VCGS Leaders in Genetic Health

the partumpost

Reproductive genetic carrier screening - is more better?

Volume 3 Issue 3 December 2019

What's so important about carrier screening?

It is estimated that 1-2% of couples have an increased chance of having a child with an autosomal recessive or X-linked genetic condition (1). In most cases, people have no knowledge of their genetic risk prior to having a family (2) and only become aware of their carrier status once an affected child is born (3). Research shows support for carrier screening from healthcare providers, the general community and families impacted by these conditions (4,5,6,7).

Carrier screening enables couples to find out about their genetic risk before or early in pregnancy. Couples with an increased risk can access reproductive options (such as IVF with pre-implantation genetic diagnosis) to prepare for or avoid having a child with the condition. Offering carrier screening provides 'reproductive autonomy' to couples, enabling them to make decisions that are consistent with their own beliefs and values (8).

What do professional guidelines say about carrier screening?

RANZCOG have recently updated their guidelines on carrier screening which now state:

Information on carrier screening for other genetic conditions should be offered to all women planning a pregnancy or in the first trimester of pregnancy.

Options for carrier screening include screening with a panel for a limited selection of the most frequent conditions (e.g. cystic fibrosis, spinal muscular atrophy and fragile X syndrome) or screening with an expanded panel that contains many disorders (up to hundreds).

Despite recommendations, research suggests most healthcare providers are not routinely offering carrier screening to their patients preconception or in early pregnancy (2,9). As carrier screening is ideally offered preconception, general practitioners have an important role in improving access to carrier screening (10).

Our experience with carrier screening

VCGS has a long history of providing carrier screening services (figure 1 below). VCGS was first to offer a multi-condition reproductive genetic carrier screen (*prepair*) in the general population and have recently celebrated 30,000 people screened. Our laboratory, clinical and research partnerships have enabled us to collect comprehensive outcome data (2).

prepair: key findings

Carrier screening is relevant to all. 1 in 20 is a carrier of CF, FXS or SMA. 90% of carriers had no family history.

Collectively these conditions are common. 1 in 240 pregnant couples were found to have an increased chance of a child with CF, FXS or SMA. 1 in 1000 had an affected pregnancy.

Access to carrier screening is variable. Screening is mostly offered in metro areas by private obstetricians. 70% screened are pregnant.

Knowing genetic risk informs reproductive planning.

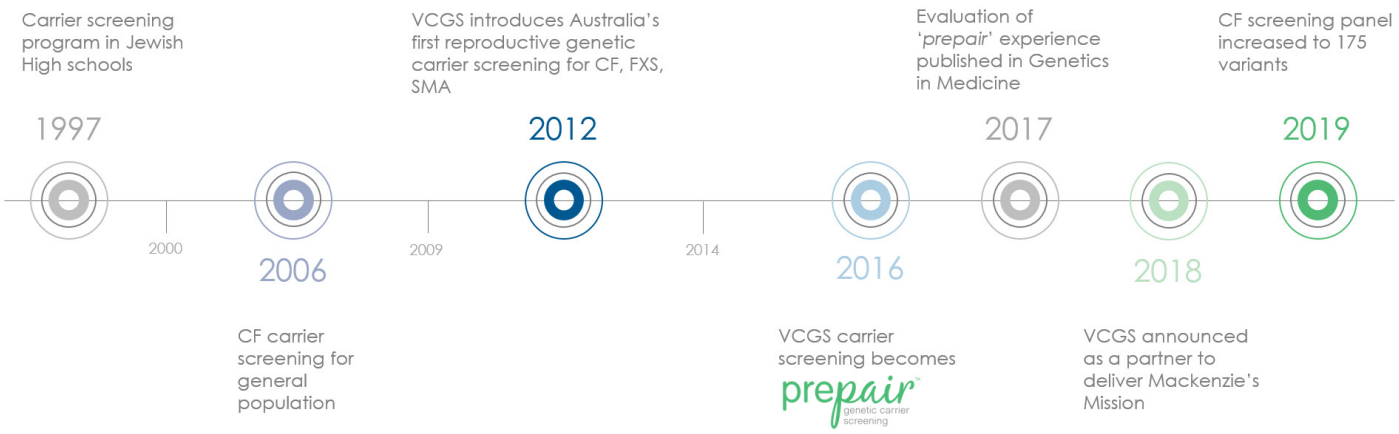

Figure 1. History of reproductive carrier screening at VCGS

Victorian Clinical Genetics Services
Murdoch Children's Research Institute
The Royal Children's Hospital
Flemington Road, Parkville VIC 3052
P +61 1300 118 247 W vcgs.org.au

Towards expanded carrier screening - is more better?

Answer: *It depends* on the conditions screened, how screening is offered and the carrier frequency of those conditions.

Understanding the conditions screened

Understanding the conditions included in these panels is important as not all are useful to screen for in a reproductive setting. Conditions that have an adult onset, mild clinical presentations, or uncertain outcomes may result in complicated decision-making and/or may cause unnecessary anxiety for couples.

A couple screening approach

It is important to be mindful that the majority of people screened using an expanded panel will be carriers for at least one condition. This means additional resources are required to provide genetic counselling about carrier results and facilitate testing of the person's reproductive partner. For this reason, a pragmatic approach is to test both members of the couple at the same time so that a combined assessment of their reproductive risk can be provided.

Considering carrier frequency

The common genetic conditions covered in *prepair* (CF, FXS, SMA) as well as haemoglobinopathies (screened through FBE & Hb electrophoresis) are responsible for the greatest proportion of inherited childhood onset conditions. Increasing the number of conditions screened will identify more couples with an increased risk. However, the number of additional increased risk couples identified diminishes as the conditions become rarer.

In the expanded carrier screening context, access to expert laboratory and genetic counselling services becomes essential for appropriate interpretation and management of results.

Expanded carrier screening at VCGS

In addition to *prepair*, VCGS currently offers expanded carrier screening through Invitae, a company in the USA. This involves screening both members of a couple for genetic changes in over 288 genes associated with serious genetic conditions. Arranging screening through VCGS is simple:

Instructions for patients requesting carrier screening

Please contact our team (+61 3 9936 6402 or screeninggc@vcgs.org.au) if you would like more information about expanded carrier screening at VCGS.

Future directions in expanded carrier screening

VCGS is excited to be a partner in delivering Mackenzie's Mission, a Medical Research Futures Fund research project aimed at understanding how to offer reproductive genetic carrier screening in Australia. More information is available here: https://www.australiangenomics.org.au/our-research/disease-flagships/mackenzies-mission/

References

1. Ropers HH. On the future of genetic risk assessment. Journal of community genetics. 2012 Jul 1;3(3):229-36.
2. Archibald AD, Smith MJ, Burgess T, Scarff KL, Elliott J, Hunt CE, Barns-Jenkins C, Holt C, Sandoval K, Kumar VS, Ward L et al. Reproductive genetic carrier screening for cystic fibrosis, fragile X syndrome, and spinal muscular atrophy in Australia: outcomes of 12,000 tests. Genetics in Medicine. 2018 May;20(5):513.
3. McClaren BJ, Metcalfe SA, Amor DJ, Aitken M, Massie J. A case for cystic fibrosis carrier testing in the general population. Medical Journal of Australia. 2011 Feb;194(4):208-9.
4. Archibald AD, Hickerton CL, Jaques AM, Wake S, Cohen J, Metcalfe SA. "It's about having the choice": Stakeholder perceptions of population based genetic carrier screening for fragile X syndrome. American Journal of Medical Genetics Part A. 2013 Jan;161(1):48-58.
5. Archibald AD, Hickerton CL, Wake SA, Jaques AM, Cohen J, Metcalfe SA. "It gives them more options": preferences for preconception genetic carrier screening for fragile X syndrome in primary healthcare. Journal of community genetics. 2016 Apr 1;7(2):159-71.
6. Beard CA, Amor DJ, Di Pietro L, Archibald AD. "I'm Healthy, It's Not Going To Be Me": Exploring experiences of carriers identified through a population reproductive genetic carrier screening panel in Australia. American Journal of Medical Genetics Part A. 2016 Aug;170(8):2052-9.
7. Ioannou L, McClaren BJ, Massie J, Lewis S, Metcalfe SA, Forrest L, Delatycki MB. Population-based carrier screening for cystic fibrosis: a systematic review of 23 years of research. Genetics in Medicine. 2014 Mar;16(3):207.
8. Delatycki MB, Alkuraya F, Archibald A, Castellani C, et al . International perspectives on the implementation of reproductive carrier screening. Prenatal Diagnosis, 2019 epub - https://obgyn.onlinelibrary.wiley.com/doi/10.1002/pd.5611
9. Leibowitz R, Archibald AD, Lewis S, Emery J, Delatycki MB. 2019. Genetic carrier screening for cystic fibrosis, fragile X syndrome and spinal muscular atrophy in general practice. GP19 conference oral presentation.
10. Delatycki MB, Laing NG, Moore SJ, Emery J, Archibald AD, Massie J, Kirk EP. Preconception and antenatal carrier screening for genetic conditions:'The critical role of general practitioners'. Australian Journal of General Practice. 2019 Mar;48(3):106.