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Norfolk and Norwich University Hospitals NHS
NHS Foundation Trust

Trust Guideline for the Inclusion of Women at Very High Risk of Breast Cancer in the NHS Breast Screening Programme

For Use in:	Norwich Breast Screening Unit, Norwich Breast Service, and NNUH Oncology Dept
By:	Director of Breast Screening, Consultant Breast Surgeons and Breast Clinicians, and Consultant Oncologists
For:	Women at high risk of Breast Cancer
Division responsible for document:	Clinical Support Services
Key words:	Very High Risk Breast Screening
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Assessed and approved by the:	Clinical Guidelines Assessment Panel (CGAP) If approved by committee or Governance Lead Chair's Action; tick here ✓
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To be reviewed by:	Director of Norwich Breast Screening Unit
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If Yes - does the strategy/policy deviate from the recommendations of NICE? If so why?	N/A

This guideline has been approved by the Trust's Clinical Guidelines Assessment Panel as an aid to the diagnosis and management of relevant patients and clinical circumstances. Not every patient or situation fits neatly into a standard guideline scenario and the guideline must be interpreted and applied in practice in the light of prevailing clinical

circumstances, the diagnostic and treatment options available and the professional judgement, knowledge and expertise of relevant clinicians. It is advised that the rationale for any departure from relevant guidance should be documented in the patient's case notes.

The Trust's guidelines are made publicly available as part of the collective endeavour to continuously improve the quality of healthcare through sharing medical experience and knowledge. The Trust accepts no responsibility for any misunderstanding or misapplication of this document.

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Version and Document Control:

Version Number	Date of Update	Change Description	Author
4.2	29/04/2020	Six-month extension given due to Covid-19	Dr Arne Juette
5	11/11/2020	See section 1 re: revision and updated in line with NHS Breast Screening Programme	Dr Arne Juette

This is a Controlled Document

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Background

This guideline replaces the previous guideline after an updated national guideline was published by the NHS BSP in September 2020.

While this trust document reflects the guideline at the time of writing on 11Nov 2020, the up-to-date national guideline can be accessed via the gov.uk website:

https://www.gov.uk/government/publications/breast-screening-higher-risk-women-surveillance-protocols/protocols-for-surveillance-of-women-at-higher-risk-of-developing-breast-cancer

This trust is adopting the national guideline in full, as is mandated by the NHSBSP.

1. Revisions to previous guidance

This guidance has been revised to clarify:

- How very high risk is defined in the NHS BSP and how that relates to the NICE
- Definitions
- What is risk equivalent to carriers of germline BRCA1 and BRCA2 pathogenic variants
- Which women aged 25 to 29 should be included in the very high risk screening
- Programme
- Who is entitled to a baseline MRI scan
- Who is entitled to very high risk screening following radiotherapy to sites involving
- Breast tissue (formerly referred to as ‘supra-diaphragmatic radiotherapy’)
- When the very high risk screening programme ends

2. Related guidance

Technical guidelines on the use of MRI for the surveillance of women at higher risk (https://www.gov.uk/government/publications/nhs-breast-screening-using-mri-with-higher-risk-women) must be followed. This includes information relating to physics quality control and guidance for radiologists reporting MRI. There are also practical guidelines (https://www.gov.uk/government/publications/breast-screening-screening-of-higher-risk-women) on setting up and providing screening for women at higher risk.

Guidance on screening very high risk women who are pregnant or lactating (https://www.gov.uk/government/publications/breast-screening-higher-risk-women-who-are-pregnantor-lactating) is also available.

Screening should be suspended during pregnancy until about 3 months after cessation of
lactation, due to the high density of the lactating breast inhibiting interpretation of images. If not breast feeding, MRI should be postponed until 3 months post partum.

3. Accessing very high risk screening

Referrals into the NHS BSP should be through:

- A genetics service by a consultant clinical geneticist, genetic counsellor or an
- Appropriately trained individual nominated by them
- An oncologist (in the case of women who received radiotherapy to sites involving
- Breast tissue). For the small number of women who received radiotherapy to sites
- Involving breast tissue for cancers other than lymphoma, oncologists are advised to
- Contact breast screening after radiotherapy dataset (bard)
- (chn-tr.bard@nhs.net) to confirm eligibility for very high risk screening
- Bard: for women who received radiotherapy to sites involving breast tissue during
- Treatment for lymphoma

3.1 Referrals by clinical genetics services or oncology centres

Women who meet the very high risk criteria should be referred to their local breast screening service.

Typically, you should refer to a named high risk coordinator or director of breast screening. Referrals should contain all the necessary information to demonstrate the individual meets the very high risk criteria and should be made using an NHS BSP referral form (https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/830844/BSP_very_high_risk_referral_form.odt).

On receipt, each referral must be reviewed to make sure the inclusion criteria have been
evidenced. This review must be completed by a consultant radiologist, consultant practitioner or breast clinician experienced in the full range of triple assessment. Once a referral has been accepted, the woman needs to be appropriately identified as very high risk on BS Select and NBSS. You should scan and upload documentation on to her BSSelect record. See more detailed information regarding these processes (https://www.gov.uk/government/publications/breast-screening-screening-of-higher-risk-women)

3.2 Referrals by BARD

BARD (https://www.christie.nhs.uk/bard) identifies all women in England below the age of 36 who have been treated with radiotherapy for lymphoma to sites involving breast tissue.

Women in this group who were treated with radiotherapy between the ages of 10 and 29
years are referred into the NHS BSP very high risk programme.

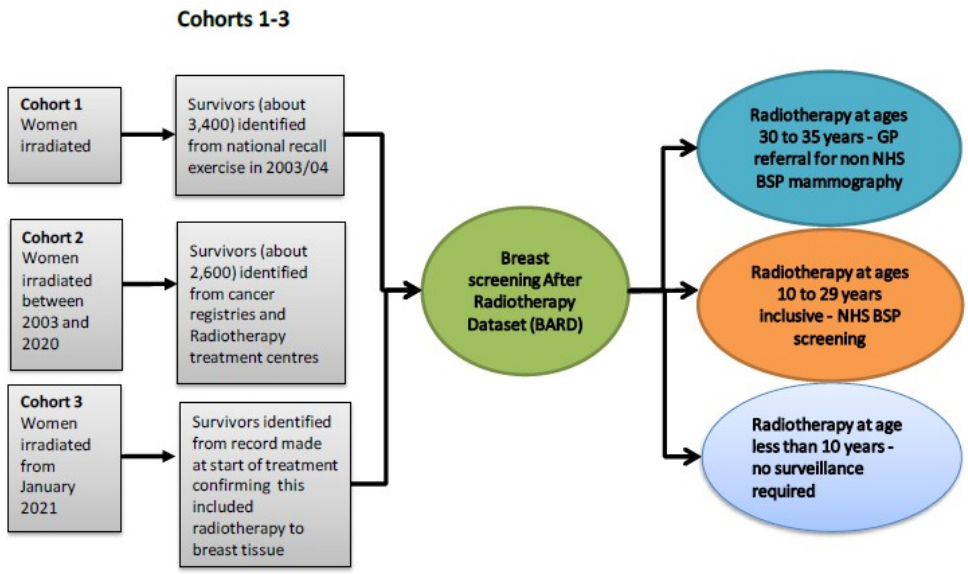
Women are identified from cancer registries and then cross matched against information
held at radiotherapy treatment centres to determine eligibility for inclusion in the NHS BSP for very high risk screening.

BARD sends details (NHS numbers) of these women who fulfil very high risk criteria to NHS Digital to determine if they are already on the BS Select call/recall system. BARD writes to the woman's GP to confirm screening remains appropriate and, if so, sends services a completed referral form. The service then issues an invitation for screening. This invitation must include the BARD patient information leaflet (https://www.christie.nhs.uk/bard).

This is sent to the service from BARD directly with the referral or is available online. The service must subsequently confirm with BARD:

- That the referred woman has been invited
- If and when the referred woman attended screening, using the referral template

  (https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/830844/bsp_very_high_risk_referral_form.odt)



BARD referrals into very high risk programme

4. Threshold for screening women in the very high risk programme

The NHS BSP screens women at very high risk of breast cancer due to:

- A proven germline pathogenic variant in BRCA1, BRCA2, TP53, A-T homozygotes, PALB2, PTEN, STK11 or CDH1 based on testing in a clinically accredited laboratory
- Having received radiotherapy to breast tissue during treatment for Hodgkin and non-Hodgkin lymphoma (Younger women treated with radiotherapy due to breast cancer are excluded from the NHS BSP very high risk programme).

The NICE familial breast cancer guidelines categorise women at increased risk of breast
cancer as moderate or high. Only a subset of those defined by NICE as being at high risk reach the very high risk group threshold used in the NHS BSP. This has previously been set at 8 times the relative risk of women in the general population.

To differentiate between the NICE and NHS BSP guidance, very high risk is defined by the NHS BSP as:

- Women with a lifetime risk of 40% or greater due to a specific genetic abnormality in the woman or her family
- Those receiving radiotherapy to breast tissue during treatment for Hodgkin and non-Hodgkin lymphoma between the ages of 10 and <30 years
- A small number of women who received radiotherapy to breast tissue during treatment
- For cancers other than lymphoma

5. How to calculate women at very high risk

A woman is considered to be at very high risk if she has a test result that identifies a germline pathogenic variant in a gene that would confer a 40% to 95% lifetime risk of breast cancer.

Some women may choose not to have genetic testing. In order to avoid a situation where a woman with a known pathogenic variant in her family is obliged to proceed with predictive genetic testing to access very high risk screening, the following risk assessment process will apply:

If a woman has not been tested, but has a first degree relative with a germline BRCA1, BRCA2 or TP53 pathogenic variant, she has a 50% chance of carrying this variant. As a result, she will be eligible for very high risk screening up to and including the age of 50.

To access this, confirmation is required from the genetics service that a first degree relative carries a germline pathogenic variant. After the age of 50 a previously untested woman will be returned to the routine screening programme.

After the age of 50, a personal test result identifying a pathogenic variant is required to access the very high risk programme. This is due to the residual lifetime risk associated with a pathogenic variant having fallen by the age of 50, which means a woman with only a 50% chance of carrying this pathogenic variant would no longer reach the 40% lifetime risk threshold to access very high risk screening. More detailed information (https://www.gov.uk/government/publications/breast-screening-screening-of-higher-risk-women) regarding these processes is available.

5.1 How to decide lifetime risk in absence of genetic test

Risk assessment should provide clear confirmation of the level of risk using an NHS endorsed computer risk modelling software programme, BOADICEA (CanRisk) or Tyrer Cuzick. The 10-year risk estimate must be submitted with the referral proforma as evidence that the woman satisfies the appropriate risk at time of screening entry.

Age 25 to 29

A small proportion of women at very high genetic risk will meet the 8% threshold for screening earlier than 30 years of age. Assess 10-year risk for each year between 25 and 29 years to determine at what age the risk meets the 8% threshold and hence age at entry to screening. A woman should have an 8% 10-year risk confirmed by an NHS clinical genetics service (required by the NHS BSP).

Age 30 to 39

Set risk at 30 years and screening if woman meets an 8% 10-year risk confirmed by an NHS clinical genetics service (required by the NHS BSP).

Age 40 to 49

Set risk at 40 years and screening if woman meets a 12% 10-year risk confirmed by an NHS clinical genetics service (required by the NHS BSP).

5.2 Women with proven pathogenic variants in high-risk genes

All referrals for women aged 30 and above with a proven germline BRCA1/2 or PALB2 pathogenic variant can be automatically accepted into the very high risk programme. Referrals for BRCA1, BRCA2 gene and PALB2 carriers aged between 25 and 29 years (https://www.gov.uk/government/publications/breast-screening-higher-risk-women-surveillanceprotocols/tests-and-frequency-of-testing-for-women-at-very-high-risk) must include evidence of risk, using an NHS endorsed computer risk modelling software programme as detailed above, to be accepted into the very high risk programme.

Surveillance starts at 20 years for TP53, at 25 years for A-T homozygotes and at 30 years for PTEN, STK11 and CDH1. A letter is required from the NHS clinical genetics service confirming the presence of a pathogenic variant and stating the name of the gene.

5.3 Women previously treated with total body irradiation

Women who have previously received total body irradiation are at an elevated risk of breast cancer in the years following treatment. However, there is insufficient evidence to show that the risk reaches the threshold to qualify this cohort of women for screening in the very high risk programme.

See Tests and frequency of tests for women at very high risk (https://www.gov.uk/government/publications/breast-screening-higher-risk-women-surveillanceprotocols/tests-and-frequency-of-testing-for-women-at-very-high-risk)

5.4 Queries over entitlement following previous radiotherapy

Most women who have had radiotherapy fields involving breast tissue at a young age are
those receiving treatment for Hodgkin or non-Hodgkin lymphoma. However, other diagnoses may also result in similar radiotherapy treatment fields.

If a woman had radiotherapy involving breast tissue below the age of 36 years but it is unclear if she is eligible for very high risk screening within the NHS BSP, contact BARD for advice chn-tr.bard@nhs.net .

6. Screening test

Where indicated, the screening test should be MRI (with or without mammography). If a woman cannot tolerate MRI, she and her lead radiologist should discuss and agree potential alternatives such as wide scanners.

Breast ultrasound is not offered as a screening tool in the NHS BSP based on current evidence.

This differs from current NICE guidance, which states:
Do not routinely offer ultrasound surveillance to women at moderate or high risk of breast cancer but consider it:

- When MRI surveillance would normally be offered but is not suitable (for example, because of claustrophobia)
- When results of mammography or MRI are difficult to interpret

Breast ultrasound is not provided by the NHS BSP as a screening tool. If a woman cannot be screened with MRI, ultrasound should only be carried out following a full discussion regarding the potential benefits and limitations of the test.

6.1 Process before MRI screening

Local protocols should be followed regarding MRI with gadolinium enhancement. There is also Royal College of Radiologists guidance (https://www.rcr.ac.uk/publication/guidancegadolinium-based-contrast-agent-administration-adult-patients).

If a woman cannot tolerate gadolinium or refuses to have MRI with a contrast agent, MRI should not be performed. Depending on the woman's age and breast density, other modalities such as mammography may be offered. This decision must be made and documented by clinicians locally.

6.2 Review of background density

Some of the screening protocols state that women require mammography with or without an MRI. The decision for MRI is based on an annual review of breast density. Women covered by this guidance should have both procedures up to and including the age of 50. At this point, and annually thereafter, breast density should be reviewed based on current images until a decision is made that MRI is no longer required. Any women who are newly referred into the programme after the age of 50 should have both MRI and mammography performed at the initial screen to review whether MRI is required at subsequent screens.

Once the decision is made that a woman no longer needs MRI, her protocol should be updated within the client record on NBSS to show mammography only for her next screening appointment. More detailed information (https://www.gov.uk/government/publications/breast-screening-screening-of-higher-risk-women)
regarding this process is available.

If the mammogram shows an entirely fatty breast (Birads A (https://www.acr.org/-/media/ACR/Files/RADS/BI-RADS/Mammography-Reporting.pdf)), MRI is unlikely to add value and should not be performed. From the age of 60 onwards, breasts are less likely to require MRI plus mammography, as most breasts are less dense.

6.3 Baseline MRIs for women

A woman newly referred into the programme and meeting the very high risk criteria is entitled to MRI screening even if she is considering risk-reducing surgery. This may help identify malignancy before surgery.

After risk-reducing surgery, a woman can either opt out of the programme by signing a form or the service can cease the woman if there is clinical evidence that bilateral mastectomy has been carried out. Details are available in the opting out of breast screening guidance (https://www.gov.uk/government/publications/opting-out-of-breast-screening), which include copies of the required form.

7. Policy for short-term recalls following screening assessment

Short-term recalls are defined as a further appointment to attend a screening assessment indicated before the normal screening interval (one year).

All women on short-term recall should have previously attended assessment. Short-term recall should not be used as a routine outcome following assessment. Every effort should be made to obtain a definitive diagnosis at initial assessment. Short-term recall should only be made in exceptional circumstances and with fully informed consent as it is associated with significant anxiety.

If recall is within 6 weeks of the original assessment then it should be part of the same episode. If recall is after 6 weeks, it should be logged as a short-term recall episode. The short-term recall should usually be 6 months after the initial assessment of the woman.

8. When very high risk screening stops

Screening should be performed as specified in this guidance.
When a woman reaches 71 years of age routine invitations for very high risk screening will stop. At this stage she is entitled to self-refer for screening. For women in the very high risk programme, this will be annual screening in accordance with her routine screening protocol.

These women should be informed they will need to ask their local screening service directly or their GP can arrange screening for them.

9. The very high risk guidance writing group

This guidance was written by a panel of experts which included:

- Professor Diana Eccles (Professor of Cancer Genetics, University of Southampton)
- Professor Gareth Evans (Professor of Medical genetics and cancer epidemiology, University of Manchester)
- Dr Sacha Howell (Senior Lecturer in medical oncology, University of Manchester)
- Jacquie Jenkins (Breast screening programme manager, PHE)
- Professor John Radford (Professor of Medical Oncology, University of Manchester, The Christie NHS Foundation Trust, Manchester, President of Lymphoma Action)
- Dr Nisha Sharma (Breast consultant and director of screening, BSBR Secretary, Leeds Teaching Hospital)
- Mr Mark Sibbering (Clinical advisor to the NHSBSP, Consultant breast surgeon, Royal Derby Hospital)
- Professor Anthony Swerdlow (Professor of Epidemiology, Institute of Cancer Research)

We consulted:

- National breast cancer experts from the NHS BSP radiology and surgery clinical and professional group
- The national advisory committee for breast cancer screening
- NHS England national commissioning team
- Screening quality assurance service
- Senior administration and IT staff

Tests and frequency of testing for women at very high risk

Contents

1. BRCA carriers and equivalent risks

This group of women at very high genetic risk of developing breast cancer includes:

- BRCA1 carriers
- BRCA2 carriers
- risk equivalent to BRCA carriers not tested [1], but have a first degree relative who has a BRCA1 or BRCA2 genetic mutation
- women who have a mutation in another high risk gene including:
  - PALB2
  - PTEN
  - STK11
  - CDH1 (E-Cadherin)

Age	Test	Frequency of testing
25 to 29 [2]	MRI	Annual
30 to 39	MRI	Annual
40 to 50	MRI + mammography	Annual
51 to 70	Mammography +/- MRI [3]	Annual

2. Women with TP53 (Li-Fraumeni) syndrome

Age	Test	Frequency of testing
20 to 70	MRI	Annual

No mammography tests for this group of women.

3. Women with A-T homozygotes

Age	Test	Frequency of testing
25 to 70	MRI	Annual

No mammography tests for this group of women.

4. Women who have had radiotherapy to breast tissue

4.1 Females irradiated below the age of 10 years

Testing is not applicable to these females.

4.2 Females irradiated between ages of 10 and 19

Age	Test	Frequency of testing
25 to 70	MRI	Annual

Surveillance starts at 25 or 8 years after first irradiation, whichever is the later.

4.3 Females irradiated between ages of 20 and 29

Age	Test	Frequency of testing
30 to 39 [4]	MRI	Annual
40 to 50	MRI +/- mammography	Annual
51 to 70	Mammography +/- MRI [5]	Annual

4.4 Females irradiated between ages of 30 and 35

These women should be referred by GP to local mammography service (non-NHS Breast Screening Programme) as they do not reach the very high risk threshold. Breast screening After Radiotherapy Dataset (BARD) will inform GPs about the need for this and the timing.

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1. Screening for untested women will stop at 50 years. After that, testing will be required to continue in the very high risk screening programme.
2. To qualify for screening under 30 years, women must also have an 8%, 10-year risk at the age when entered (when aged 25 to 29 years).
3. Review MRI annually on basis of background density from 50 years.
4. Surveillance starts at 30 or 8 years after first irradiation, whichever is the later
5. Review MRI annually on basis of background density from 50 years.

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Summary of development and consultation process undertaken before registration and dissemination

The authors listed above drafted this guideline in accordance to national guidance.

This version has been endorsed by the Clinical Guidelines Assessment Panel.

Distribution list / dissemination method

Trust Intranet