NHS England

NHS North Thames
NHS Genomic Medicine Service Alliance

The NHS Jewish BRCA Testing Programme

JEWISH MEDICAL ASSOCIATION UK

Queen Mary University of London

ICR The Institute of Cancer Research

The ROYAL MARSDEN NHS Foundation Trust

Jnetics

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- **Summary**
- **Overview**
- **Programme Pathway**
- **Background information**
- **Additional Resources**

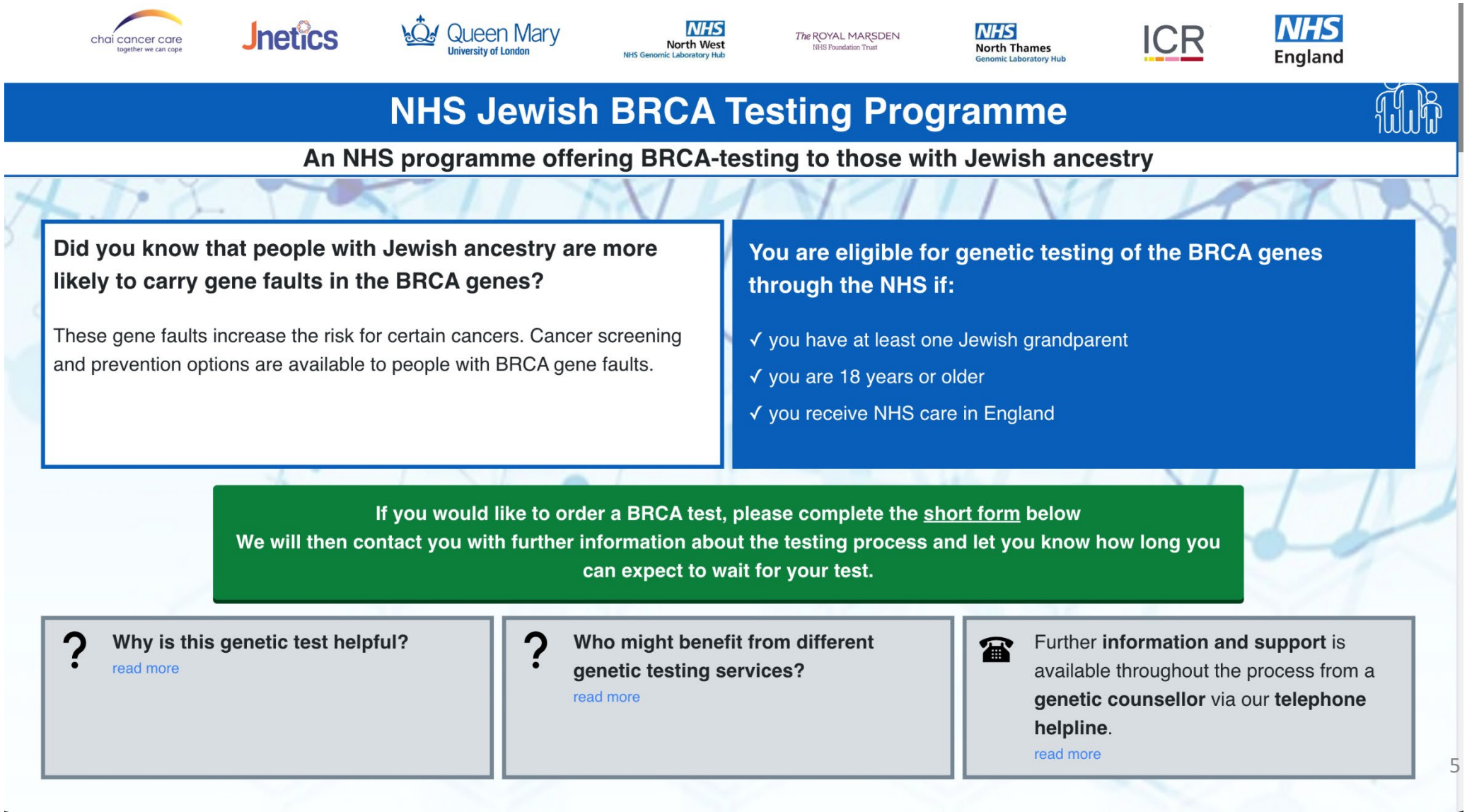
SUMMARY….

- 1 in 40 Ashkenazi Jews and 1 in 100-140 Sephardi Jews carry a *BRCA1* or *BRCA2* Pathogenic Variant or mutation or genetic alteration. This compares to 1 in 200-250 in the general population.
- Women carrying a *BRCA* mutation have a 17-44% risk of ovarian cancer and ~70% risk of breast cancer. These cancers are potentially preventable.
- Up to 10% of breast cancers and 40% of ovarian cancers in the Jewish population are due to BRCA mutations.
- BRCA carriers can opt for screening and/or preventive interventions
- Despite 25 years of testing in the NHS ~90% of *BRCA* carriers remain unidentified
- Offering testing to everyone of Jewish ancestry irrespective of family history (Population testing) can identify 150% additional BRCA carriers than standard family history or clinical criteria based testing policy
- Population *BRCA* testing is associated with reduction in anxiety compared with family history criteria based testing
- This approach is cost-effective for the NHS and cost saving in most scenarios.
- It can prevent many more breast and ovarian cancers, saving both lives and money.

SUMMARY….

- In the Jewish BRCA testing (JBRCA) programme, NHS England is offering genetic testing of the *BRCA1* and *BRCA2* genes to people with Jewish ancestry (at least one Jewish grandparent)
- The JBRCA testing is free, supported by the NHS England Cancer Programme, and coordinated through the North Thames GMSA
- This is available to both men and women, over the age of 18 years
- Interested individuals need to self register through a web site/ web portal – https://nhsjewishbrcaprogramme.org.uk/
- Registered individuals are sent an information pack, a saliva sample collection kit, and consent form.
- Written information (pre-test booklet) is made available along with the option of speaking to a genetic counsellor over the telephone.
- Before anyone undergoes testing they should consider the implications of a positive result for themselves and their family members
- People can contact the NHS dedicated helpline for counselling and support.
- Support is also available through community charities (e.g. Chai Cancer Care)
- Consenting individuals post sample and consent form back through Royal Mail (local post office) in a pre-paid plastic mailing bag.
- *BRCA* test results are returned via post. Post test counselling is provided by the NHS JBRCA programme counsellor and is mandatory for those with positive results.
- The GP is informed of the result. Participants with positive results are referred to the relevant Regional Genetics service
- Referrals for those who are eligible for the high risk breast cancer screening programme, are made by the NHS JBRCA Programme team.
- Cascade testing for family members of individuals identified to carry a *BRCA* mutation through the programme is also available.

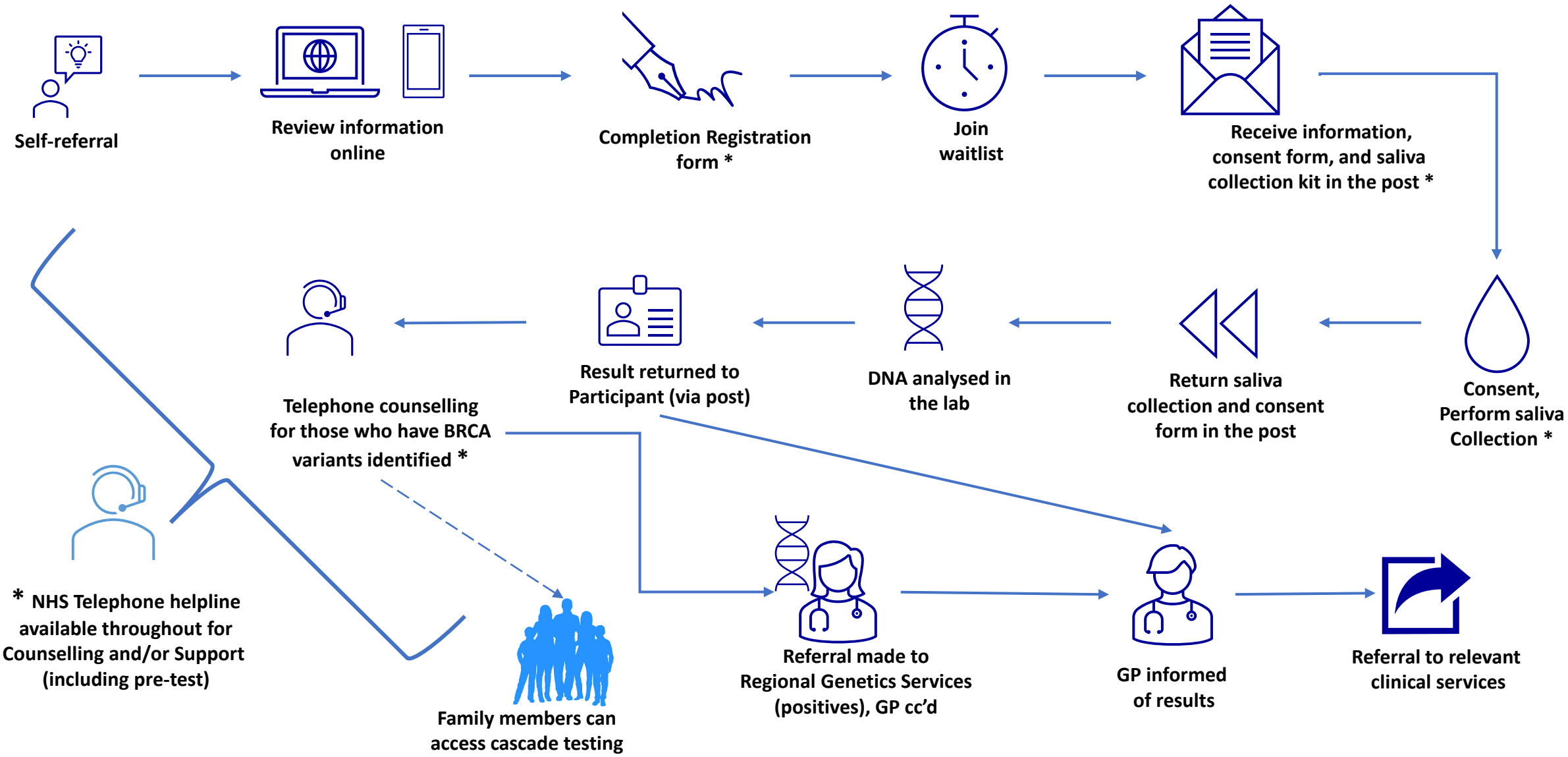
NHS Portal: https://nhsjewishbrcaprogramme.org.uk/



ADDITIONAL INFORMATION….

- **Further information can also be obtained through the JBRCA Programme NHS Genetics Helpline at +44 20 3437 6001 or Email: jewishbrca.programme@nhs.net**
  - **The Helpline is open, Monday to Friday, 9:00am to 5:00pm (extended hours to 7:00pm on Wednesdays)**
- **Jnetics (https://www.jnetics.org/getting-tested/nhs-brca-screening/)**
  - **A cross community charity dedicated to the prevention and diagnosis of Jewish genetic disorders**
- **Chai Cancer Care (https://chaicancercare.org/ or Tel: 0808 808 4567)**
  - **Expert support services for any member of the Jewish community affected by cancer, with concerns about BRCA or identified as having a BRCA gene mutation.**
- **www.Jewishbrca.org**
  - **Website with additional resources related to BRCA testing, information on the programme and a link to sign up**
- **Jewish Medical Association (https://jewishmedicalassociationuk.org/)**

Overview of pathway



Eligibility Criteria

- ≥1 Jewish Grandparent
- Over 18 years age
- Eligible for NHS care in England

Self Referral NHS JBRCA Website

https://nhsjewishbrcaprogramme.org.uk/

- Review Information on website
- Genetic counsellor Helpline- accessible for information, counselling & support

Registration

Complete a Registration Form:

- Name, Date of birth, Sex (at birth), Email, Postal address, NHS number, Jewish Denomination

Join a Waitlist

JBRCA Pack (sent via post) → JBRCA pack contains:

- Pre-test Information booklet
- Consent form, Personal details form
- Saliva collection kit with instructions
- Prepaid plastic mailing bag for return of sample and signed consent form
- Contact details for the Genetics Helpline

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Decision Making →

- Review Pre-test Information booklet
- Contact Helpline via telephone or email for any queries, further information or support, counselling needs, technical or administrative needs
- Pre-test counselling is available (but is not mandatory)

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Decision to undergo BRCA Testing →

- Fill and sign Consent form and Personal details form
- Provide Saliva sample as per instructions (follow instructions carefully)*

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Return of Sample to NHS Lab →

- Sample and filled Forms returned by Royal Mail via Local Post office, in prepaid plastic mailing bag.
- Follow instructions carefully.* Do not post using a street post box

See Slide xx for Sample collection & postage instructions

Receipt of Sample by NHS Lab

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Processing of Sample by NHS Lab →

- Full gene sequencing for both BRCA1 and BRCA2
- A very small proportion of saliva samples may fail quality control. If this happens, a repeat sample will be requested from the participant.
- If the second saliva sample fails, then a blood sample will be requested

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Return of Result via post to participant →

- Results can take approximately 12-18 weeks
- Results will be returned to the participant via post.
- Result letter will have a front sheet, so that the participant can choose when to read the result, and also chose to have access and support from a genetic counsellor whilst reading the result. For this the participant can contact the Genetics Helpline.
- Results are shared with the GP (unless the participants declines this)

Post-test Counselling →

- Post-test counselling is available to any participant who wants it through the JBRCA Genetics Helpline.
- Participants with a Positive Result (Pathogenic Variant present) will receive a follow-up post-test counselling telephone appointment with a genetic counsellor from the JBRCA programme, within a week of the result.
- Participants may themselves telephone the Genetics Helpline and speak to a genetic counsellor sooner, and at a time of their choosing
- There is no limit on the number of post-test counselling appointments the Participant can schedule.
- Community support accessible through community organisations (e.g. Chai Cancer Care)

Referrals by JBRCA Counsellor →

- Participants with a positive result will be referred to their Regional Genetics Service by the NHS JBRCA counsellor.
- Participants with Positive Result, will be referred to the high risk breast cancer screening programme by the JBRCA team if they are eligible for screening.
- The GP is cc'd in the referral and informed of the test result.

Considerations for the GP ⟶

- Individuals with a strong family history of cancer should still be referred to the regional genetics service by the GP, if they fulfil the NHS referral criteria for a 'strong family history'. They may be eligible for panel genetic testing (not just BRCA testing) and this assessment can be made by the genetics team. This should also be the case if they participated and tested negative for *BRCA1/BRCA2* in the JBRCA programme.
- Regional genetics services, following review, will refer patients for risk management advice by the high risk breast team and the high risk gynaecology team. The GPs too can make these referrals if needed/appropriate.
- *BRCA2* patients can access research trials for pancreatic cancer screening (EUROPAC study).
- *BRCA2* men can access trials for prostate cancer screening (PROFILE study)
- See slide 13 for types of results, slide 15 for cancer risks, slides 17-19 for risk management options, slide 20 for PGT, slides 6, 23-26 for additional information and resources

Cascade Testing ⟶

- Relatives (on the same side of the family) in whom a *BRCA* gene mutation (Pathogenic variant) has been identified, also have a high risk of carrying the same familial mutation. This is 50% for FDRs and 25% for SDRs
- Cascade testing for the familial mutation is available for all relatives through the JBRCA programme. This can be accessed through the same web portal through self referral following the same process described earlier. https://nhsjewishbrcaprogramme.org.uk/

Types of BRCA test results…….

There can be 3 broad types of results

No variant or mutation identified (Negative Result) →

- No *BRCA* associated increased cancer risk identified
- It does not mean the person cannot get cancer. The cancer risk is similar to the rest of the general population of similar age
- Continue to participate in routine general population NHS screening programmes

Pathogenic or Likely Pathogenic variant or mutation identified (Positive Result) →

- A *BRCA* mutation associated increased cancer risk is present
- Most of the results will reflect one of the 3 *BRCA* founder mutations commonly seen in the Jewish population
- Around 10% of results (5-13%) may be a non-founder mutation
- Participant should access screening or prevention options available
- Family members will be eligible for cascade testing on the NHS JBRCA programme

Variant of uncertain significance identified (Uncertain Result) →

- This is rare.
- There remains some uncertainty around the interpretation of this variant.
- This is currently treated as a negative result
- With time as more information becomes available, most of these will get reclassified as a negative result (benign or likely benign variants)
- A very small proportion may get reclassified as pathogenic, in which case the result is then treated as a positive result.

Sample Collection and Postage Instructions….

❖ Consent Form

- Review and sign the Genetic Test Consent Form

❖ Personal Details Form

- Fill in the requested information on the Personal Details Form

❖ Saliva Sample Collection

- Wait at least 30 minutes after eating or drinking before sample collection
- Wash your hands thoroughly
- Rinse your mouth well with water to clear away any food
- Fill the tube with your saliva up to the line
- Screw on the lid and check it is tight
- Wash your hands again thoroughly
- Write the date of saliva collection on the adhesive label, then stick the label on the saliva collection tube
- Place the labelled saliva collection tube into the transport tube, making sure the transport tube is shut tightly
- Place the transport tube into the small padded envelope

❖ Postage from a Post Office

- Place both forms and the packaged saliva sample in the pre-paid plastic mailing bag
- Take the package to your local post office. Nearest post office can be found at: www.postoffice.co.uk/branch-finder
- This package should **NOT** be posted using a street post box

For any queries, contact the Genetics Helpline at

- **+44 20 3437 6001**
- **or Email jewishbrca.programme@nhs.net**

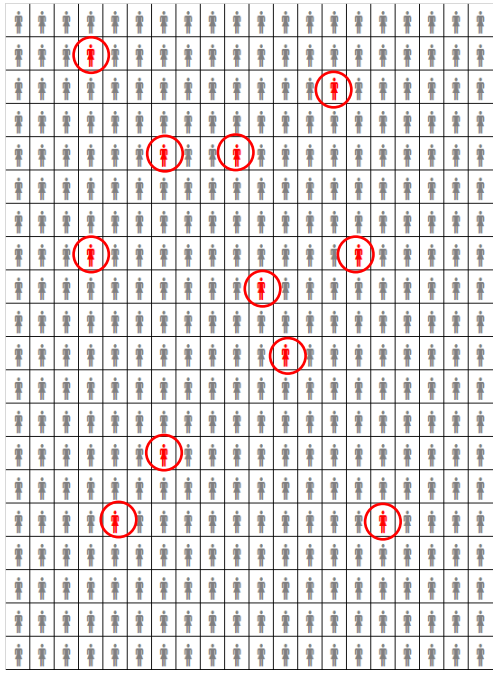
Cancer Risks associated with *BRCA1* and *BRCA2* mutations (pathogenic variants)

Female Cancer Risk Over Lifetime (to age 80)			
Cancer	General population	With **BRCA1**	With **BRCA2**
Breast	11.5%	**72% (65-79%)**	**69% (61-77%)**
Ovarian	1.5%	**44% (36-53%)**	**17% (11-25%)**
Pancreatic	1.0%	Not elevated	2% (1-4%)

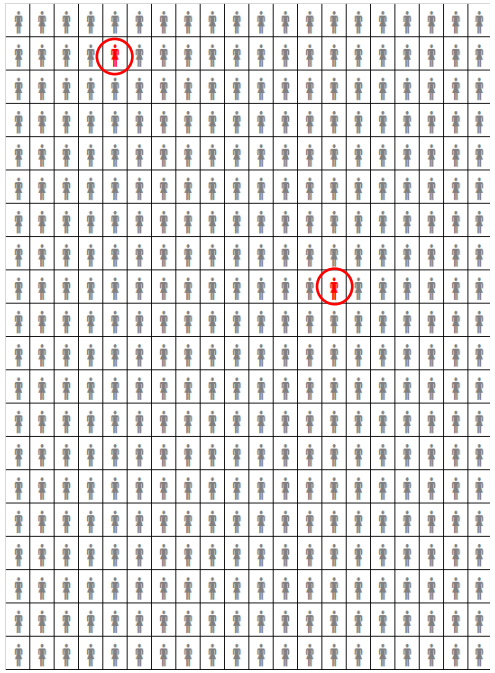
Male Cancer Risk Over Lifetime (to age 80)			
Cancer	General population	With **BRCA1**	With **BRCA2**
Breast	Less than 0.1%	0.4% (0.1-1.5%)	4% (2-8%)
Prostate	12.5%	Not elevated	27% (21-35%)
Pancreatic	1.0%	Not elevated	3% (2-5%)

- *The tables above show the detailed cancer risks for females and males*
- *The values in brackets indicate the range of risks (95% confidence intervals)*
- *The risk to each individual can depend on multiple factors including family history*
- *The main cancers caused by BRCA1 and BRCA2 mutations are female breast cancer and ovarian cancer*
- *BRCA1 and BRCA2 mutations are not associated with childhood cancers, except in very rare cases where a child has faults in both copies of their gene.*
- *The inheritance of these mutations is autosomal dominant*

BRCA Prevalence



1:40 Ashkenazi Jewish individuals carry a *BRCA* mutation



1:200-250 general population individuals carry a *BRCA* mutation

40% Breast Cancers & 10% Ovarian Cancers in the Jewish population are associated with *BRCA* mutations. This is 2.5x higher than the general population.

Managing Cancer Risk

Breast Cancer

Enhanced (high risk) breast screening:
This includes annual MRI and/or mammograms, from age 30 years (as per NICE guidelines). BRCA carriers are eligible for this. Referral to the National High Risk Screening Programme is made by the JBRCA Counsellor.

Risk Reducing Mastectomy:
This provides the maximum level of breast cancer risk reduction.
Referral to the high risk breast service can be made by the Regional genetics service or the GP

Medical Prevention:
This reduces the risk of ER+ breast cancer.
Tamoxifen (premenopausal women) or Anastrazole (post-menopausal women) can be offered.

NICE Familial Breast Cancer Guideline https://www.nice.org.uk/guidance/cg164

Managing Cancer Risk

Ovarian Cancer

Risk reducing salpingo-oophorectomy (RRSO):
This is the most effective method of preventing ovarian cancer. It is offered from the ages of 35-40 years once woman has completed her family. Referral to the high risk gynaecology/ gynae-oncology clinic to discuss this option can be made by the Regional genetics service or the GP.

Screening or Surveillance for Ovarian Cancer:
A new NICE Guideline NG241 (Ovarian cancer: identifying and managing familial and genetic risk https://www.nice.org.uk/guidance/ng241) provides updated guidance on management of women at increased risk of familial ovarian cancer (published on 20/03/2024). It highlights surveillance is not an alternative to risk reducing surgery in BRCA carriers. But a potential role for surveillance as an interim risk management strategy in those delaying risk reducing surgery could be considered. This involves 4 monthly Ca125 assessed by an algorithm with oversight from a high risk gynaecology MDT and annual decision review.

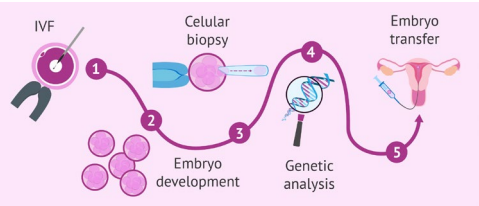
Risk reducing early salpingectomy and delayed oophorectomy (RRESDO):
This new two-step ovarian cancer surgical prevention strategy which involves excision of tubes as a first step and subsequent ovarian removal at a later date, at or near menopause. This enables risk reduction in ovarian cancer risk, while avoiding early menopause. This is only advised within a research study and can currently be accessed in the UK through a study called PROTECTOR.
Website- http://protector.org.uk/ (Email- bci-protector@qmul.ac.uk or protector.study@nhs.net)

Managing Cancer Risk

Pancreatic Cancer	Screening for Pancreatic cancer is available in a research study. Details for the EUROPAC study are available at https://www.europactrial.com/ Email: europac@liverpool.ac.uk
Prostate Cancer	Screening for Prostate cancer is available in a research study. Details for the PROFILE study are available at https://www.royalmarsden.nhs.uk/profile-study Email: Prostate.Research@rmh.nhs.uk
Male Breast Cancer	There is no screening for male breast cancer. *BRCA2* men need to be breast aware.

- *The increase in risk for these cancers is much lower*

Pre-implantation genetic testing for monogenic disorders (PGT-M)……

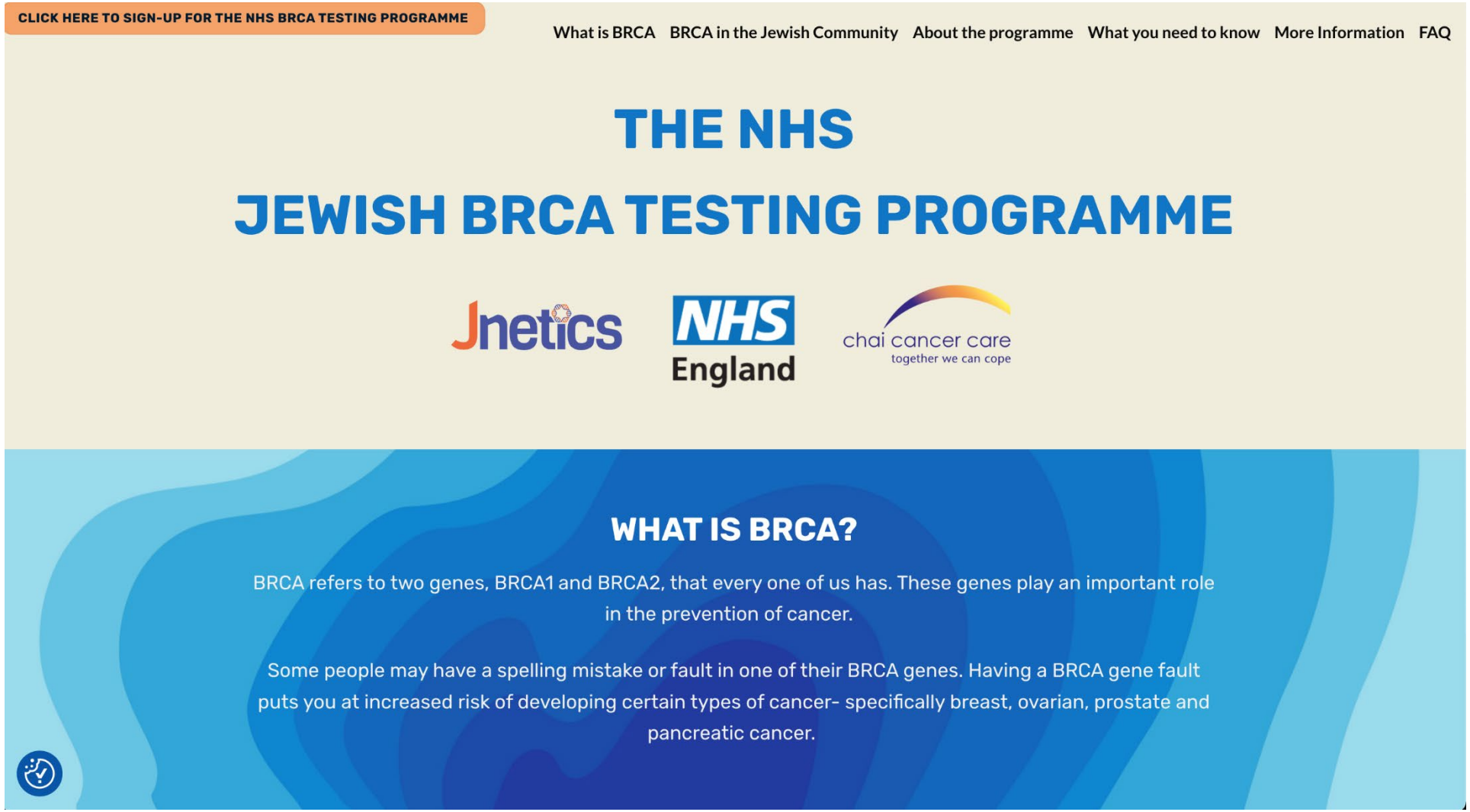


- Pre-implantation genetic testing can be used by people who have a *BRCA* mutation to avoid passing it onto their children
- PGT-M was previously known as preimplantation genetic diagnosis (PGD)
- This is licensed for *BRCA* carriers
- It involves needing to have IVF, even in the absence of fertility problems
- The embryos are checked for the familial BRCA mutation.
- Embryos free of the inheritable BRCA mutation are placed back into the womb to continue to develop
- Regional Genetics Services can make referral to NHS PGT teams for those wishing to discuss this
- More details are available on the HFEA website

  https://www.hfea.gov.uk/treatments/embryo-testing-and-treatments-for-disease/pre-implantation-genetic-testing-for-monogenic-disorders-pgt-m-and-pre-implantation-genetic-testing-for-chromosomal-structural-rearrangements-pgt-sr/

  https://geneticalliance.org.uk/information/service-and-testing/nhs-genetic-services-in-the-uk-2/

Jnetics Website https://jewishbrca.org/



Abbreviations

ER – Estrogen Receptor

FDR – First Degree Relative

SDR – Second Degree Relative

GMSA – Genomic Medicine Service Alliance

GP – General Practitioner

JBRCA Programme – NHS Jewish BRCA testing Programme

For any queries regarding the NHS Jewish BRCA Programme, contact the NHS JBRCA team using the Genetics Helpline at

- **+44 20 3437 6001**
- **or Email jewishbrca.programme@nhs.net**

NHS England

NHS North Thames
NHS Genomic Medicine Service Alliance

Additional Resources /references on Jewish Population Testing

Population Testing in the Jewish population

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ICR The Institute of Cancer Research

The ROYAL MARSDEN NHS Foundation Trust

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Papers linked to ovarian cancer risk management

1. NICE. Ovarian cancer: identifying and managing familial and genetic risk. In NICE guideline [NG241], National Institute of Health and Care Excellence: UK, 2024; p https://www.nice.org.uk/guidance/ng241.
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