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| SOP Title | Genomic Testing for Inherited Ovarian and Endometrial Cancers |
| Version |  |
| Author |  |
| Issued by |  |
| Date Issued |  |
| Date Updated |  |
| Directorate |  |

Introduction

Around 22,000 women are diagnosed with a gynaecological cancer in the UK each year; within this collective group, there are five separate gynaecological cancers: endometrial, ovarian, vulval, cervical and vaginal.[[1]](#footnote-1) Approximately 15-20% of ovarian cancers are associated with an inherited pathogenic genetic alteration, *BRCA1* or *BRCA2* account for the majority of these.[[2]](#footnote-2) NICE Guidelines recommend that anyone with a diagnosis of endometrial cancer is tested for Lynch Syndrome if their tumours display mismatch repair deficiency. Lynch Syndrome is an inherited condition which is associated with pathogenic alterations in the mismatch repair genes. This change increases the risk of several cancers, primarily colorectal and endometrial cancer.

Next Generation Sequencing technology has made it possible to sequence multiple genes simultaneously, at lower cost, thus maximising the health benefits to patients with a suspected inherited cause of their cancer. These tests are available to teams delivering cancer care via the National Genomic Test Directory. Included in the Directory are the R207 and R210 panels for inherited Ovarian and Endometrial Cancers.*[[3]](#footnote-3)*

Knowing if a patient has pathogenic alterations helps to ensure they are given the most appropriate and effective treatment for them. It can also aid in preventing future cancers, both for the patient and their families. Lifetime risk (until age 80 years) of other cancers, (such as breast cancer) associated with *BRCA1* pathogenic variants are estimated to be 65–79% and for *BRCA2* pathogenic variants, 61–77%; within this group, the risk of developing a second breast cancer is estimated to be between 40-60%.[[4]](#footnote-4) Other cancers associated with the genes in the R210 panel (Lynch Syndrome) include, stomach cancer, ovarian cancer, cancers of the gastrointestinal tract (sigmoid, colon, duodenum), brain cancer, bladder and kidney cancer and pancreatic cancer.[[5]](#footnote-5)

Genetic testing of cancer patients and their unaffected relatives facilitates the implementation of risk-reducing strategies and more effective treatment including: targeted therapies, enhanced surveillance, chemoprevention and risk-reducing surgery (bilateral mastectomy and/or bilateral salpingo-oophorectomy). Awareness of pathogenic variants in the R207 and R210 gene panels can guide the surgical treatment and appropriateness of adjuvant therapies for those patients considering risk reducing surgery and systemic anti-cancer therapy (SACT).[[6]](#footnote-6)

This SOP is designed to guide appropriately trained doctors and Clinical Nurse Specialists to undertake counselling and consenting of patients who fall under the mainstreaming criteria for Germline testing as set out in NHS England’s National Genomic Test Directory (2023). This is to ensure all patients receive a safe and effective high-quality service by facilitating patients’ timely access to the most appropriate treatment.

Responsibility

It is the responsibility of the MDT including surgeons, oncologists, nurses and allied healthcare professionals to follow this SOP in accordance with the Trust Escalation Policy and Corporate Strategy.

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| **Team Members** | **Details** |
| **Consultants** |  |
| **Lead Breast Nurse** |  |
| **Clinical Nurse Specialists** |  |

TESTING CRITERIA

1. The National Genomic Test Directory (NGTD) sets out the test criteria for R207 (inherited ovarian cancer) testing:

**Living affected individual** (proband) with ovarian cancer where the individual +/- family history meets one of the criteria. The proband has:

* High grade non mucinous epithelial ovarian cancer (EOC) **at any age.**

**OR**

* Epithelial ovarian cancer (EOC) **AND:**
  + **1 or more** first degree relatives with EOC

**OR**

* + **1 or more** second degree relatives with EOC (where the separating relative has had a BSO, is male or is a deceased female).

**OR**

* + **2 or more** second/third degree relatives with EOC.
* Deceased affected individual where criteria above is met (or Manchester Score of 20) **AND:**
  + **Appropriate tissue is available** (tumour or normal)

**AND:**

* + **No living affected individual is available for genetic testing.**

1. The National Genomic Test Directory (NGTD) sets out the test criteria for R210 (Lynch Syndrome) testing :
2. **Criteria for germline testing an affected individual:**

* A dMMR tumour where additional testing results suggest Lynch Syndrome:
  + *BRAF* testing in *MLH1* deficient colorectal cancers.
  + *MLH1* hypermethylation testing in *BRAF* negative colorectal cancers.
  + ALL *MLH1* deficient uterine cancers.
* A positive family history of modified Amsterdam Criteria (regardless of dMMR tumour status).
* **Personal or family history** suggestive of CMMRD (Constitutional Mismatch Repair Deficiency) with Wimmer score of **3 or more.**

1. **Criteria for MSI/IHC testing on a stored tumour sample prior to germline testing:**

* Personal/family history of colorectal cancers reaching Modified Amsterdam Criteria (≥ 3 cases of Lynch related cancer over ≥2 generations with ≥1 case diagnosed under 50yrs.
* Any lynch-related cancer\* **under 50 years** (excluding isolated pancreas, prostate or gastric cancers)
* Two Lynch-related cancers (**any age**, if one is colorectal or endometrial)
* Lynch-related cancer and **1 or more** first degree relative has Lynch-related cancer (both occurred **60 years or less**, one is colorectal or endometrial)
* Lynch-related cancer and **2 or more** relatives (first / second / third degree relatives) have Lynch-related cancer (all occurring ≤75years, one is colorectal or endometrial)
* Lynch-related cancer and **3 or more** relatives (first / second / third degree relatives) have Lynch-related cancer (occurring any age, one is colorectal or endometrial)

1. **Criteria for somatic (tumour) Lynch syndrome panel testing:**

* Individual has colorectal or endometrial cancer with a dMMR tumour with normal *BRAF* and *MLH1* hypermethylation analysis **AND** germline testing did not reveal a pathogenic mutation.
* Personal/family pattern of disease whereby demonstration of acquired MMR mutations (and therefore exclusion of constitutional MMR abnormality) enables downscaling of surveillance
* Deceased affected individual with colorectal or endometrial cancer ≤60 years AND tumour featuring high/intermediate MSI or loss of staining of MMR protein(s) on IHC, AND one first degree relative with Lynch-related cancer ≤60 AND no living affected individual is available for genetic testing.

1. **Clinical Criteria for germline testing in an unaffected individual: (see note on testing)**

* First degree relative affected with Lynch-related cancer, AND
* Family history of colorectal cancer/Lynch-related cancers reaches Amsterdam Criteria (≥3 cases over ≥2 generations with ≥1 case affected <50 years) AND
* Tumour sample analysis from affected family member has been attempted and is not possible, failed, indeterminate or indicates MMR deficiency (via IHC or MSI), AND
* Somatic sequencing is not possible, or failed, AND

No living affected individual is available for genetic testing

*NOTES*

*All new diagnoses of colorectal and endometrial cancers should have tumour MSI/IHC testing completed.*

*This may include BRAF testing in MLH1 deficient colorectal cancers and MLH1 hypermethylation testing in BRAF negative colorectal cancers and all MLH1 deficient uterine cancers. MLH1 hypermethylation testing is included on the Cancer Test Directory under* ***M1.5****.*

***Testing of unaffected individuals can only be carried out by Clinical Genetics Services.***

*Please refer to the National Genomic Test Directory for other tests related to Colorectal Cancer.*

testing pathway

\*\*INSERT LOCAL PATHWAY HERE\*\*

TESTING PROTOCOL

* Germline sample to include 4-5ml EDTA (purple-top tube) total 10-20ml. \*AMEND TO REFLECT LOCAL PROCEDURES \*
* Cancer clinician may include Surgeon, Oncologist, Registrar, Clinical Nurse Specialist etc, who has completed appropriate training on counselling and consenting.



Training to take consent

* Complete additional genomics courses/training depending on the individual Clinical Nurse Specialist’s learning needs. Recommended courses include the following from Genomic Education Programme (***available for free for NHS and UK Universities via NHS England’s Elearning for Health porta***l [Online courses Archives - Genomics Education Programme (hee.nhs.uk)](https://www.genomicseducation.hee.nhs.uk/product-category/online-courses/)):
  + Genomics 101 – Taking and Drawing a Genetic Family History
  + Genomics 101 – Genomics in Healthcare
  + Genomics 101 --Genomics Medicine Service: Introduction to Offering Genomic Tests
  + Genomics 101 - Talking Genomics: Tips and Tools for Communicating
* Obtain copies of patient information leaflets, consent forms and test request forms. These are subject to local Trust Governance and approval.
* Complete local Trust eLearning module “318 Consent ESR eLearning”.
* Spend time shadowing clinician who is competent in consenting for mainstreaming testing then complete consenting under their supervision until deemed competent.
* Optional - shadowing the genetic counsellor via Microsoft Teams platform or clinic.

Key documents:

* **Consent form**
* **Patient results letters: Normal, VUS, Variant found.**
* **Referral to clinical genetics form**
* **GMS Test Request Form (Blood sample form)**
* **Patient information leaflet**
* **Competency Training Checklist**

**Competency training and evidence form: facilitating germline genomic testing**

*Note: This framework has been designed to be a developmental tool to support individuals and organisations, and is not intended to be used as a grading or assessment tool. This form is an optional resource that may be used to demonstrate evidence of competence for use in clinical practice; it may be useful for individual records, appraisals or CPD records. Further information can be found at* [www.genomicseducation.hee.nhs.uk/consent-a-competency-framework/](http://www.genomicseducation.hee.nhs.uk/consent-a-competency-framework/)

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| **Start date:** |  | **Trainee Name:** |  | | | **Position:** |  |
| **Trainer(s):** |  | | | | | | |
| **Assessed and signed by:** |  | | | **Date:** | | |  |
| **Competency** | | | | **Tick** | **Comments** | | |
| 1 Ensures the process of recording consent for a genomic test follows national and local processes and governance arrangements, and is appropriate for the test being requested | | | |  |  | | |
| Demonstrates familiarity with the National Genomic Test Directory and adheres to this guidance when offering genomic testing, including the funding model, sample requirements and local requesting pathways. | | | |  |
| Understands the national and local processes for changes to consent (i.e. at age 16 with capacity, for additional tests, when a patient changes their mind about having the test). | | | |  |
| Demonstrates familiarity with principles of the Human Tissue Act 2004, Data Protection Act 2018 and/or General Data Protection Regulation 2018 as they apply to the use of DNA and genomic data. | | | |  |
| **Date discussed with trainer:** | |  | | **E-signature/initials of trainer:** | | | |
| 2 Demonstrates up-to-date knowledge of the conditions occurring within their specialist area for which genetic or genomic testing may be offered | | | |  |  | | |
| Understands general genetic concepts, the inheritance and mechanism of disease. | | | |  |
| Is able to elicit a family history to assess the risk of one or more conditions. | | | |  |
| Understands how conditions may present and the variability of clinical presentations. | | | |  |
| Knows the likelihood of the patient’s presenting condition having a genetic basis, versus other possible factors (i.e. behavioural, social, environmental) that may contribute. | | | |  |
| Recognises the different implications of somatic versus germline analysis. | | | |  |
| **Date discussed with trainer:** | |  | | **E-signature/initials of trainer:** | | | |
| 3 Assesses where genomic testing is appropriate in the patient’s clinical pathway | | | |  |  | | |
| Knows why a test may or may not be offered. | | | |  |
| Considers ethnic and/or population-specific factors that may influence the type of test being offered. | | | |  |
| Is aware of alternative tests to the genomic test being offered, if applicable. | | | |  |
| Knows of possible future test options and choices, pending the results. | | | |  |
| **Date discussed with trainer:** | |  | | **E-signature/initials of trainer:** | | | |
| 4 Conveys to patients the purpose and process of the clinical test being offered | | | |  |  | | |
| Explains the context of the test (diagnostic, predictive or carrier). | | | |  |
| Outlines the scope and limitations of the test based on the technology being used. | | | |  |
| Explains the possible results and the turn-around time and feedback process for any results. | | | |  |
| Describes the potential relevance of the test for that patient/family, including clinical actions that may or may not be taken. | | | |  |
| Explains possible unexpected results (incidental findings). | | | |  |
| Describes the potential uncertainty of genomic information, and the iterative nature of analysing results | | | |  |
| Describes how samples and data may be used, stored and accessed. | | | |  |
| Outlines the familial implications of results and the importance of sharing results with relatives. | | | |  |
| Understands the Code on Genetic Testing and Insurance. | | | |  |
| **Date discussed with trainer:** | |  | | **E-signature/initials of trainer:** | | | |
| 5 Explains and answers questions relating to the National Genomic Research Library\* where applicable | | | |  |  | | |
| Outlines the potential benefits and risks of data and sample use, storage and sharing on personal, familial and societal levels. | | | |  |
| Describes how samples and data may be used, stored and accessed. | | | |  |
| Explains the process of partial or complete withdrawal of consent for research at any time. | | | |  |
| **Date discussed with trainer:** | |  | | **E-signature/initials of trainer:** | | | |
| 6 Applies core clinical skills to the genomic test conversation | | | |  |  | | |
| Assesses capacity according to the Mental Capacity Act 2005 and other guidelines (such as Gillick competency). | | | |  |
| Establishes the patient’s understanding and expectations of the genomic test being offered. | | | |  |
| Employs effective communication skills to support decision making and enable patients to make a choice without coercion or bias. | | | |  |
| Tailors provision of information based on the patient’s cognitive ability, age and language. | | | |  |
| Engages with all individuals present in the discussion and incorporates the potentially different views of family members. | | | |  |
| Addresses the psychosocial impact of genomic testing and risk, taking into consideration the impact of disease on the individual and/or family. | | | |  |
| Considers the factors that may influence an individual’s choice to consent, including additional physical and mental health history; cultural, religious, familial and personal values; and timing of the conversation with respect to the patient’s care and/or other life events. | | | |  |
| Respects the patient’s right to decline the genomic test, and is able to explain potential implications, limitations, and/or alternatives for the patient’s care. | | | |  |
| **Date discussed with trainer:** | |  | | **E-signature/initials of trainer:** | | | |
| 7 Recognises one’s ongoing responsibilities to the patient and acts when appropriate | | | |  |  | | |
| Understands that duty of care may extend beyond the initial feedback of genomic findings. | | | |  |
| Is able to inform relevant professionals involved in managing the patient’s care and initiate onward referrals to other specialists. | | | |  |
| Knows of patient resources, support groups, and eligibility criteria for research (where applicable). | | | |  |
| **Date discussed with trainer:** | |  | | **E-signature/initials of trainer:** | | | |
| 8 Seeks further assistance, where relevant, based on scope of practice | | | |  |  | | |
| Knows how to contact their local genomics laboratory, Clinical Genetics service and multidisciplinary review meetings if relevant. | | | |  |
| Can recognise and understand one’s professional responsibilities and boundaries, and when to refer to relevant specialists for further support or patient management. | | | |  |
| Knows how to access educational resources to support learning where relevant (such as Good Clinical Practice training and Genomics Education Programme courses). | | | |  |
| **Date discussed with trainer:** | |  | | **E-signature/initials of trainer:** | | | |
| **Further reflection notes:** | | | | | | | |
| e.g. any suggested resources or actions to support competency development, recommendations | | | | | | | |

1. The Eve Appeal (2023) *Gynaecological Cancers. https://eveappeal.org.uk/gynaecological-cancers/* [↑](#footnote-ref-1)
2. Sobocan, M., Chandrasekaran, D., Sideris, M., et al. (2023) “Patient decision aids in mainstreaming genetic testing for women with ovarian cancer: A prospective cohort study” *British Journal of Obstetrics and Gynaecology,* 00:1-10. Accessible at: DOI: 10.1111/1471-0528.17675 [↑](#footnote-ref-2)
3. NHS England. *National Genomic Test Directory v5* (London, 2023). Accessible at: https://www.england.nhs.uk/wp-content/uploads/2018/08/rare-and-inherited-disease-eligibility-criteria-v4.pdf. [↑](#footnote-ref-3)
4. Ain, Q, Richardson, C., Mutebi, M., George, A., Kemp, Z., Rusby, J. “Does Mainstream BRCA Testing affect surgical decision-making in newly-diagnosed breast cancer patients?” *The Breast*, 67 (Feb 2023): 30-35. Accessible at: https://www.thebreastonline.com/action/showPdf?pii=S0960-9776%2822%2900193-X [↑](#footnote-ref-4)
5. Ryan et al (2020) “Lynch Syndrome for the Gynaecologist” *The Obstetrician and Gynaecologist,* 23 (1), 9-20. Accessible at: <https://doi.org/10.1111/tog.12706> [↑](#footnote-ref-5)
6. Ain, Q, Richardson, C., Mutebi, M., George, A., Kemp, Z., Rusby, J. “Does Mainstream BRCA Testing affect surgical decision-making in newly-diagnosed breast cancer patients?” *The Breast*, 67 (Feb 2023): 30-35. Accessible at: https://www.thebreastonline.com/action/showPdf?pii=S0960-9776%2822%2900193-X [↑](#footnote-ref-6)