GP referral guide for BRCA1 and BRCA2 risk assessment

Who is this decision aid for?

This guide will help general practitioners (GPs) understand BRCA1 and BRCA2-related cancers.

How will this decision aid help you?

GPs have an important role in identifying patients that are at risk of having a variant in BRCA1 and BRCA2. This guide will provide GPs with information about BRCA1 and BRCA2 testing as well as guidance on when and how to refer a patient to a familial cancer centre for further investigations.

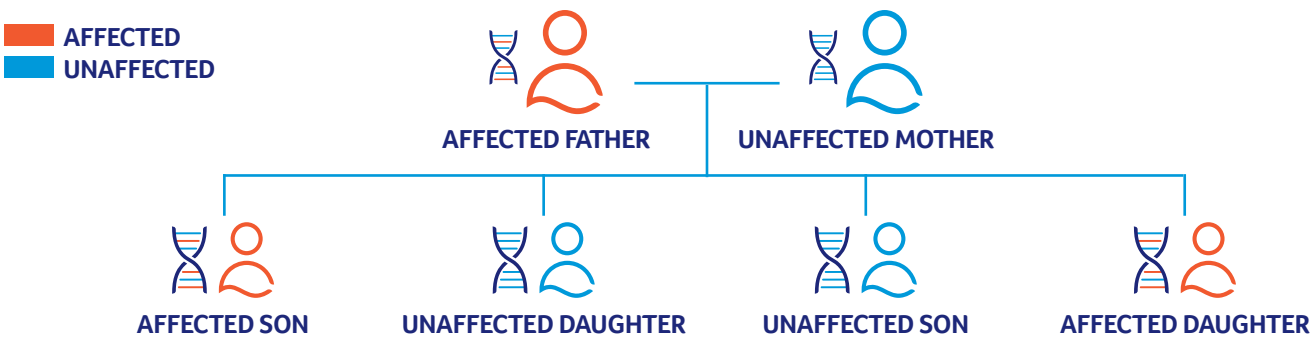
What are BRCA1 and BRCA2-related cancers?

Of all breast cancer cases, approximately 5% are familial,[1,2] and a significant proportion of familial breast cancer cases are caused by pathogenic variants in BRCA1 and BRCA2 genes.

Gene	Syndrome	Contribution to familial breast cancer
BRCA1	Breast/Ovarian (1:1,000)	20–40%
BRCA2	Breast/Ovarian (1:1,000)	10–30%

What causes BRCA1 and BRCA2-related cancers?

- BRCA1 and BRCA2 are tumour suppressor genes that look for and repair errors that occur during DNA replication.
- Pathogenic variations in BRCA1 and BRCA2 can lead to the accumulation of errors that have occurred during DNA replication and this can result in cancer cell proliferation.
- The inheritance of BRCA1 and BRCA2 pathogenic variations follows an **autosomal dominant inheritance pattern**, meaning that an individual who has a pathogenic variant has a 1 in 2 chance of passing this pathogenic variant to their children.
- Most individuals who inherit this variant will develop cancer, but some will not; this is because BRCA1 and BRCA2 express incomplete penetrance.



Source: www.blueprintgenetics.com/resources/impact-of-inherited-cardiovascular-conditions/

Cancer Council

BRCA1 and BRCA2-related cancers

Cancer type	Lifetime risk		
	General population	BRCA1 pathogenic variant	BRCA2 pathogenic variant
Breast	12.5%	**72%** to age 80yrs*	**69%** to age 80yrs*
Ovarian/Fallopian tube/ Primary peritoneal	1.2%	**44%** to age 80yrs*	**17%** to age 80yrs*
Pancreatic	<1%	May be increased	<5.0%
Male breast	<1.0%	1.2%	7.0%
Prostate	5.3%	8.6%	15%

*Residual lifetime risk is dependant on age at consultation

When do I refer to familial cancer centres?

Using a family history risk assessment tool such as **I-prevent** may help you in your risk assessment of BRCA1 and BRCA2-related cancers: **www.petermac.org/iprevent**

Refer to a familial cancer centre if any of the following features are present[3]

1. Two first-degree or second-degree relatives on the same side of the family diagnosed with breast or ovarian cancer, plus one or more of the following features on the same side of the family:
   - Additional relative(s) with breast or ovarian cancer
   - Breast cancer diagnosed before age 40 years
   - Bilateral breast cancer
   - Breast and ovarian cancer in the same woman
   - Ashkenazi Jewish ancestry
   - Breast cancer in a male relative
2. One first-degree or second-degree relative diagnosed with breast cancer aged <45 years plus another first-degree or second-degree relative on the same side of the family with sarcoma (bone/soft tissue) aged <45 years
3. Any member of a family where a mutation in one or more cancer risk genes has been found in the patient or a relative
4. Any woman with:
   a. High grade ovarian/Fallopian/peritoneal cancer (non-mucinous)
   b. Breast cancer <30 years or HER2-positive breast cancer <35 years
   c. Triple negative breast cancer either <50 years or at any age if they also have a close relative with breast or ovarian cancer
   d. Bilateral breast cancer where first cancer was <50 years
5. A woman with breast cancer who has:
   a. A close relative with breast cancer (where 1<40 years or 1 is male or 1 is bilateral or both cancers occurred <50 years)
   b. Two or more close relatives with breast cancer
   c. A close relative with sarcoma or brain or adrenal cancer where 1<46 years and 1<56 years
6. Any man with breast cancer
7. Anyone with Ashkenazi ancestry and breast or ovarian cancer

If unsure about the significance of the family history, seek advice from a familial cancer centre regarding referral. Familial cancer centres will assess individual risk and determine utility of genetic testing.

What do I include in the referral?

Checklist:	Including:
☐ I have recorded a detailed family history	• Cancer diagnoses in 3 generations where available • Age of onset of any cancers in the family • Type of cancer (including whether cancer is metachronous) • Ethnicity of patient (as some pathogenic variations are more prevalent in some ethnicities)
☐ I have provided information about the patient's health history	• Any recent investigations (blood results, histopathology reports, operation notes and any diagnostic imaging) • Current medications • Relevant clinical information
☐ I have provided a reason for referral	• Whether it is urgent (give reason) or non-urgent • How long the referral is valid for
☐ I have provided contact details	• Contact information for the patient • Your contact details in case there are any questions about the referral

Genetic testing

Types of genetic testing:

- **Genetic variant detection** is offered to individuals with cancer suspected to be associated with a pathogenic BRCA gene variant. Testing will be done on the family member with the highest probability of finding a pathogenic BRCA gene variant.
  - Genetic variant detection is generally only offered and/or funded if the calculated risk of an underlying pathogenic variant is greater than 10%.
  - If a pathogenic variant is found, then predictive testing is offered to other family members.
- **Predictive testing** is only available for families with a known pathogenic variant.
  - If no variant is found after predictive testing this does not mean the unaffected individual will not develop cancer. The negative result indicates the individual has a population risk of developing cancer related to the BRCA gene variant.

Surveillance options and recommendations

It's important that individuals are aware that they have BRCA1 or BRCA2 pathogenic variant because as a GP, it is recommended that you offer the patient tailored surveillance and prevention. Risk management is varied and depends on factors such as age, sex and which pathogenic variant is inherited.

Ongoing surveillance may include:

- Regular clinical breast examination
- Breast imaging with mammogram and ultrasound
- Breast magnetic resonance imaging (MRI) in certain populations
- Consideration of ovarian cancer risk

Surgery:

- Bilateral risk-reducing mastectomy
- Risk-reducing bilateral salpingo-oophorectomy

Other strategies:

- Lifestyle modifications

Breast cancer risk-reducing medications:

- Tamoxifen/Raloxifene have been effective in reducing breast cancer risk[4,5]
- Anastrozole has been shown to effectively reduce incidence of breast cancer in high-risk postmenopausal women[4]

Familial cancer services in Victoria

Clayton

Monash Medical Centre

Familial Cancer Centre
Special Medicine Building
246 Clayton Rd, Clayton 3168

Ph: (03) 9594 2009
Fax: (03) 9594 6046
E: familial.cancer@monashhealth.org

Regional clinics:

- Frankston
- Moe

Heidelberg

Austin Hospital

Genetics in the North East
145 Studley Road,
Heidelberg 3084

Ph: (03) 9496 3027
Fax: (03) 9496 4385
E: genetics@austin.org.au

Regional clinics:

- Albury/Wodonga
- Shepparton
- Ballarat

Parkville

The Parkville Familial Cancer Centre

The Royal Melbourne Hospital

Level 2 Centre, Infill Building,
Grattan Street, Parkville 3050

Ph: (03) 9432 7151
Fax: (03) 9342 4267
E: familycancer@mh.org.au

Regional clinics:

- Geelong
- Warrnambool

Peter MacCallum Cancer Centre

Level 1, 305 Grattan Street
Melbourne 3000

Ph: (03) 8559 5322
Fax: (03) 8559 5329
E: familialcancer@petermac.org

Regional clinics:

- Bendigo
- Mildura

Further resources

BreastScreen Victoria www.breastscreen.org.au/breast-cancer-and-screening/your-breast-cancer-risk/family-history/

Cancer Australia canceraustralia.gov.au/publications-and-resources/cancer-australia-publications/advice-about-familial-aspects-breast-cancer-and-epithelial-ovarian-cancer

Cancer Australia GP guides canceraustralia.gov.au/clinical-best-practice/breast-cancer/gp-guides-and-resources

Cancer Connections www.cancerconnections.com.au

Cancer Council Australia cancer.org.au/about-cancer/causes-of-cancer/family-cancers/

Cancer Council Victoria www.cancervic.org.au/cancer-information/genetics-and-risk

Centre for Genetics Education www.genetics.edu.au

EviQ www.eviq.org.au

National Health and Medical Research Council www.nhmrc.gov.au

RACGP Clinical Guidelines:

- www.racgp.org.au/clinical-resources/clinical-guidelines/key-racgp-guidelines/red-book
- www.racgp.org.au/clinical-resources/clinical-guidelines/key-racgp-guidelines/genomics-in-general-practice

References

1. Winship I & Southey MC. (2016). Gene panel testing for hereditary breast cancer. *Medical Journal of Australia, 204(5),* 188–90. doi: 10.5694/mja15.01335
2. Kirk J, Barlow-Stewart K, Poplawski NK, Glesson M, Tucker K & Friedlander M. (2018). Medicare-funded cancer genetic tests: a note of caution. *Medical Journal of Australia, 209(5),* 193–6. doi: 10.5694/mja17.01124
3. Peter MacCallum Cancer Centre. *Familial Cancer Centre: Referral Guideline* [Guidelines]. Retrieved from www.petermac.org/services/treatment/familial-cancer-centre
4. Cuzick J, Sestak I, Forbes JF, Dowsett M, Knox J, Cawthorn S, & Howell A. (2014). Anastrozole for prevention of breast cancer in high-risk postmenopausal women (IBIS-II): an international, double-blind, randomised placebo-controlled trial. *The Lancet,* 383(9922), 1041–8. doi:10.1016/S0140-6736(13)62292-8
5. Vogel VG, Costantino JP, Wickerham DL, Cronin WM, Cecchini RS, Atkins JN, & Wolmark N. (2006). Effects of tamoxifen vs raloxifene on the risk of developing invasive breast cancer and other disease outcomes: the NSABP Study of Tamoxifen and Raloxifene (STAR) P-2 trial. *Journal of the American Medical Association, 295*(23), 2727–41. doi:2710.1001/jama.2295.2723.joc60074.

July 2020

Cancer Council

AP1625