



Genetic carrier screening

This statement has been developed and reviewed by the Genomics Advisory Working Group & Women's Health Committee and approved by the RANZCOG Board and Council.

A list of Women's Health Committee Members & Genomics Advisory Working Group can be found in [Appendix A](#).

Disclosure statements have been received from all members of this committee.

Disclaimer This information is intended to provide general advice to practitioners. This information should not be relied on as a substitute for proper assessment with respect to the particular circumstances of each case and the needs of any patient. This document reflects emerging clinical and scientific advances as of the date issued and is subject to change. The document has been prepared having regard to general circumstances.

First endorsed by RANZCOG: March 2019
Current: March 2019
Review due: March 2022

Objectives: To provide health professionals with advice on the counselling of women and couples prior to and in the early stages of pregnancy in relation to genetic carrier screening.

Target audience: All health professionals providing care to women and couples prior to and in the early stages of pregnancy.

Values: The evidence was reviewed by the Women's Health Committee (RANZCOG), and applied to local factors relating to Australia and New Zealand.

Background: This statement was first developed by the Genomics Advisory Working Group & Women's Health Committee in March 2019.

Funding: The development and review of this statement was funded by RANZCOG.

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1. Plain language summary

There are many hundreds of inherited genetic conditions that can affect human health, and most are very rare. However, when all these inherited conditions are considered together, they affect up to 1 in 400 people. The majority of children born with such conditions are born into families with no other affected family members. This occurs because a healthy couple can pass on genetic changes to their child without knowing that they are carriers of that condition. The two major types of inheritance that can lead to a healthy couple having children with serious genetic conditions are called autosomal recessive and X-linked recessive.

In **autosomal recessive inheritance**, a person inherits a faulty gene from each parent. Genes are the inheritance particles. We have about 23,000 pairs of genes, one in each pair inherited from each parent. For an autosomal recessive condition, if a person has one faulty gene and one healthy gene, they will not have the condition. They are a so-called “carrier” of the condition. We are all carriers of on average two severe autosomal recessive conditions. It is only if both members of a couple are carriers of the same faulty gene that there is a 1 in 4 chance of having a child affected by that condition. The most common types of autosomal recessive conditions in our community are thalassaemia and cystic fibrosis.

X-linked inheritance is closely related to the sex of the individual, with males generally being more severely affected than females. Genes lie on chromosomes, which can be thought of as long strings with the genes as beads on the string. Males have an X and a Y chromosome whilst females have two X chromosomes. When there is a faulty gene on the X chromosome, females are generally unaffected or more mildly affected than males since they have a second unaffected copy of the gene. Males only have one X chromosome and so if there is a faulty gene on their X chromosome they are more severely affected by the condition since they do not have a second X chromosome to compensate. If a woman is a carrier for an X-linked condition, there is a 1 in 4 chance of having an affected son with each pregnancy. The most common X-linked recessive condition is fragile X syndrome.

Testing for inherited conditions

Babies are already tested for a large number of genetic conditions via the **newborn screening** ‘heel prick’ test. However, it is also possible to test healthy adults to see if they have an increased chance of having a child with an autosomal or X-linked genetic condition *before* conception or birth. This is called **reproductive carrier screening**. If both members of a couple are known carriers of the same autosomal recessive condition or a woman is a carrier of an X-linked condition, there are a number of options available. These options include:

1. Having a child naturally and testing after birth to see if the child is affected.
2. Conceiving naturally and having diagnostic testing during pregnancy to determine if the fetus is affected. This is usually performed with an invasive test (amniocentesis or chorionic villus sampling).
3. Conceiving the pregnancy by *in vitro* fertilisation (IVF) and testing embryos by preimplantation genetic diagnosis (PGD). Unaffected embryos would then be selected for achieving pregnancy.
4. Using donor sperm, egg or embryo from unaffected individuals.
5. Adoption.
6. Not having children.

Carrier screening can be performed at any time, but it is preferable to screen before a couple conceives so that they have time to understand and consider their reproductive options, such as preimplantation genetic

diagnosis. The most common conditions for which carrier screening is available are thalassaemia, cystic fibrosis, spinal muscular atrophy and fragile X syndrome.

There are some ethnic-specific patterns of genetic inheritance, which may lead to a specific offer of additional testing. For example, couples of Eastern European (Ashkenazi) Jewish descent, may wish to have carrier testing for Tay Sachs disease, Niemann Pick disease type A, Fanconi anaemia group C, familial dysautonomia, Bloom syndrome, Canavan disease and mucopolidosis type IV in addition to screening for thalassaemia, cystic fibrosis, spinal muscular atrophy and fragile X syndrome.

Reproductive carrier screening generally incurs out of pocket expenses where there is no family history of the condition. Where there is a family history of a genetic condition, referral to a clinical geneticist or genetic counsellor may be indicated and testing for carrier status for the condition may be funded by the government.

Further information regarding genetic carrier screening can be found at:

<https://www.ranzcog.edu.au/Womens-Health/Patient-Information-Guides/Patient-Information-Pamphlets>

2. Summary of recommendations

Recommendation 1	Grade
All couples intending to have children, or who are pregnant, should have a family history taken with a view to identifying relatives with heritable genetic disorders, as well as the presence of consanguinity. Those identified with a family history of a specific inherited disorder should be offered referral to a genetic counselling service for information about carrier screening and prenatal diagnosis/ pre-implantation genetic diagnosis for the condition.	Consensus-based recommendation
Recommendation 2	Grade
All pregnant women should be offered basic screening for thalassaemia carrier status by a full blood examination at initial presentation. Screening with specific assays for haemoglobinopathies (such as HPLC or EPG and haemoglobinopathy DNA testing) should be considered in high probability ethnic or population groups.	Consensus-based recommendation
Recommendation 3	Grade
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).	Consensus-based recommendation
Recommendation 4	Grade
For individuals of Eastern European (Ashkenazi) Jewish descent, additional screening for Tay Sachs disease, Niemann Pick disease type A, Fanconi anaemia group C, familial dysautonomia, Bloom syndrome, Canavan disease and mucopolidosis type IV should be offered.	Consensus-based recommendation
Good Practice Point	Grade
Screening can be sequential or couple screening. In sequential screening, one member of the couple is screened (usually the woman since the woman's carrier	Consensus-based recommendation

status for X-linked conditions is relevant) and the second member of the couple is only screened if the first member is a carrier of one or more autosomal recessive conditions. In couple screening both members of the couple are screened at the same time.	
Recommendation 5	Grade
Women wanting more information about carrier screening should be given the opportunity to have a more detailed discussion about carrier screening with an informed clinician. Informed consent for screening should be obtained and this should include any out of pocket expenses that are required for this testing.	Consensus-based recommendation
Recommendation 6	Grade
Laboratories should only report carrier status for class 4 and 5 mutations. Variants of unknown significance should not be reported.	Consensus-based recommendation
Recommendation 7	Grade
All couples with a high chance of having a child with one of the conditions screened for should be referred for genetic counselling to be informed of available reproductive options and to assist with prenatal testing if the woman in the couple found to have a high chance is pregnant when the result becomes known.	Consensus-based recommendation
Good Practice Point	Grade
It may be appropriate to refer couples with a high probability of having a child with a genetic condition to see a clinician with the relevant clinical expertise. The couple should also be offered the opportunity to access community resources and/or a patient support group if available.	Consensus-based recommendation

3. Introduction

Population carrier screening is defined as the detection of carrier status of autosomal and X-linked recessive diseases in couples or people who do not have an a priori increased chance of being a carrier based on their or their partners' personal or family history¹. It does not refer to testing an individual with a strong family history of a known or possible genetic condition – these people should be offered direct referral to a specialist clinical genetics service.

Carrier screening for genetic conditions has been available since the 1970s with screening for Tay Sachs disease by testing of hexosaminidase A levels in blood and for haemoglobinopathies by full blood examination and haemoglobin electrophoresis². Since the late 1980s, screening by directly testing for genetic mutations has been possible.

Carrier screening for selected genetic conditions of highest population frequency

Testing has been widely offered for conditions common in particular ethnic groups such as cystic fibrosis in Caucasians, Tay Sachs disease and a number of other conditions in Ashkenazi Jewish individuals, and haemoglobinopathies in those of Mediterranean, African and Asian ethnicity. The carrier and affected frequencies for cystic fibrosis, spinal muscular atrophy and fragile X syndrome are shown in table 1. The results from an Australian study found that approximately 1 in 20 individuals accessing self-funded carrier screening were carriers of cystic fibrosis, spinal muscular atrophy and/or fragile X syndrome³.

Table 1 - frequency of carrier and affected individuals for cystic fibrosis, spinal muscular atrophy and fragile X syndrome from 12,000 screened individuals in Australia³

Condition	Carrier	Affected	Main clinical features of the condition
Cystic fibrosis	1 in 35	1 in 4925*	Recurrent lung infections, malabsorption, shortened life span
Spinal muscular atrophy	1 in 50	1 in 9917*	Severe muscle weakness, death usually during childhood
Fragile X syndrome	1 in 332	1 in 7143 males ^	Intellectual disability, autism

* = inferred from the carrier frequency

^ = based on a meta-analysis of data⁴

Prenatal diagnosis has been available for inherited genetic conditions since 1977. The current rate of prenatal diagnosis for an increased chance of single gene condition is approximately 1 in 500 births⁵. The three most common inherited genetic conditions for which prenatal diagnosis is currently performed are thalassaemia, cystic fibrosis, and fragile X syndrome.

Expanded carrier screening

The development of next generation sequencing means it is now possible to ascertain the nucleotide sequence of all 23,000 genes for a fraction of the cost than was the case prior to this technology becoming available. This has resulted in the ability to offer carrier screening for over 1000 autosomal recessive and X-linked conditions. From a study of over 30,000 people screened by next generation sequencing of over 100 genes, 1 in 3.4 people were a carrier of at least one condition.⁶ Screening can involve sequencing of the nucleotide sequence of multiple entire genes or testing for specific mutations in multiple genes. The former has the advantage of identifying the maximum number of carriers but has the disadvantage of identifying variants of uncertain significance (VUS). A VUS is an alteration in a gene that cannot be categorised with certainty as a mutation or a benign polymorphism.

Reproductive carrier screening for cystic fibrosis has been shown to be cost effective in Australia.⁷ Screening by next generation sequencing is more cost effective than screening for selected mutations in genes.⁶ The absolute cost effectiveness of expanded reproductive carrier screening has not been studied, however. As the cost of testing is reduced and expensive treatments for genetic disorders become available, it is anticipated that screening for multiple conditions will become more cost effective in the future.

Reproductive options after carrier screening

Where both members of a couple are found to be carriers of an autosomal recessive condition or a woman is found to be a carrier of an X-linked condition, and thus have a 1 in 4 chance of each pregnancy being affected by the condition, a number of reproductive options are available including:

1. Having a child naturally and testing after birth to see if the child is affected.

2. Conceiving naturally and having diagnostic testing during pregnancy to determine if the fetus is affected. This is usually performed with an invasive test (amniocentesis or chorionic villus sampling).
3. Conceiving the pregnancy by in vitro fertilisation (IVF) and testing embryos by preimplantation genetic diagnosis (PGD). Unaffected embryos would then be selected for achieving pregnancy.
4. Using donor sperm, egg or embryo from unaffected individuals.
5. Adoption.
6. Not having children.

4. Discussion and recommendations

4.1 Family history

Recommendation 1	Grade
All couples intending to have children, or who are pregnant, should have a family history taken with a view to identifying relatives with heritable genetic disorders, as well as the presence of consanguinity. Those identified with a family history of a specific inherited disorder should be offered referral to a genetic counselling service for information about carrier screening and prenatal diagnosis/ pre-implantation genetic diagnosis for the condition.	Consensus-based recommendation

All women/couples should be questioned about genetic conditions that are present in their family as well as the presence of consanguinity. This information may inform specific carrier screening and/or chromosomal testing for the couple. Referral to a clinical genetic health professional should be considered where a family history of a genetic condition is identified.

4.2 Who should be offered screening?

Recommendation 2	Grade
All pregnant women should be offered basic screening for thalassaemia carrier status by a full blood examination at initial presentation. Screening with specific assays for haemoglobinopathies (such as HPLC or EPG and haemoglobinopathy DNA testing) should be considered in high probability ethnic or population groups.	Consensus-based recommendation

All women and couples planning pregnancy should be offered screening for genetic conditions irrespective of the presence or absence of a family history of a genetic condition or the ethnicity of the individuals. Screening should ideally be prior to a pregnancy so reproductive options are available to the couple but if the woman/couple present for the first time in early pregnancy, testing should still be offered at that time.

4.3 What conditions should be offered?

Recommendation 3	Grade
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).	Consensus-based Recommendation
Recommendation 4	Grade
For individuals of Eastern European (Ashkenazi) Jewish descent, additional screening for Tay Sachs disease, Niemann Pick disease type A, Fanconi anaemia group C, familial dysautonomia, Bloom syndrome, Canavan disease and mucopolidosis type IV should be offered.	Consensus-based Recommendation

The conditions for which genetic screening is offered should be a cause of major diminution of quality of life and/or reduction in lifespan.

Information on carrier screening for the most common inherited genetic conditions in our population, that is **thalassaemia, cystic fibrosis, spinal muscular atrophy, and fragile X syndrome**, should be offered to all women planning pregnancy or in early pregnancy. Screening the general population for a limited range of high frequent single gene disorders is called **panethnic screening**.

For individuals of Eastern European (Ashkenazi) Jewish descent, additional **ethnic-specific screening** for Tay Sachs disease, Niemann Pick disease type A, Fanconi anaemia group C, familial dysautonomia, Bloom syndrome, Canavan disease and mucopolidosis type IV should be offered.

With the introduction of new genomic sequencing techniques, carrier screening for multiple autosomal and X-linked recessive conditions – “**expanded carrier screening**” - is now available for couples who have no family history of a genetic disorder.⁸ Clinicians should be aware that expanded carrier panels may vary substantially in their content, mutation coverage, and reporting strategies, depending on the provider⁹. This is a rapidly evolving field and the Federal Government has invested in a large trial of expanded carrier screening which is expected to inform future service delivery and funding¹⁰. Currently, “expanded carrier screening” should only be offered in the context of well-defined clinical pathways for pre- and post-test genetic counselling, as up to 24% of adults will be found to be a carrier of at least one recessive disorder^{8, 11}

Panethnic and expanded carrier screening are both acceptable approaches for prepregnancy and prenatal carrier screening. Health services and clinicians should develop a consistent approach to carrier screening according to their local context, and ensure that appropriate clinical services for pre- and post-test genetic counselling are available.

4.4 How should screening be performed?

Good Practice Point	Grade
Screening can be sequential or couple screening. In sequential screening, one member of the couple is screened (usually the woman since the woman's carrier status for X-linked conditions is relevant) and the second member of the couple is only screened if the first member is a carrier of one or more autosomal recessive conditions. In couple screening both members of the couple are screened at the same time.	Consensus-based recommendation

Screening is usually provided as either (i) sequential screening, or (ii) couple screening.

(i) Sequential screening (also called two step screening) refers to where one member of the couple is offered testing first (usually the woman). If she/he is a carrier of an autosomal recessive condition, the other member of the couple is then offered screening. It is generally the female member of the couple who is offered screening in the first instance since for X-linked conditions such as fragile X syndrome, it is the female member's carrier status that is important. The advantage of sequential screening is that it reduces overall costs of testing for most couples (as most couples only require one member to be tested). It also allows for cascade testing of relatives of carriers. Cascade testing refers to testing of relatives of a person who is affected by or is a carrier of a genetic condition and who therefore has a higher probability of being a carrier than an unrelated individual.

(ii) Couple screening (also called one step screening) refers to testing both members of a couple simultaneously with the provision of a combined "low probability" or "high probability" result. A high probability result is provided if both members of the couple are carriers of the same autosomal recessive condition or the woman is a carrier of an X-linked condition. All other couples are provided with a low probability result. ***Those provided with a low probability result may or may not be informed of the individual results of carrier testing.*** The advantages of couple screening over sequential screening are (i) that the result for the couple is available in the same time period as for the first member of the couple for sequential screening; (ii) far fewer individuals/couples require genetic counselling since the number of carrier couples is far lower than the number of carriers identified by sequential screening (iii) anxiety from waiting for the partner result once the first person is found to be a carrier of one or more conditions is minimised since most will be identified as low probability as a couple. The disadvantages are that (i) test costs are higher, and (ii) the opportunity for cascade testing is largely lost if the individuals are not made aware of the conditions that they carry, and (iii) the results also become invalid if the individuals change reproductive partners for future pregnancies.

4.5 Informed consent

Recommendation 5	Grade
Women wanting more information about carrier screening should be given the opportunity to have a more detailed discussion about carrier screening with an informed clinician. Informed consent for screening should be obtained and this should include any out of pocket expenses that are required for this testing.	Consensus-based Recommendation

All individuals/couples having screening should provide written informed consent that should include:

- (i) Acknowledgement that screening will not identify carrier status for all mutations in the tested genes and therefore that there is a residual chance of the couple having a child with one of the conditions screened for.
- (ii) Acknowledgement that there is a small chance of identifying the individual tested as affected by one of the conditions screened for. An example is the identification of homozygous/compound heterozygous mutations in the *CFTR* gene in an individual with no symptoms, congenital bilateral absence of the vas deferens and/or pulmonary symptoms.
- (iii) If couple screening is offered, the members of the couple need to be informed that if they have children with a different partner that they require rescreening to define the reproductive risk for that new couple.

4.6 What genetic findings should laboratories report?

Recommendation 6	Grade
Laboratories should only report carrier status for class 4 and 5 mutations. Variants of unknown significance should not be reported.	Consensus-based recommendation

Laboratories should only report carrier status for class 4 (likely pathogenic) and 5 (pathogenic) mutations. Variants of unknown/uncertain significant (VUS) should not be reported.

4.7 Carrier couples of autosomal recessive conditions / female carriers of X-linked conditions

Recommendation 7	Grade
All couples found to have a high probability of having a child with one of the conditions screened for should be referred for genetic counselling to be informed of available reproductive options and to assist with prenatal testing if the woman in the couple found to have a high chance is pregnant when the result becomes known.	Consensus-based recommendation
Good Practice Point	Grade
It may be appropriate to refer couples with a high chance of having a child with a genetic condition to see a clinician with the relevant clinical expertise. The couple should also be offered the opportunity to access community resources and/or a patient support group if available.	Consensus Based Recommendation

All couples found to have a higher chance of having a child with one of the conditions screened for should be referred for genetic counselling to be informed of available reproductive options.

4.7.1 The **preconception period** is the preferred timing for carrier screening as advances in preimplantation genetic diagnosis (PGD) now provide couples with a means to avoid having a pregnancy affected by a heritable disorder altogether. For many couples, undergoing *in vitro* fertilisation (IVF), PGD and selective transfer of an unaffected embryo is ethically more acceptable than conceiving by chance, undergoing prenatal diagnosis, and considering termination of an affected pregnancy.^{12, 13} Other options for couples wishing to avoid conception of an affected pregnancy include gamete or embryo donation, adoption or forgoing pregnancy.

4.7.2 If a couple are found to have an increased chance **during pregnancy**, genetic counselling and prenatal diagnosis should be offered. Diagnostic testing (usually involving amniocentesis or chorionic villus sampling) may allow couples to prepare for the birth of a child with a genetic condition, to consider the option of terminating an affected pregnancy, or, in some rare cases, to allow *in utero* treatment.

4.7.3. Regardless of the timing of diagnosis, it may be appropriate to refer the couple to see a physician with expertise in the condition that the couple are found to have an increased probability of. An example is referral of a couple found have a high chance of having a child with cystic fibrosis to a respiratory paediatrician. The couple should also be offered the opportunity to access community resources and/or a patient support group if available.

4.8 Costs of screening and equity of access

Currently genetic carrier screening for low probability couples is only available on a user pays basis, apart from haemoglobinopathy screening, which is commonly performed via a full blood examination. Individuals and couples should be informed that there is an out of pocket expense for this screening. It is acknowledged that there is inequity of access to reproductive carrier screening as the current average cost of \$400 represents a substantial financial barrier for many couples. The responsible and ethical implementation of genomic advances in medicine requires equal access for all couples regardless of socioeconomic factors. Development of funding models that provide for equitable access to screening should be an urgent health policy priority.

4.9 Laboratory accreditation and standards

All laboratories currently undertaking carrier screening should be accredited by the National Association of Testing Authorities (NATA) in Australia, and International Accreditation New Zealand (IANZ) in New Zealand.

Laboratories that undertake carrier testing should undertake audit and monitoring of their carrier screening programs and participate in external quality assurance activities.

All pathology laboratories in Australia receiving funding via Medicare must be accredited by the National Association of Testing Authorities (NATA)/RCPA Laboratory Accreditation Program. The Standards are set by the National Pathology Accreditation Advisory Council (NPAAC). The Standards are based on the international standard ISO 15189 Standard for Medical Laboratories. In New Zealand laboratories are accredited via IANZ using the same ISO 15189 as their basis(<https://www.rcpa.edu.au/Patients/Lab-Accreditation>).

4.10 Implications for maternity and genetics workforce

Reproductive carrier screening on a population basis is a new area of practice for many maternity clinicians. Educational resources and training for health professionals should be developed prior to the introduction of screening into routine clinical care.

Health professionals caring for reproductive age women should have up-to-date knowledge of the options available for carrier screening, awareness of appropriate patient resources, and established clinical pathways for referrals to specialist genetic services.

4.11 Community engagement

RANZCOG recognises that increasing uptake of carrier screening may have broader implications for community perceptions of disability and genetic probability. It is important that expanding opportunities for carrier screening, prenatal diagnostic testing, and reproductive choice do not lead to negative consequences for individuals living with genetic conditions, such as a reduction in health services, or stigmatisation. To this end, carrier screening programs should be developed in consultation with consumer

representatives, health advocacy groups and other stakeholders to ensure that community values and distributive justice are maintained within our health system.

5. References

1. Henneman L, Borry P, D C, al e. Responsible implementation of expanded carrier screening. *Eur J Hum Genet.* 2016;24:e1-e12.
2. Delatycki MB. Population screening for reproductive risk for single gene disorders in Australia: now and the future. *Twin Res Hum Genet.* 2008;11(4):422-30.
3. Archibald AD, Smith MJ, Burgess T, Scarff KL, Elliott J, Hunt CE, et al. Reproductive genetic carrier screening for cystic fibrosis, fragile X syndrome, and spinal muscular atrophy in Australia: outcomes of 12,000 tests. *Genet Med.* 2018;20(5):513-23.
4. Hunter J, Rivero-Arias O, Angelov A, Kim E, Fotheringham I, Leal J. Epidemiology of fragile X syndrome: a systematic review and meta-analysis. *Am J Med Genet A.* 2014;164A(7):1648-58.
5. Poulton A, Lewis S, Hui L, J. H. Preimplantation and prenatal diagnosis for single gene disorders: a population based study from 1977 to 2016. *Prenatal diagnosis.* 2018.
6. Norman R, van Gool K, Hall J, Delatycki M, J. M. Cost-effectiveness of carrier screening for cystic fibrosis in Australia. *J Cyst Fibros.* 2012;11:281-7.
7. Azimi M, Schmaus K, Gregor V, Neitzel D, Rochelle R, T. D. Carrier screening by next-generation sequencing: health benefits and cost effectiveness. *Mol Genet Genomic Med.* 2016;4:292-302.
8. Edwards JG, Feldman G, Goldberg J, Gregg AR, Norton ME, Rose NC, et al. Expanded carrier screening in reproductive medicine-points to consider: a joint statement of the american college of medical genetics and genomics, american college of obstetricians and gynecologists, national society of genetic counselors, perinatal quality foundation, and society for maternal-fetal medicine. *Obstetrics and gynecology.* 2015;125(3):653-62.
9. Chokoshvili D, Vears D, P. B. Expanded carrier screening for monogenic disorders: where are we now? . *Prenatal diagnosis.* 2018;38(1):59-66.
10. Mackenzie mission access to pre-pregnancy genetic screening 2018. Available from: <http://www.abc.net.au/news/2018-03-01/mackenzie-mission-access-to-pre-pregnancy-genetic-screening/9496734>.
11. Lazarin GA, Haque IS, Nazareth S, Iori K, Patterson AS, Jacobson JL, et al. An empirical estimate of carrier frequencies for 400+ causal Mendelian variants: results from an ethnically diverse clinical sample of 23,453 individuals. . *Genet Med.* 2013;15(3):178-86.
12. Cameron C, R. W. Is There an Ethical Difference Between Preimplantation Genetic Diagnosis and Abortion? . *Journal of medical ethics.* 2003;29:90-2.
13. Karatas J, Strong K, Barlow-Stewart K, McMahon C, Meiser B, C. R. Psychological Impact of Preimplantation Genetic Diagnosis: A Review of the Literature. . *Reproductive BioMedicine Online.* 2010;20:83-91.
14. National Health and Medical Research Council. NHMRC additional levels of evidence and grades for recommendations for developers of guidelines. Canberra2009.

6. Other suggested reading

ACOG Committee Opinion No. 690, March 2017. Carrier screening in the Age of Genomic Medicine. <https://www.acog.org/Clinical-Guidance-and-Publications/Committee-Opinions/Committee-on-Genetics/Carrier-Screening-in-the-Age-of-Genomic-Medicine>

ACOG Committee Opinion No.691 March 2017 Carrier screening for Genetic Conditions. <https://www.acog.org/Clinical-Guidance-and-Publications/Committee-Opinions/Committee-on-Genetics/Carrier-Screening-for-Genetic-Conditions>

ACMG position statement on prenatal/preconception expanded carrier screening. Genetics in Medicine volume 15, pages 482–483 (2013). <https://www.nature.com/articles/gim201347>

7. Links to other College statements

[Prenatal screening and diagnostic testing for fetal chromosomal and genetic conditions \(C-Obs 59\)](#)

8. Patient information

A range of RANZCOG Patient Information Pamphlets can be ordered via:

<https://www.ranzcog.edu.au/Womens-Health/Patient-Information-Guides/Patient-Information-Pamphlets>

9. Appendices

Appendix A Women's Health Committee Membership

Name	Position on Committee
Professor Yee Leung	Chair and Board Member
Dr Gillian Gibson	Deputy Chair, Gynaecology
Dr Scott White	Deputy Chair, Obstetrics and Subspecialties Representative
Associate Professor Ian Pettigrew	Member and EAC Representative
Dr Kristy Milward	Member and Councillor
Dr Will Milford	Member and Councillor
Dr Frank O'Keeffe	Member and Councillor
Professor Sue Walker	Member
Dr Roy Watson	Member and Councillor
Dr Susan Fleming	Member and Councillor
Dr Marilyn Clarke	ATSI Representative
Associate Professor Kirsten Black	Member
Dr Thangeswaran Rudra	Member
Dr Nisha Khot	Member and SIMG Representative
TBC	Midwifery Representative
TBC	Community Representative
Dr Alicia Mulligan	Trainee Representative
Prof Caroline De Costa	Co-opted member (ANZJOG member)

Genomics Advisory Working Group

Name	Position on Committee
Professor Steve Robson	Chair
Associate Professor Lisa Hui	Member
Professor Martin Delatycki	HGSA Representative
Ms Julie Cini	Community Representative

Appendix B Overview of the development and review process for this statement

i. Steps in developing and updating this statement

This statement was originally developed in March 2018. The Genomics Advisory Working Group & Women's Health Committee carried out the following steps in reviewing this statement:

- Declarations of interest were sought from all members prior to reviewing this statement.
- Structured clinical questions were developed and agreed upon.
- An updated literature search to answer the clinical questions was undertaken.
- At the March 2018 face-to-face committee meeting, the existing consensus-based recommendations were reviewed and updated (where appropriate) based on the available body of evidence and clinical expertise. Recommendations were graded as set out below in Appendix B part iii)

ii. Declaration of interest process and management

Declaring interests is essential in order to prevent any potential conflict between the private interests of members, and their duties as part of the Women's Health Committee.

A declaration of interest form specific to guidelines and statements was developed by RANZCOG and approved by the RANZCOG Board in September 2012. The Women's Health Committee members were required to declare their relevant interests in writing on this form prior to participating in the review of this statement.

Members were required to update their information as soon as they become aware of any changes to their interests and there was a standing agenda item at each meeting where declarations of interest were called for and recorded as part of the meeting minutes.

There were no significant real or perceived conflicts of interest that required management during the process of updating this statement.

iii. Grading of recommendations

Each recommendation in this College statement is given an overall grade as per the table below, based on the National Health and Medical Research Council (NHMRC) Levels of Evidence and Grades of Recommendations for Developers of Guidelines.¹⁴ Where no robust evidence was available but there was sufficient consensus within the Women's Health Committee, consensus-based recommendations were developed or existing ones updated and are identifiable as such. Consensus-based recommendations were agreed to by the entire committee. Good Practice Notes are highlighted throughout and provide practical guidance to facilitate implementation. These were also developed through consensus of the entire committee.

Recommendation category		Description
Evidence-based	A	Body of evidence can be trusted to guide practice
	B	Body of evidence can be trusted to guide practice in most situations
	C	Body of evidence provides some support for recommendation(s) but care should be taken in its application
	D	The body of evidence is weak and the recommendation must be applied with caution
Consensus-based		Recommendation based on clinical opinion and expertise as insufficient evidence available
Good Practice Note		Practical advice and information based on clinical opinion and expertise

Appendix C Full Disclaimer

This information is intended to provide general advice to practitioners, and should not be relied on as a substitute for proper assessment with respect to the particular circumstances of each case and the needs of any patient.

This information has been prepared having regard to general circumstances. It is the responsibility of each practitioner to have regard to the particular circumstances of each case. Clinical management should be responsive to the needs of the individual patient and the particular circumstances of each case.

This information has been prepared having regard to the information available at the time of its preparation, and each practitioner should have regard to relevant information, research or material which may have been published or become available subsequently.

Whilst the College endeavours to ensure that information is accurate and current at the time of preparation, it takes no responsibility for matters arising from changed circumstances or information or material that may have become subsequently available.