

The emerging new paradigm in pregnancy care. Reproductive Genetic Carrier Screening: a review of 12,000 cases shows high clinical utility.

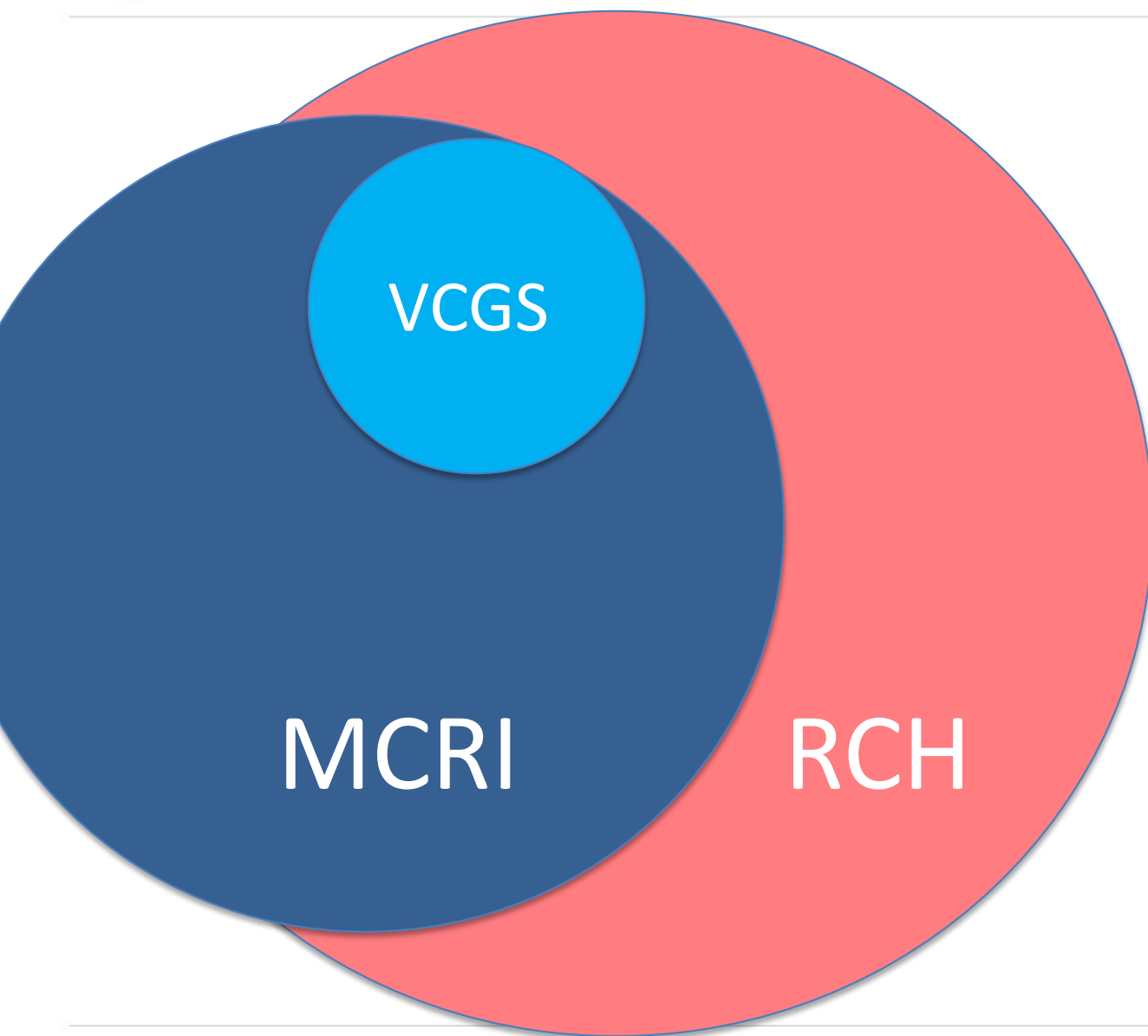
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Senior scientist,

Victorian Clinical Genetics Services

Murdoch Children's Research Institute

Honorary Fellow, Department of Paediatrics, University of Melbourne



Not-for profit subsidiary of Murdoch Children's Research Institute at Royal Children's Hospital

Comprehensive laboratory and clinical genetics service

Key role in research and development, translational research, and policy development

Service provider for public & private Non-invasive Prenatal Testing & carrier screening in New Zealand

Population screening programs

1960-70's

Newborn screening

- Severe childhood onset metabolic conditions
- Interventions can result in normal/greatly improved development outcomes
- >20 conditions screened for in Aus and NZ - government funded programs

1970's

Haemoglobinopathies

- Mediterranean countries. Ad hoc reproductive screening

1990's

Tay-Sachs (1970's internationally)

- School age screening within local Ashkenazi Jewish comm.
- 2003 nation wide program in Israel - 90% reduction in Tay-Sach's

1990-2012

Maternal serum screening/NIPT

- 2nd trimester, CFTs and Non-invasive prenatal testing

2005

Cystic fibrosis

- Population based reproductive screening

2013

Reproductive Genetic Carrier Screening

- Fragile X syndrome and spinal muscular atrophy

2015

Expanded screening

- 100's of autosomal recessive and X-linked genetic conditions



April 2015

*Consensus-based recommendation: Where available, screening of low risk women for carrier status of the more common genetic conditions (e.g. cystic fibrosis, spinal muscular atrophy, fragile X syndrome) **may be offered**.*

“Every baby is at a small risk of having a chromosomal or genetic condition. Prenatal screening for some chromosomal conditions is offered in maternity care to provide the pregnant woman with more information about her unborn baby. All such testing **should be voluntary** and only undertaken when the pregnant woman has been **informed** about the nature of the screening test, the possible result, and the option available to her.”

March 2017

All patients who are considering pregnancy or are already pregnant, regardless of screening strategy and ethnicity, **should be offered** carrier screening for cystic fibrosis and spinal muscular atrophy, as well as a complete blood count and screening for thalassemia's and hemoglobinopathies.

Screening guidelines

ACMG, ACOG,
ECHG, RANZCOG

Disorders

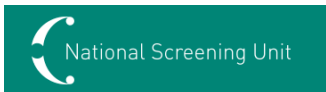
- Approx. 2000 known recessive conditions
- Should be childhood onset
- Severe (cognitive disability, life shortening)
- Clinically actionable (alter pregnancy management)
- Relative high frequency

Test

- Should have high specificity
- Accurate
- Etiology of disorder well defined
- Ideally the ethnic prevalence is known

Support

- Increasing research supports population based screening
- Special interest groups support testing
- Families are strongly advocating to include information about screening prior to pregnancy



Jaydin's story

"I cannot speak highly enough of the benefits of the medical team right from the start."

Jaydin, born in 1998

Read

Soc Sci Med. 2001 Nov;53(9):1149-62.

Goddard M¹, Smith P.

Author information

Abstract

The pursuit of equity of access to health care is a central objective of many health care systems.



NEXT

The real impact of genetic testing on New Zealand families

GPPULSE
THE ROYAL NEW ZEALAND COLLEGE OF GENERAL PRACTITIONERS

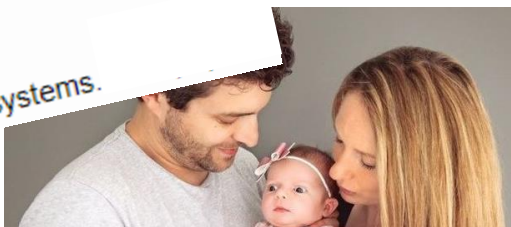
Mother urges GPs to ensure patients have genetic carrier testing choice

The Auckland mother of a child with cystic fibrosis (CF) is urging GPs to ensure their patients (tūroro) receive information about all pre-conception and prenatal tests available to them, now that private genetic carrier screening for single gene disorders, such as CF, is available.



Jobs Motoring Real Estate Obituaries Classifieds ALL

little baby



"We are broken by our new reality"



NEWS



Lobbying for pre-birth & newborn screening



Laboratory

- Cystic fibrosis (CF)
- Spinal muscular atrophy (SMA)
- Fragile X syndrome (FXS)

Clinical

- Pre and post test genetic counselling
- Specialist paediatricians
- Prenatal diagnostic testing
- Education for health professionals



**The Royal Children's
Hospital Melbourne**

Conditions most recommended for screening



prepair

Cystic
fibrosis

CF is a condition affecting breathing and digestion. Requires life long physiotherapy and hospital visits. Shortened life span (30-40).

Spinal
muscular
atrophy

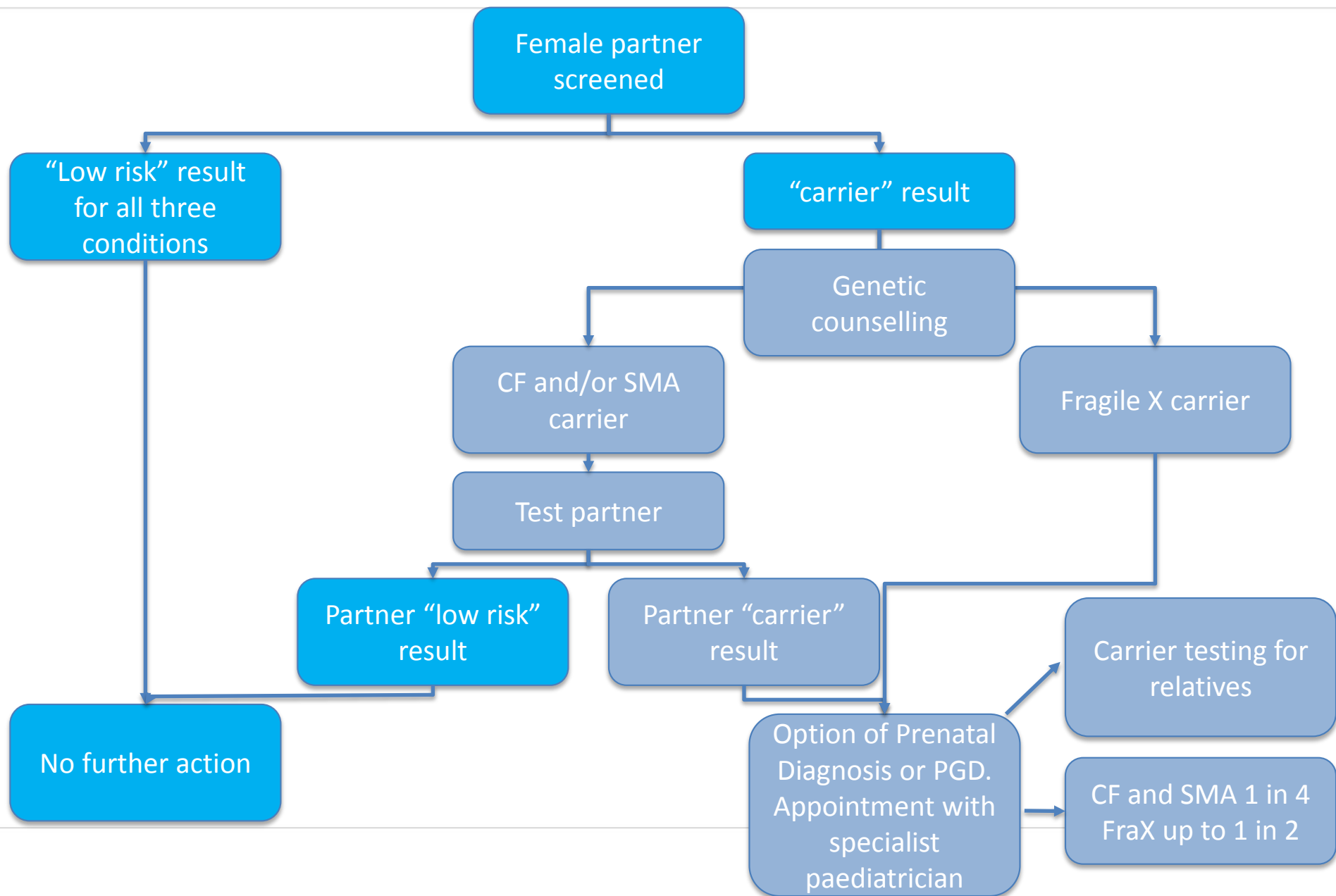
SMA is a condition that affects nerves in the spinal cord and causes muscles to get weaker. SMA type 1 is the most severe. Babies with SMA type 1 usually do not live past 2 years of age.

Fragile X

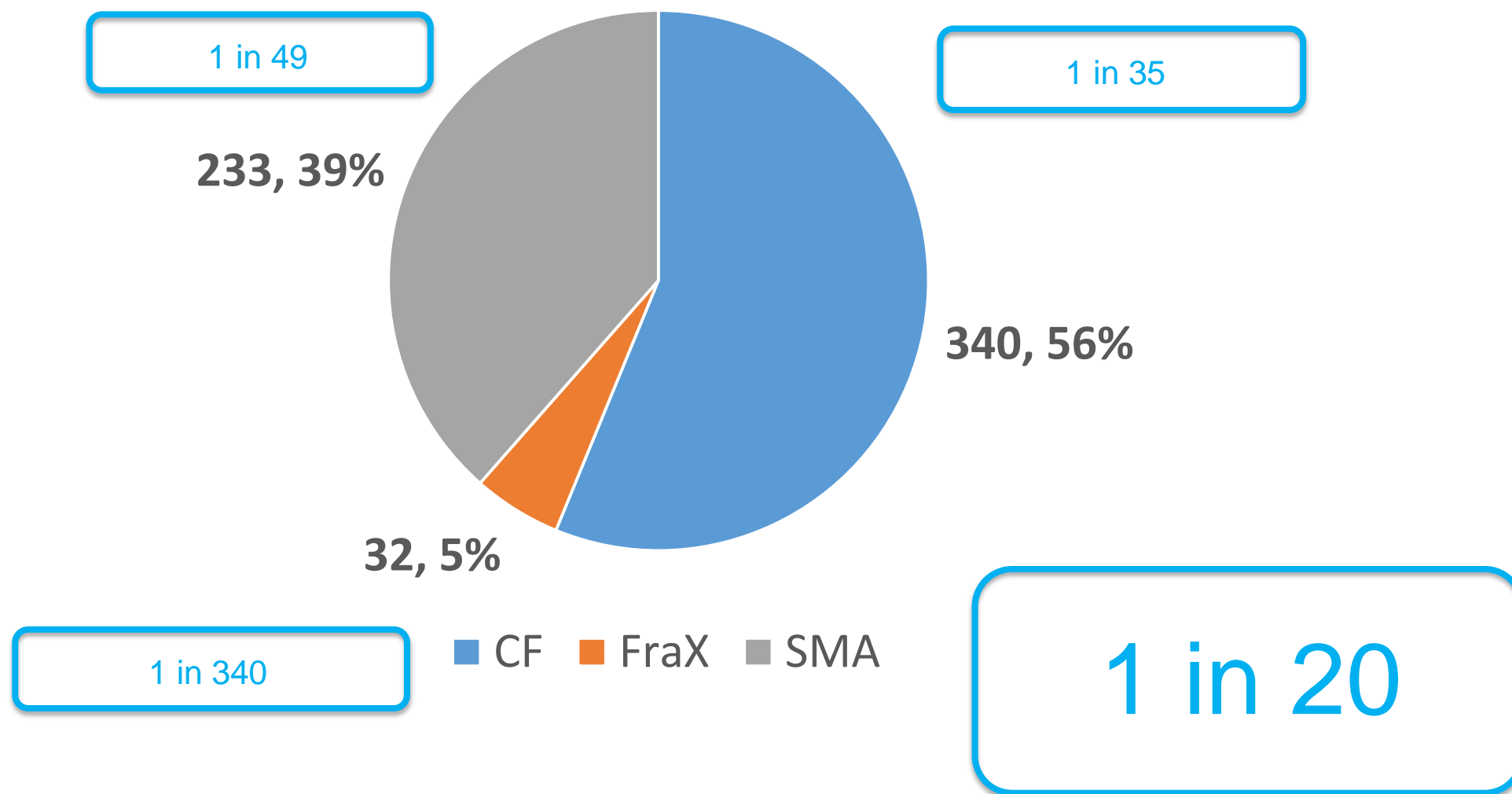
FXS is the most common cause of inherited intellectual disability. People with FXS can have developmental delay, learning difficulties, anxiety, autism and epilepsy. Males are more severely affected than females. Some female carriers have early menopause.

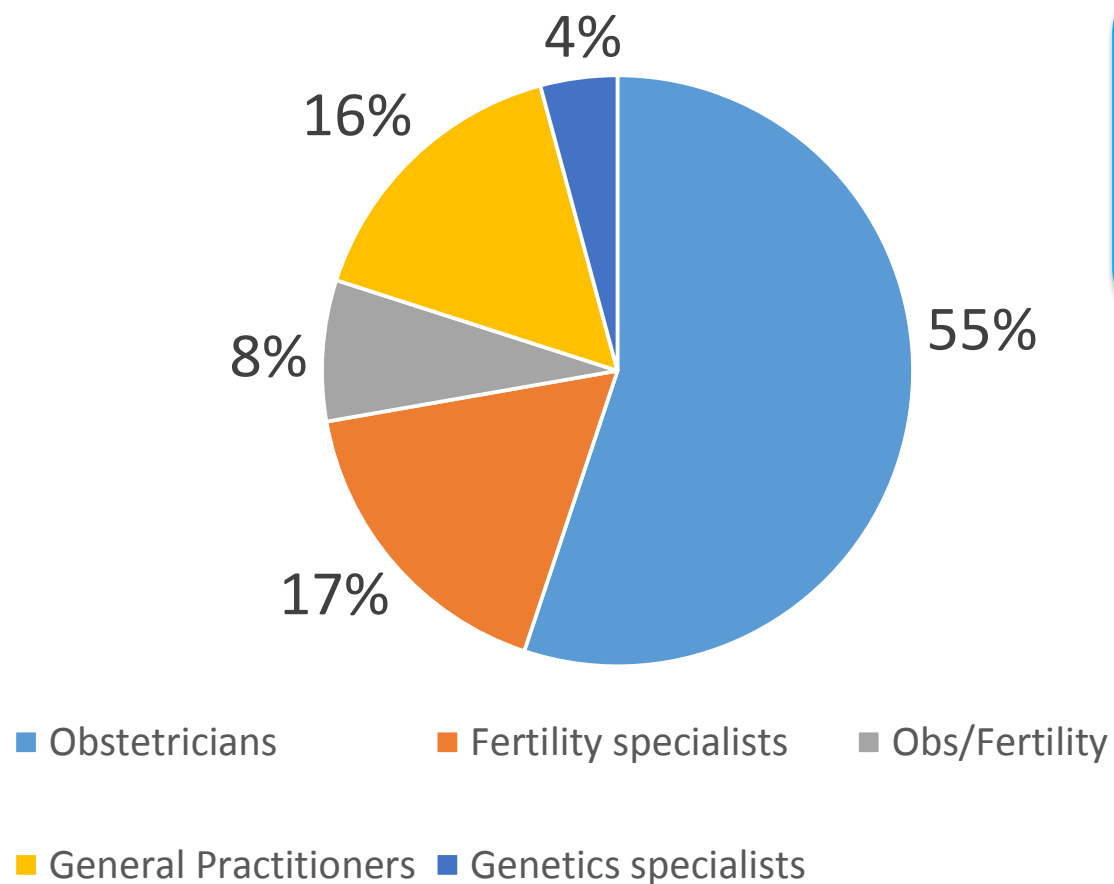
	No. of people who are carriers	No. of people with the condition	Detection rate
CF	1 in 25	1 in 2000-2500	90%
SMA	1 in 40	1 in 6000-10000	95%
FraX	1 in 250-350	1 in 4000	>99%

Many people are carriers of CF, FXS or SMA even though they do not have anybody in their family who has the condition.



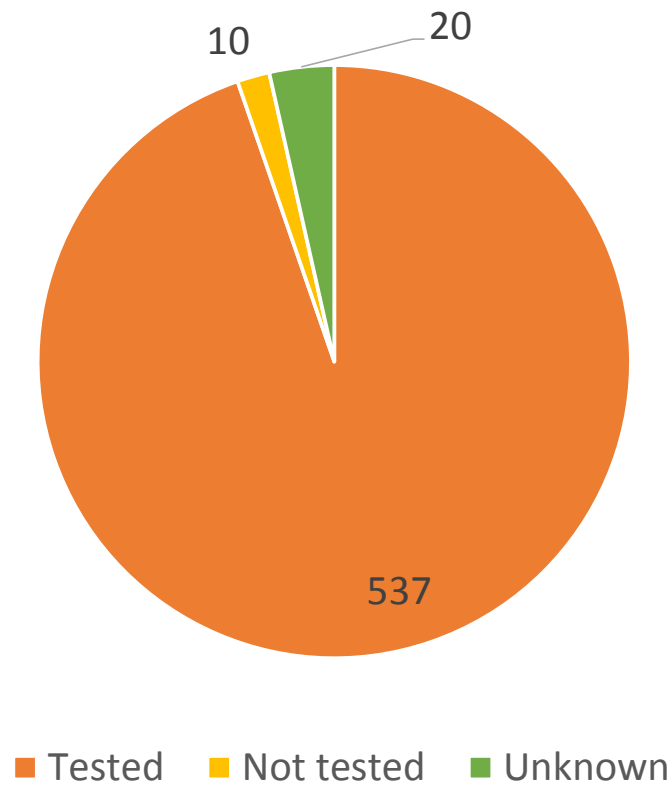
Carriers detected (n=605)





69% pregnant at
time of testing

Proportion of partners tested



CF and SMA partner testing (577)

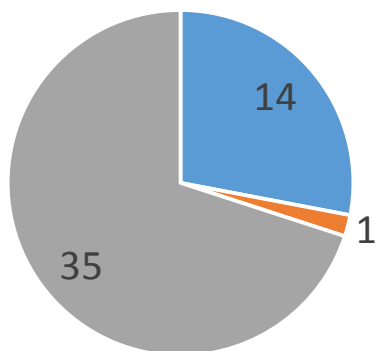
- 537 (94.7%) tested
- 20 (3.5%) unknown
- 10 (1.8%) not tested

Reasons partners not tested:

- No partner
- Partner declined testing
- Ethnicity of partner
- Partner result would not change pregnancy plan

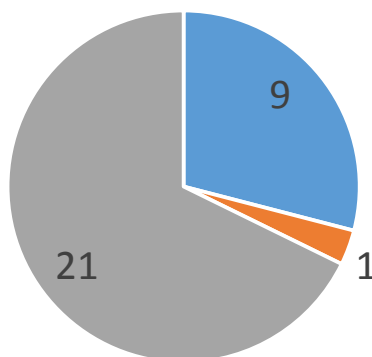
High risk couples & affected pregnancies

High risk couples



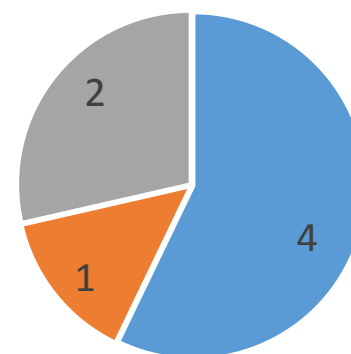
■ CF ■ SMA ■ FraX

Pregnant high risk couples



■ CF ■ SMA ■ FraX

Affected pregnancies

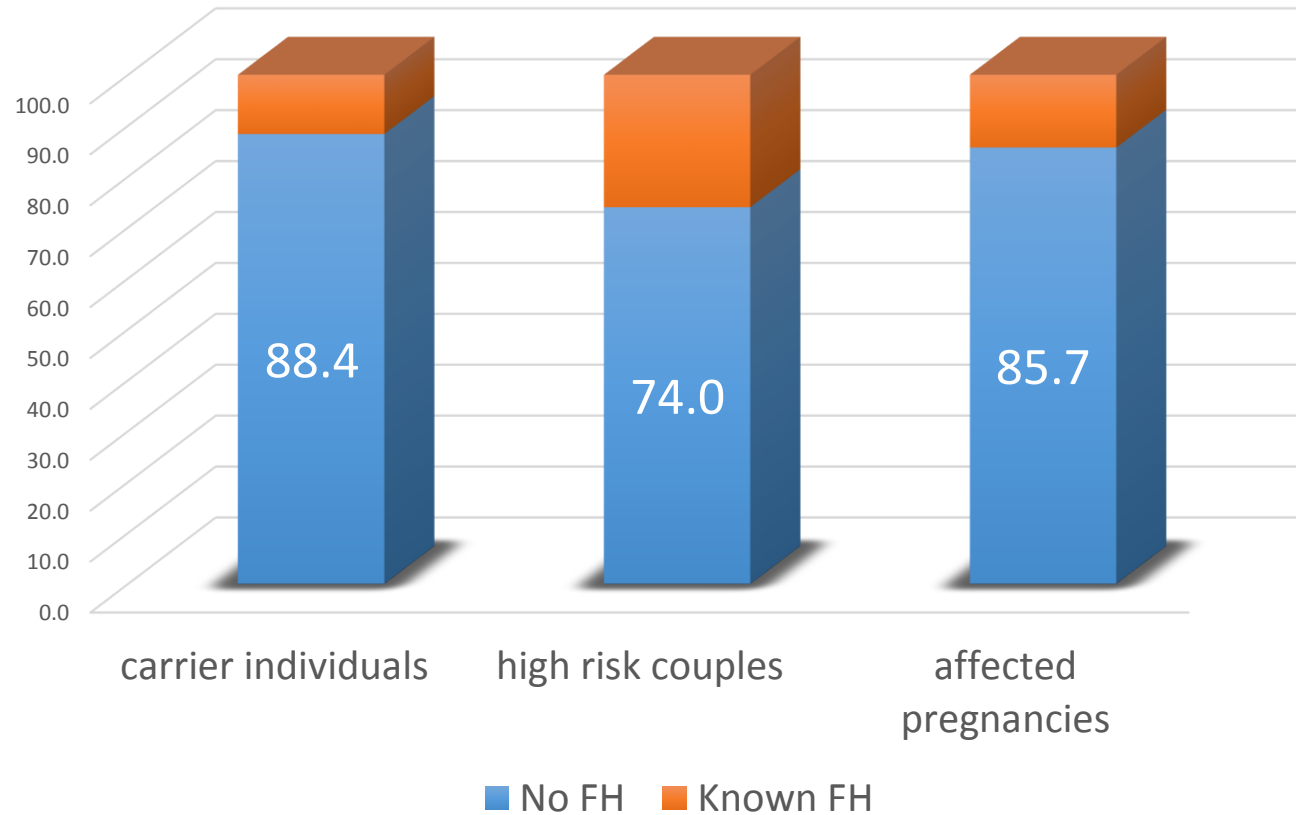


■ CF ■ SMA ■ FraX

1 in 240

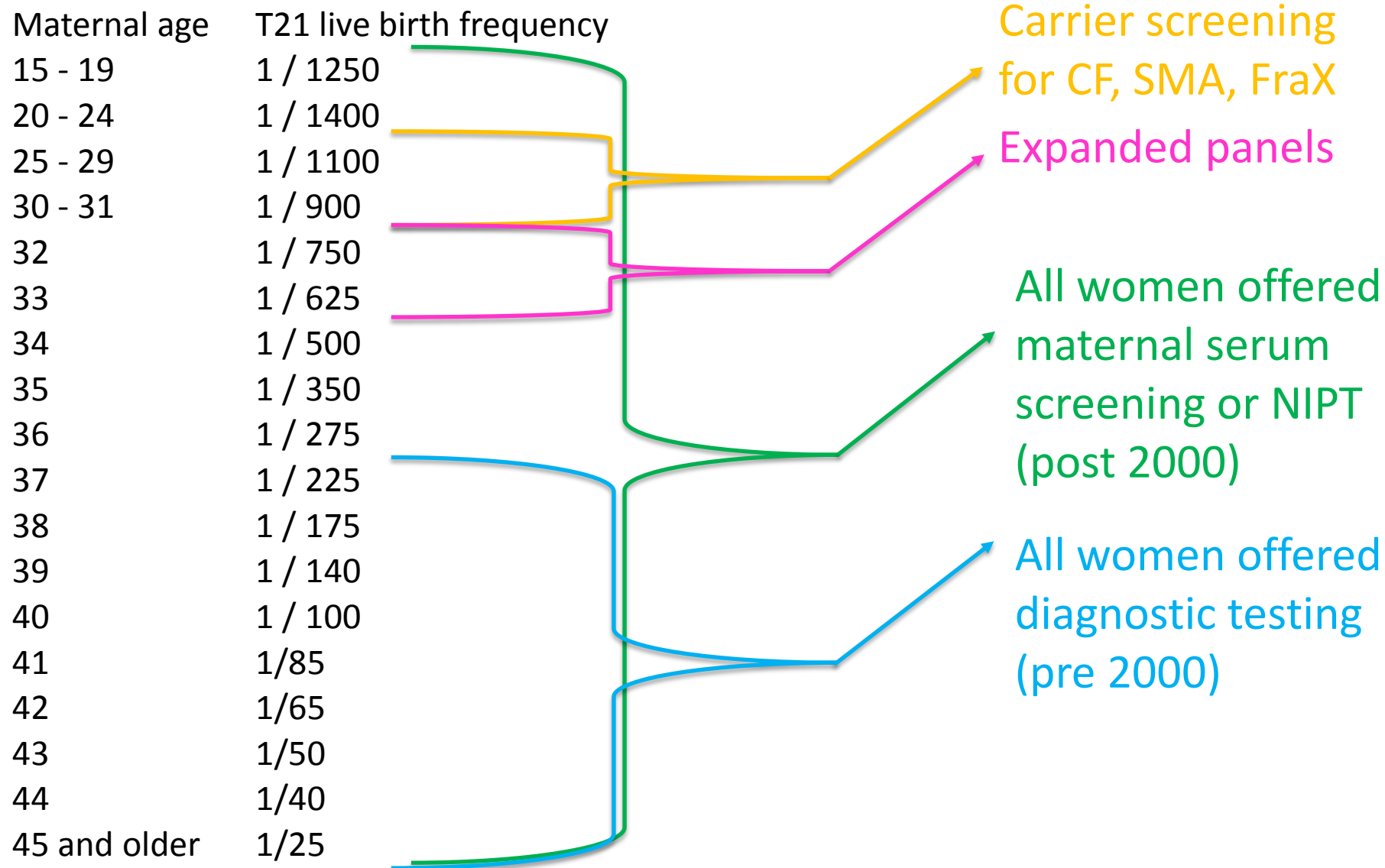
1 in 1000

Prior known family history

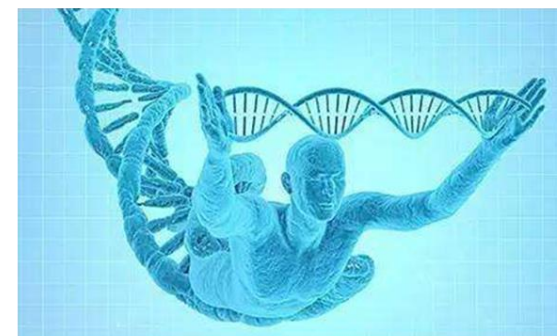
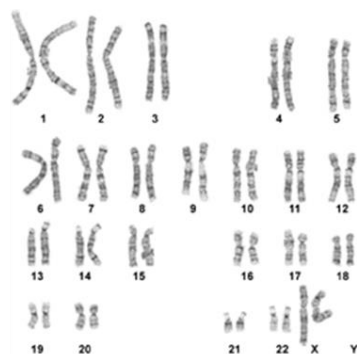


The common misconception

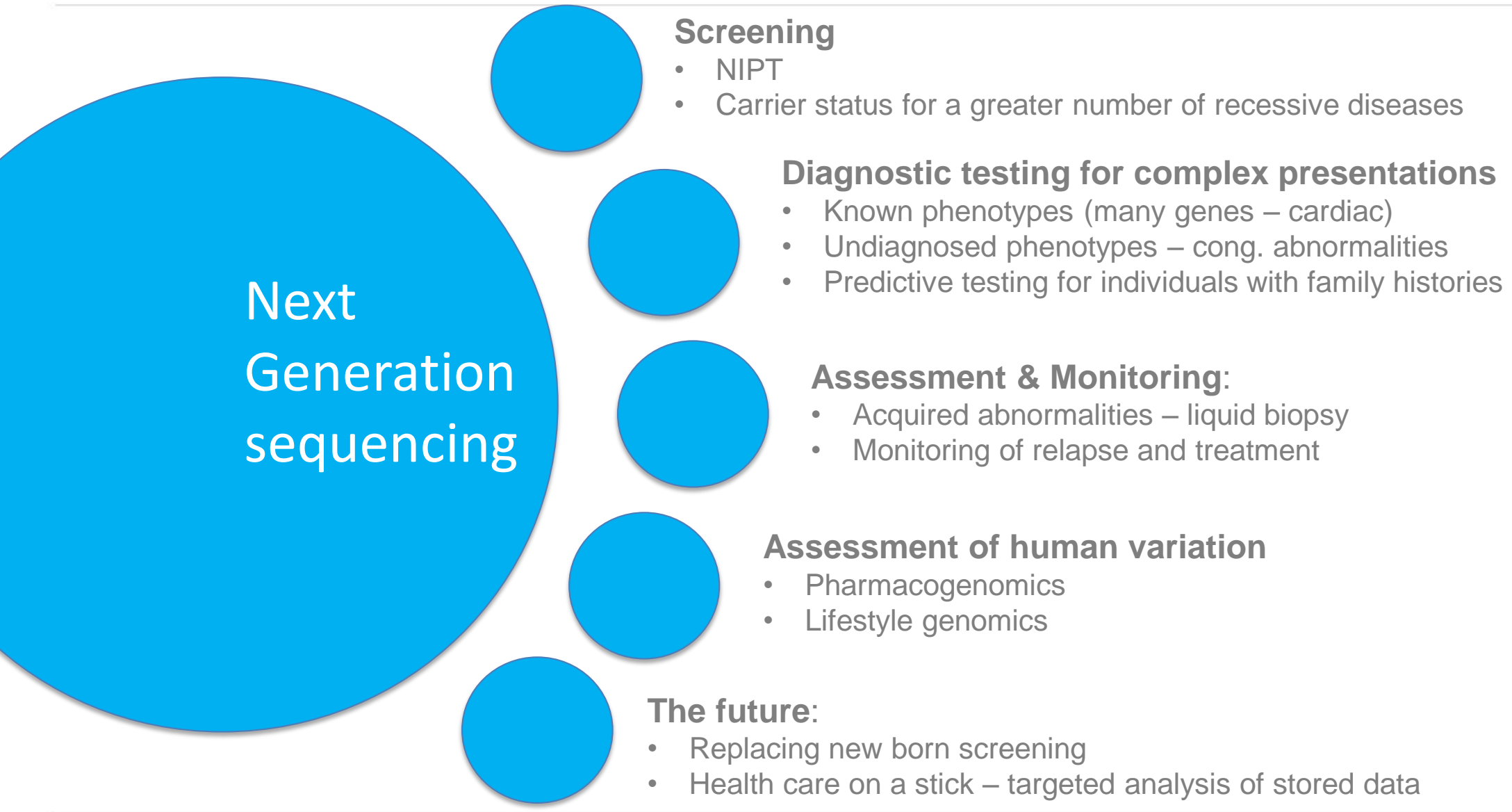
Clinical utility of carrier screening



A digital revolution



Next generation sequencing



Next Generation sequencing

Screening

- NIPT
- Carrier status for a greater number of recessive diseases

Diagnostic testing for complex presentations

- Known phenotypes (many genes – cardiac)
- Undiagnosed phenotypes – cong. abnormalities
- Predictive testing for individuals with family histories

Assessment & Monitoring:

- Acquired abnormalities – liquid biopsy
- Monitoring of relapse and treatment

Assessment of human variation

- Pharmacogenomics
- Lifestyle genomics

The future:

- Replacing new born screening
- Health care on a stick – targeted analysis of stored data

Summary

Most carriers, high risk couples and couples with an affected pregnancy have no known family history

Recessive genetic conditions individually rare, but combined have risks akin to Down syndrome

Availability of genetic counselling is an important part of any program.

Professional bodies are now recommending patients be made aware of carrier screening

Testing for recessive conditions is likely to become a part of standard pregnancy care

Laboratory team (VCGS)

- Dr. Desiree Du Sart
- Dr. Mark Pertile
- Ms. Melanie Smith
- Ms. Chelsea Holt
- Ms. Lisa Ward
- Ms. Vanessa Siva Kumar
- Ms. Karina Sandoval
- Mr. Trent Burgess

Clinical team (VCGS)

- Prof. Martin Delatycki
- Prof. David Amor
- Dr Alison Archibald
- A/Prof Zornitza Stark
- Dr. Kate Scarff
- Ms. Clare Hunt
- Ms. Justine Elliott



Clinical team (RCH)

- A/Prof John Massie (Respiratory physician - CF)
- Dr. Eppie Yiu (Neurologist – SMA)

Support organisations

- Fragile X Association of Australia
- Cystic fibrosis Victoria
- Spinal Muscular Atrophy Association of Australia