Cancer Mainstream Genetic Testing Pack

These packs has 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. They 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, consent requirements, and potential limitations and ramifications of genetic testing for both the patient and their families. If you have any questions or concerns after reviewing this information, please 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 any specific cancer associated gene in their lifetime; therefore, please confirm that **the most appropriate test is requested (usually a panel based rather than single gene test) and that no prior testing has been undertaken**. Genetic tests which do not meet the MBS criteria may attract large unexpected out of pockets costs for the patient or requesting service.

The Available Mainstreaming Resources include:

General Pack for Ordering Clinicians

- Clinician Information Sheet
- Considerations for Ordering Mainstream Cancer Genetic Testing Leaflet
- Cancer Genetics Mainstream Testing Flowchart
- Consent To Mainstream Cancer Genetic Testing Form

Cancer Type Specific Packs (Breast, Ovarian, Prostate and Lynch Syndrome)

- Genetic Testing Criteria and Checklist
- Scoring Criteria to Determine Eligibility (when applicable)
- Consent To Mainstream Cancer Genetic Testing Form
- SA Pathology Request Forms (partially pre-filled)
- Patient Leaflet - Information about Genetic Testing and Cancer Leaflet
- Patient Leaflet - Information for People Considering Genetic Testing of their Tumour Leaflet (when applicable)

Patient Supplemental Information and Resources

- Variant of Unknown Significance Leaflet
- Talking to Family and Friends About Your Test Result Leaflet
- Coping Strategies for People with a Cancer Gene Variant Leaflet
- Emotional Response Following Genetic Testing Leaflet

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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

Previously, some types of genetic testing could impact a patient's ability to obtain private underwritten insurance policies. This would generally NOT be applicable in the setting of a cancer affected patient undergoing a test of cancer associated genes. Additionally, the law is now changing, and new genetic discrimination protections are being implemented.

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 (that 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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CLINICIAN INFORMATION SHEET

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

- **Patient Information Video** (scan the QR code or use the link) https://t2m.io/zr5HM4O0
- 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 T 08 7074 2697, F 08 8429 6112, adultgenetics@sa.gov.au

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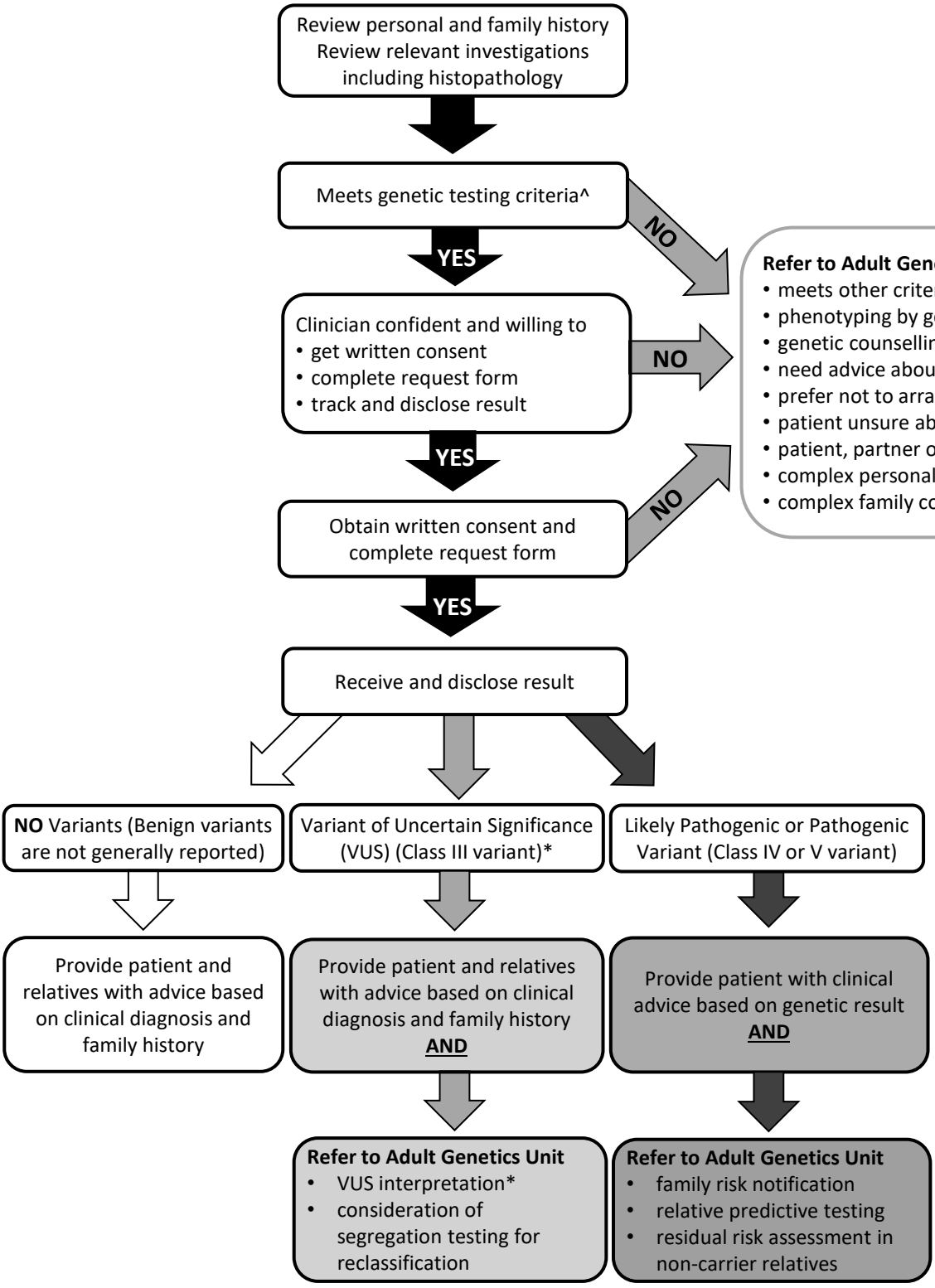
Cancer Genetics Mainstream Testing Flowchart



^ 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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