



**Genomic Diagnostics**  
LEADING THE WAY TO IMPROVE HEALTH

# Breast and Ovarian Cancer

CLINICIAN GUIDE FOR GENETIC TESTING



## When should genetic testing in breast and ovarian cancer be considered?

Genetic testing in breast and ovarian cancer can be considered in two main settings. DIAGNOSTIC testing is performed after a diagnosis of cancer, and PREDICTIVE testing is performed in unaffected individuals to determine the future risk of cancer. This guide is intended to assist specialist clinicians treating patients with a breast/ovarian cancer diagnosis.

### Diagnostic Testing

Testing for BRCA variants and other cancer risk genes is performed to determine if there is a genetic contribution to a diagnosis of breast or ovarian cancer.

Hereditary (also known as germline) mutations in cancer risk genes such as BRCA1 and BRCA2 are commonly detected through testing of blood samples. Independent of heritable changes, it is also possible a tumour may have mutations (somatic variants) which is not identifiable through germline testing.

Detection of variants in known cancer risk genes can be used to inform therapeutic and prophylactic options for the patient. These can include determining potential benefit from PARP inhibitor therapy, risk of recurrence, and improved prediction of progression free survival and overall survival.

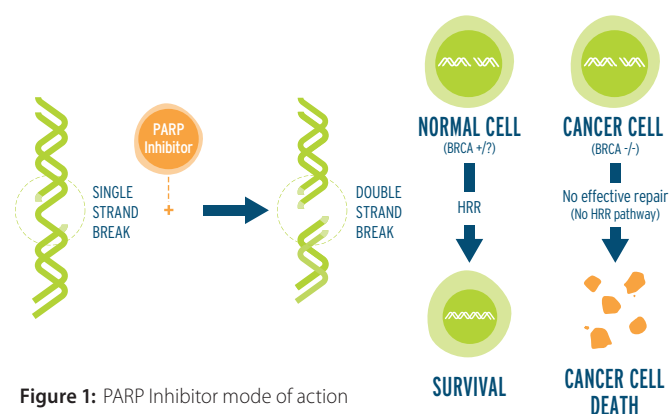


Figure 1: PARP Inhibitor mode of action

### Clinical features suggesting diagnostic testing may be necessary\*

1. A diagnosis of bilateral breast cancer
2. Onset of breast cancer before the age of 40 years
3. Relapsed platinum-sensitive ovarian cancer to determine eligibility for olaparib treatment
4. Ovarian cancer before the age of 70 years
5. Diagnosis of breast and ovarian cancer at the same or at different times
6. Ashkenazi Jewish ancestry
7. A male patient diagnosed with breast cancer
8. Triple negative breast cancer

\* Germline testing. Adapted from EviQ guidelines, February 2017

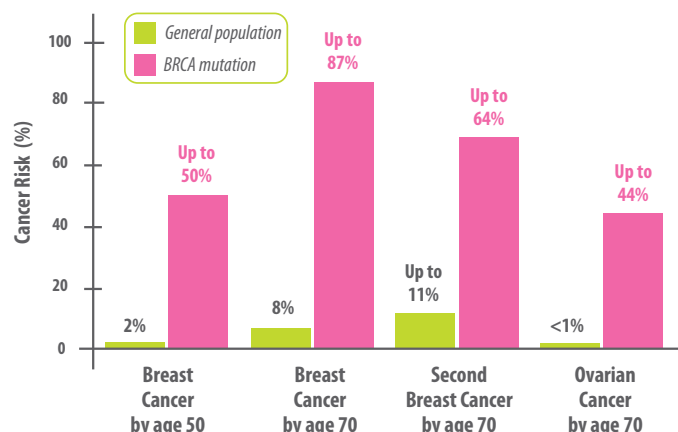


Figure 2: Mutations significantly increase the risk of developing cancer  
Source: www.cancer.gov

### Predictive testing

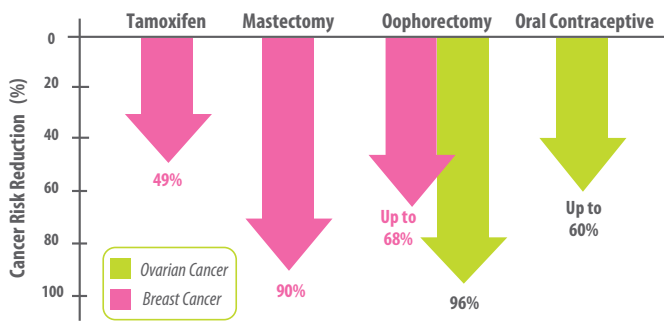
Predictive testing<sup>†</sup> should be considered in patients who have a high risk of developing breast cancer, due to one of the following reasons:

1. Where diagnostic genetic testing in a relative has identified the presence of a high risk breast cancer pathogenic DNA variant. This is now covered by Medicare when requested by a specialist after the provision of genetic counselling.
2. A family history which is strongly suggestive of an underlying genetic contribution, for example:
  - Two or more close relatives (first or second degree) on the same side of the family diagnosed with breast or ovarian cancer <50 years
  - Jewish ancestry
  - Breast cancer in a male
  - Cancer risk score assessed >10%

<sup>†</sup> Prior to predictive testing referral for assessment and pre-test genetic counselling with an appropriately qualified clinical geneticist or genetic counsellor should be given.

**Awareness of inherited cancer susceptibility can alter medical management. Options which could be considered and discussed when a pathogenic or likely pathogenic variant is identified include:**

- Consideration of prophylactic risk-reducing surgery
- Altered chemotherapeutic treatment: some SERMs (selective oestrogen receptor modulators) or aromatase inhibitors may reduce the risk of developing hormone receptor positive breast cancer in women at high risk
- Increased breast screening and imaging (including MRI)
- Identification and testing of other at-risk family members
- Assisting couples with reproductive decision making (e.g. options for assisted reproduction, including pre-implantation genetic diagnosis)



**Figure 3:** Reduce risk and pre-empt cancer with proven medical management  
Source: [www.cancer.gov](http://www.cancer.gov)

## Calculating Risk of Familial Cancer

Cancer risk prediction models, based on epidemiologic data, calculate an individual's likelihood of developing cancer, identify an individual's risk of carrying a genetic mutation for a specific cancer (eg, BRCA 1 or BRCA 2), or both. There are a number of publicly available tools to perform these calculations with some listed in the table below.

RISK CALCULATOR	SOURCE	BACKGROUND
Manchester Score	Medical Genetic Unit, St. Mary's Hospital, Manchester	Simple, manual scoring system to estimate chance of identifying mutation in BRCA1 and BRCA2 gene
BOADICEA	Cambridge University – Centre for Cancer Genetic Epidemiology	Computer program used to calculate the risks of breast and ovarian cancer in women based on their family history
Penn II Risk Model	University of Pennsylvania	Ten questions used to predict pre-test probability (prior probability) that a person has a BRCA 1 or BRCA2 mutation

**Table 1:** List of some commonly referenced risk calculators.

## Pre-test Genetic Counselling

Optional pre-test genetic counselling support is available for our referrers in patients eligible for MBS Item Number 73296. Counselling is provided by Genetic Counselling Australia by qualified genetic counsellors. Please request by writing "genetic counselling" or "G.C" on the patient request form.

A referral form will be required. You may complete this form with the request, or you will be contacted to complete this.

## Why Genomic Diagnostics?

### Our extensive experience:

- With more than 10 years' experience in diagnostic genetics we are your reliable partner for genetic testing

### We are responsive:

- We are committed to delivering the fastest possible turnaround times
- Our dedicated and knowledgeable customer care team are available to assist you and address your queries

### Our commitment to quality is reflected in our testing service:

- We are NATA/RCPA accredited for diagnostic genetic testing
- We participate in regular external quality assurance programs for all tests
- We welcome your queries and are happy to discuss test results and interpretation
- Our expert staff are highly skilled in interpretation of genetic results

## Testing Options Available

TEST	DESCRIPTION	DETAIL
BraOVO (ATM, BRCA1, BRCA2, BRIP1, CHEK2, CDH1, PALB2, PTEN, RAD51C, RAD51D, STK11, TP53)	Multi-gene test that analyses 12 high risk & moderately high risk breast & ovarian cancer susceptibility genes.	This test is bulk-billed at no cost to patients under item 73296 for patients who fit the MBS criteria, otherwise an out-of-pocket fee applies.
Comprehensive BRCA1 and BRCA2 Mutation Screen	Full length BRCA1 and BRCA2 sequencing and deletion / duplication (large re-arrangement) analyses.	This test is bulk-billed for patients who fit the MBS criteria under Medicare item 73296 or an option where only BRCA1 and BRCA2 status is required.
"Predictive Familial Cancer Test" Targeted Mutation Testing	For specified familial or ethnic specific mutations.	Testing of patients with a known familial mutation. This is bulk billed at no cost to patients under item 73297.

## How to Organise Testing

### BraOVO – Diagnostic testing in women with breast or ovarian cancer who qualify for a Medicare rebate Medicare item 73296

For patients with breast or ovarian cancer and a familial pathogenic mutation >10% risk score. To organise testing;

1. Use your standard SDS Network pathology request form. Please request “BraOVO” test and indicate clinical condition (Breast/Ovarian cancer). Please indicate on the request form if patient DOES NOT qualify for the Medicare rebate.
2. Discuss option of genetic counselling# with your patient and if you and your patient agree that this would be of value please write “Genetic Counselling” on the pathology request form when requesting the Breast and Ovarian Cancer genetic test. Genomic Diagnostics will facilitate the genetic counselling process. Please see Breast and Ovarian Cancer Genetic Counselling Service FAQ sheet for further information.
3. Patient attends a collection centre and results are returned to you using your preferred method.

#Genetic counselling is available for the BraOVO test only when ordered under the Medicare rebate

#### MBS Item Descriptor

*Characterisation of germline gene mutations, requested by a specialist or consultant physician, including copy number variation in BRCA1 and BRCA2 genes and one or more of the following genes STK11, PTEN, CDH1, PALB2, or TP53 in a patient with breast or ovarian cancer for whom clinical and family history criteria, as assessed by the specialist or consultant physician who requests the service using a quantitative algorithm, place the patient at >10% risk of having a pathogenic mutation identified in one or more of the genes specified above.*

### BRCA1 and BRCA 2 Test – Diagnostic testing for eligibility for Olaparib - Medicare item 73295

#### MBS Item Descriptor

*Detection of germline BRCA1 or BRCA2 gene mutations, in a patient with platinum-sensitive relapsed ovarian, fallopian tube or primary peritoneal cancer with high grade serous features or a high grade serous component, and who has responded to subsequent platinum-based chemotherapy, requested by a specialist or consultant physician, to determine whether the eligibility criteria for olaparib under the Pharmaceutical Benefits Scheme (PBS) are fulfilled.*

### Diagnostic testing in women with breast or ovarian cancer who do not qualify for a Medicare rebate

#### Choose either the Comprehensive BRCA1 and BRCA2 test or the BraOVO test

1. Use your standard SDS Network pathology request form. Please request “BraOVO” test or “BRCA 1 and 2” test and indicate clinical condition (Breast/Ovarian cancer) and indicate the patient DOES NOT qualify for the Medicare rebate.
2. Patient calls 1800 822 999 to pre-pay for the test and identify a convenient collection location.
3. The test is performed and results are returned using your preferred method.

### Predictive familial cancer test - Medicare item 73297

#### Massively parallel sequencing is used for targeted mutation testing for this item.

#### MBS Item Descriptor

*Characterisation of germline gene mutations, requested by a specialist or consultant physician, including copy number variation in BRCA1 and BRCA2 genes and one or more of the following genes STK11, PTEN, CDH1, PALB2, or TP53 in a patient who is a biological relative of a patient who has had a pathogenic mutation identified in one or more of the genes specified above, and has not previously received a service under item 73296.*

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