

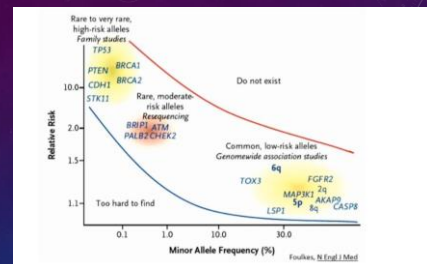
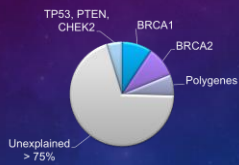
GENETIC COUNSELLING AND GENE TESTING FOR BREAST CANCER

DR MICHAEL GATTAS
16 NOVEMBER 2024

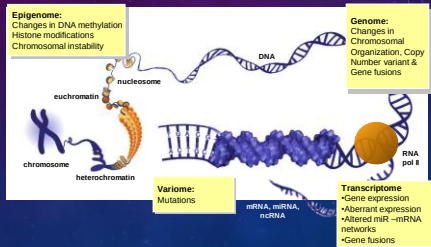
OVERVIEW

- Background Information
- Women who have a family history of cancer
- Women who have a diagnosis of breast cancer

MOST FAMILIES WITH BREAST CANCER DO NOT HAVE A GENE FAULT WE CAN IDENTIFY

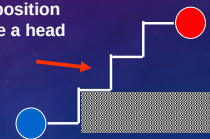


MOLECULAR EVENTS DRIVING TUMORIGENESIS



BASIC CONCEPTS

Familial predisposition means you have a head start



AUTOSOMAL DOMINANT INHERITANCE

- Most of our genes are autosomal
- Most cancer causing genes are inherited in a dominant fashion



The screenshot shows the Cancer Institute NSW eviQ website. The page title is "BRCA1 or BRCA2 – risk management (female)". The page includes a search bar, navigation links, and a list of related pages. The related pages list includes:

- Interpreting family members about hereditary cancer
- Cancer predisposition genes: population carrier frequency
- BRCA1 and BRCA2 – genetic testing
- BRCA1 or BRCA2 – risk management (male)
- Facts for people and families with a faulty BRCA1 gene
- Facts for people and families with a faulty BRCA2 gene

BRCA1 or BRCA2 – risk management (female)

Lifetime risk of cancer/tumour

Cancer/tumour type	Average risk for BRCA1 pathogenic variant carrier	Average risk for BRCA2 pathogenic variant carrier	General female population risk**
Breast	72% to age 80 years (95% CI, 65% to 79%) [†]	69% to age 80 years (95% CI, 61% to 77%) [†]	11.9% to age 80 years
Ovarian/fallopian tube/peritoneal	44% to age 80 years (95% CI, 26% to 59%) [†]	17% to age 80 years (95% CI, 11% to 25%) [†]	0.84% ^{††} to age 80 years
Peritoneal (post BRSO, if no STC is found at BRSO)	<1.0% at 10 years post BRSO (95% CI, 0.6% to 1.4%) [†]	<1.0% at 10 years post BRSO (95% CI, 0.6% to 1.4%) [†]	Rare
Peritoneal (post BRSO, if STC is found at BRSO)	28% at 10 years post BRSO (95% CI, 16% to 44%) [†]	28% at 10 years post BRSO (95% CI, 16% to 44%) [†]	Rare
Pancreatic	<2% [†]	<4% [†]	1.1% to age 80 years
Uterine	2.4% to age 75 years (95% CI, 2.2% to 4.4%) [†]	2.2% to age 75 years (95% CI, 1.1% to 3.2%) [†]	1.7% to age 75 years

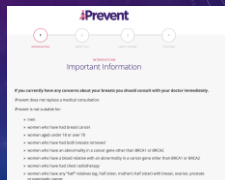
Abbreviations: BRSO – risk-reducing salpingo-oophorectomy; STC – serous tubal intraepithelial cancer
[†] These are average risks; an individual's risk can be substantially more or less than average depending on other factors (e.g. family history and non-genetic (lifestyle) factors). Individualised risk information for breast and ovarian cancer should be provided using iPrevent[®] (see 'Further info').
^{††} Source: Australian Institute of Health and Welfare (AIHW) 2022 Cancer Data in Australia, Canberra. AIHW website (www.aihw.gov.au/reports/cancer/cancer-data-in-australia/cancer-risk-data-in-australia) (2024 data, published for comparison monthly).

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WOMEN WITH A FH OF BREAST CANCER

- First assess if they might have breast cancer
- Assess her FH using iPrevent or similar
- Gene test comes last



MBS ITEM NUMBER 73297

- Characterisation of germline gene variants, including copy number variation:
1. in one or more of the following genes:
 1. BRCA1;
 2. BRCA2;
 3. STK11;
 4. PTEN;
 5. CDH1;
 6. PALB2;
 7. TP53; and
 2. in a patient who:
 1. is a biological relative of a patient who has had a pathogenic or likely pathogenic gene variant identified in one or more of the genes mentioned in paragraph 1; and
 2. has not previously received a service to which item 73295, 73296 or 73302 applies.
- requested by a specialist or consultant physician
 - **Fee:** \$400.00 **Benefit:** 75% = \$300.00 85% = \$340.00

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MBS ITEM NUMBER 73296

- Characterisation of germline gene variants, including copy number variation where appropriate, requested by a specialist or consultant physician:
- (a) in genes associated with breast, ovarian, fallopian tube or primary peritoneal cancer, which must include at least:
 - (i) BRCA1 and BRCA 2 genes, and
 - (ii) one or more STK11, PTEN, CDH1, PALB2 and TP53 genes; and
- (b) in a patient:
 - (i) with breast, ovarian, fallopian tube or primary peritoneal cancer; and
 - (ii) for whom clinical and family history criteria place the patient at greater than 10% risk of having a pathogenic or likely pathogenic gene associated with breast, ovarian, fallopian tube or primary peritoneal cancer
- Once per cancer diagnosis
- Fee: \$1,200.00 Benefit: 75% = \$900.00 85% = \$1,106.80
- (See para 20.0.22 of explanatory notes to this Category)

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EVIQ BREAST CANCER TEST

Target population

- Individual with breast cancer who meets one of the following criteria:
- a pathogenic variant of probability of $\geq 10\%$ using the Manchester score or CanRisk-12 (validated pathogenic variant prediction tools)
 - diagnosed age ≤ 40 years¹
 - bilateral breast cancer or 2 or more synchronous or asynchronous breast cancers with first cancer diagnosed age ≤ 50 years¹
 - triple negative breast cancer (TNBC) diagnosed age ≤ 60 years¹ or at any age if the patient would potentially be eligible for adjuvant therapy with a PARP inhibitor
 - hormone receptor positive, HER2 negative, early breast cancer with one or more high risk features (grade 3, lymph node positive, size ≥ 20 mm), diagnosed at any age, if the patient would potentially be eligible for adjuvant therapy with a PARP inhibitor
 - male breast cancer diagnosed at any age
 - testing criteria for one or more other gene(s) included in the panel.

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THE PENN II RISK MODEL

Part A: Select the side of the family being evaluated: **Maternal** **Paternal**

Part B: Please provide the following information:

1. Presence of Ashkenazi (Eastern European) Jewish ancestry in the family?	☐ Yes ☒ No
2. Number of women in the family diagnosed with both breast and ovarian cancer?	(0-100)
3. Number of women in the family diagnosed with ovarian, fallopian tube, or primary peritoneal cancer (in the absence of breast cancer)?	(0-100)
4. Number of breast cancer cases in the family diagnosed in women under the age of 50?	(0-100)
5. What is the age of the youngest breast cancer diagnosis in the family?	(18-130)
6. Presence of mother-daughter breast cancer diagnoses in the family?	☐ Yes ☒ No
7. How many women with bilateral breast cancer in the family? (Note: Count women with cancer in both breasts, not two primaries in one breast.)	(0-100)
8. Number of men diagnosed with breast cancer in the family?	(0-100)
9. Presence of pancreatic cancer in the family?	☐ Yes ☒ No
10. Number of men diagnosed with prostate cancer in the family?	(0-200)

Part C: Closest relative with breast or ovarian cancer:

Part D: Patient Information (Optional - For use on printable report only):

1. Patient's first name	
2. Patient's last name	
3. Patient's age	
4. Clinic location	

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MBS ITEM NUMBER 73295

- Detection of germline BRCA1 or BRCA2 pathogenic or likely pathogenic gene variants, requested by a specialist or consultant physician, to determine eligibility for treatment with a poly (adenosine diphosphate [ADP]-ribosyl) polymerase (PARP) inhibitor under the Pharmaceutical Benefits Scheme (PBS) in a patient with:
 - (a) advanced (FIGO III-IV) high-grade serous or high-grade epithelial ovarian, fallopian tube or primary peritoneal cancer for whom testing of tumour tissue is not feasible; or
 - (b) triple negative early breast cancer; or
 - (c) hormone receptor positive, HER2-negative, early breast cancer with one or more high-risk characteristics.
- Applicable once per lifetime.

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Research

Universal genetic testing for women with newly diagnosed breast cancer in the context of multidisciplinary team care

Dilanka L De Silva^{1,2,3,4*}, Lesley Stafford^{1,5,6*}, Anita R Skandarajah^{1,4}, Michelle Sinclair¹, Lisa Devereux^{1,6}, Kirsten Hoog^{1,7}, Maira Kentwell^{1,7}, Allan Park⁸, Luci Lai^{1,9,10}, Magnus Zethoven¹¹, Madawa W Jayawardana¹⁰, Fiona Chan⁹, Phyllis N Butow⁹, Paul A James^{12,13}, G Bruce Mann^{14,15}, Ian G Campbell^{16,17}, Geoffrey J Lindeman^{12,13,18} 

The known: Medicare-funded genetic testing is available to people with newly diagnosed breast cancer if the likelihood of finding a pathogenic germline variant, based on family history and tumour pathology, is at least 10%.

The new: Germline testing identified pathogenic variants in 31 of 474 women with newly diagnosed invasive breast cancer (6.5%), eighteen of whom did not meet the 10% risk criterion for guideline-based testing.

The implications: Routine testing removes barriers to testing.

Abstract

Objective: To determine the feasibility of universal genetic testing of women with newly diagnosed breast cancer, to estimate the incidence of pathogenic germline variants and their impact on patient management, and to evaluate patient and clinician acceptance of universal testing.

Design, setting, participants: Prospective study of women with invasive or high grade *in situ* breast cancer and unknown germline status discussed at the Parkville Breast Service (Melbourne) multidisciplinary team meeting. Women were recruited to the pilot.

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3 Classification of 31 participants found to carry pathogenic germline variants, by gene, estimated risk of having a pathogenic germline variant*, and effect on treatment recommendations



*Estimated with the CanRisk or Manchester algorithms. Further information is available in the Supporting Information table 4.

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MOST WOMEN WITH
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SHOULD HAVE A
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TEST

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