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| SOP Title | Genomic Testing for Prostate Cancer |
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Introduction

Prostate cancer is the second most diagnosed cancer in men, with an estimated 1.4 million diagnoses and 375,000 deaths worldwide in 20201.

In 2018, the UK ranked 7th amongst the 31 European countries studied for the incidence of prostate cancer, with 172 in every 100,000 men being diagnosed with the condition2.

There are around 55,100 new prostate cancer cases in the UK every year, that's around 150 every day (2017-2019). In males in the UK, prostate cancer is the most common cancer, and accounts for 28% of all new cancer cases in males in the UK (2017-2019)3.

Each year around a third (34%) of all new prostate cancer cases in the UK are diagnosed in males aged 75 and over (2017-2019). Around 3,100 cases of prostate cancer each year in England are linked with lower deprivation3.

Family history and ethnic background are associated with an increased prostate cancer incidence suggesting a genetic predisposition4.

**Prostate cancer susceptibility genes**

**BRCA 1 and BRCA2**

Men with BRCA mutations have an increased risk of getting prostate, breast or pancreatic cancer. For example, 12 or 13 men in every 100 will get prostate cancer before the age of 80. But out of every 100 men who have the BRCA2 gene mutation, 20 will develop prostate cancer in their lifetime.

**ATM** (ataxia telangiectasia mutated gene)

Men with a germline mutation in the ATM gene have an increased risk of developing prostate cancer, and the prostate cancer might develop at a younger age.

If a person **does have** the faulty ATM gene:

* they can pass it on to their children.
* each child has a 50% (1 in 2) chance of being born with it. Pregnancy planning options are available to people who want to prevent the faulty gene from being passed on.

**CHEK2**

Men with a germline mutation in the CHEK2 gene have an increased risk of prostate cancer.

**MLH1, MSH2, MSH6, PMS2**

Germline mutations in these genes are associated with Lynch Syndrome and have associated increased risk of prostate cancer and other cancers (include link to lynch syndrome information)

Germline gene mutations have two important implications for patients: potential prostate cancer treatment planning and potential family cancer risk.

Next Generation Sequencing technology has made it possible to sequence multiple genes simultaneously, at lower cost, thus maximising the health benefits to patients with cancer. These tests are available to teams delivering cancer care via the National Genomic Test Directory. Included in the Directory5

Knowing if a patient has pathogenic alterations helps to ensure they are given the most appropriate and effective treatment for them.

1. Culp, M.B., et al. Recent Global Patterns in Prostate Cancer Incidence and Mortality Rates. Eur Urol, 2020. 77: 38.<https://pubmed.ncbi.nlm.nih.gov/31493960>
2. Office of National Statistics, Cancer survival in England: national estimates for patients followed up to 2018, 2019. Available via: <https://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/conditionsanddiseases/bulletins/cancersurvivalinengland/stageatdiagnosisandchildhoodpatientsfollowedupto2018>
3. Cancer Research UK web content, <https://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/prostate-cancer/incidence>, Accessed August 2024.
4. Hemminki, K. Familial risk and familial survival in prostate cancer. World J Urol, 2012. 30: 143. <https://pubmed.ncbi.nlm.nih.gov/22116601>
5. National Genomic Test Directory

This SOP is designed to guide appropriately trained doctors and Clinical Nurse Specialists to undertake mainstreaming criteria for testing as set out in NHS England’s National Genomic Test Directory. 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** |  |
| **Clinical Nurse Specialists** |  |

TESTING CRITERIA

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

**Somatic testing M218 panel criteria:**

M218.1 Multi-target NGS panel - small variant (BRCA1, BRCA2) for somatic/tissue testing

* Patient is eligible for NICE approved PARP inhibitor and has a diagnosis of metastatic castration-resistant prostate cancer. Somatic analysis should be performed first, germline analysis (R444.2) should only be performed should there be insufficient tissue, or the somatic analysis has failed.

M218.2 Multi-target NGS panel - structural variant (TMPRSS2-ERG, NTRK1, NTRK2, NTRK3)

* Only required if there is a doubt over the aetiology of a tumour on the basis of morphology and prostate carcinoma is in the differential

M218.3 TMPRSS2-ERG FISH

* Only required if there is a doubt over the aetiology of a tumour based on morphology and prostate carcinoma is in the differential.

**Germline testing R430 for inherited prostate cancer:**

**Testing criteria:**

* Proband (first person in family) diagnosed with prostate cancer under 50 years of age.
* Ashkenazi Jewish ancestry and prostate cancer at any age.
* Proband diagnosed with metastatic prostate cancer under 60 years of age.
* Proband diagnosed with prostate cancer with a family history of prostate cancer where estimated likelihood of identifying a pathogenic variant in the relevant target genes is at least 10%.

Genetic testing may occasionally be appropriate outside these criteria following discussion at a specialist MDT with a cancer geneticist present.

**Overlapping indications**

* R208 inherited breast cancer and ovarian cancer – proband (first person in family) affected by prostate cancer who has a personal/family history of other BRCA related cancers see R208 (BRCA related cancers = breast, ovarian, pancreatic, prostate).
* R210 inherited MMR deficiency (Lynch syndrome) prostate cancer with a personal/family history of Lynch related cancers see R210 (Lynch related

cancers *Colorectal cancer, Endometrial cancer, Epithelial ovarian cancer, Ureteric cancer, Transitional cell cancer of renal pelvis, cholangiocarcinoma, small bowel cancer, Glioblastoma, endocervical cancer, multiple sebaceous tumours, prostate, gastric and pancreas***).**

* R444 NICE approved PARP inhibitor treatment indication Metastatic, castration-resistant prostate cancer where somatic tumour testing (M218.1) has failed.
* M218 somatic prostate cancer testing

Referrals for testing are triaged by the genomic laboratory and targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

Testing should be at presentation and be requested by clinical genetics, oncology, or urology.

All tests below are undertaken within R430 unless clinical presentation or initial results indicate all are not necessary.

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| Code | Target type | Target Name | Method |
| R430.1 | Small panel of genes | BRCA1, BRCA2, MLH1, MSH2, MSH6, ATM, PALB2, CHEK2 | Small panel |
| R430.2 | Small panel of genes | BRCA1, BRCA2, MLH1, MSH2, MSH6, ATM, PALB2, CHEK2 | Exon level CNV detection by MLPA or equivalent |

Associated tests - 2444.2

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| --- | --- | --- | --- |
| Code | Target type | Target Name | Method |
| R4444.2  NICE, approved PARP inhibitor treatment prostate cancer | Small panel of genes | BRCA1, BRCA2 | Small panel |

testing pathway

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

Training

* 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 – 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:

* **GMS Test Request Form (Blood sample form)**
* **Patient information leaflet**
* **Competency Training Checklist**

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| **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 | | | |