CLINICIAN INFORMATION SHEET

Breast and Ovarian Cancer Mainstream Genetic Testing Pack

These packs have been developed by a working group within the SA Cancer Clinical Network to improve access to and provide consistency of genetic testing in cancer patients throughout South Australia. These packs provide essential information and documents to facilitate mainstream testing of cancer patients by non-genetics health care professionals. They are designed to support rather than replace a discussion between the managing specialist and the patient about genetic testing.

The information in these packs is general in nature and may not apply to all clinical scenarios. It is **strongly recommended that any specialist ordering mainstream genetic testing undertake formal education and training** focused on understanding the types, role, and potential limitations and ramifications of genetic testing for both the patient and their families (e.g. COSA online mainstream genetic testing training). If you have any questions or concerns after reviewing this information, please feel free to contact the Adult Genetics Unit (AGU) at the Royal Adelaide Hospital for further information or assistance.

Please also carefully review the Medicare Benefits Schedule (MBS) item numbers (as noted) to ensure compliance prior ordering a genetic test. A patient is only entitled to one germline genetic test of the cancer associated genes in their lifetime; therefore, please confirm that **the most appropriate test is requested and that no prior testing has been undertaken**. Genetic tests which do not meet the MBS criteria may attract unexpected out of pockets costs for the patient or requesting service.

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Considerations for Ordering Mainstream Cancer Genetic Testing

This leaflet is for non-genetic health care professionals who order genetic tests in the cancer setting (mainstream genetic testing). This information is general in nature and does not constitute formal medical advice. Please contact the Adult Genetics Unit if you require further advice or support.

Setting Expectations

When a patient has a medical test, they usually expect to receive definitive results and often think that the test has a high chance of producing meaningful results. However, with genetic testing:

- The pick-up rate varies for each test and clinical indication, and in many contexts is low, ranging from 10% upwards.
- It is possible to receive complex or uncertain results.

Setting realistic expectations about the potential outcomes of a genetic test helps to minimise disappointment and confusion when a patient receives their results.

Familial Implications

Genetic testing has benefits and risks that are different from those associated with other pathology tests. This is because of the predictive nature of certain genetic tests, and the shared familial implications and ownership of genetic information.

As genetic test results may have implications for relatives in addition to the person being tested, it is important to mention this during the consent process.

- Introduce the idea that the patient is being tested as a representative of the family.
- Briefly discuss the role of information sharing in the family and notification of at risk family members if a disease-causing variant is identified.

Insurance Implications

Some types of genetic testing may impact a patient's ability to obtain private underwritten insurance policies. However, this is generally NOT applicable in the setting of a cancer affected patient undergoing a test of cancer associated genes. Please see the separate Insurance Information leaflet for more details.

Types of Testing

The evolution of genetic knowledge means that there are now a number of genes associated with most cancer predisposition conditions. The evolution of genetic testing technologies means that most testing is undertaken using next generation sequencing platforms that analyse multiple genes in parallel. Therefore, in most cancer focused genetic testing, a panel-based test, which characterises a small number of genes, is the most appropriate test. Single gene testing is rarely the best option either clinically or financially.

For example:

- If Lynch syndrome testing is requested, a panel including the following genes should be considered: MLH1, MSH2, MSH6, PMS2 and EPCAM deletions (alter MSH2 gene activity).
- If breast and/or ovarian cancer testing is requested, a panel including at least the following genes should be considered: BRCA1, BRCA2, PALB2, ATM, CHEK2, RAD51C, RAD51D and TP53.

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Request Form

Both the clinical context and the family history are needed for the laboratory to accurately interpret the genetic test result. Prior to ordering a genetic test:

- Take a minimum three generation family history.
- Summarise the relevant clinical information and family history on the request form, including ancestry information if non-Caucasian.

Consent

Consent is required for all genetic tests. The Adult Genetics Unit recommends obtaining written consent. A genetic test consent form:

- Provides the basis for a structured conversation about the potential benefits and limitations of genetic testing.
- Documents permission to share genetic test results with relatives and other clinical services.

Results

When undertaking consent, you need to inform patients of the possible results of genetic testing and their implications, including:

- A disease-causing variant is NOT identified (uninformative or negative result). Please note, benign variants are generally not included on a genetic testing report.
- A disease-causing variant IS identified, this includes likely pathogenic variants [class IV] and pathogenic variants [class V].
- A variant of unknown significance (VUS) is identified [class III]. A VUS should NOT be interpreted as clinically actionable or used in clinical decision making and should NOT be confused with a disease-causing variant. Patients found to have a VUS should be referred to the Adult Genetic Unit for counselling and consideration of further testing.
- An incidental or unexpected finding is possible but unlikely in the cancer gene panel setting.

Care should be taken when deciding whether a variant is disease-causing. Sometimes the answer is not straight-forward. Advice should be sought from a genetics specialist.

The Adult Genetics Unit

The Adult Genetics Unit can support genetic testing in many ways, including:

- Providing clinician training and support for mainstream genetic testing.
- Providing genetic counselling for patients and their families including assistance with decision making about genetic testing, reproductive risk counselling and support for adjustment to genetic test results.
- Co-ordination of family risk notification and predictive genetic testing when a disease-causing variant is identified.
- Interpretation of complex genetic test results.

Other Useful Resources

- COSA Mainstream Education https://www.mainstreamgenetictesting.com.au
- eviQ Cancer Genetics https://www.eviq.org.au/cancer-genetics/adult
- NSW Centre for Genetics Education https://www.genetics.edu.au/
- Adult Genetics Unit, Royal Adelaide Hospital, level 8F 401.52 (MDP 63)

  Tel: 08 7074 2697, Fax: 08 8429 6112, Email: adultgenetics@sa.gov.au

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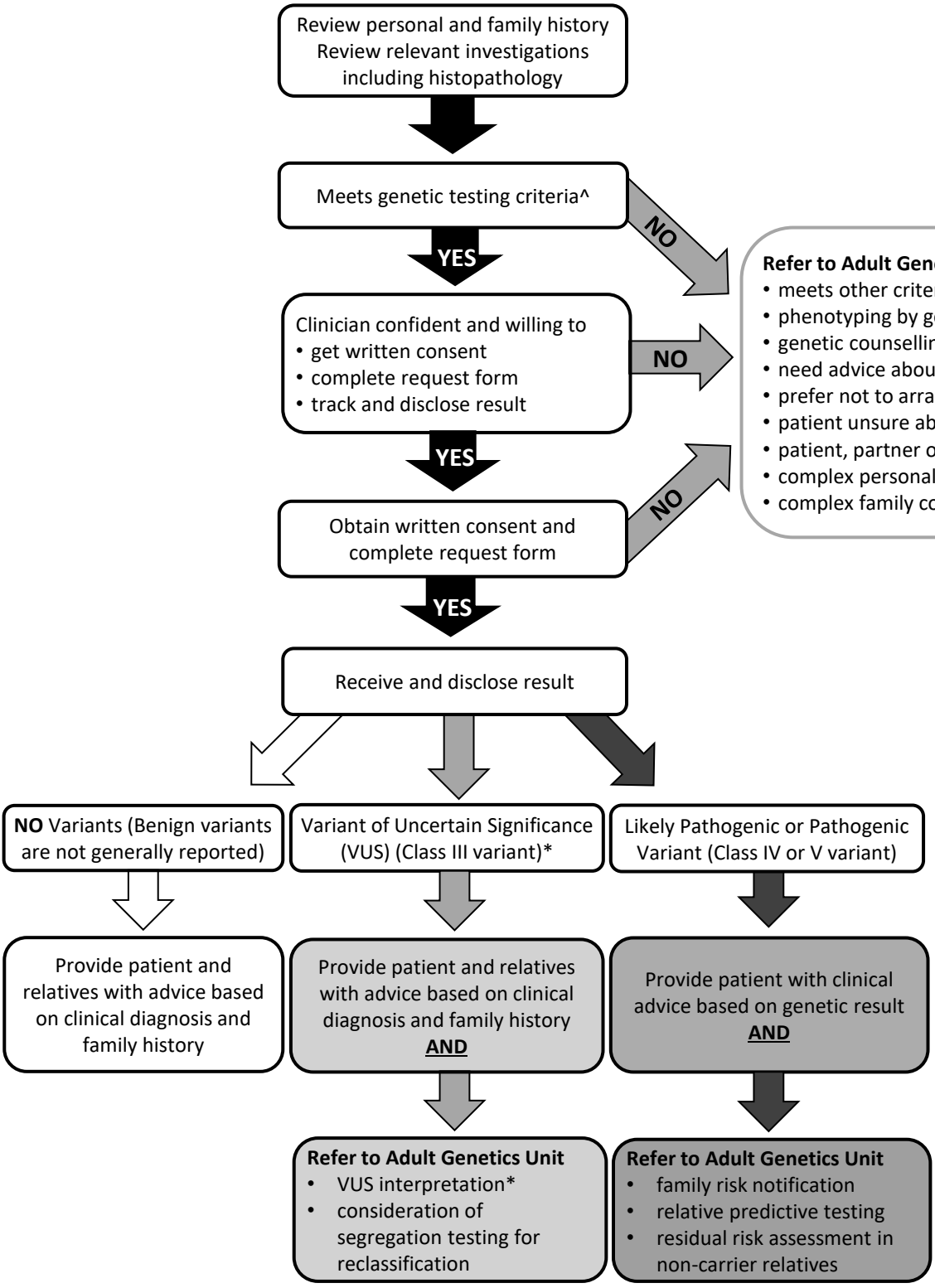
Cancer Genetics Mainstream Testing Flowchart



^ Criteria will differ depending on the cancer type and clinical scenario – please see individual guidelines.
* The clinical relevance of a VUS is by definition unknown. Some VUS will be reclassified overtime; they may be either downgraded to benign/likely benign OR upgraded to likely pathogenic/pathogenic. Therefore a VUS should NOT be used to make clinical decisions for a patient or their family.

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Consent to Mainstream Cancer Genetic Testing

PATIENT LABEL (if available)

Name of person to be tested		**DOB**
Hospital		**UR**
Sample to be collected	☐ Tumour Tissue (somatic) ☐ Blood (germline) ☐ Other (_____)	

I consent to a genetic test for _____

The gene(s)/gene panel being tested is _____

I understand that:

1. The meaning of the result is based on what is known now. This could change in the future.
2. There are limitations to genetic testing:
   - We do not know all the genes that cause cancers.
   - Genetic variants may be found that cannot be interpreted. These are called variants of unknown significance or VUS. A VUS cannot be used to guide clinical care.
3. Rarely, there may be a technical problem with a genetic test. Further sample(s) may be needed.
4. Test results may have implications for both my treatment/cancer risks AND for my family members.

I am aware that:

1. Samples will be stored after testing for at least the period required by laboratory guidelines.
2. I can change my mind about testing at any point before a report is issued.

I consent to the genetic testing described above.
I have had the chance to ask questions and I am satisfied with the answers I have been given.

I give permission for this genetic test result to be retained confidentially by the Adult Genetics Unit and/or given to health care services looking after other members of my family: ☐ Yes ☐ No

Patient signature:..... Date:.....

If I am unable to receive my genetic test result, I nominate the following individual(s) to receive it on my behalf:

Name and Contact Information:.....

Person obtaining consent:..... Signature: .....

Position and specialty of person obtaining consent:.....

Responsible Consultant (please print in capitals): .....

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Breast and Ovarian Cancer Genetic Testing Criteria

Criteria for Mainstream Medicare Funded Testing (MBS Item #73296)

- ❑ Breast cancer with a Manchester score ≥15 or CanRisk score ≥10% OR
- ❑ FIGO Stage III-IV high-grade epithelial (non-mucinous) ovarian, fallopian tube or primary peritoneal cancer

If not eligible on above criteria, do not offer mainstream genetic testing. Consider referral to the Adult Genetics Unit for the following patients:

Genetic testing will be offered by the Adult Genetics Unit for the following patients:

- Male breast cancer
- Invasive breast cancer (any receptor status) diagnosed ≤40 years of age
- Triple negative breast cancer
- Breast cancer and/or high-grade serous endometrial cancer with Ashkenazi Jewish ancestry

Genetic testing may be offered by the Adult Genetics Unit for the following patients:

- Breast cancer diagnosed <50 years of age with a small and/or male dominant family structure (limited female relatives)
- Bilateral breast cancer diagnosed ≤ 60 years of age
- Bilateral lobular breast cancer

Adult Genetics Unit
Tel: (08) 7074 2697
Fax: (08) 8429 6112
Email: adultgenetics@sa.gov.au

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Breast and Ovarian Cancer
Mainstream Genetic Testing Checklist

Patient name:
DOB:
UR:
EMR Visit:
(or patient label)

- ❑ Patient's family history taken and documented
- ❑ Provide patient with genetic testing information leaflets
- ❑ Discuss genetic testing with patient
- ❑ Complete Consent to Genetic Testing form
- ❑ Provide patient with completed SA Pathology request form
  - 4mL blood in EDTA tube
  - Cc: Responsible Consultant
  - Cc: Adult Genetics Unit, Royal Adelaide Hospital
- ❑ Place a copy of consent form and this checklist in patient notes (Paper or scan to EMR)
- ❑ Ensure patient follow-up appointment in 3 months to discuss results (date of appointment _ _ / _ _ / _ _)

MO Signature: _____ Date _ _ / _ _ / _ _

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MANCHESTER Scoring System with pathology adjustment (2017)

DATE	NAME	DOB	UR

Cancer (age at Dx) count invasive breast cancer & DCIS; do **not** count LCIS	**Score**	**Patient's score** pathology adjust Br+Ov	**Relatives' scores** pathology adjust Ov only
Female Breast Ca <30	**11**		
Female Breast Ca 30-39	**8**		
Female Breast Ca 40-49	**6**		
Female Breast Ca 50-59	**4**		
Female Breast Ca >59	**2**		
Male Breast Ca <60	**13**		
Male Breast Ca >59	**10**		
Epithelial ovarian (any grade) <60	**13**		
Epithelial ovarian Ca (any grade) >59	**10**		
Pancreatic Ca	**1**		
Prostate Ca <60	**2**		
Prostate Ca >59	**1**		
Adjust for breast cancer histology (for index case only)			
DCIS only	**-2**		no adjustment needed
Lobular histology	**-2**		no adjustment needed
Adjust for grade and receptors (for index case with ductal cancer or DCIS only)			
Grade 3	**2**		no adjustment needed
Grade 2	**0**		no adjustment needed
Grade 1	**-2**		no adjustment needed
ER positive	**-1**		no adjustment needed
ER negative	**1**		no adjustment needed
Triple negative	**4**		no adjustment needed
HER2 positive	**-6**		no adjustment needed
Ovarian cancer pathology adjustment (for all cases in the family)			
High grade serous <60	**2**		
Do **not** score mucinous, germ cell, borderline	**score 0**		
Adjustment for lack of family history (adjust once only)			
Adopted or no knowledge of blood relatives	**4**		no adjustment needed
	Total	**A=**	**B=**
Manchester Score (add A+B)			**CanRisk** (if done)

Scoring BrCa: Bilateral breast cancer is counted separately (i.e. score each breast cancer); DCIS is included as invasive breast cancer (all cases); lobular breast cancer is included as invasive breast cancer; LCIS is **not** counted.

Histology: For DCIS and invasive ductal breast cancer adjust for histology, grade and/or receptors (where available) for the **index case** only (e.g. grade 3 triple negative = +2 for G3 and +4 for TN). Grade and/or receptor adjustment is **not** made for invasive lobular breast cancer.

Scoring OvCa: Only score epithelial ovarian cancer; do **not** score mucinous, germ cell or borderline ovarian tumours.

In the case of bilinear family history, the highest score from either side is used (do not add together).

Reference: Evans et al. J Med Genet 2017 54(10):674-681

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PATHOLOGY REQUEST FORM
Mainstream Genetic Testing (V1 Nov 2022)

SA PATHOLOGY

AFFIX BARCODE HERE

PERSON BEING TESTED *(all samples must include at least two patient identifiers)*

Family Name	Date of Birth	Sex	Ethnicity *(if known)*	Your Ref
Given Name(s)	Medicare No.			Telephone
Address: *(Number, Street)*	Suburb			Postcode

Patient Status at the time of the service or when the specimen was collected:
- ☐ a private patient in a private hospital or approved day hospital facility
- ☐ a private patient in a private recognised hospital
- ☐ a public patient in a recognised hospital
- ☐ an outpatient public of in a recognised hospital

Medicare Assignment "Section 20A of the Health Insurance Act 1973"
I offer to assign my right to benefits to the approved pathology practitioner who will render the requested pathology service(s) and any eligible pathologist determinable services(s) established as necessary by the practitioner.

Patient Signature & Date _____

Your doctor has recommended that you use SA Pathology. You are free to choose your own pathology provider. However, if your doctor has specified a particular pathologist on clinical grounds a Medicare rebate will only be payable if that pathologist performs the service. You should discuss this with your doctor.

REQUESTING DOCTOR DETAILS

Requesting Clinician:

Responsible Consultant & provider number:

COPY REPORTS TO

Adult Genetics Unit
Royal Adelaide Hospital
via email: adultgenetics@sa.gov.au

CLINICAL SETTING

- ☒ Diagnostic test ☐ Predictive test
- ☐ Carrier Test ☐ Prenatal *(please tick one)*
- ☒ Affected
- ☐ Unaffected *(please tick one)*

TEST TYPE *(please tick)*

☐ Common mutation screen ☒ Full gene mutation analysis ☐ Known familial mutation(s)

CLINICAL NOTES

Personal and Family History of

This is a <u>Medicare Funded</u> Mainstream Genetic Test (MBS item number 73296)

Consent Obtained ☐ YES ☐ NO

MBS & Mainstream Criteria

☐ Breast cancer and Manchester score ≥15 or CanRisk ≥10% ☐ High grade non-mucinous ovarian cancer

TESTS REQUESTED

EDTA	BUCCAL SWAB	OTHER

4ml blood in EDTA tube for:

Genetic testing: Breast and Ovarian Cancer gene panel analysis (sequencing and del/dup studies)

Doctor's Signature & Date

I have verified FULL NAME, DOB and URN on the sample label and request form verbally with the patient and/or checking the patient's ID band.

Collector's Signature: Specimen Collected: / / : Hrs

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Information for people considering genetic testing of their tumour

This leaflet is for people who are thinking about having genetic testing done on their tumour or cancer tissue. It is intended to help people understand and make decisions about this testing. It does not replace a discussion with your managing specialist. If you have any further questions or concerns after reading this leaflet, ask or managing specialist or contact the Adult Genetics Unit.

Genes and Genetic Testing

Genes are the instructions for the body to grow, develop and work. Genes are coded by DNA. Genetic testing involves collecting a sample (blood, hair, tumour tissue), extracting DNA from the sample, and testing the DNA to look for changes in the genes.

Tumour Genetic Testing

This is usually done in consultation with a cancer specialist (i.e. your oncologist), as part of your clinical care, or possibly as part of research or a clinical trial.

- Tumour testing looks for genetic changes in tumour or cancer cells.
- Tumour genetic testing can sometimes help make decisions about the best treatment for a cancer.

Somatic Genetic Changes

A cancer forms when certain genetic changes develop in a cell. The genetic changes allow the cancer cells to grow and spread abnormally. This type of change is called a “somatic genetic change”

- Somatic genetic changes develop as you age; you are not born with these changes.
- Somatic genetic changes are only found in certain cells in the body, like cancer cells.
- Somatic genetic changes cannot be passed on to children.
- To find somatic genetic changes, testing is done on a sample of tumour or cancer, often from a biopsy or surgery.

Germline Genetic Changes

We are all born with genetic changes that are in all the cells of our body. This type of change is called a “germline genetic change”.

- Germline genetic changes make us each unique.
- Germline genetic changes are usually passed down from a parent, and they can be passed down to a child (inherited).

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Germline Genetic Changes and Health

- Most germline genetic changes are harmless and do **not** affect your health, they are called normal variants.
- Some germline genetic changes can affect your health or cause a health problem.
- Germline genetic changes that cause a health problem are called disease-causing variants, mutations, or genetic faults/errors.

The Overlap Between Somatic and Germline Changes

- Germline and somatic (tumour) genetic testing sometimes overlap.
- Because germline genetic changes are present in all the cells of the body, they are also present in the cells of a cancer or tumour.
- This means tumour genetic testing can sometimes find germline genetic changes that are important for both the person with cancer **and** for other family members.
- This sort of genetic test result is uncommon and usually unexpected.

Emotions, Family and Tumour Genetic Testing

Genetic test results can have emotional impacts for both the person having the test and their family. If you are having any sort of genetic test, think about:

- How you might feel receiving the results, including unexpected results.
- How you will share the results with your family members.
- How to be open with, and supportive and respectful of other family members' responses to a genetic test result.

More Information

If you have questions or worries about a genetic test, you can talk to your specialist. In some situations your specialist may refer you to a Clinical Genetics Service.

Other places to get information:

Seattle Children's Hospital leaflet (Somatic and Germline Cancer Testing)
www.seattlechildrens.org/globalassets/documents/for-patients-and-families/pfe/pe2960.pdf

Centre for Genetics Education
http://www.genetics.edu.au/

If you have further questions or concerns, you can speak to your cancer specialist or contact:

The Adult Genetics Unit
Royal Adelaide Hospital (8F401.52, MDP 63)
Port Road, ADELAIDE, SA 5000
Telephone: 08 7074 2697 Fax: 08 8429 6112

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Information about Genetic Testing and Cancer

This leaflet was written for people who are thinking about having a genetic test following a cancer diagnosis. This leaflet does not replace a discussion with your managing specialist. If you have any questions or concerns after reading this leaflet, please discuss them with your managing specialist or contact the Adult Genetics Unit.

What are genes?

The human body is made up of millions of cells. Each cell contains DNA. DNA spells out the genetic instructions (genes) the cells need. Some genes tell cells how to grow, divide and work properly. Some genes help keep DNA healthy. Other genes tell worn-out cells when to self-destruct (die). These genes work together to control cell growth.

What is cancer?

The DNA in our cells is continually damaged by the things we are exposed to in our environment, for example UV light or cigarette smoke, and the process of aging. This DNA damage is usually repaired but the repair process is not perfect. This means that damage can build up in our DNA. If a cell has too much DNA damage it normally dies.

Cancer occurs when abnormal cells do not die and start to grow in an uncontrolled way. These abnormal cells can damage or invade the nearby tissues or spread to other parts of the body; this is called a cancer.

What is familial cancer?

Rarely, a person is born with a genetic error (called a variant or mutation) in a cell growth-control gene or a DNA-repair gene. These genetic errors increase the chance of developing a cancer. Usually, the genetic error has been inherited from the person's mother or father. If a genetic error is inherited, other blood relatives may also have an increased chance of developing cancer. This is called familial or hereditary cancer.

What is a genetic test?

A genetic test involves collecting a sample, usually blood. Genetic material (DNA) is extracted from the sample and analysed looking for genetic errors or variants.

- Everyone's genes have differences or variants, this makes us each unique.
- Most genetic variants are harmless and do not cause problems.
- Some genetic variants change how a gene works and **do** cause a problem, like an increased risk of developing a cancer.
- The names for a variant that causes a medical problem include a disease-causing variant, mutation, genetic error or genetic fault.
- Most genetic tests analyse a number of genes that are all known to cause a particular health problem, like an increased risk of cancer. This is called a gene panel test.
- Genetic testing is part of the standard care for patients with certain types of cancer. This genetic testing is not research based or part of a clinical trial.

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Why have a genetic test?

There are many reasons a doctor may suggest having a genetic test in the setting of a cancer diagnosis, including:

- To help identify the best treatments for some specific types of cancer.
- To help family members understand their cancer risks.
- To help family members manage and reduce their cancer risks through early cancer screening tests and other management options.

What are the possible outcomes of a genetic test?

1. No genetic variants are found. This is the most common result and is called a negative or uninformative test. This may mean that the cancer did not have an inherited genetic cause or that an inherited genetic cause cannot be found using the currently testing technology.
2. A genetic variant that explains the cancer is found. This is a less common result. This may influence cancer treatments. It also means that other family members may have the variant and can choose to have their own genetic test.
3. A variant that is not understood is found. This is an uncommon result and is called a variant of unknown significance or VUS. A VUS is neither good nor bad; its meaning is just not known yet. Sometimes more testing can help to understand the meaning of a VUS, or the meaning may become clearer overtime. A VUS cannot be used to influence cancer treatments or offer testing to other relatives.
4. An unexpected variant is found. This is a rare result called an incidental finding. It occurs when a genetic variant that causes a different medical problem is found.

What do I tell my family about genetic testing?

A genetic variant found in you may be relevant for your blood relatives. Genetic variants can occur in both sexes and both sexes can usually pass a genetic variant down to their children. Telling your family members about a genetic variant can be difficult but may help them understand and manage or reduce their cancer risks.

What about genetic tests and insurance?

A genetic test result is part of a person's health history. In Australia, premiums for private health insurance do **not** depend on health history. However, other types of insurance like income protection and life insurance may be impacted by personal or family health history, including genetic testing. This is usually not relevant for a person with a cancer but may be relevant for their family. Ask for an Insurance Information leaflet if you have more questions or concerns about genetic testing and insurance.

Where can I get more information or support?

- Genetic Alliance Australia https://www.geneticalliance.org.au/
- NSW Centre for Genetics Education https://www.genetics.edu.au/
- Pink Hope https://www.pinkhope.org.au/
- Lynch Syndrome Australia https://lynchsyndrome.org.au/
- Adult Genetics Unit, Royal Adelaide Hospital Tel: 08 7074 2697

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