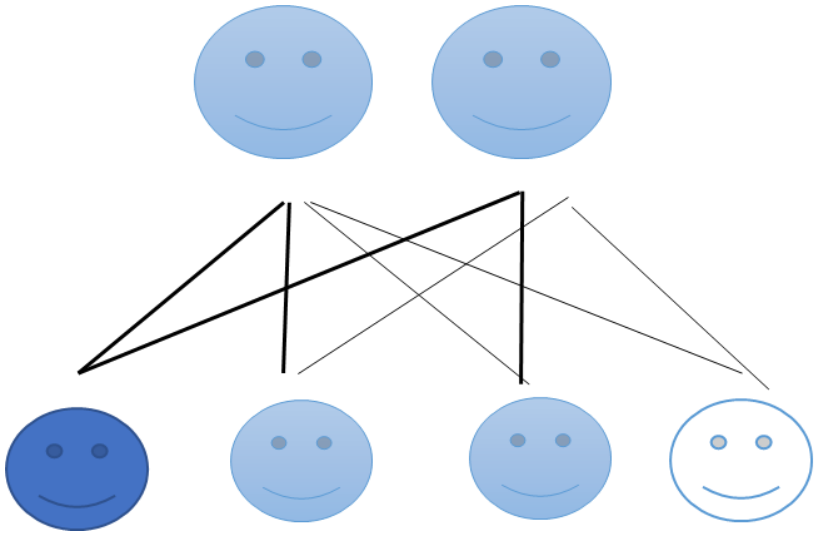
What I will discuss today

- Expanded carrier testing
- Couple-based testing: results as a couple
- Testing prior to pregnancy, rather than during or neonatally
- Implications might differ in general population compared to ART setting
- How to decide what to test for

Autosomal recessive inheritance

Carrier-couple





Risk 1 in 2
Unaffected: Heterozygous carrier

Risk 1 in 4
Unaffected: homozygous with two functional alleles

Risk 1 in 4
Affected: homozygous with two non-functional alleles

Previous approaches to carrier testing

- General population:
  - Most children with AR conditions born unexpectedly
  - Family history
  - Ethnicity (haemoglobinopathies) or founder populations such as Ashkenazi Jews
- Donor gametes
  - in UK based on ethnicity eg. CF

Expanded preconception carrier testing

- Using next generation sequencing to test for carrier status of many (rare) autosomal recessive conditions simultaneously before pregnancy
- Testing **all couples** regardless of prior risk

Risk of being a carrier couple: 0.5-1%

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My PhD: Expanded Preconception Carrier Couple Testing

Researching the ethical and practical issues in two health care settings:

general practice and fertility care

Why carrier testing prior to pregnancy?

- Enable meaningful options after a positive couple result
  - Prenatal diagnosis
  - **IVF&PGD**
  - Refrain from having children
  - Use of gamete donors
  - Adoption

- **Future possibilities:**
  - Earlier treatment during pregnancy or soon after birth

What is a responsible test-offer?

- Several issues to consider:
  - Clinical utility (wide range of conditions/different panel composition/offer during pregnancy)
  - Quality of counselling: facilitating informed choice
  - Equity in access
  - Providing balanced information
  - Psychosocial implications

- Available private offer – ethical concerns

Test-provision: how and by whom?

- As part of routine clinical care
  - Primary care
  - Fertility clinic/ PGD
  - Clinical genetics
  - Obstetrics
- Population screening
  - National screening programme
  - Pre-marital screening
- Private offer

How to design a panel?

- Only very severe conditions
- Early onset
- High carrier frequency
- Only conditions without available treatment
- Clear genotype-phenotype relationship

- Mild/ adult onset conditions
- Adult onset conditions
- As many (rare)conditions as possible
- Low penetrant conditions/ Variable expression
- NGS or targeted panel

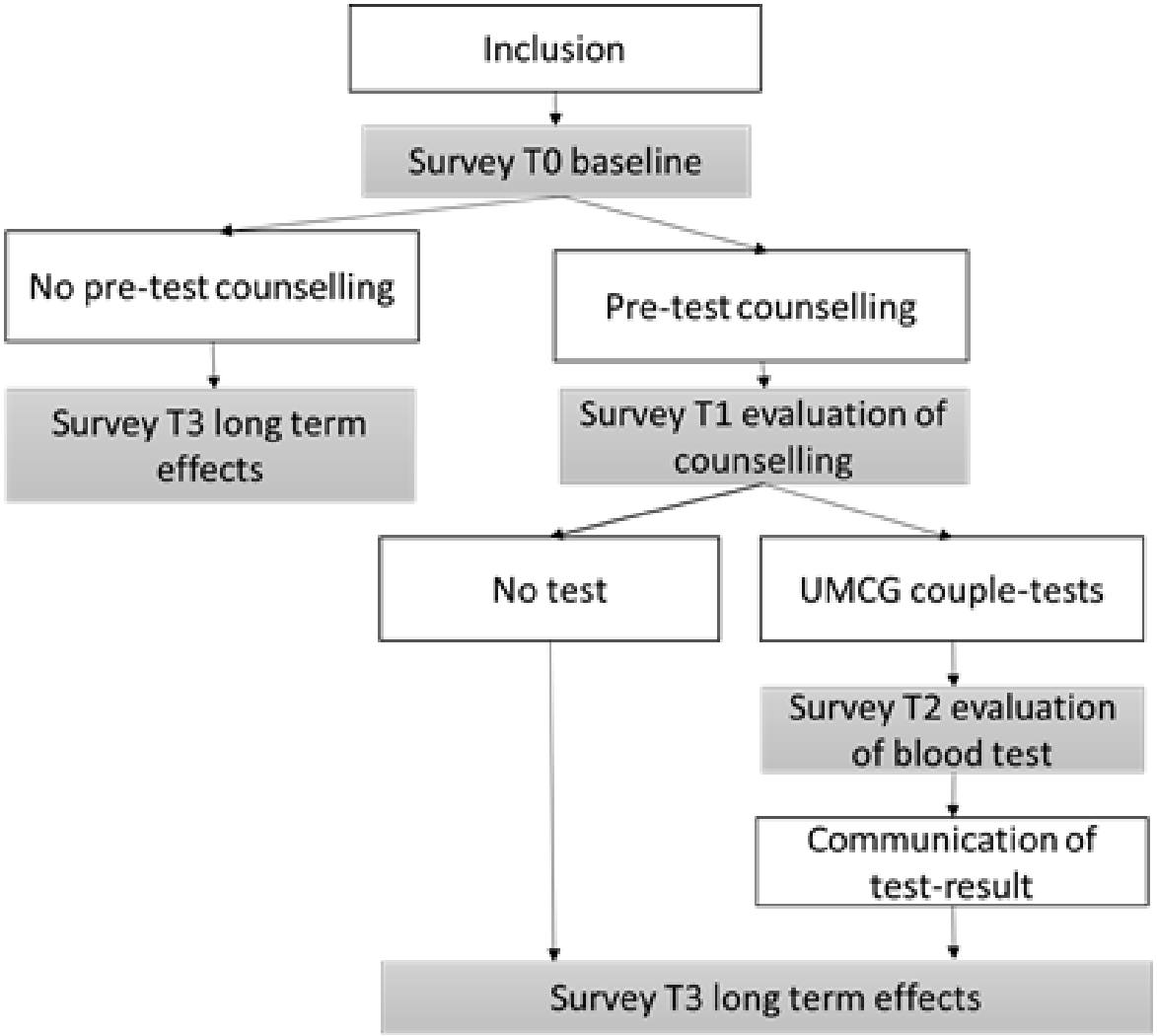
Results so far

- Test developed by: Department of Genetics, UMC Groningen
  - Next generation sequencing: screening 70 genes/50 diseases
  - very serious autosomal recessive conditions
  - 1:150 positive result
  - Carrier **couple** result

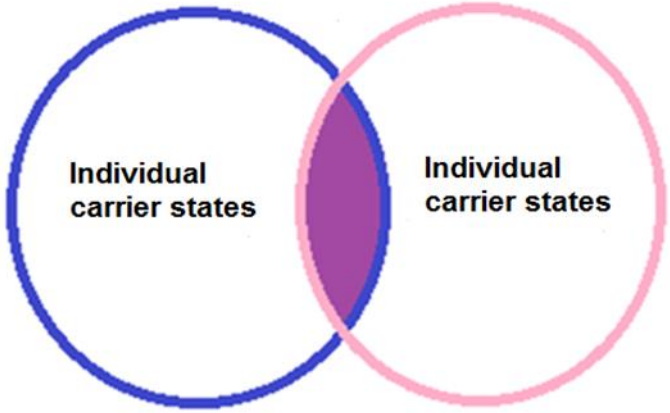
Implementation study in general population

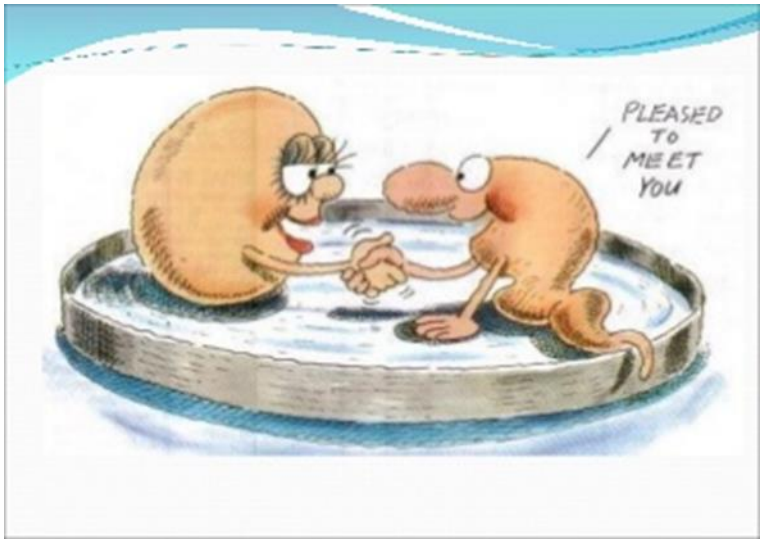
- Test-offer by trained general practitioners
  - Inclusion criteria:
    - Women age 18-40
    - Having a male partner
    - Planning to have children
    - Not pregnant
- Study aims:
  - Uptake
  - Feasibility (GPs' experiences)
  - Psychological impact and informed choice

Study overview



Couple result





Couple-based approach

- Individual results not or of little clinical utility
- Perceived utility of individual results
- Different for couples from general population compared to fertility couples?
- What about donors?
- What about new partner?

UK PhD- carrier testing for those using fertility treatment

- Focus groups with health care professionals
- Interviews with couples using fertility treatment

- *What are their views on and experiences with carrier screening?*
- *What are the ethical and practical implications of couple results?*

Summary

- Clinical practice has not offered pre-conception screening in past because chance so low, do we need to amend in light of NGS?
- UMCG panel restricted to severe conditions but overall carrier couple frequency 0.5-1%
- Couple-based approach raises ethical issues, different for general population compared to couples using fertility treatment
- My PhD looks at the ethical and practical implications of carrier **couple** screening in two different health care settings

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Questions

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